ORGANS AT RISK
&
DOSE-VOLUME CONSTRAINS

Primož Strojan

Bucharest, November 2013

OAR – ORGANS AT RISK

= normal tissues whose radiation sensitivity may significantly influence treatment planning and/or absorbed-dose prescription

(ICRU Report 50)

- In principal: all non-target tissues
- “critical normal structures”: spinal cord, mandible, parotids…
- Dose-volume constrains for OARs: NTCP curves
  (retrospective 2D data, prospective 3D data)

TISSUE ORGANISATION

FSUs = functional subunits (Withers et al. 1988)

- the largest tissue volume (unit of cells) that can be regenerated from a single surviving clonogenic cells
- FSUs are sterilized independently by irradiation
- severity of damage ~ no. of sterilized FSUs

  - intrinsic radiosensitivity
  - dose
  - fractionation
  - overall treatment time

- arrangement of the FSUs $\rightarrow$ clinical consequences

ARRANGEMENT

PARALLEL

- independent functioning of FSUs
- clinical effect = no. of surviving FSUs ↓ to sustain physiological organ function
- importance of threshold volume
- distribution of the total dose more important than indiv. “hot spots”

parotid
lung
liver

SERIAL

- organ function depends on the function of each indiv. FSU (chain)
- clinical effect = inactivation of one FSU (binary response)
- “hot spots” more important than dose distribution

spinal cord, nerve
intestine, esophagus

INTERMEDIATE TYPE

= kidney
glomerulus – parallel
distal tubules – serial

OAR

DOSE-VOLUME CONTRAINS

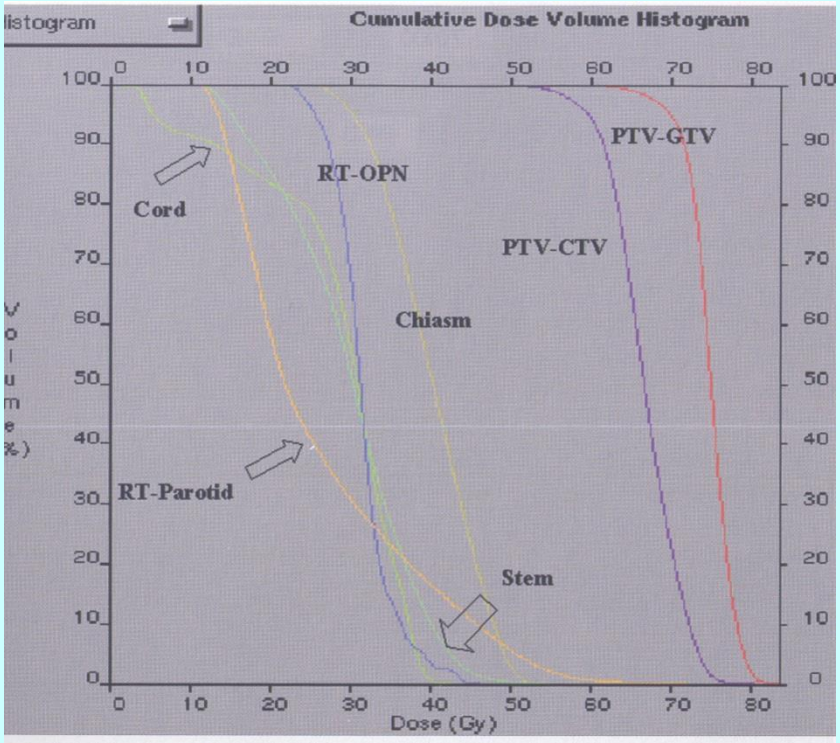
- serial: threshold-binary response (AD_{max} to a given volume)
- parallel: graded AD response (AD_{mean} or V_{AD})

