IMRT for HNC

a New Standard of Care

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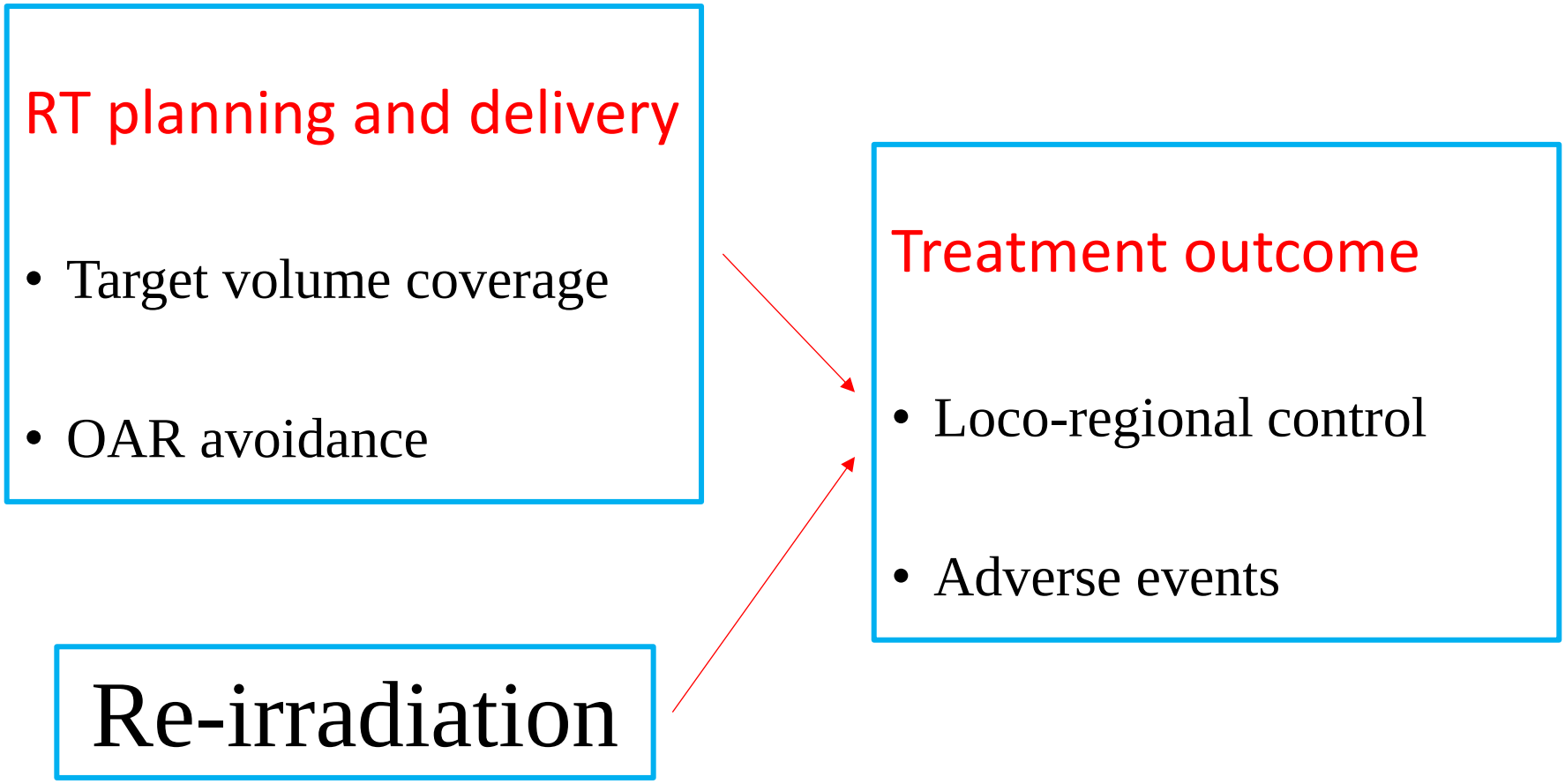
Contents

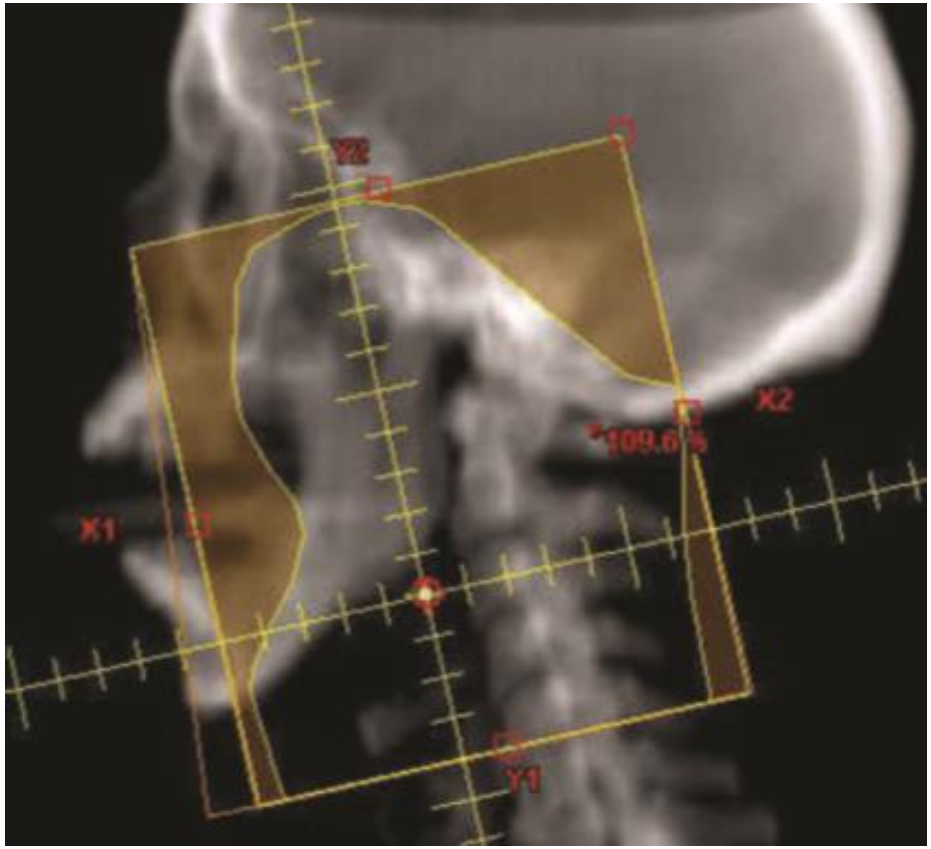
- IMRT: A new standard of care
- Precision & Accuracy in IMRT
- Future steps ?

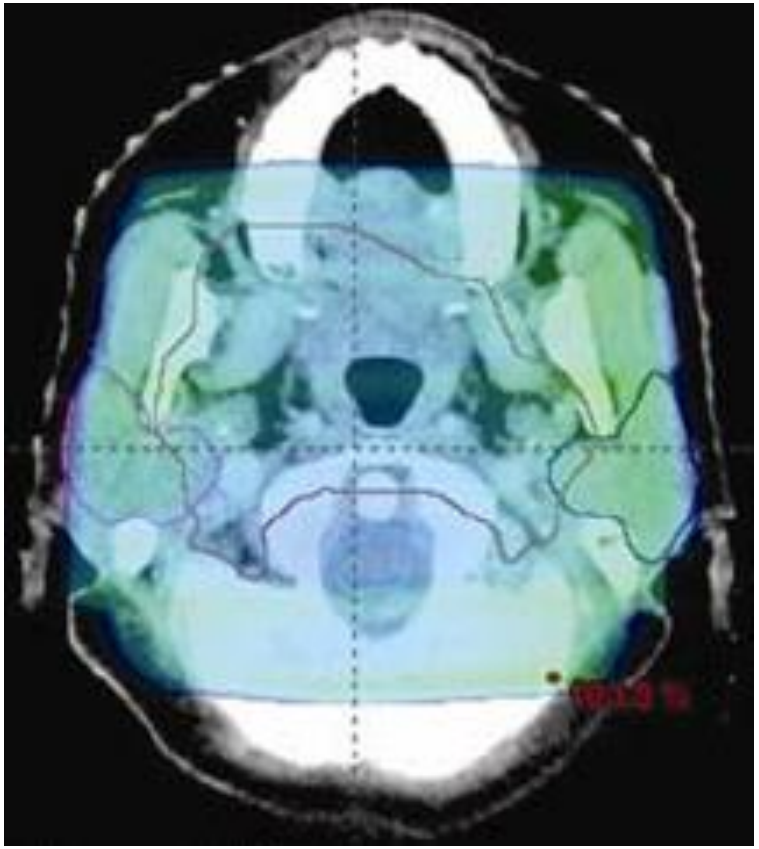
75% of HNSCC patients will receive RT as part of their primary or adjuvant treatment.

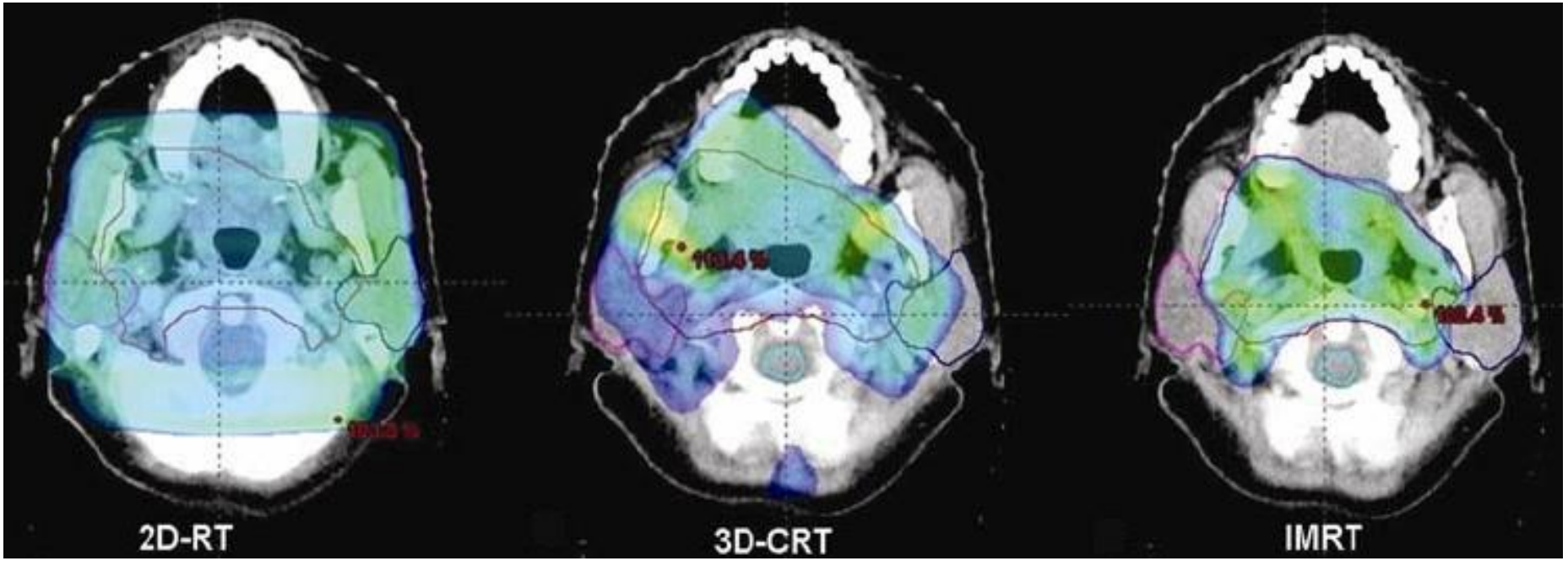
Grégoire V et al. J Clin Oncol 2015;33(29):3277-84.


RT planning and delivery
• Target volume coverage
• OAR avoidance
Treatment outcome
• Loco-regional control
• Adverse events
Re-irradiation

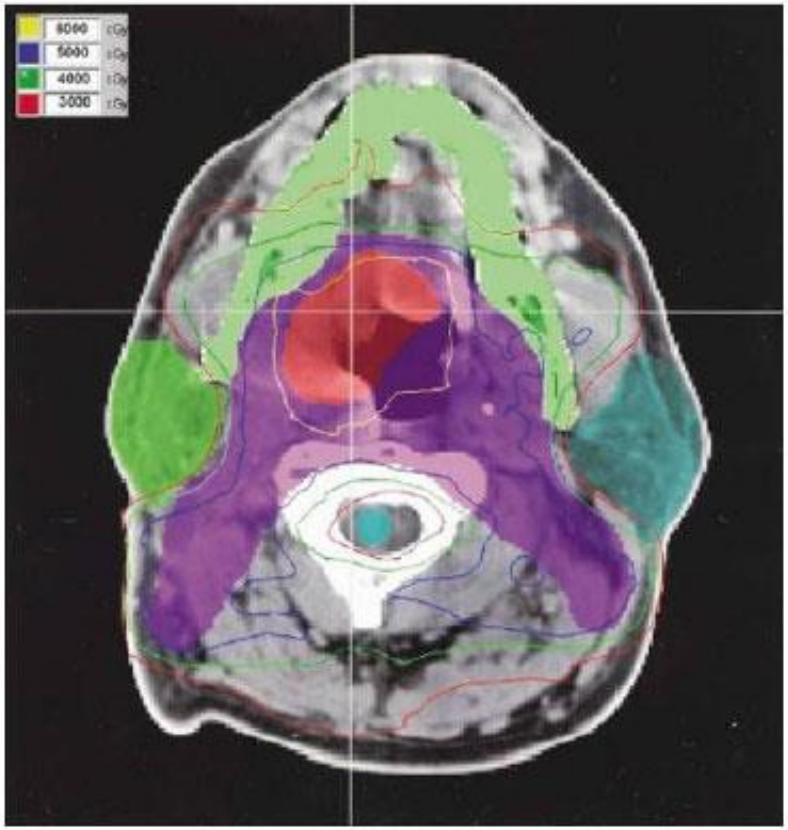
2D

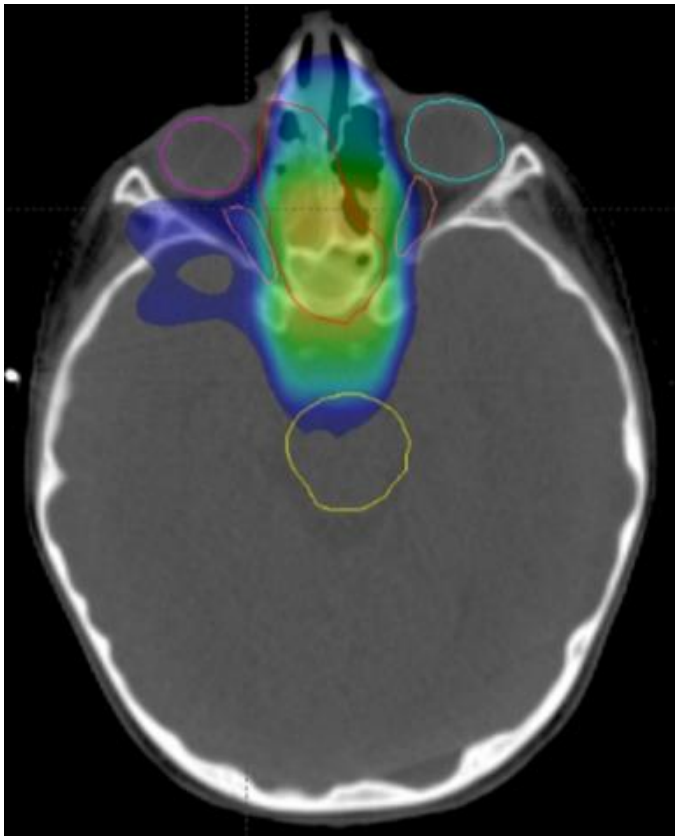





2D-RT
3D-CRT
IMRT

IMRT

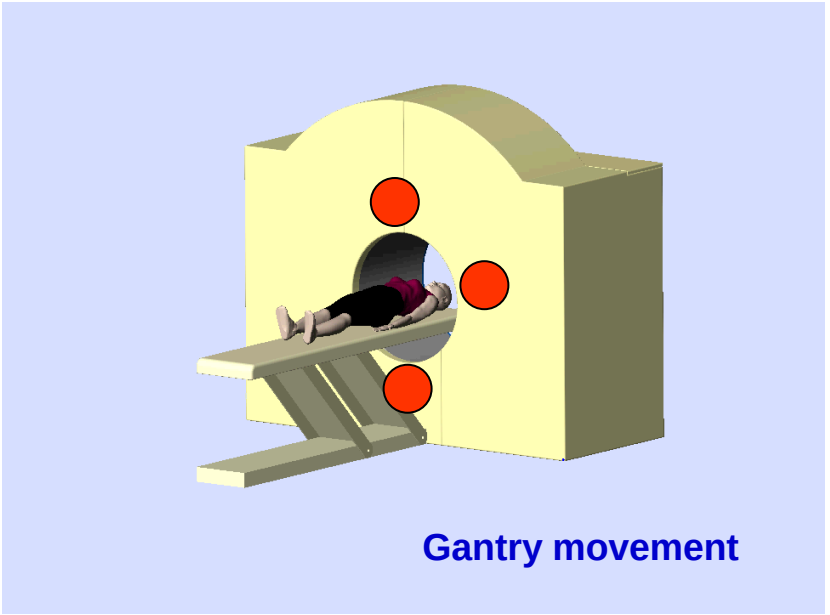




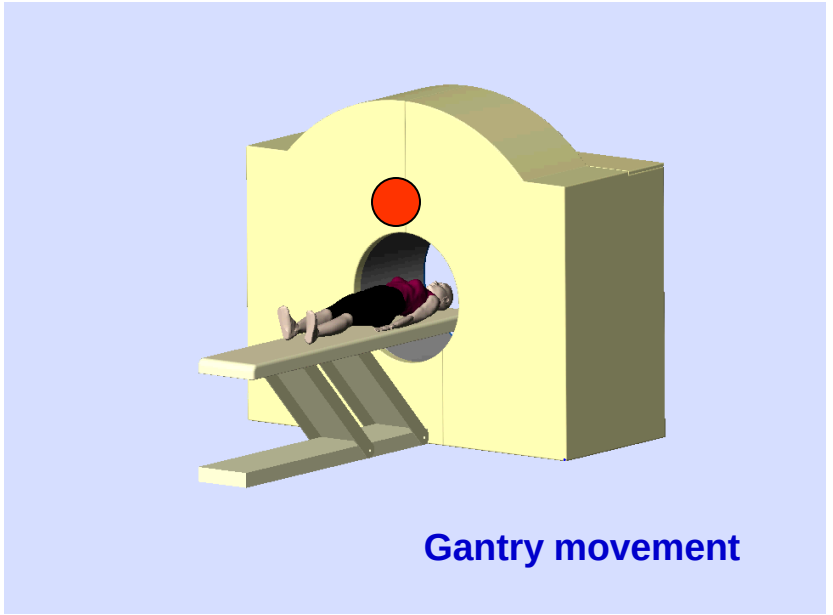
Non IMRT

IMRT

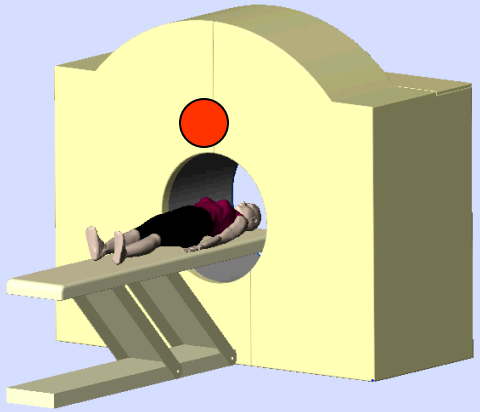
Step & shoot



VMAT



TomoTherapy



Gantry movement

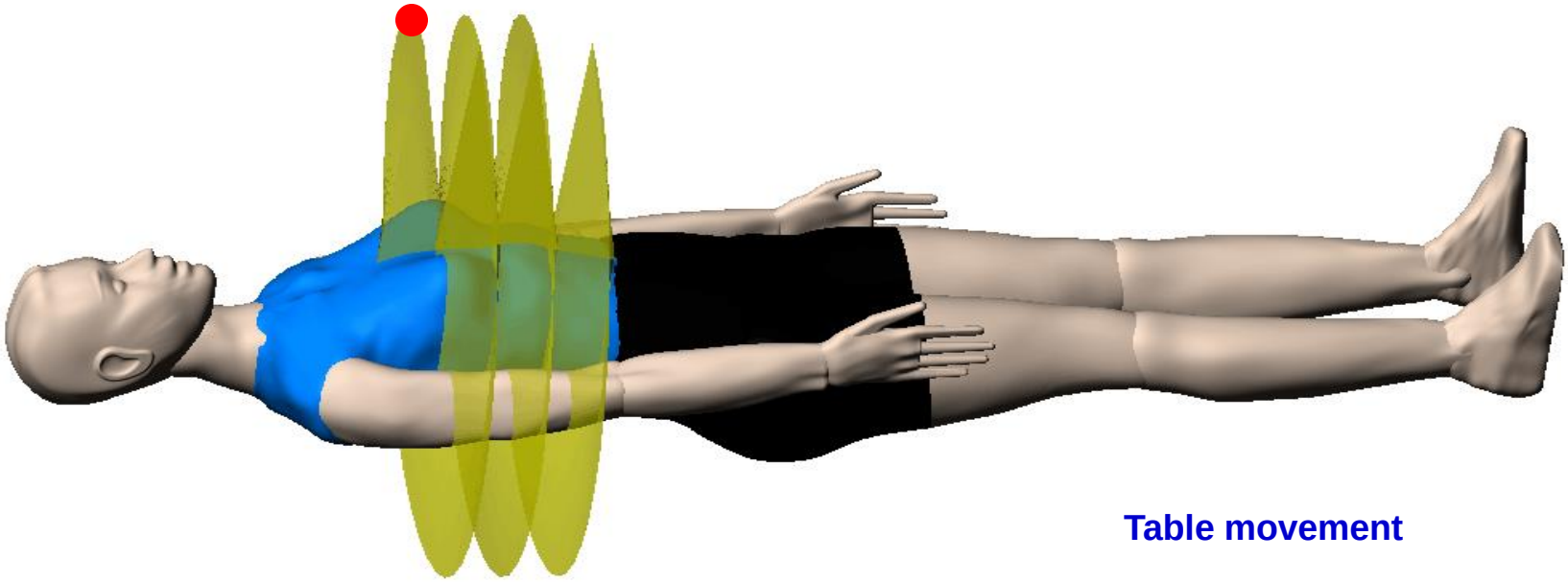


Table movement

- IMRT: advanced form of conformal RT that can generate highly optimized dose distribution with steep dose gradient.

- Dose conformality possible with IMRT makes it particularly effective for HNC because it is a complex anatomic region and CTV is contiguous to OAR.

- Studies have demonstrated the IMRT benefit of improving target coverage and decreasing OAR dose.

Nishimura Y. IMRT. Springer Japan 2015.

Disease Control: OPC

	Number	CS IV	T4	N2b	OS	LCR	PFS
Sher	163	75	7	54	86@5Y	86@5Y	
Garden	774	74	17	58	84@5Y	90@5Y	82@5Y
Setton	442	73	13.8	69.5@N2–3	84.9@3Y	LR5.4 %@3Y	
Daly	107	85	29	83@N2-3	83.3@3Y	92@3Y	81@3Y
Huang	71	76	11	72@N2-3	83.3@3Y	90@3Y	81@3Y
Clavel	100	87	12	87@N2–3	92.1@3Y	95.1@3Y	85@3Y

Nishimura Y. *IMRT*. Springer Japan 2015.

Disease control: NPC

Five-Year Treatment Outcome With Intensity-Modulated Radiotherapy

Study	No. of Patients	Dose (Gy)		Chemotherapy (%)	Local Control (%)	Nodal Control (%)	Distant Control (%)	OS (%)	T4 Disease (%)		Serious Neurologic Complications (%)
		Total	Per Fraction						Patients	Local Control	
Lai et al	512	NR	2.27	81	93	97	84	NR	52 (T3 to T4)	82	NR
Peng et al	306	70	2.12	60	91	92	NR	80	17*	82	TLN, 13.1 CN, 3.9 OP, 1.6
Lin et al	414	66 to 70.95 30 to 33 fractions	—	81	95	97	82	80	21	NR	NR
Wu et al	249	68 to 72 (30 to 32 fractions) 30 to 32 fractions	—	100	87	88	78	78	33	85 (T3 to T4)	TLN, 2.6 CN, 1.5 OP, 1.8
Sun et al	868	68	2.27	83	92	96	85	NR	19	83	TLN or BS, 5.5
Ng et al	444	70	2 to 2.12	83	86	92	83	80	23	74	TLN, 0.5 CN, 1.6
Yi et al	271	70 (T1 to T2) 74 (T3 to T4)	2.12 2.24	52	87	NR	70	79	25	54 and 76†	NR

Abbreviations: BS, brainstem injury; CN, cranial nerve injury; NR, not reported; OP, optice nerve or chiasm injury; OS, overall survival; TLN, temporal lobe necrosis.
*Randomized study; percentage is based on both treatment arms of 616 patients.
†With and without concurrent chemotherapy, respectively.

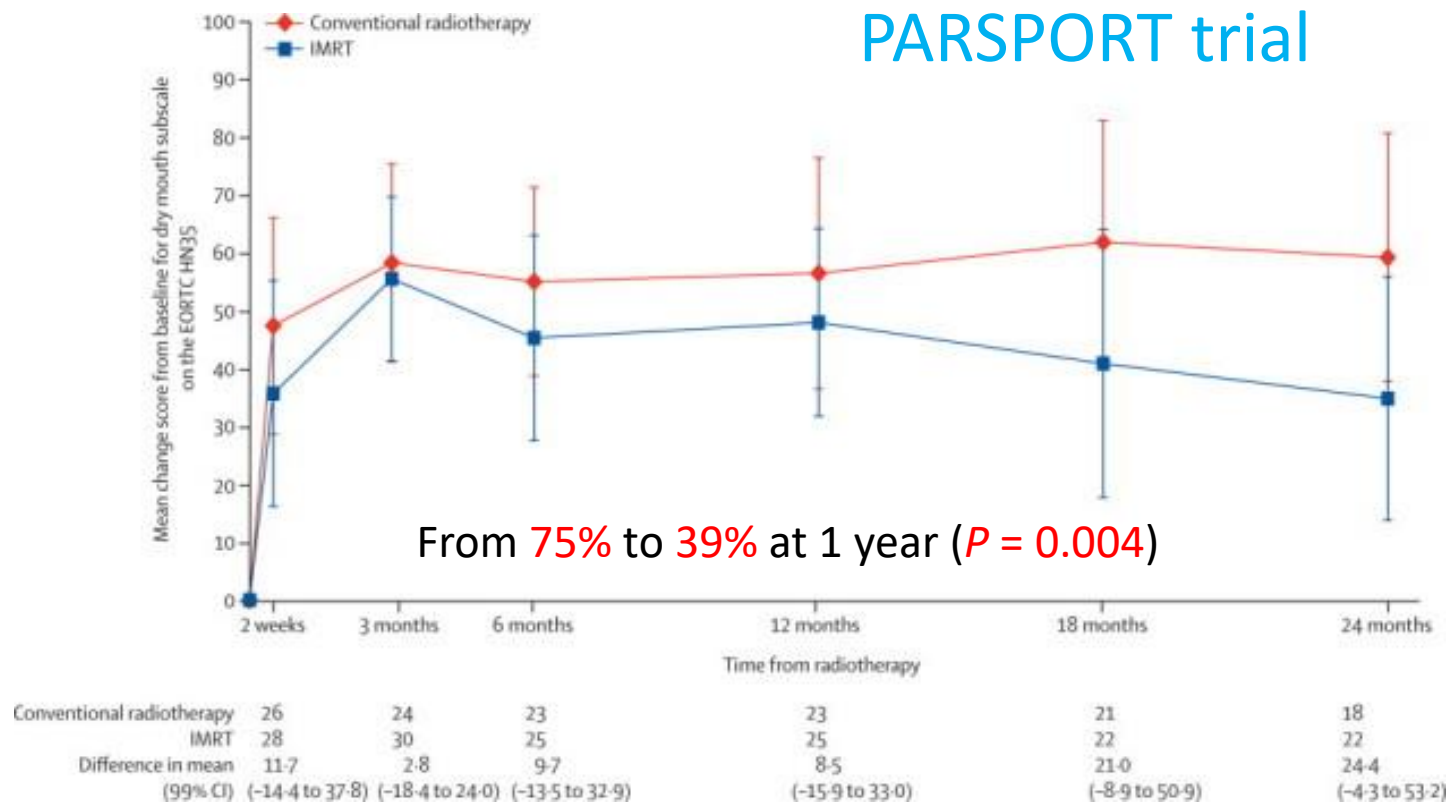
Lee AW et al. J Clin Oncol 2015;33(29):3356-64.

Meta-analyses (LC and OAS)

- Zhang et al (2015) meta-analysis (8 studies, 3570 patients with NPC): both 5-year OAS and LC were better in patients treated with IMRT compared to those treated with 2D or 3DCRT.

- Gupta et al (2018) meta-analysis: with the limitation of small sample size and low statistical power, NPC were the only HN subsite in which IMRT allowed a better response in OAS and LRC.

Salivary function: OPC



- Phase III randomized trial of 88 patients: IMRT reduced xerostomia compared to 2D RT. No significant difference in locoregional PFS.

Nutting C et al. Lancet Oncol. 2011;12(2):127–36.

Salivary function: NPC

- Two phase III randomized trials: 2D vs IMRT with 1 year FU.
- Both studies showed improved xerostomia with IMRT.
- 1st trial: IMRT has superior QoL.
- 2nd trial: benefits of IMRT in observer-rated xerostomia, patient-reported xerostomia, and parotid function preservation.

Nishimura Y. IMRT. Springer Japan 2015.

Treatment compliance: NPC

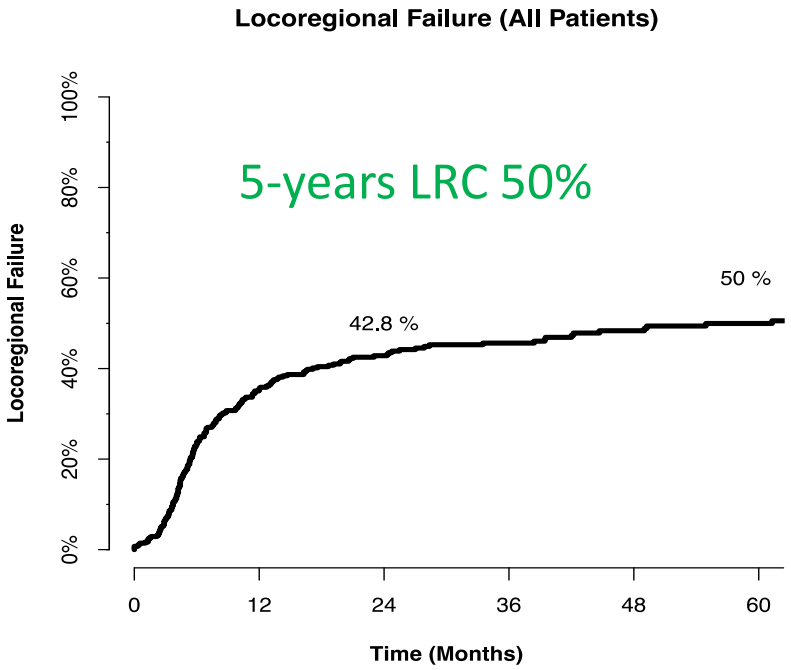
- Lesser toxicity by IMRT improve treatment compliance (patients' ability to tolerate the prescribed treatment).

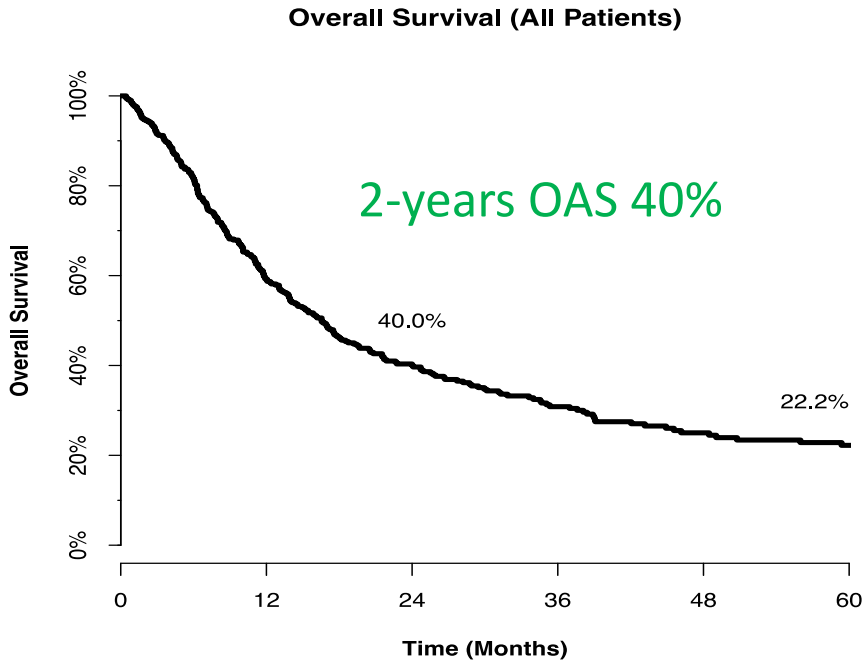
- RTOG 0225, IMRT multi-institutional trial, showed that 90 % of patients were able to receive the full 70-Gy dose and 88% of the patients with ≥T2b or N+ were able to receive the full 3 cycles of concurrent cisplatin. (compared favorably to 2D RT studies e.g., CT compliance was 63 % in the Intergroup 0099 trial, 71 % in a Singapore randomized trial, and 52 % in the Hong Kong NPC-9901 trial).

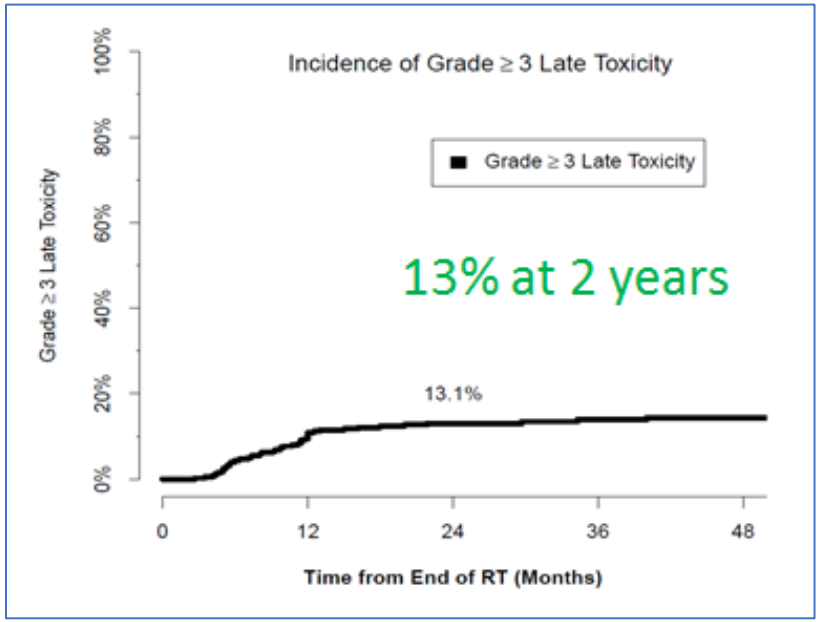
Lee N et al. J Clin Oncol 27(22):3684-90
Nishimura Y. IMRT. Springer Japan 2015.