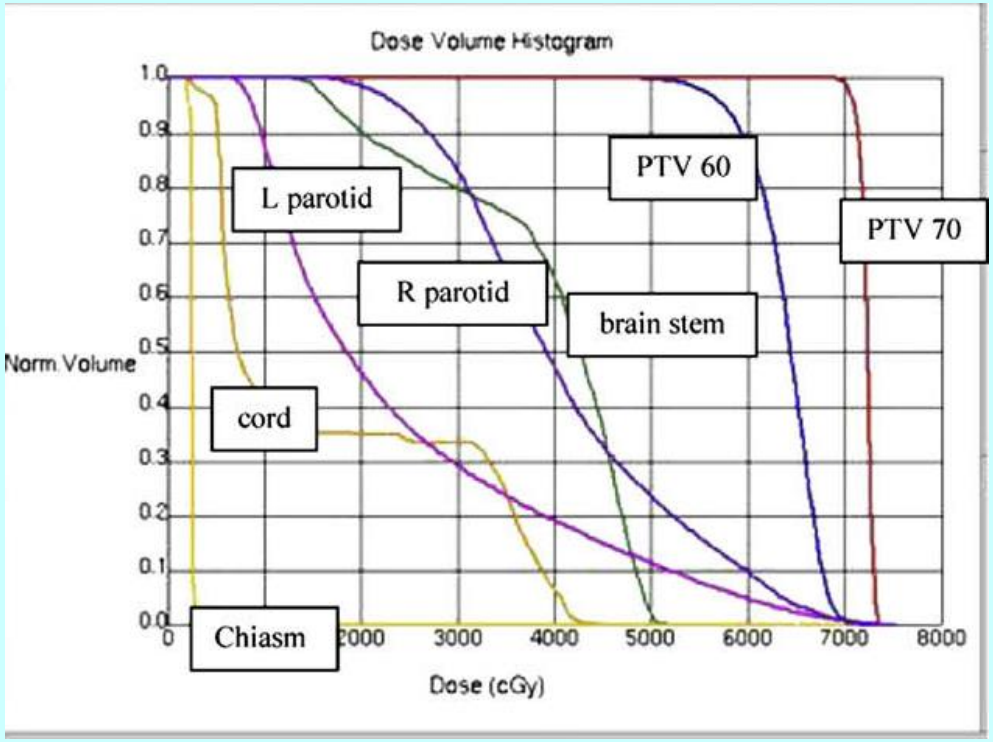
DELINEATION

- serial: $V_{irradiated}$ – ↓ impact on the assessment of the organ tolerance → delineate wall, surface…
- parallel: volume assessment is crucial – complete organ delineation is required

Routine → DVHs

= 2D presentation of 3D dose distribution
(what % of volume is raised to a defined dose)





DVHs

= tool for the evaluation & comparison of treatment plans

- no info on the spatial dose distribution in a DVH
- no info on the functional status of irradiated organ or volume
- all regions in the target equally important (doesn't differentiate between functionally or anatomically different subregions within the organ)
- as good as is the anatomic information provided
  - how accurately routine imaging reflect underlying anatomy?
  - marked inter-physician differences in image segmentation

OAR

DOSE-VOLUME CONSTRAINS

- serial: treshold-binary response (AD_{max} to a given volume)
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OAR – Delineation guidelines

Radiotherapy and Oncology 93 (2009) 545–552

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Xerostomia

Delineation guidelines for organs at risk involved in radiation-induced salivary dysfunction and xerostomia

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Radiotherapy and Oncology 101 (2011) 394–402

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Radiotherapy and Oncology

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Morbidity in head and neck radiotherapy

Delineation of organs at risk involved in swallowing for radiotherapy treatment planning

Miranda E.M.C. Christianen [a], Johannes A. Langendijk [a,*], Henriëtte E. Westerlaan [b], Tara A. van de Water [a], Hendrik P. Bijl [a]

DEVELOPMENT AND VALIDATION OF A STANDARDIZED METHOD FOR CONTOURING THE BRACHIAL PLEXUS: PRELIMINARY DOSIMETRIC ANALYSIS AMONG PATIENTS TREATED WITH IMRT FOR HEAD-AND-NECK CANCER

William H. Hall, M.D.,* Michael Guiou, Ph.D.,* Nancy Y. Lee, M.D.,† Arthur Dublin, M.D.,‡ Samir Narayan, M.D.,* Srinivasan Vijayakumar, M.D.,* James A. Purdy, Ph.D.,* and Allen M. Chen, M.D.*

OAR – Delineation guidelines

Table 1
Delineation guidelines: The anatomic boundaries of the organs at risk involved in radiation-induced salivary dysfunction and xerostomia.