IMRT-based Re-Irradiation for HNC

Multi-Institution Re-Irradiation (MIRI) Collaborative (ASTRO 2016)







Multi-Institution Re-Irradiation (MIRI) Collaborative (ASTRO 2016)

Does IMRT help ?

Yes, it deceases adverse events while improving tumor control.

“bath dose”

- On the other hand, a larger volume of normal tissues receive a low-radiation dose.

- Produced new toxicities such as anterior oral mucositis, occipital scalp hair loss, headache, nausea, and vomiting and irradiation of a small part of the brainstem (dorsal vagal complex), irradiation of the posterior fossa (postulated to be one cause of fatigue).

Contents

- IMRT: A new standard of care
- Accuracy & Precision in IMRT
- Future steps ?

Accuracy & Precision

Accurate
not Precise

Accurate and Precise

Precise
not Accurate

GTV Delineation: Molecular Imaging

Precision

- PET influences primary tumor delineation, at least for locally advanced tumors (PET-based TV smaller compared to CT or MRI).

- Compared with the pathologic specimen as the ground truth, PET-based GTV was closer to the pathologic specimen.

- PET has no added value for TV delineation in the neck (same sensitivity and specificity for neck-node detection as CT or MRI).

Grégoire V et al. J Clin Oncol 2015;33(29):3277-84.

Precision

Dirix et al (2009) compared between CT, PET, and DW-MRI:

- Both GTV-PET and GTV-DW-MRI were significantly smaller than GTV-CT.

- With median FU of 30 months, 7 patients had recurrent disease; all recurrences were located within the area of overlap between the 3 sets.

Dirix P et al. J Nucl Med 2009;50:1020-7.

Precision

- No randomized study compared PET-CT–based dose distribution and patient outcome, but a few prospective studies show that PET planning translated into more conformal dose distribution and fewer late adverse events, without compromising LRC.

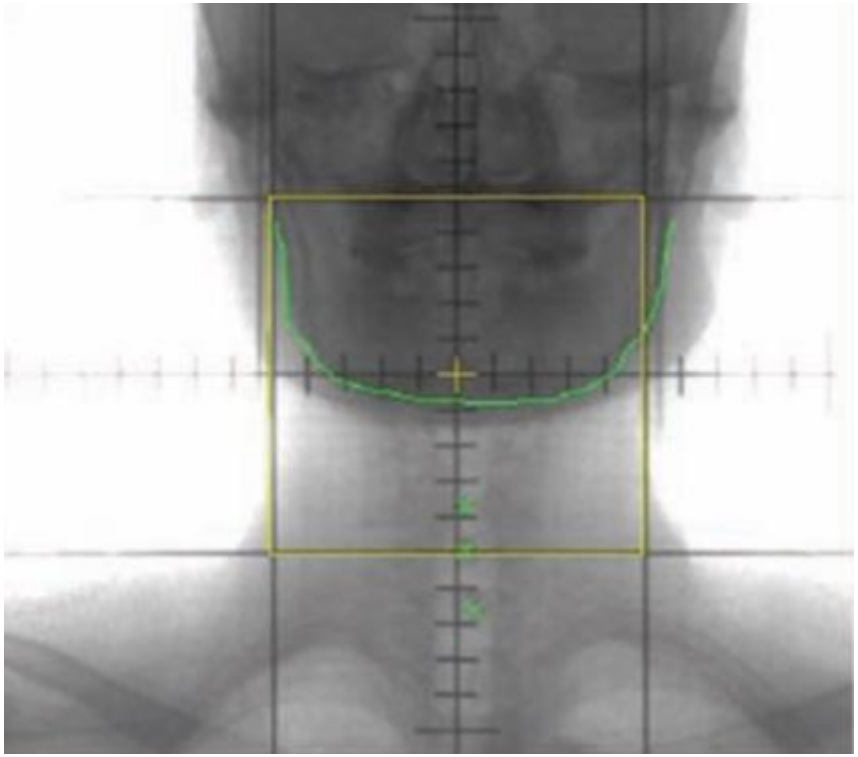
- In the study by Leclerc et al (2012) the advantage of PET was mainly observed for OPC (lower dose to parotid and oral cavity).

Leclerc et al. Radiother Oncol 2012;103(suppl 1):S175-6.
Grégoire V et al. J Clin Oncol 2015;33(29):3277-84.

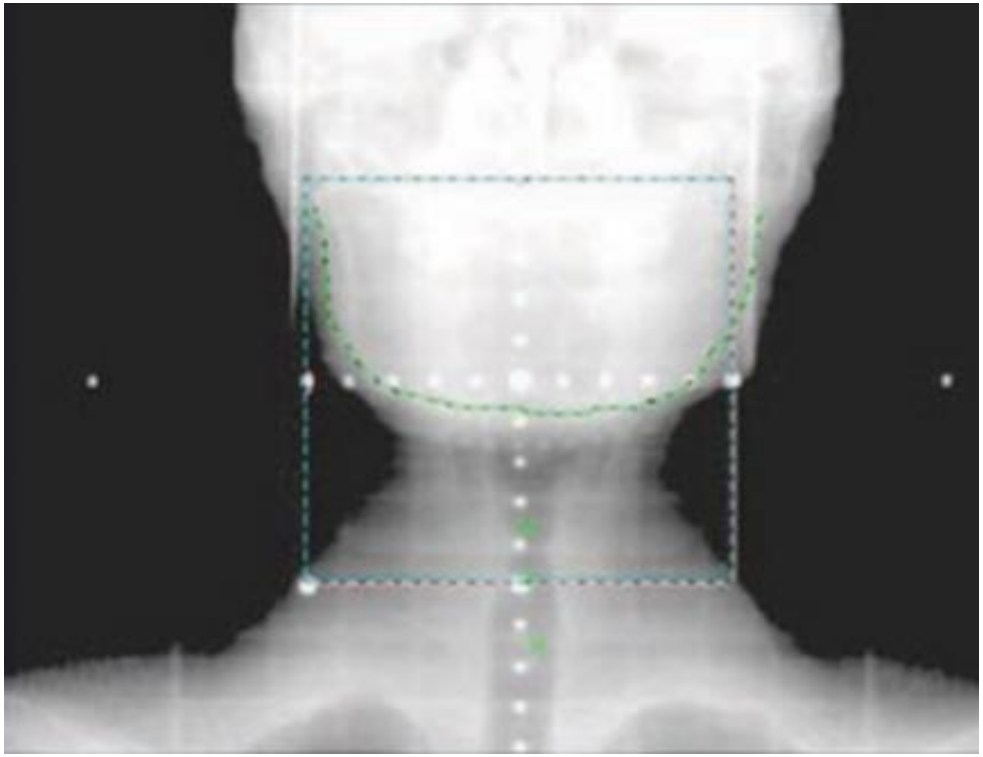
Accuracy

IGRT

Portal Imaging



DRR

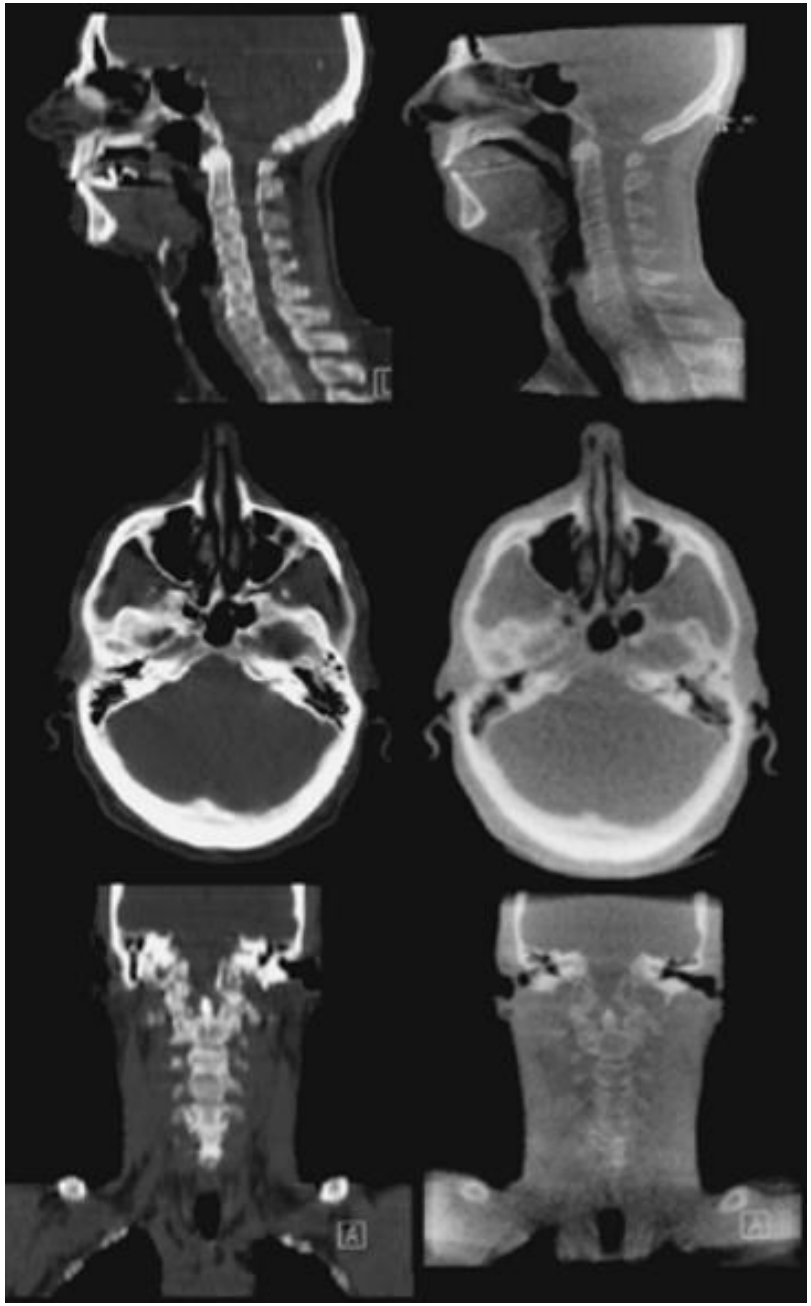


EPI

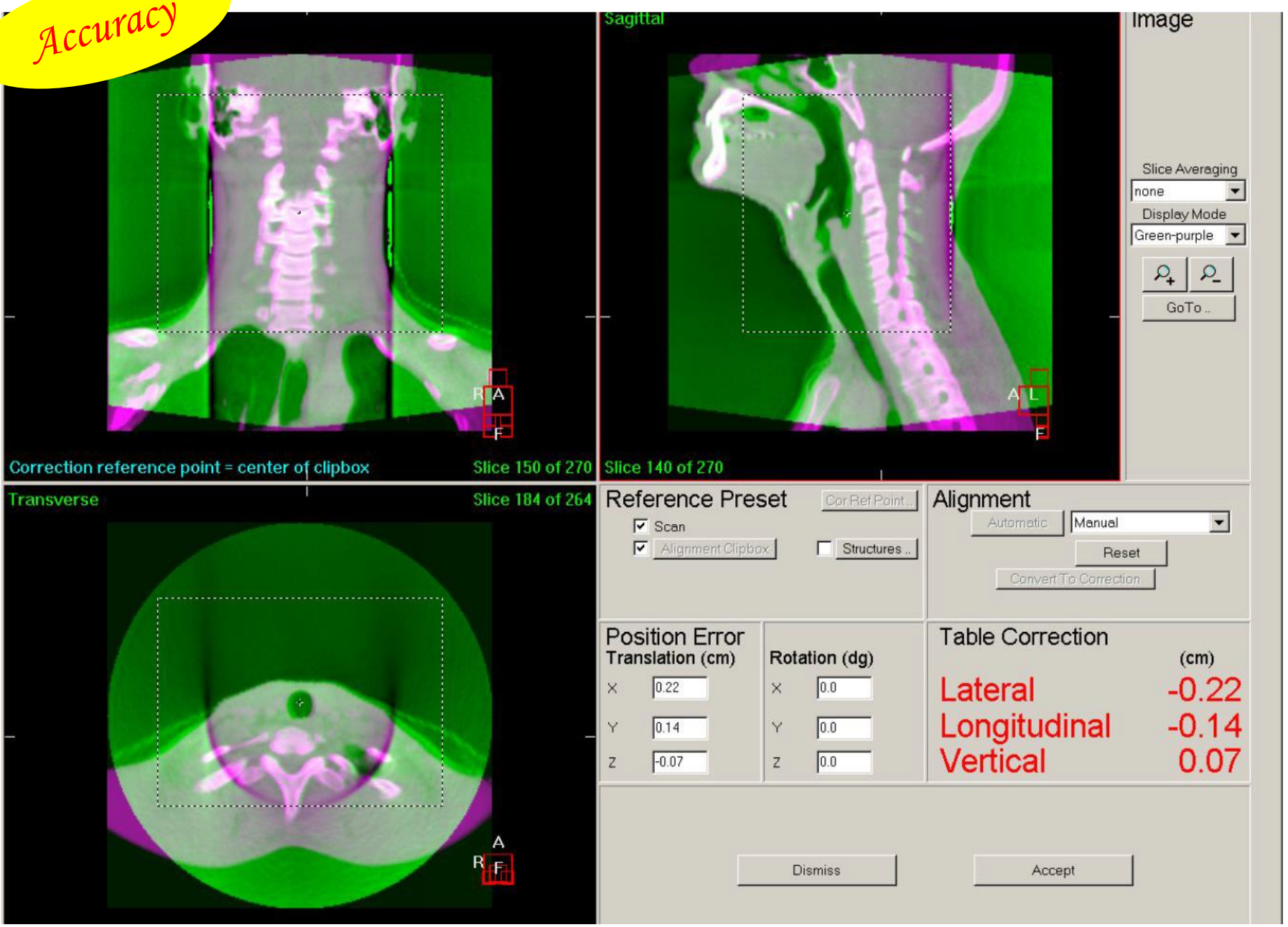
Accuracy

IGRT

CBCT



Accuracy


Sagittal
Image
Slice Averaging
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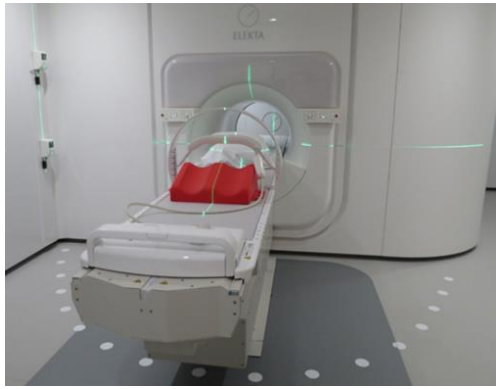
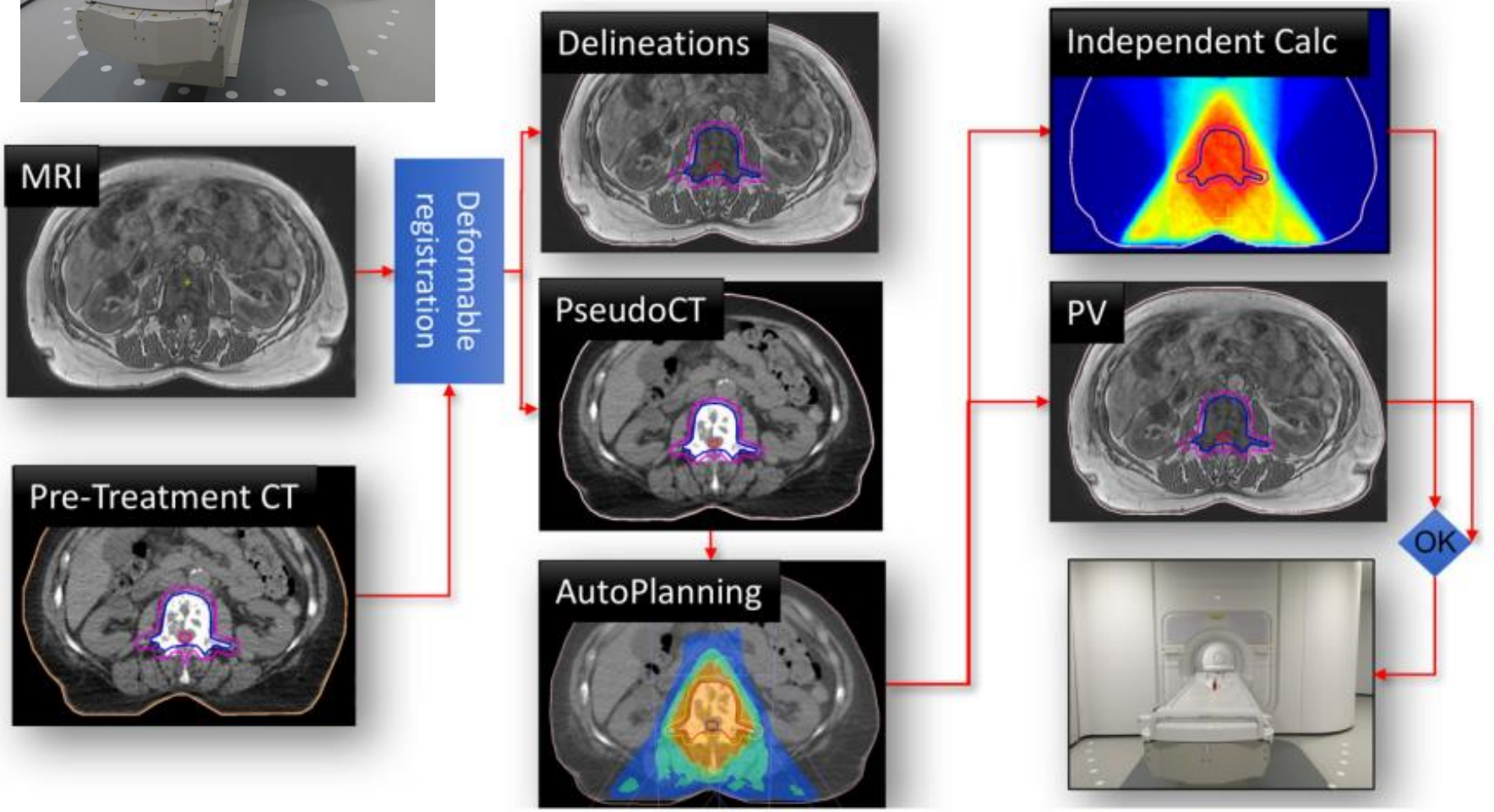
Display Mode
Green-purple
GoTo ..
Correction reference point = center of clipbox
Slice 150 of 270
Slice 140 of 270
Transverse
Slice 184 of 264
Reference Preset
Cor Ref Point ..
Scan
Alignment Clipbox
Structures ..
Alignment
Automatic
Manual
Reset
Convert To Correction
Position Error
Translation (cm)
Rotation (dg)
X 0.22
Y 0.14
Z -0.07
X 0.0
Y 0.0
Z 0.0
Table Correction
(cm)
Lateral -0.22
Longitudinal -0.14
Vertical 0.07
Dismiss
Accept

MRI-Linac





The online MRI is registered to the pre-treatment CT to generate a warped CT and to propagate the pre-treatment contours. An IMRT plan is generated automatically and is validated via independent dose calculations and after position verification (PV) by an additional MRI, beam delivery is started.