Organ at risk	Anatomic boundaries					
	Cranial	Caudal	Anterior	Posterior	Lateral	Medial

Overview of all SWOARs and their corresponding anatomic borders.

Organ at risk	Anatomic borders					
	Cranial	Caudal	Anterior	Posterior	Lateral	Medial
Superior PCM	Caudal tip of the pterygoid plates (hamulus)	Lower edge of C2	Hamulus of pterygoid plate; mandibula; base of tongue; pharyngeal lumen	Prevertebral muscle	Medial pterygoid muscle	Pharyngeal lumen
Middle PCM	Upper edge of C3	Lower edge of hyoid bone	Base of tongue; hyoid	Prevertebral muscle	Greater horn of hyoid bone	Pharyngeal lumen
Inferior PCM (thyropharyngeal part)	First slice caudal to the lower edge of hyoid bone	Lower edge of the arythenoid cartilages	Soft tissue of supraglottic/ glottic larynx	Prevertebral muscle	Superior horn of thyroid cartilage	
Cricopharyngeal muscle	First slice caudal to the arytenoid cartilages	Lower edge of the cricoid cartilages	Posterior edge of cricoid cartilage	Prevertebral muscle	Thyroid cartilage, fatty tissue, thyroid gland	
Esophagus inlet muscles	First slice caudal to lower edge of the cricoid cartilage	1 cm caudal to the superior border	Tracheal lumen	Prevertebral muscle	Fatty tissue, thyroid gland	
Cervical esophagus	1 cm caudal to the lower edge of the cricoid cartilage	Sternal notch				
Base of tongue	Lower edge of anterior tubercle of atlas	Upper edge of hyoid bone	Posterior one third from mandibular bone to pharyngeal lumen	Pharyngeal lumen	Width of the pharyngeal lumen	
Supraglottic larynx	Tip of epiglottis	First slice cranial to the upper edge of the arytenoid cartilages	Hyoid bone, pre-epiglottic space, thyroid cartilage	Pharyngeal lumen, inferior PCM	Thyroid cartilage	Pharyngeal lumen (lumen excluded)
Glottic larynx	Upper edge of the arythenoid cartilages	Lower edge of cricoid cartilage (if soft tissue is present)	Thyroid cartilage	Inferior PCM, pharyngeal lumen/ cricoid cartilage	Thyroid cartilage	Pharyngeal lumen (lumen excluded)

Abrreviations: PCM = pharyngeal constrictor muscle, C2 = second cervical vertebra, C3 = third cervical vertebra, cm = centimeter.

alveolar process maxilla	mandible	post. edge maxilla	

Abbreviations: m., muscle; med., medial; lat., lateral; post., posterior; ant., anterior.
[a] These structures have a constant thickness of 4 mm.

OAR – Delineation guidelines

3D Variation in delineation of head and neck organs at risk

Radiation Oncology 2012, **7**:32

Charlotte L Brouwer[1*], Roel JHM Steenbakkers[1], Edwin van den Heuvel[2], Joop C Duppen[3], Arash Navran[3], Henk P Bijl[1], Olga Chouvalova[1], Fred R Burlage[1], Harm Meertens[1], Johannes A Langendijk[1] and Aart A van 't Veld[1]

Conclusions: Variation in delineation is traced to several regional causes. Measures to reduce this variation can be: (1) guideline development, (2) joint delineation review sessions and (3) application of multimodality imaging. Improvement of delineation practice is needed to standardize patient treatments.