Accuracy & Precision

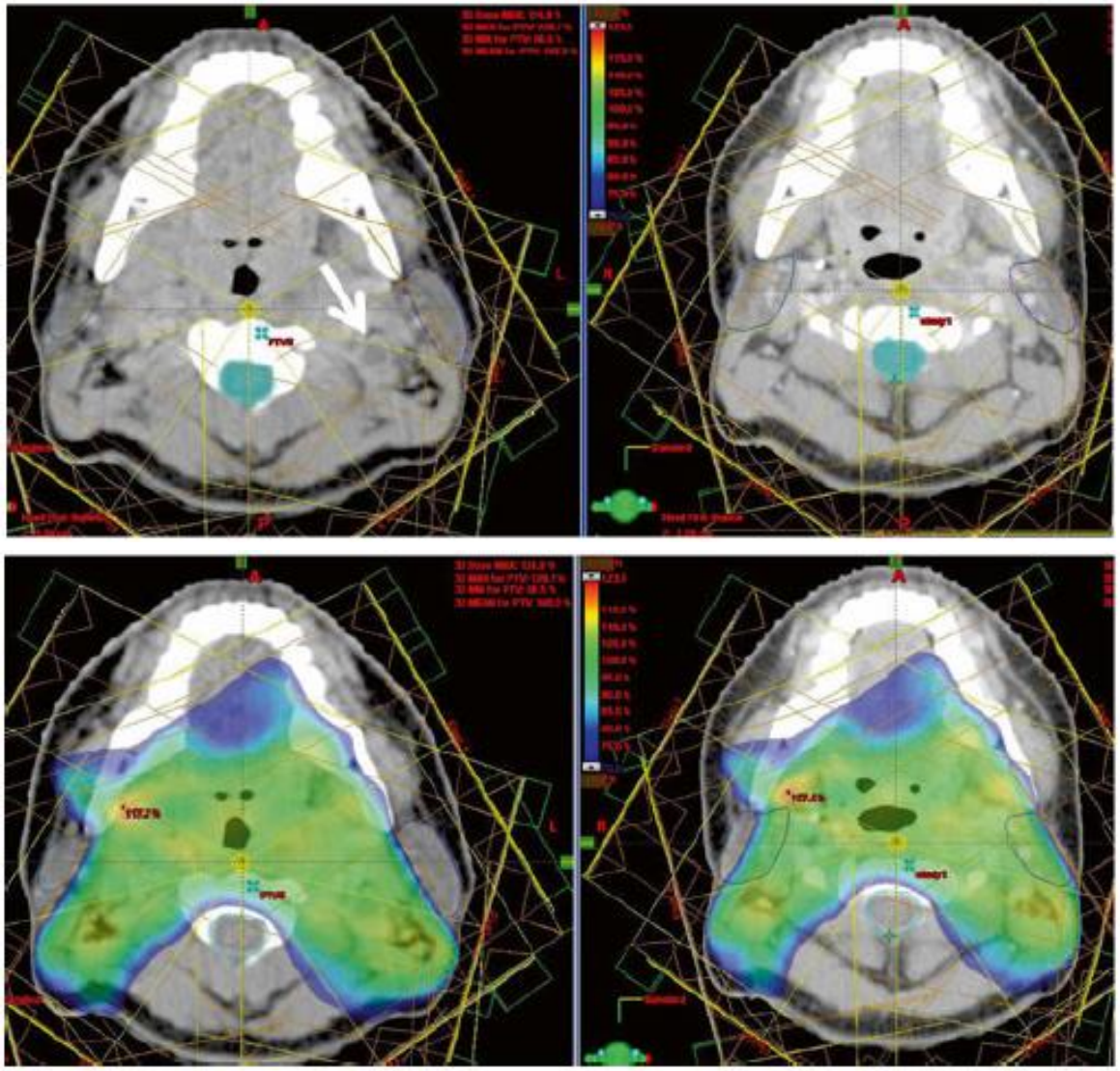
Adaptive Radiotherapy

- Barker et al (2004) evaluated 14 HNC patients treated by an integrated CT-LINAC that allows CT imaging at daily RT sessions.
- GTV decreased at a median rate of 1.8 % per day.
- Absolute volume loss was larger for large tumors. At the end of treatment, the GTV median relative loss was 70 %, and the mass center was displaced by a median 3.3 mm.
- Parotid gland volume: at the end of treatment, median loss was 28%, and the median medial shift was 3.1 mm.

Barker et al. Int J Radiat Oncol Biol Phys 2004;59:960-70.

Accuracy & Precision

CT-1 CT-2



Shrinkage of the neck diameter and the LN is evident on CT-2 obtained after 38Gy/19f for NPC patient.

Dose distributions on CT-1 and the same plan transferred onto CT-2. Most of both parotid glands is included in the 70 % dose level (*blue color*).

Nishimura Y. *IMRT*. Springer Japan 2015.

Accuracy & Precision

- Zhao et al (2011) retrospectively evaluated 175 NPC patients treated with IMRT, 158 showed anatomic changes before 20 fractions (33 had replan, 66 matched control had no replan, outcomes were compared).

- IMRT replanning improved the 3-year local PFS in T3–T4 tumors and also reduced late effects in large LNs (N2, N3).
- Conclusion: recommend ART for advanced NPC (T3-4 or N2-3).

Zhao L et al. Radiother Oncol 2011;98:23-7.

Functional ART

- Along with anatomical modifications, the new concept of ART according to tumor metabolic changes evaluated by either FDG- or FMISO- PET, and/or functional MRI is currently under investigation.

- The principal aim: increase the RT dose in tumor areas considered to be more radioresistant.

IMRT:
Wide margins for Intra-and intertreatment changes of tumor and normal tissues

IGRT or ART !!

IGRT:
Daily setup correction by in-room imaging can reduce margins

Goal: correct set-up errors and minimize PTV margin.

Does not modify the original plan but reposition the patient.

ART:
Detection of changes in anatomy by images acquired during treatment, followed by online or offline replanning

Goal: account for changes in anatomy.

Modify the treatment plan.

Accuracy & Precision

Accurate but not Precise
2D or 3DCRT

Precise but not Accurate
IMRT + PET-CT

Precise and Accurate
IMRT + PET-CT + IGRT ± ART

Contents

- IMRT: A new standard of care
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LC in advanced disease

- Dose painting by IMRT

AEs in early disease

- Carotid sparing IMRT
- Single vocal cord irradiation
- Swallowing sparing IMRT

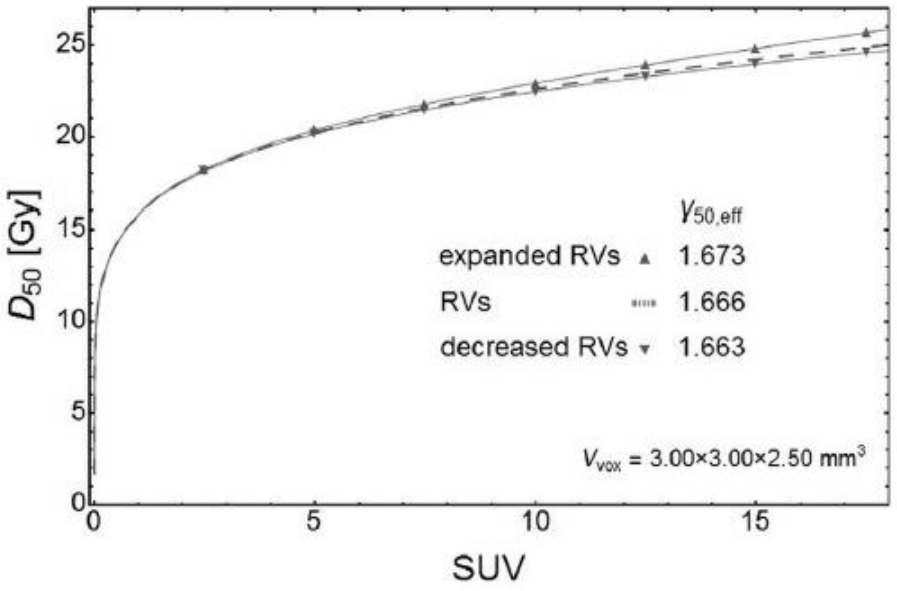
Dose painting IMRT

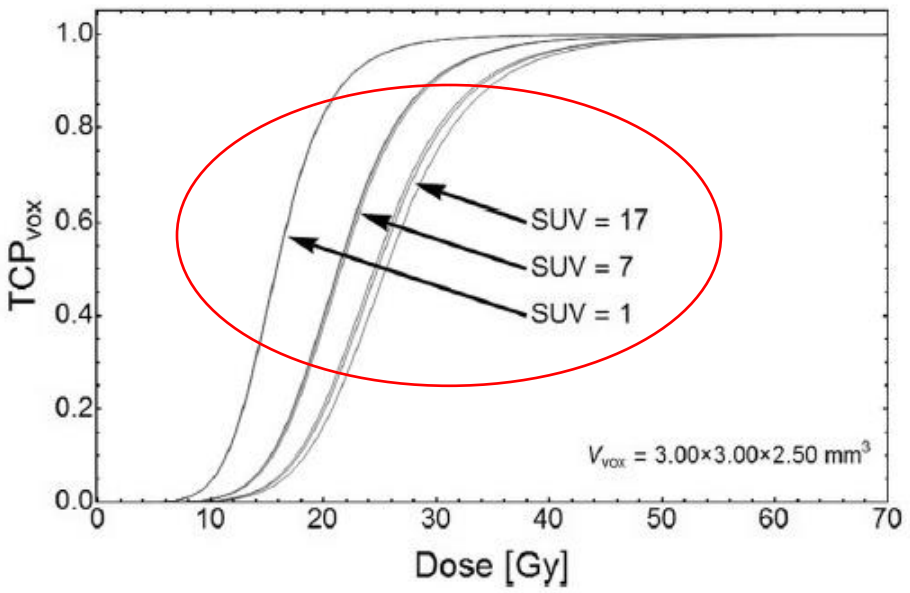
- Main causes of RT failure:
  - Tumor burden
  - Tumor cell proliferation
  - Tumor hypoxia

- Partial dose escalation with IMRT using functional imaging that can define subvolumes at high risk of failure within GTV.

Grégoire V et al. J Clin Oncol 2015;33(29):3277-84.
Nishimura Y. IMRT. Springer Japan 2015.

Increasing radioresistance with increasing SUV

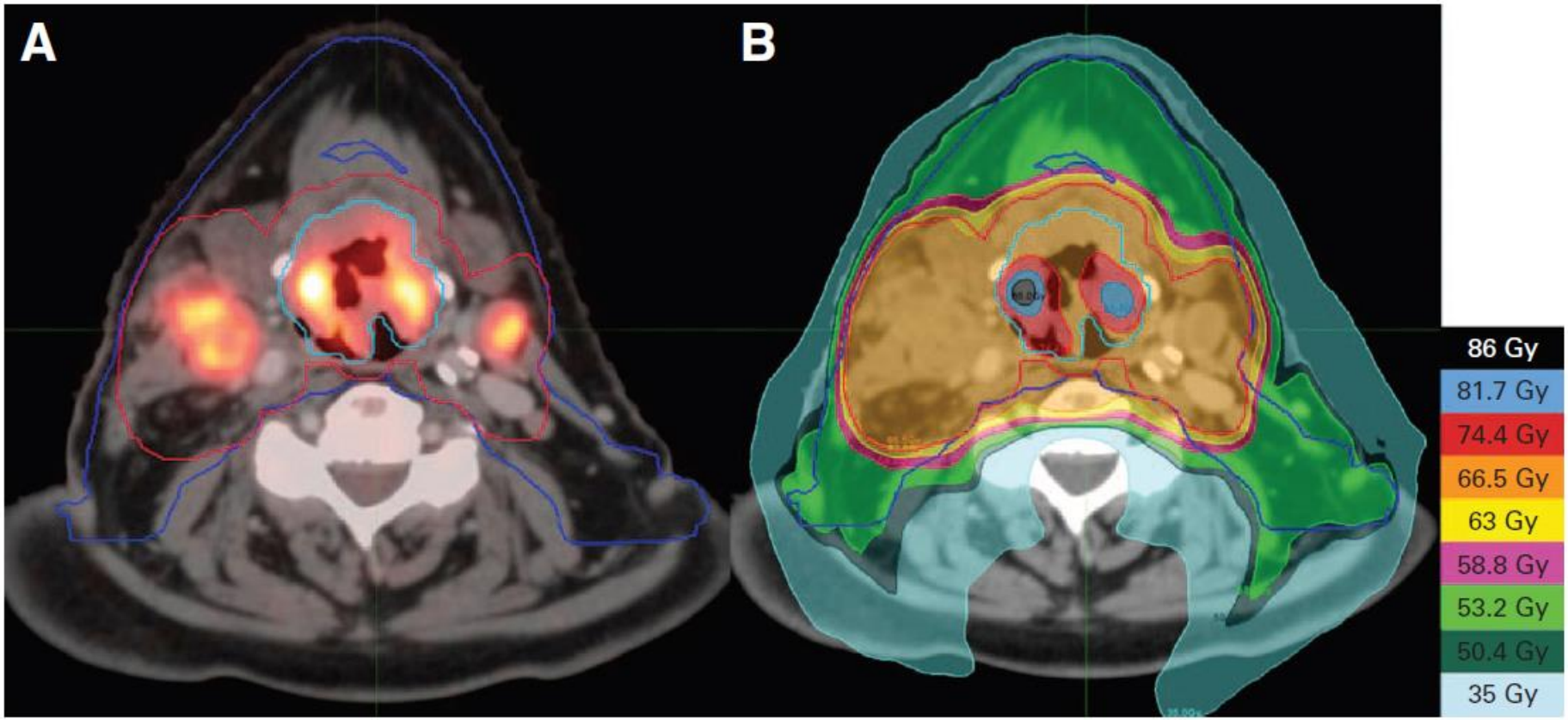




(Left) D50 as a function of SUV and the determined c50,eff values solved for the linearized LCR functions for the different delineation scenarios. (Right) SUV driven dose–response functions for the different delineation scenarios for three different SUV. At SUV = 1 and SUV = 7 the functions for the different delineation scenarios not distinguishable from each other, while for at SUV = 17 a slight separation is observed with the expanded RVs rightmost and the decreased RVs leftmost.

Grönlund E et al. Radiother Oncol 2017;122(2):236-41.

FDG–PET–based dose painting



PET-CT of T4N2cM0 OPC; image was segmented into levels, which were used for dose escalation from 70 to 86 Gy.

Corresponding dose distribution obtained with TomoTherapy. PTV70 (red), PTV56 (deep blue), GTV-PET (light blue).

Grégoire V et al. J Clin Oncol 2015;33(29):3277-84.

- The possible increase in TCP compared to a conventional treatment varied from 0.1% to 14.6%.

- Improvement was greater for patients with large tumor volume and large spread in SUV.

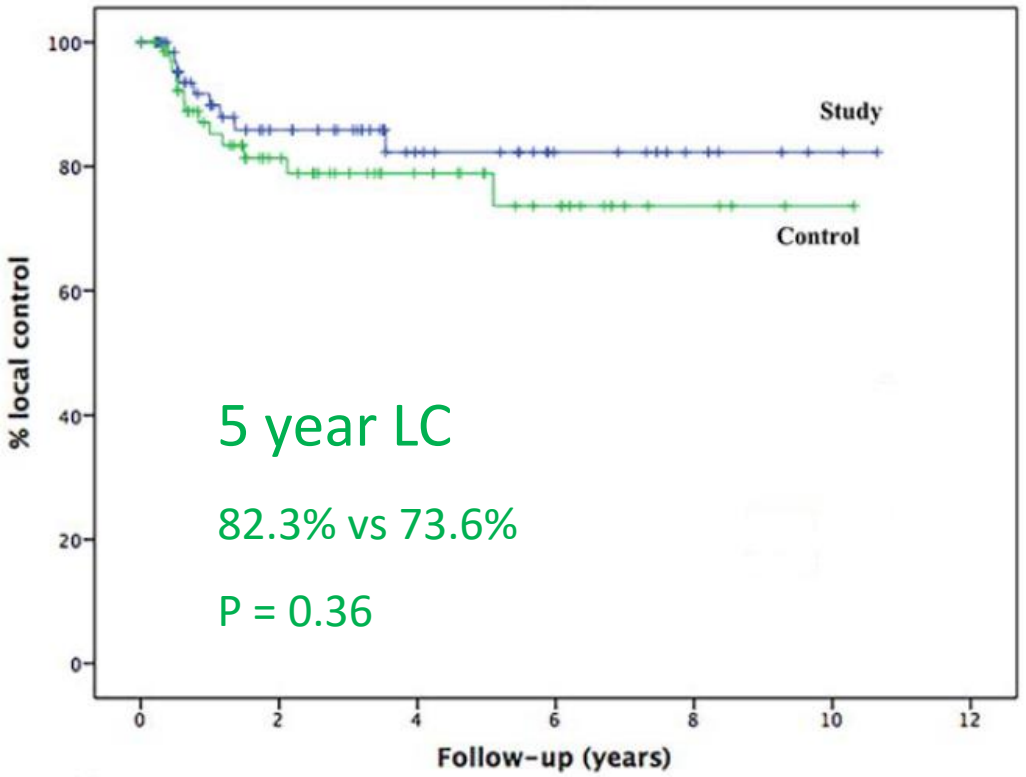
- The average increase was 5% for the whole group, so the patient cohort TCP (71%) would raise to 76% by dose painting.

Grönlund E et al. Radiother Oncol 2017;122(2):236-41.

Seventy-two patients treated with dose painting (PET-guided DPBC or DPBN to 85.9Gy/32f) were compared with 72 matched control.

Median FU 87.7 m.

No difference in regional and distant control, 5 year OAS and DSS.



Dose-painting increased rates of acute (P 0.004) and late dysphagia (P 0.005) and late grade 4 mucosal ulcers (9/72 vs 3/72, P 0.11).

Berwouts et al. Head & Neck. 2017;39:2264-75.

In dose-searching phase I trial in patients with locally advanced HNSCC, a median dose of 86 Gy to the FDG-avid sub-GTV was associated with late mucosal necrosis in 5 of 14 patients, and the maximum-tolerated median dose was 81 Gy.

Madani I et al. Radiother Oncol 2011;101:351-5.

ARTFORCE Trial

- Multicenter phase III randomized trial, 221 patients, T3-4N0-3M0 were assigned to either receive a dose 64-84Gy/35f with adaptation at the 10th fraction (rRT) or conventional 70Gy/35f (cRT). Both arms received concurrent cisplatin.
- 2-year LRC was 81 vs 74 % in the rRT and cRT arm (P=.31). Toxicity rates were similar, with exception for a significant increased grade ≥ 3 pharyngolaryngeal stenoses in the rRT arm (0 vs 4 %, P=.05).
- Subgroup analyses: rRT improved LRC for N0-1 (HR 0.21) and oropharyngeal ca (HR 0.31), regardless of HPV.

(de Leeuw A et al., Radiother Oncol 2024)

Carotid Sparing IMRT

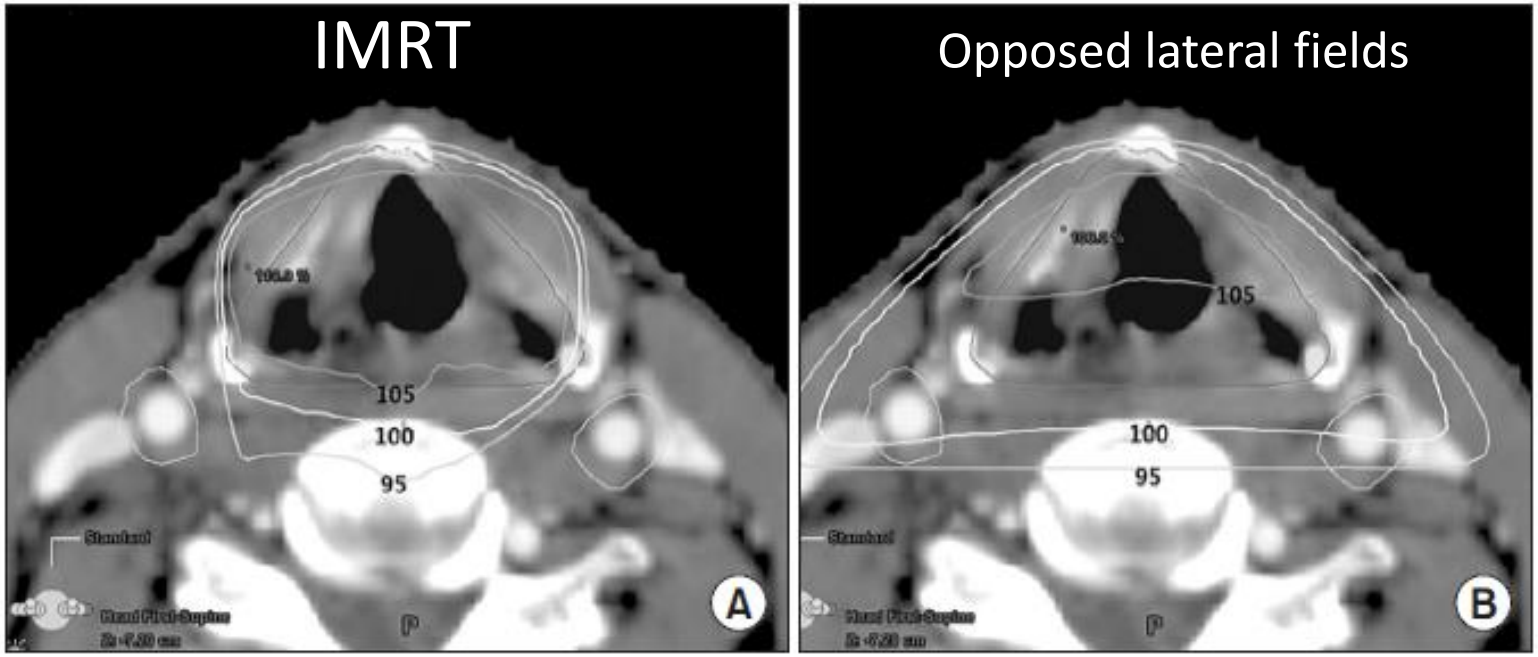
- Carotid arteries are in the beam pathway of conventional RT for early glottic cancer and exposed to relatively high dose almost identical to the target dose.

- Gujral et al (2014): RT → increase thickness of carotid intima-media → increase carotid artery stenosis risk → increase CVA risk (CVA risk can be further increased by atherosclerosis risk factors).

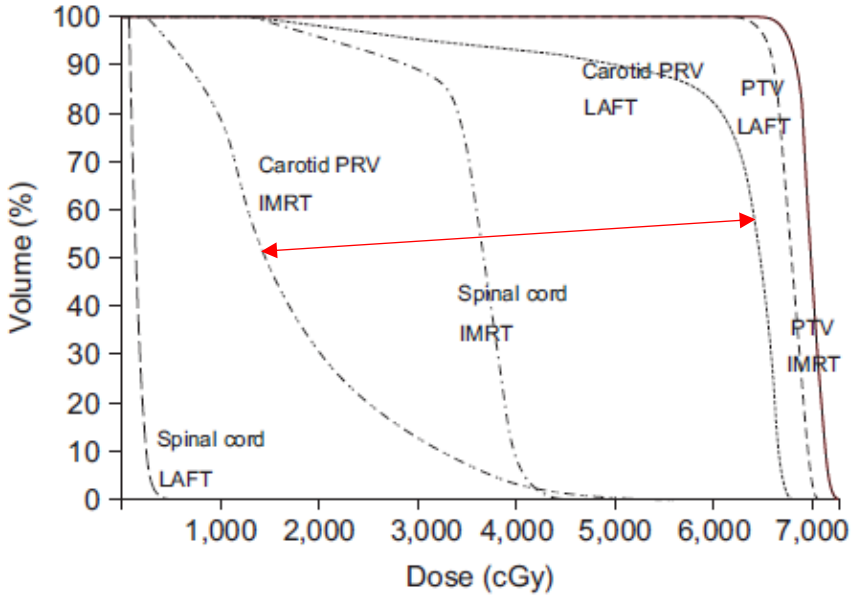
Gujral et al. Clin Oncol 2014;26:94-102.
Choi H et al. Radiat Oncol J 2016;34(1):26-33.

- RT causes carotid artery stenosis:
  - Cheng et al (2000): risk of carotid artery stenosis increased in patients who received neck RT for more than 5 years.
  - Brown et al (2005): incidence of carotid artery stenosis was higher in the irradiated neck than in the contralateral unirradiated neck.
- RT increased CVA risk:
  - Dorresteijn et al (2002): 15-year risk of stroke after neck RT was 12% and there was a 5.6 times higher chance of stroke in patients received neck RT than those who did not.
  - Smith et al (2008): 10-year incidence of CVA was increased by 9% in HNC patients treated with RT.

Cheng SW et al. Arch Otolaryngol Head Neck Surg 2000;126:517-21.
Brown PD, et al. Int J Radiat Oncol Biol Phys 2005;63:1361-7.
Dorresteijn LD et al. J Clin Oncol 2002;20:282-8.
Smith GL et al. J Clin Oncol 2008;26:5119-25.



- T1N0 glottic cancer with at least one atherosclerosis risk factor.
- 66 Gy/33f/7w by 3 fields IMRT.
- **Carotid** PRV constraints: V30 <20% and V10 <50%.



Choi H et al. Radiat Oncol J 2016;34(1):26-33.

Dosimetric data in IMRT and LAFT plans

	IMRT plan	LAFT plan	p-value
PTV (%)			
$V_{95\%}$	99.5 (99.1–99.9)	99.7 (99.2–99.9)	0.209
$V_{100\%}$	95.5 (95.3–95.7)	94.6 (93.9–94.7)	0.005
HI (%)	11.6 (11.0–12.1)	8.5 (7.9–9.1)	0.005
CI	1.4 (1.1–1.9)	5.1 (4.7–5.5)	0.005
Mean Carotid PRV dose (Gy)	14.7 (13.4–15.7)	53.9 (51.3–60.2)	0.005
Carotid PRV (%)			
V_{5Gy}	90.0 (84.5–94.8)	99.1 (96.8–100)	0.005
V_{25Gy}	13.5 (8.1–15.3)	89.0 (85.1–95.5)	0.005
V_{50Gy}	0 (0–0)	77.3 (50.1–83.4)	0.005
Maximum spinal cord dose (Gy)	37.2 (35.7–39.1)	2.5 (1.5–3.3)	0.005
Mean PCM dose (Gy)	61.2 (55.9–66.1)	64.6 (61.2–69.8)	0.009
PCM (%), V_{50Gy}	88.7 (77.3–93.7)	99.8 (90.3–99.9)	0.007

Choi H et al. Radiat Oncol J 2016;34(1):26-33.

Carotid sparing IMRT

	Target coverage (IMRT vs. LAFT)	Carotid artery dose (IMRT vs. LAFT)
Dosimetric comparison studies		
Hong et al.	CI/HI (0.65/1.09 vs. 0.32/1.06)	$V_{35Gy}/V_{50Gy}/V_{63Gy}$ (0.3%/0%/0% vs. 33.9%/18.5%/8%)
Kim and Yeo	D_{min}/D_{max} (50 Gy/66.8 Gy vs. 51.6 Gy/65.7 Gy)	V_{35Gy}/V_{50Gy} (21.1%/2.8% vs. 41.1%/38.2%)
Ki et al.	-	Mean dose (26.3 Gy vs. 38.5 Gy)
Chera et al.	-	Median dose (10 Gy vs. 38 Gy)

	No. of patients	Median follow-up (mo)	Local control rate (%)
Clinical studies			
Rosenthal et al	11	NA	NA
Zumsteg et al	48	43	88
Choi et al	10	10	100

Rosenthal et al. Int J Radiat Oncol Biol Phys 2010;77:455-61.
Zumsteg et al. Oral Oncol 2015;51:716-23.
Choi H et al. Radiat Oncol J 2016;34(1):26-33.

MD Anderson retrospective study:

- T1 glottic cancer, 153 patients, 71% were treated using CRT and 29% using IMRT. Median FU was 68 months.
- 3-year LRC with CRT was 94% vs 97% with IMRT (P=0.4).
- 3-year OS with CRT was 92.5% vs 100% with IMRT (P=0.1).
- 12 of 14 patients with LR underwent salvage surgery with 5-year ultimate LRC of 98.5% and 97.1% in the CRT and IMRT, respectively (P = 0.7).
- Post-RT cerebrovascular events were in 4 patients in the CRT (3%), whereas no patients in the IMRT suffered any events.

Mohamed A et al, Laryngoscope, 2020;130:146-153.

Recommendations

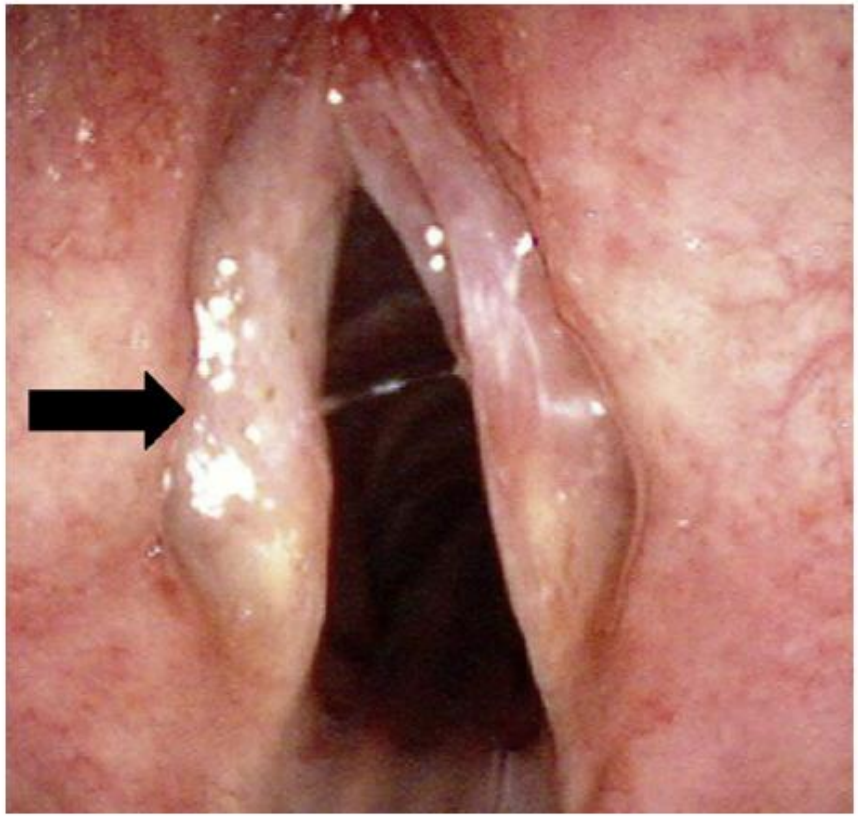
(target volume delineation, dose constraints and reporting)

carotid-sparing IMRT in early larynx cancer

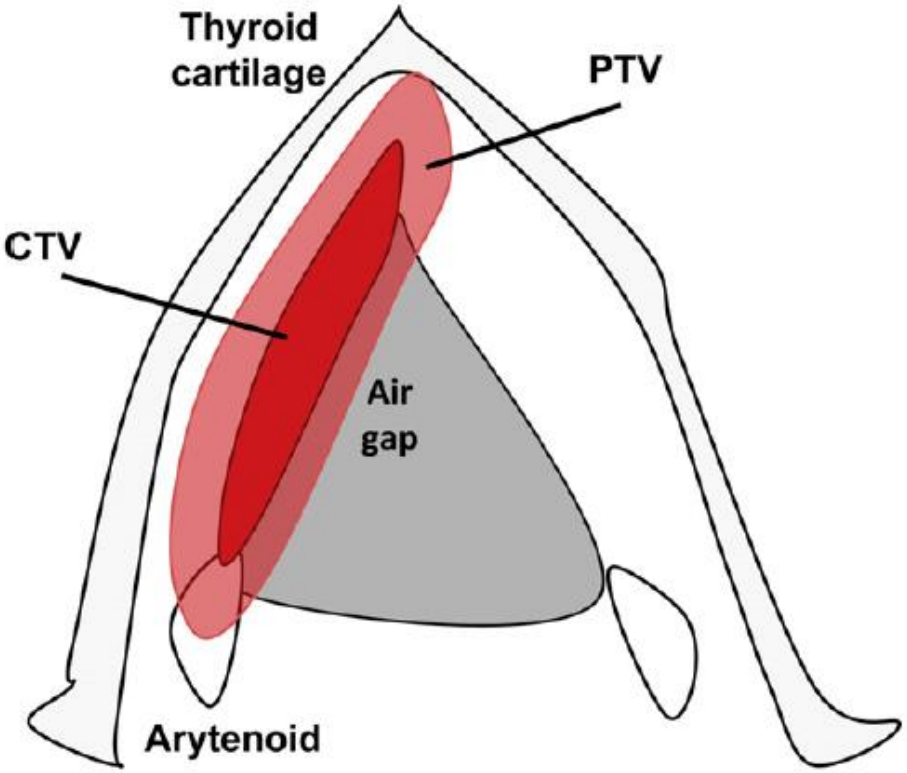
Dose prescription 55 Gy/20 fractions	GTV	CTV	PTV	Spinal cord OAR	Carotid OAR
Target volume delineation	Bilateral TVCs	GTV + 1 cm – edited back to cartilages	Arytenoids, FVCs, anterior and posterior commissure, TVCs, and 1–1.5 cm of subglottis	Foramen magnum superiorly to 2.5 cm below PTV	Extracranial extent of carotid artery (inferiorly from the aortic arch and the brachiocephalic trunk
Dose constraints	<110% prescribed dose	<110% prescribed dose	95–107% prescribed dose	Maximum <39 Gy (<45 Gy in 2 Gy/fraction) PRV maximum <41 Gy (<48 Gy in 2 Gy/fraction)	Maximum < 35 Gy to carotid OAR + 1 mm Mean carotid PRV dose as low as possible (aim < 20 Gy)
Dose reporting	Maximum, median, mean	Maximum, median, mean	Maximum, median, mean	Maximum	Maximum, median, mean dose to left and right carotid OAR and PRV

Gujral D et al. Clinical Oncology 2017;29:42-50.