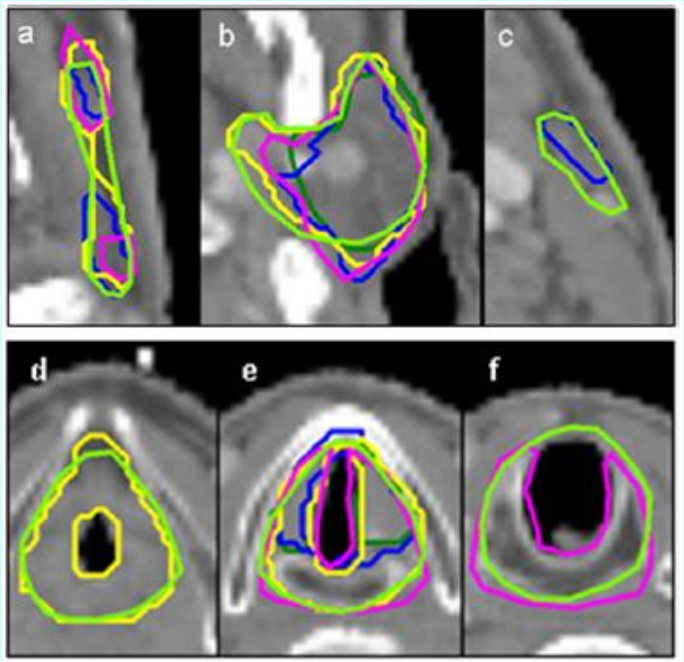


Figure 3 Delineation variation of a parotid gland and a glottic larynx. Left parotid gland and glottic larynx delineations in a typical cranial (**a** and **d**), central (**b** and **e**) and caudal (**c** and **f**) transverse CT slice. Each colour corresponds to one observer.