Single vocal cord irradiation by IMRT



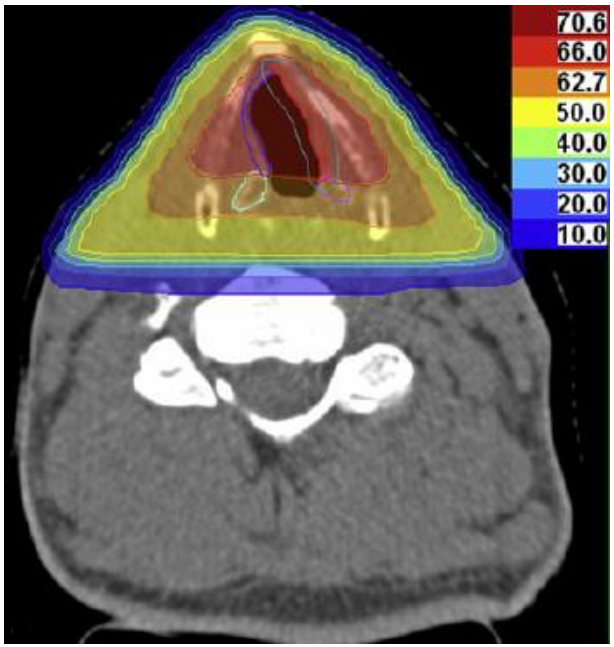
Tumor on left vocal cord

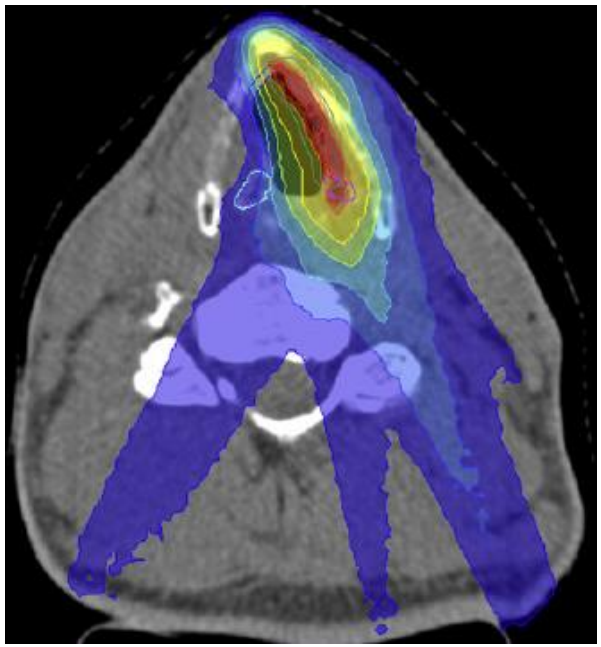


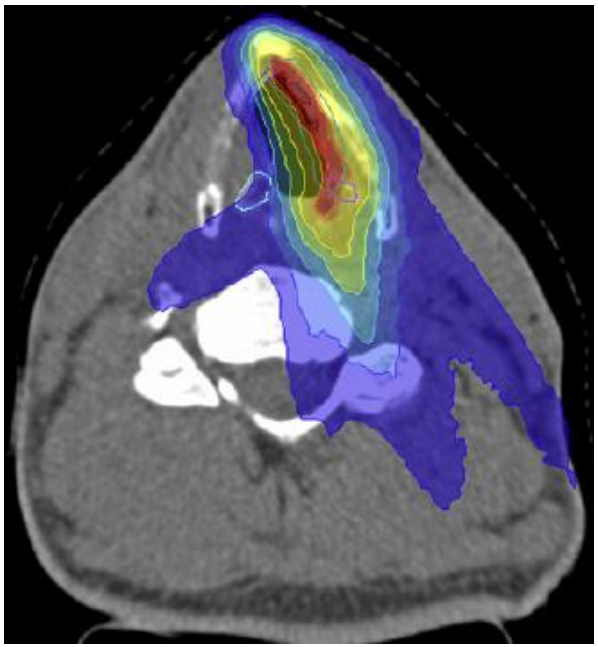
CTV and PTV

Osman S et al. Int J Radiat Oncol Biol Phys 2012;82(2):989-97.

10 patients with T1a glottic ca. Dose: 66 Gy/33f.







Conventional	Coplanar IMRT	Non-coplanar IMRT
66Gy	39Gy Contralateral vocal cord dose	36Gy

IMRT reduced contralateral vocal cord dose

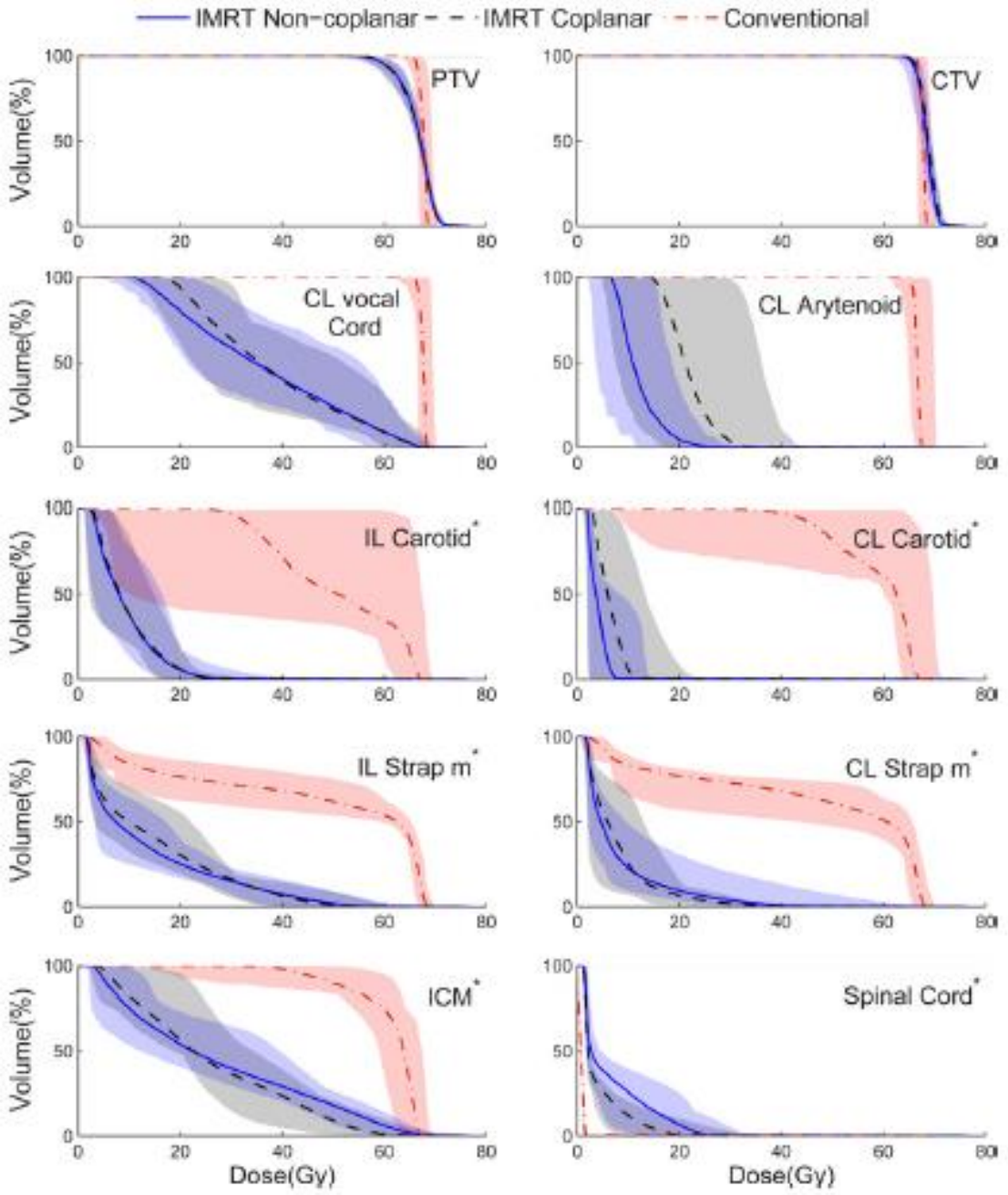
Osman S et al. Int J Radiat Oncol Biol Phys 2012;82(2):989-97.

DVH from different planning techniques for OARs.

No difference in PTV dose

IMRT reduced OAR dose

- Shaded areas indicate ranges.
- Asterisk indicates partially contoured OAR.
- CL = contralateral
- IL = ipsilateral
- m = muscle
- ICM = inferior constrictor muscle



Osman S et al. Int J Radiat Oncol Biol Phys 2012;82(2):989-97.

- Al-Mamgani et al (2015): 30 patients with T1a glottic ca (SVCI by IMRT, 58Gy/16F). Prospectively assessed by voice-handicap index (VHI).

- Median FU of 30 months, 2-year LC 100%. No grade 3 acute or serious late toxicity.

- The control group, treated to the whole larynx, had comparable LC (92.2% vs 100%, P=.24) but more acute grade ≥2 toxicity (66% vs 17%, P<.0001) and higher VHI (P<.0001).

Al-Mamgani A et al. Int J Radiat Oncol Biol Phys 2015;93(2):337-43.

Single Vocal Cord Irradiation Vs Whole Laryngeal Hypofractionated Radiotherapy for Early Stage Glottic Cancer

A Prospective Randomized Trial

Mohamed Mortada Elsharief

Supervised by

Prof. Tarek Shouman
Professor of Radiation Oncology

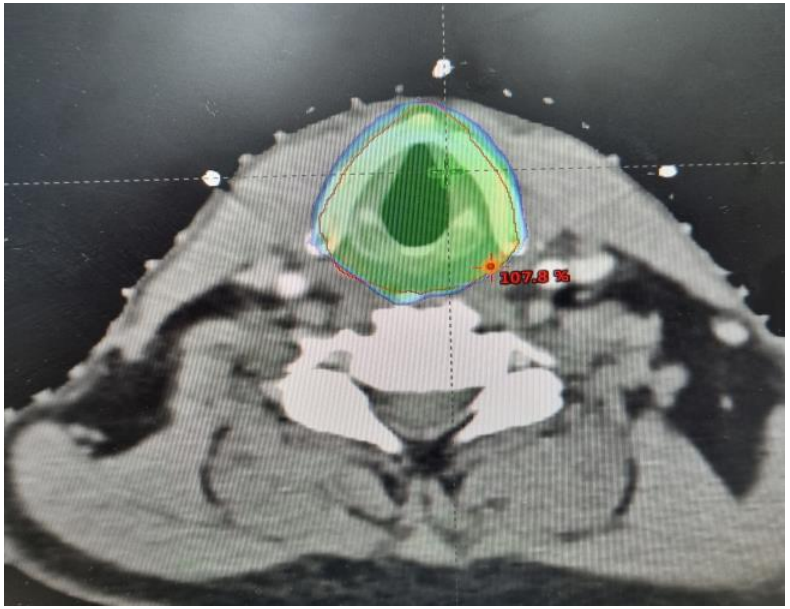
Prof. Ashraf Hassouna
Professor of Radiation Oncology

Dr. Sherweef Abdelfattah
Lecturer of Radiation Oncology

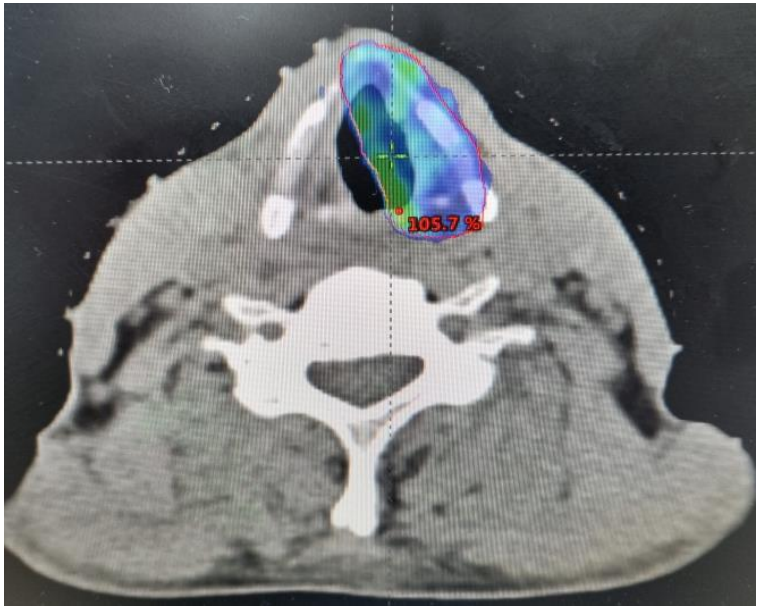
T1aN0 Glottic Cancer

Randomisation
1:1

Arm A (Standard arm)
Whole larynx
63Gy/28F

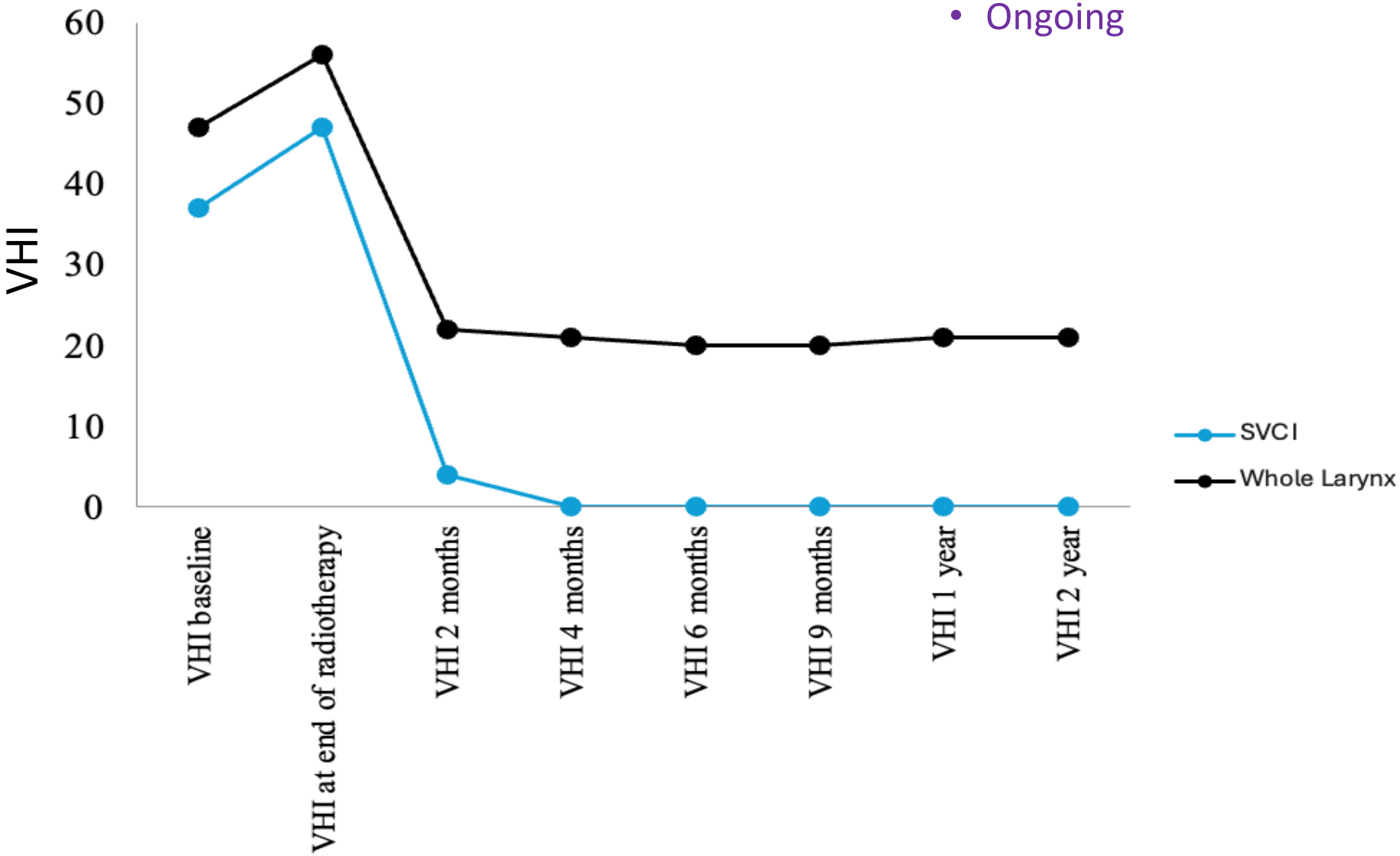


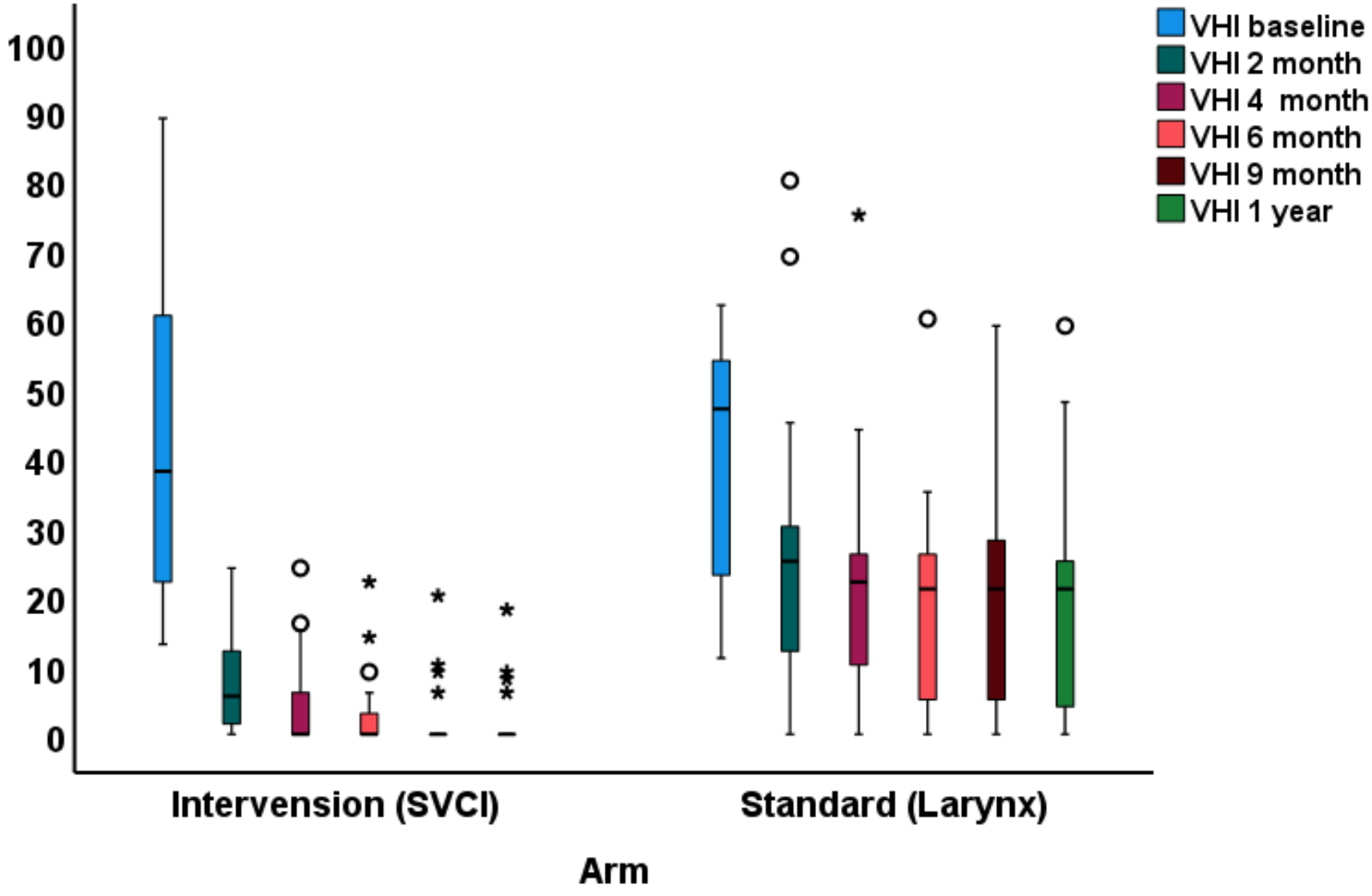
Arm B (experimental)
SVCI
58Gy/16F



Preliminary results

- Patients accrued: 57
- Started: 12.2019
- Ongoing




VHI baseline
VHI 2 month
VHI 4 month
VHI 6 month
VHI 9 month
VHI 1 year
100
90
80
70
60
50
40
30
20
10
0
Intervension (SVCI)
Standard (Larynx)
Arm

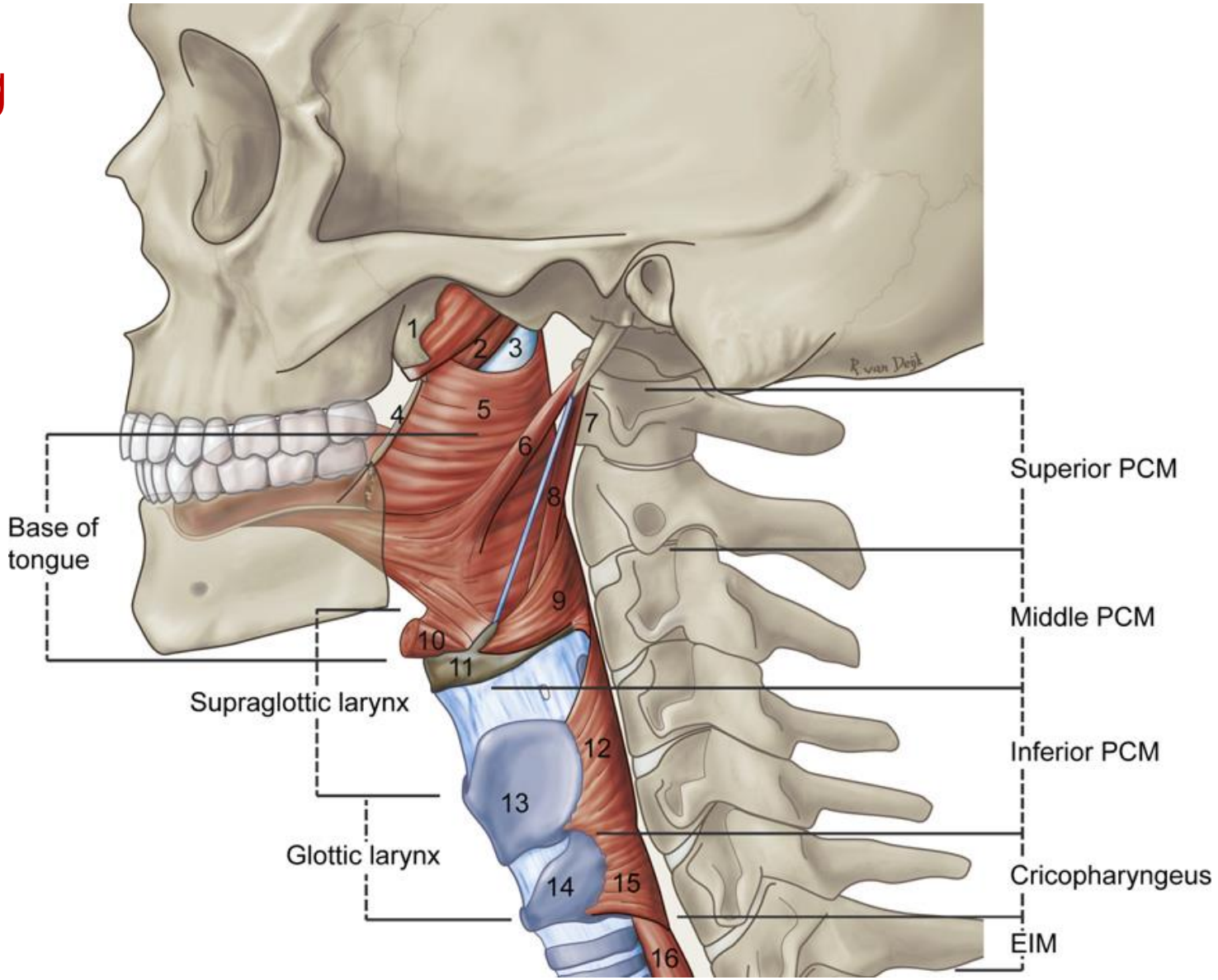
Swallowing Sparing IMRT

- Late dysphagia results when tissue become fibrotic, leading to rigidity and loss of function.
- Persistent dysphagia is seen in 20% of patient after CCRT, with Staar et al (2001) reporting a rate of 51% at 2 years.
- IMRT reduced the frequency and severity of xerostomia, but dysphagia remains a significant long-term side effect with a major impact on QoL.

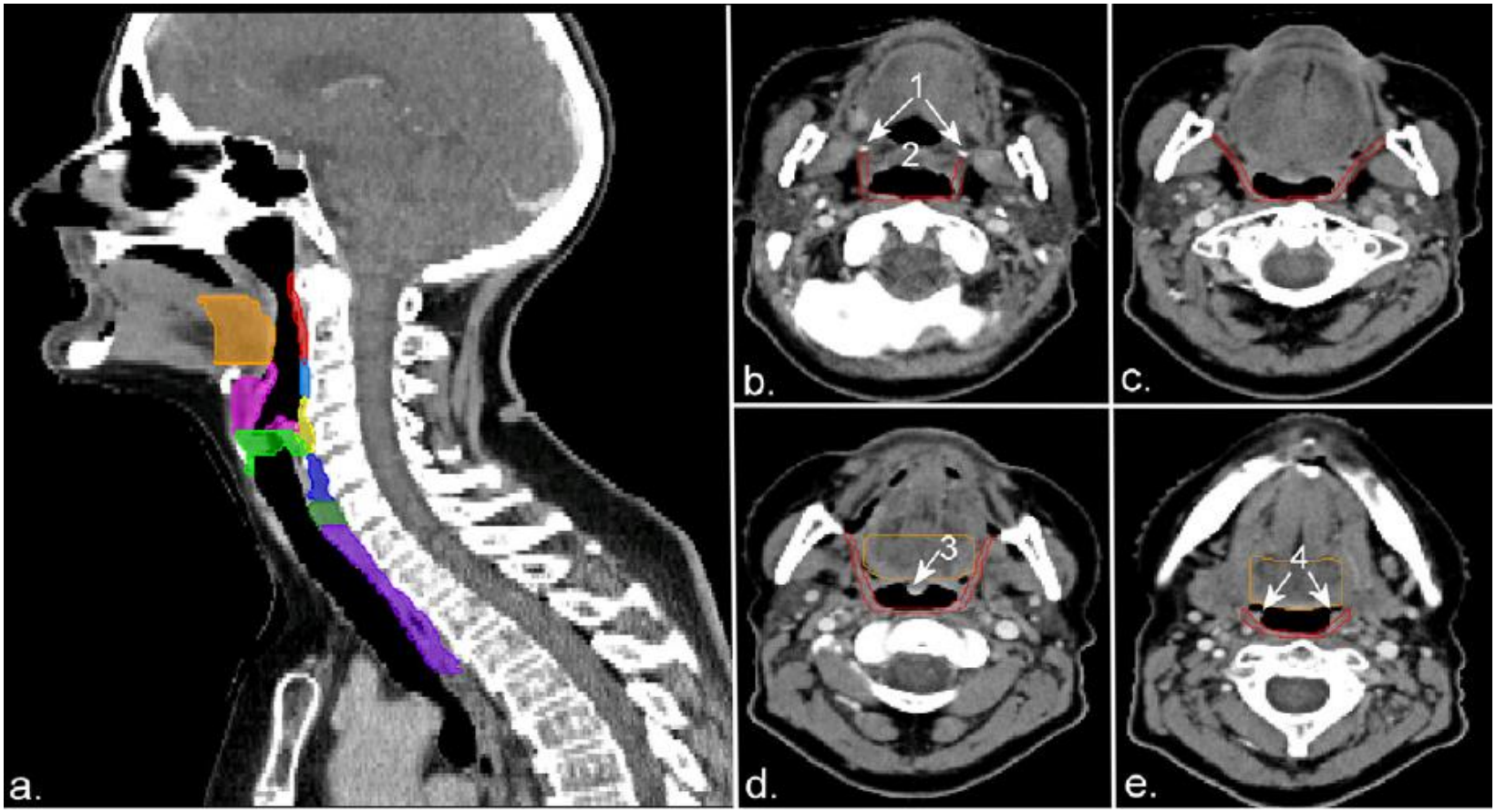
Söderström K et al. Radiother Oncol 2017;122(2):192-9.

Staar S et al. Int J Radiat Oncol Biol Phys 2001;50(5):1161-71.

Swallowing OARs (SWOARs)



Christianen M et al. Radiother Oncol 2011;101:394–402.



- The anatomical location of SWOARs, inside PTV, makes them difficult to spare.
- Tumor PTV cannot be compromised so as not to affect LRC, but for the elective PTV, the benefits of treatment are to be weighed against the risk of side effects.

Christianen M et al. Radiother Oncol 2011;101:394–402.
Söderström K et al. Radiother Oncol 2017;122(2):192-9.

SW-IMRT Prospective Clinical Trials

Reference	No. /Site	Evaluation method	Results
Feng et al, 2007	36/Mixed	VF, HN QoL, UW QoL, CTCAE, RTOG Late RT morbidity score	Significant correlation between VF based aspiration and mean dose to the PCMs, glottis and supraglottic larynx. All patients with aspiration had received mean dose to PC>60 Gy or PC V65>50%, and GSL V50>50%.
Bhide et al, 2009	37/Mixed	RTOG Late RT morbidity score, MDADI	No statistically significant correlation between the PC dose and observer assessed dysphagia grade or patient reported MDADI questionnaire in 1 year.
Feng et al, 2010	73/OPC	Observer rated, patient reported scores, VF	3 year DFS and locoregional RFS were 88% and 96% respectively. All measures of dysphagia worsened soon after therapy. Observer rated and patient reported scores recovered over time, but VF score did not.
Schwartz et al, 2010	31/OPC	PAS, PSS, MDADI, VF	V30 <65% and V35 <35% for oral cavity and V55 <80% and V65 <30% for high SPC predictive for objective swallowing dysfunction after 6, 12 and 24 months.
Eisbruch et al, 2011	73/OPC	CTCAE V3, VF	Dmean >50 Gy to each part of the PCs significantly correlated with all dysphagia measures, with SPC demonstrating highest correlation.
Hunter et al, 2013	72/OPC	VF, Observer rated QoL	Observer rated toxicities worsened 1-3 months after therapy and improved through 12 months with minor further improvement through 24 months.
Van der laan et al, 2013	100/Mixed	RTOG late RT morbidity score	SW-IMRT benefits depends significantly on neck RT, tumor site and the amount of overlap between swallowing OAR and PTVs according to NTCP models.
Van der molen et al, 2013	55/Mixed	VF, QoL	IPC volume receiving ≥60Gy and mean dose to IPC were significantly predictors for PAS at 10 weeks post treatment.