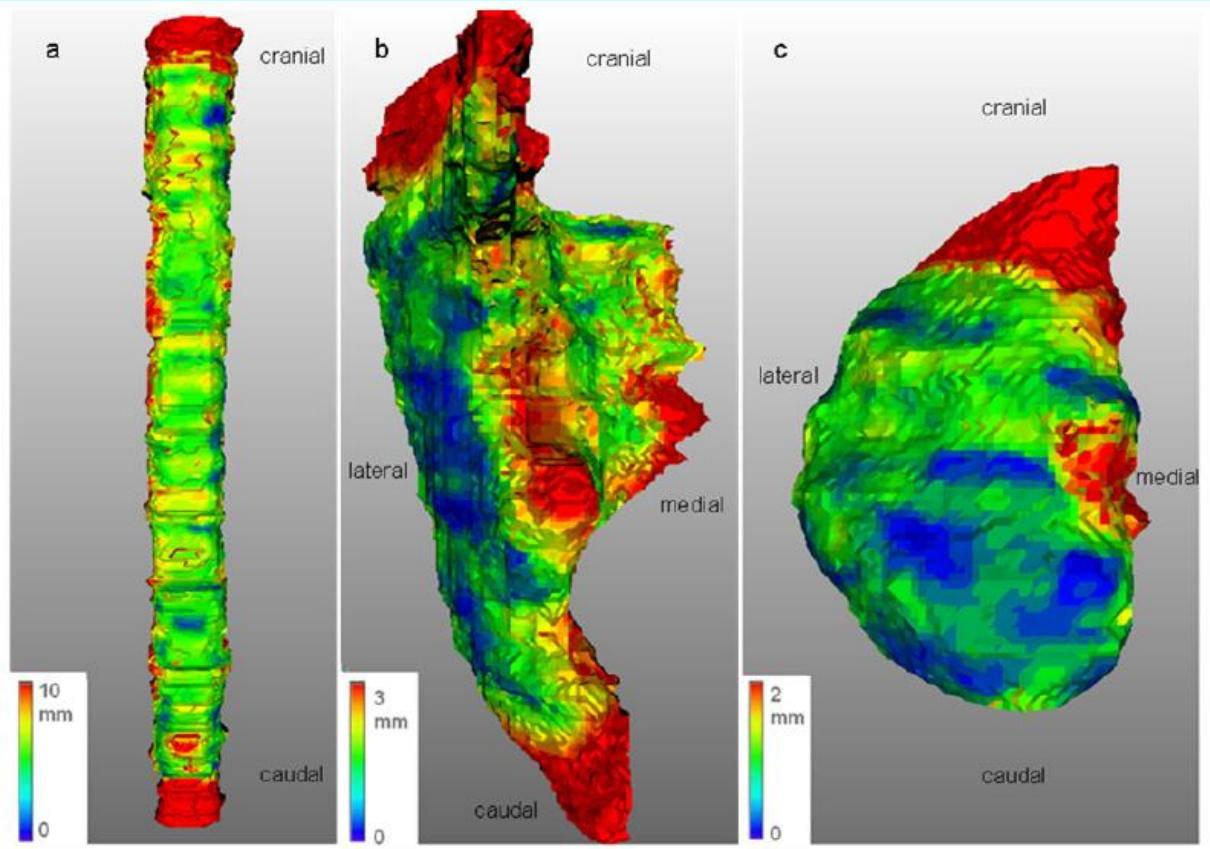


Figure 4 3D delineation variation of a spinal cord, a right parotid and submandibular gland. 3D Standard Deviations (SDs) for a typical patient plotted in colour scale on the median contour surface of the organ. Note the different scalings. Spinal cord (**a**), right parotid gland (**b**) and right submandibular gland (**c**), frontal view.

PRV – PLANNING ORGAN AT RISK VOLUME

To consider:

- ORs = subjects of variations in the position of during treatment

PRV = OR + margin

- the same principle as for the PTV
- PTV and PRV may overlap
  - report absorbed dose in the full PTV and PRV
  - calculation of the OAR-PRV margin: random & systemic uncertainties

DOSE-VOLUME CONSTRAINS

- 2D, 3D data (AD vs. volume vs. organ damage)
- NTCP curves

Which of the DVH-derived parameters is optimal for prediction of NTCP?

QUANTEC

QUantitative Aalysis of Normal Tissue Effects in the Clinic

Int J Radiation Oncol Biol Phys 2010; 76(3, Suppl)

H&N – PAROTIDs, SMGs

- Parallel organization of FSUs = marked volume effect

  parotid = serous fluid
  submandibular = mucin

- Hyposalivation (within 1 wk, <10-15 Gy)
- Spearing ≥1 PG → appears to eliminate xerostomia
  ≥1 SMG → appears to ↓ xerostomia risk
- ENDPOINT: severe xerostomia:

  = long-term salivary function <25% of baseline

H&N – PAROTIDs, SMGs

RECOMMENDED DOSE-VOLUME LIMITS
(QUANTEC, Deasy JO et al. IJROBP 2010)

- Severe xerostomia can be avoided if: 1 PG – $D_{mean} \leq 20$ Gy
  2 PGs – $D_{mean} \leq 25$ Gy
- Partial parotid irradiation (IMRT): D_{mean} = as low as possible
  (lower $D_{mean} \rightarrow$ better function, to each of PG)
- SMG sparing: $D_{mean} < 35$ Gy
  (if oncologically safe, might $\downarrow$ xerostomia)