FEES= flexible endoscopic evaluation of swallowing; GSL= Glottic supraglottic larynx; GT = gastrostomy tube; MDADI= MD Anderson Dysphagia Inventory; MPC= middle pharyngeal constrictor; PAS= penetration aspiration scale; PC= pharyngeal constrictors; PCMs= pharyngeal constrictor muscles; SPC= superior pharyngeal constrictor; UW-QoL= University of Washington QoL Revised; VF= video-fluoroscopy

SW-IMRT vs ST-IMRT

in the Treatment of HNC

Phase III Prospective Randomized Trial

May Ashour, Tarek Shouman, Ashraf Hassouna

Reem Emad, Ayda Youssef

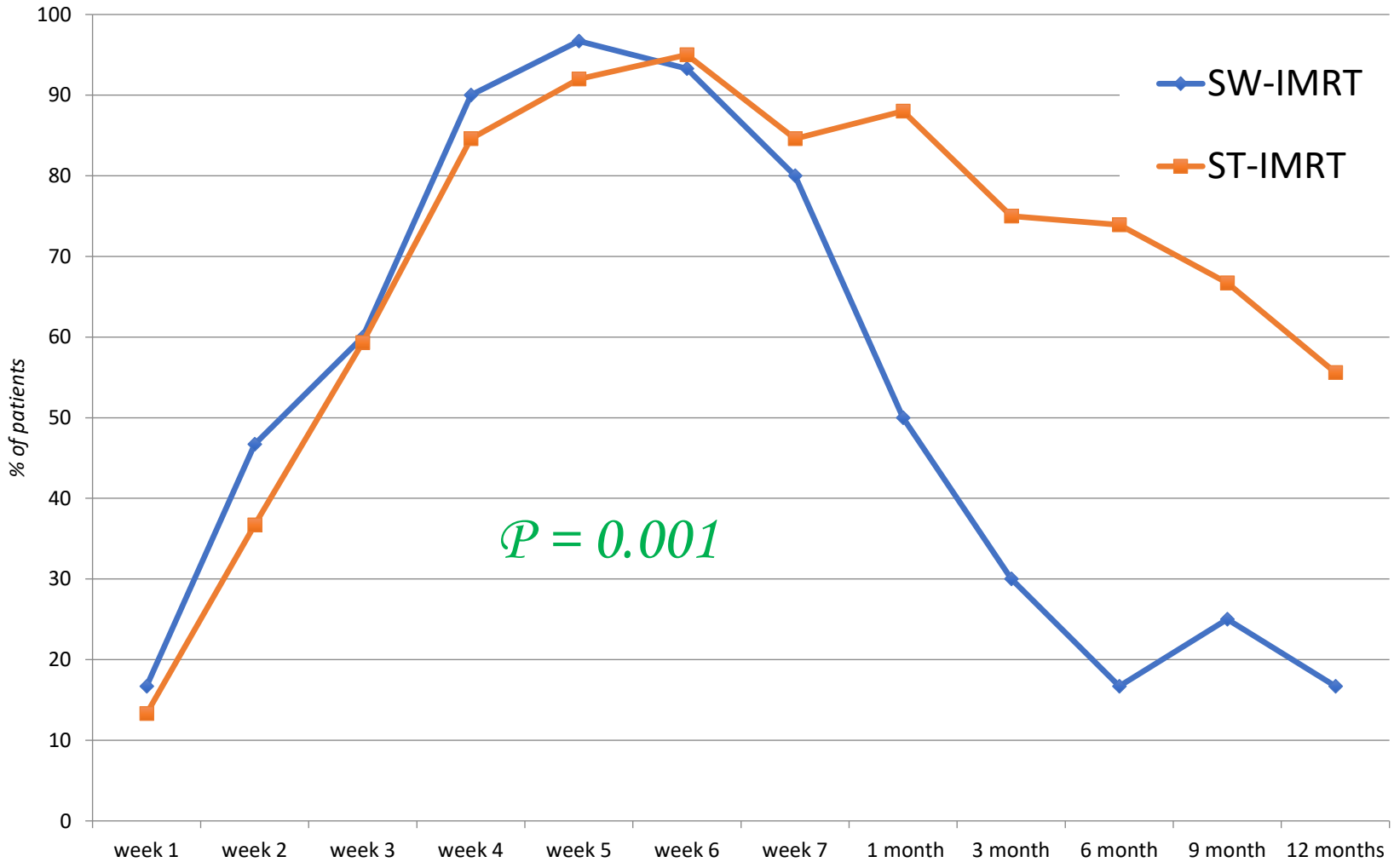
146 patients accrued

Rational	No. (%)
Radical treatment	122 (84)
Post-operative	24 (16)

Site	No. (%)
Larynx	41 (28)
Nasopharynx	51 (35)
Oral cavity	28 (19)
Hypopharynx	14 (10)
Oropharynx	10 (7)

- Objective assessment of swallowing: video-fluoroscopy (VF).
- Patient-reported dysphagia (PRD): Head and Neck Quality of Life questionnaire (HNQOL).
- Observer-rated dysphagia (ORD): NCI CTCAE-4 on FU visits.

Patients developed ≥ G1 dysphagia



Dysphagia at 6 months post-RT

Evaluation Method		ST-IMRT No (%)	SW-IMRT No (%)	P
CTCAE v4	No dysphagia	6 (26)	20 (83)	0.001
	≥ G1	17 (74)	4 (17)	
VF (DIGEST)	0-1	11 (48)	21 (88)	0.004
	2-4	12 (52)	3 (12)	
VF (PSS)	1	2 (9)	13 (54)	0.001
	2-7	21 (91)	11 (46)	
QOL Questionnaire	1	10 (44)	20 (83)	0.004
	2-4	13 (56)	4 (17)	

ESTRO 2018

Swallowing sparing IMRT vs parotid sparing IMRT in head and neck cancer phase III randomized trial

May Ashour[1], Tarek Shouman[1], Ashraf Hassouna[1], Reem Emad El Din[1], Maha Mokhtar[2], Ayda Youssef[3], Shaymaa Abd algeleel[4]

Radiation Oncology[1], Radiation Physics[2], Radiology[3], Statistics[4], National Cancer Institute- Cairo University, Egypt.

Objective

To clinically validate whether SW-IMRT actually reduce the occurrence of swallowing dysfunction as compared to ST-IMRT.

Material and Methods

130 patients with head and neck cancer required bilateral neck irradiation were randomized, planned and treated by simultaneous integrated boost IMRT technique. Doses of 70, 60 and 54 Gy (over 33 daily fractions) were prescribed to gross disease, high-risk nodal regions and low-risk nodal regions, respectively. In the post-operative setting, two volumes were identified: CTV1 for the tumor bed and high risk nodal regions and CTV2 for elective lymphatic areas. These volumes were irradiated to a total dose of 60 Gy/30fx and 54 Gy/30fx, respectively. Pharyngeal constrictor muscles (PCM; superior, middle, inferior), cricopharyngeus muscle, esophageal inlet, cervical esophagus, base of tongue, glottic and supraglottic larynx (SGL) were considered organs at risk related to swallowing dysfunction (SW-OARs). They were outlined in all cases. In standard IMRT arm parotids only were spared.

		ST-IMRT No. (%)	SW-IMRT No. (%)	Total No. (%)	P value
Dysphagia					
At 1 m	No dysphagia	9 (12)	35 (58)	18 (32.7)	0.003
	≥ G1	22 (88)	25 (42)	37 (66.1)	
	Total	25 (100)	30 (100)	55 (100)	
At 3 m	No dysphagia	6 (25)	21 (70)	27 (50)	0.001
	≥ G1	18 (75)	9 (30)	27 (50)	
	Total	24 (100)	30 (100)	54 (100)	
At 6 m	No dysphagia	8 (26.1)	20 (83.3)	28 (55.3)	<0.001
	≥ G1	17 (73.9)	4 (16.7)	21 (45.8)	
	Total	23 (100)	24 (100)	47 (100)	
Video fluoroscopy (DIGEST)					
At 3 m	0-1	10 (41.7)	24 (80)	34 (63)	0.004
	2-4	14 (58.3)	6 (20)	20 (37)	
	Total	24 (100)	30 (100)	54 (100)	
At 6 m	0-1	11 (47.8)	21 (87.5)	32 (68.1)	0.004
	2-4	12 (52.2)	3 (12.5)	15 (31.9)	
	Total	23 (100)	24 (100)	47 (100)	
QOL					
At 3 m	1	8 (37.5)	22 (73.3)	31 (57.4)	0.008
	2-4	15 (62.5)	8 (26.7)	23 (42.6)	
	Total	24 (100)	30 (100)	54 (100)	
At 6 m	1	10 (43.5)	20 (83.3)	30 (63.8)	0.004
	2-4	13 (56.5)	4 (16.7)	17 (36.2)	
	Total	23 (100)	24 (100)	47 (100)	

In SW-IMRT arm parotids and SW-OAR outside the high risk PTV were spared. Assessment of dysphagia included objective and subjective evaluation.

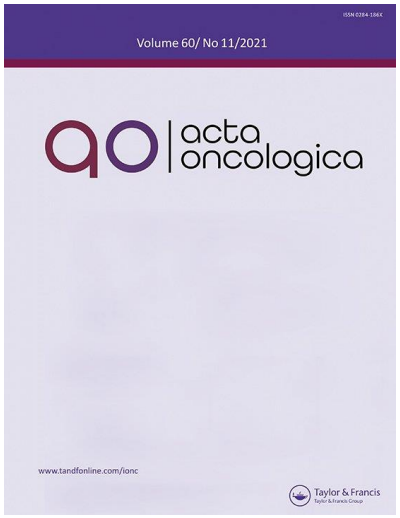
Results

We present the preliminary results of the first 60 patients with a median follow up 15.9 months (range, 6 - 24 months). Dose distribution demonstrated comparable PTV coverage and no difference in parotid glands sparing between the 2 arms. SW-IMRT plans reduce the dose to all SW-OARs with statistically significant difference. Dose reductions with SW-IMRT differ according to tumour location and its overlap with SW-OARs. SW-IMRT was associated with less dysphagia at 1,3 and 6 months using subjective and objective methods with a statistically significant difference (p=0.003, 0.001, <0.001 and NA, 0.004, 0.004 respectively). No difference between arms regarding acute dysphagia (p=0.15), acute xerostomia (p= 0.85), disease free survival (p= 0.13), and overall survival (p=0.4).

Figure (1): Pattern of dysphagia

Conclusion

We reported a randomized phase III clinical trial to found that SW-IMRT is significantly better than ST-IMRT regarding subjective and objective assessment of swallowing dysfunction at 1,3 and 6 months post treatment.



ACTA ONCOLOGICA
https://doi.org/10.1080/0284186X.2021.2022198

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ORIGINAL ARTICLE

Swallowing sparing intensity modulated radiotherapy versus standard parotid sparing intensity-modulated radiotherapy for treatment of head and neck cancer: a randomized clinical trial

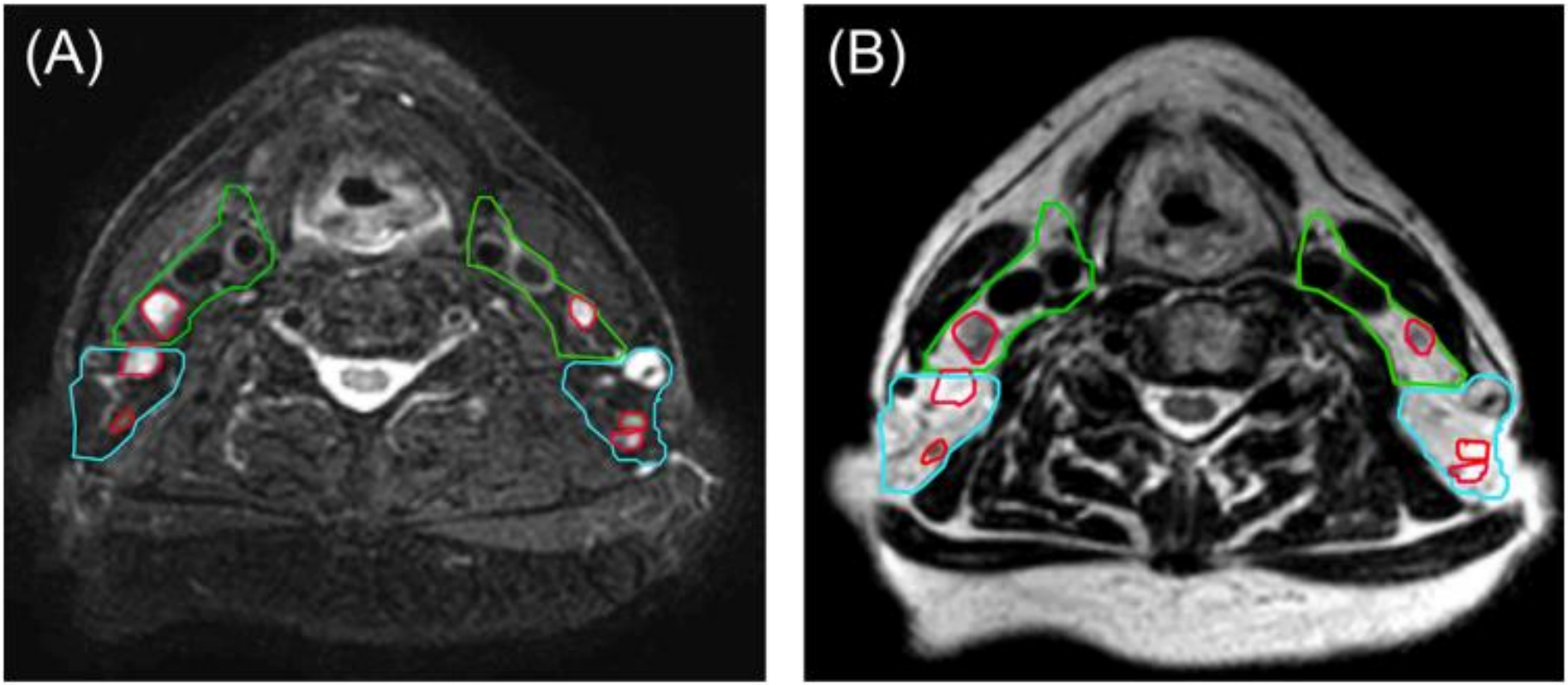
May Gamal Ashour[a], Tarek Hamed Shouman[a], Ashraf Hamed Hassouna[a], Maha Hassan Mokhtar[b], Reem Emad El Din[a], Ayda Aly Youssef[c], Mohammed Mohammed Gomaa[c] and Shaimaa Abdelgeleel[d]

[a]Radiation Oncology Department, National Cancer Institute Cairo University, Cairo, Egypt; [b]Physics Unit, National Cancer Institute Cairo University, Cairo, Egypt; [c]Radiology Department, National Cancer Institute Cairo University, Cairo, Egypt; [d]Statistics Department, National Cancer Institute Cairo University, Cairo, Egypt

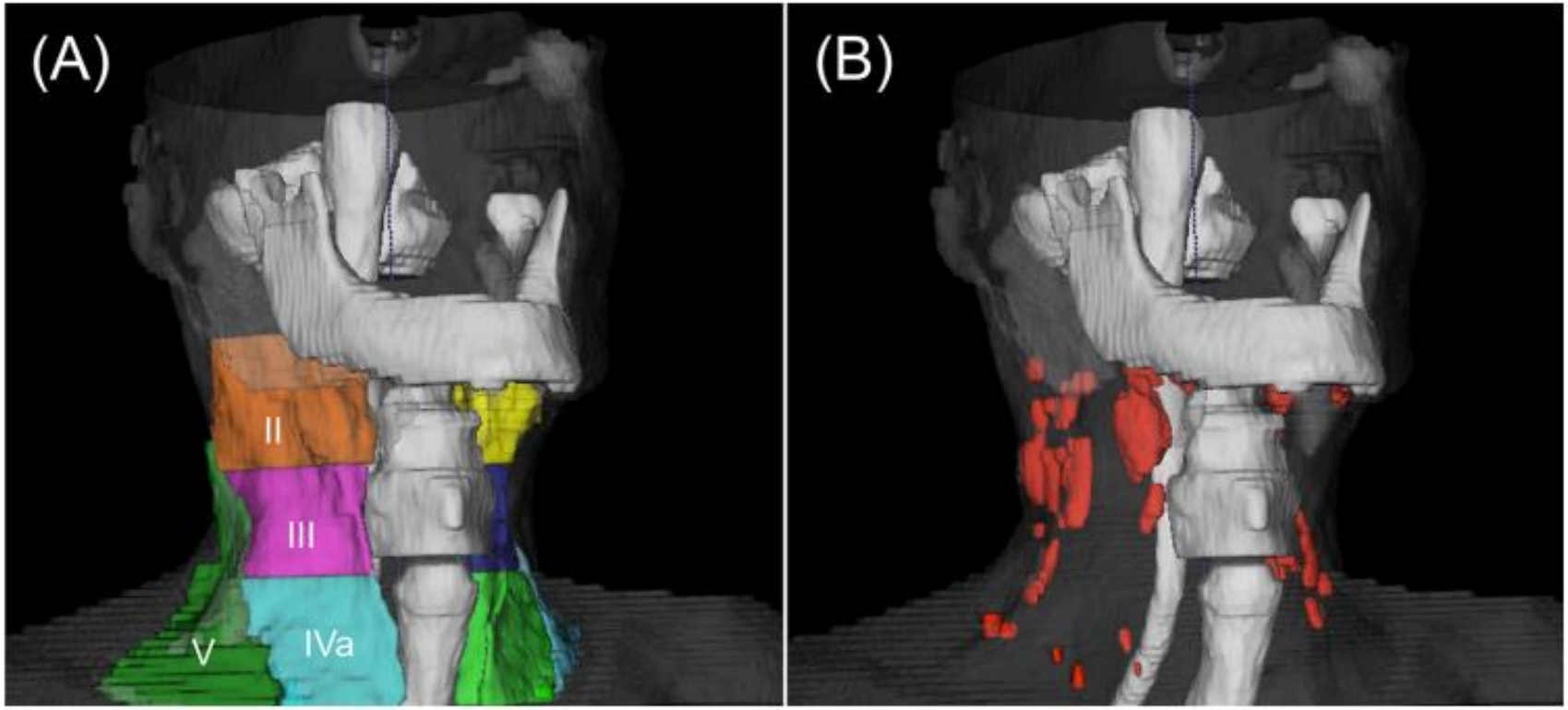
Elective nodal vs elective lymph node irradiation

The radiation dose to the surrounding tissues can be further reduced by converting ENI target volumes from conventional lymph node levels to individual lymph nodes within these levels.

These so-called “elective lymph nodes” are not suspected of containing overt metastases based on histology or radiology, but there is a risk of occult metastases, warranting elective treatment.



Transverse water-only image (A) and in-phase image (B) of a T2 mDixon TSE MRI of a HNSCC patient depicting individual lymph nodes (red), lymph node levels III (green), and level V (blue). The visibility of individual lymph nodes is better on the water image, whereas the borders of the lymph node levels are better visible on the in-phase image.



3D example of automatic segmentations of lymph node levels II/III/IV/V on the left side (A) and individual lymph nodes on the right side (B) in one HNSCC patient produced by a trained neural network (nnU-Net).

In this study, a median of 56 lymph nodes (range 46–68) were segmented on MRI, lower than the 34–46 lymph nodes found in several pathology studies. However, we excluded lymph nodes only visible in one transverse MRI slice, and small lymph nodes may have been missed due to 3 mm slice thickness.

(Reinders et al., 2024)

- MRI Linac (MR-Linac) will be used for this new treatment concept, as elective lymph nodes of HNSCC are better visualized with MRI due its superior soft tissue contrast.
- Moreover, day-to-day dose delivery can be closely monitored, and RT plans can be adapted if necessary.
- In a planning study comparing the new concept with conventional treatment, significant reductions in the mean dose of >5 Gy were achievable in the submandibular gland, carotid arteries, and thyroid gland.

Thank You

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