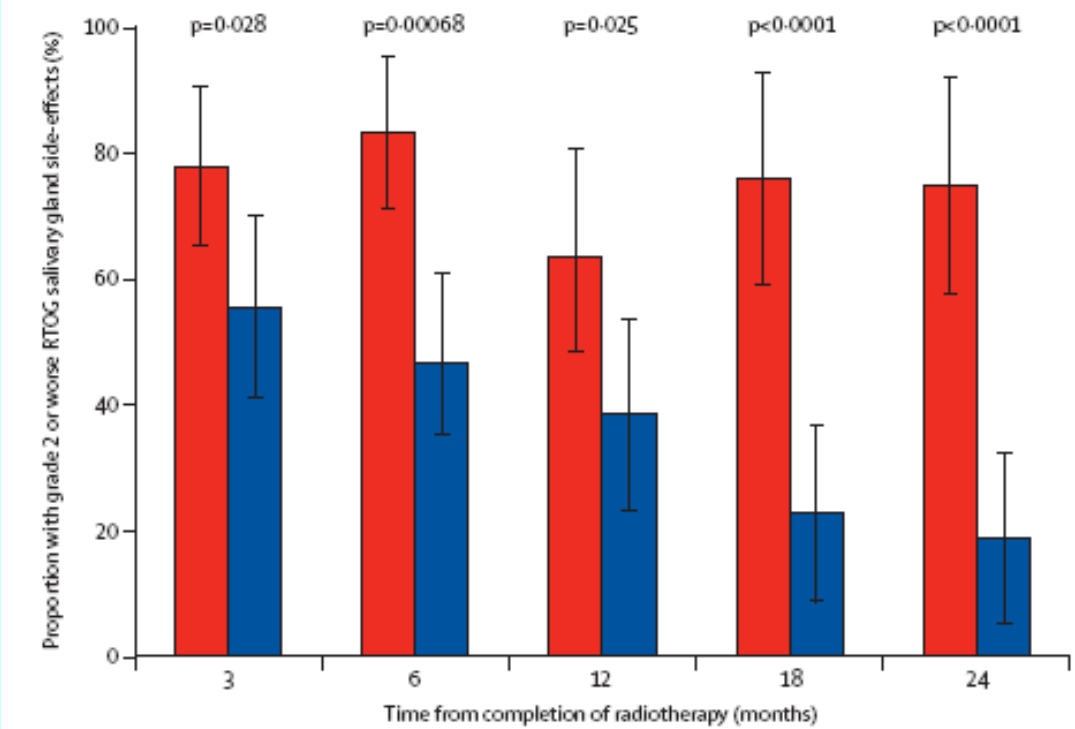
Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial

Lancet Oncol 2011;12:127-36

Christopher M Nutting, James P Morden, Kevin J Harrington, Teresa Guerrero Urbano, Shreerang A Bhide, Catharine Clark, Elizabeth A Miles,

IMRT:

- planning constraint to the contralateral PG D_{mean}<24 Gy



Novel approaches to improve the therapeutic index of head and neck radiotherapy: An analysis of data from the PARSPORT randomised phase III trial

Florian Buettner [a,*], Aisha B. Miah [b], Sarah L. Gulliford [a], Emma Hall [c], Kevin J. Harrington [b], Steve Webb [a], Mike Partridge [a], Christopher M. Nutting [b]

Radiotherapy and Oncology 103 (2012) 82–87

Results: The predictive accuracy of dose–response models improved significantly when including regional variations of radiosensitivity of the parotid glands compared to standard mean-dose models ($p = 0.001$, t-test). Beneficial dose-pattern analysis demonstrated the importance of minimising dose to the lateral and cranial component of the human parotid gland in order to avoid xerostomia. Furthermore we found an evidence that surgical removal of the sub-mandibular gland significantly increases the risk of radiation-induced xerostomia.

Conclusion: Dose–response models which take the shape of the dose-distribution into account predicted xerostomia significantly better than standard mean-dose models. Our novel model could be used to rank potential treatment plans more reliably according to their therapeutic index and may be useful to generate better treatment plans.

1.
2.

H&N – LARYNX/PHARYNX

- Laryngeal edema (inflammation, lymphatic disruption)
  + fibrosis

  Laryngeal dysfunction (hoarseness, dysphagia, aspiration)

RECOMMENDED DOSE-VOLUME LIMITS
(QUANTEC, Rancati T et al. IJROBP 2010)

- <u>Vocal dysfunction</u>

  non-involved larynx: D_{mean} 40–45 Gy
  D_{max}<63–66 Gy (if possible)

- <u>Dysphagia/aspiration</u>

  (ph. constrictors, Lx/Ph – spec. anat. points)

  to minimize/reduce $V_{ph.constrictors\&Lx}$ ≥60 Gy/50 Gy
  (if possible)

Strategies to reduce long-term postchemoradiation dysphagia in patients with head and neck cancer: an evidence-based review

Head Neck, in press

Vinidh Paleri, MS, FRCS (ORL-HNS),[1]* Justin W. G. Roe, MSc,[2] Primož Strojan, MD,[3] June Corry, MB, BS, FRANZCR,[4] Vincent Grégoire, MD, PhD,[5] Marc Hamoir, MD,[6] Avraham Eisbruch, MD,[7] William M. Mendenhall, MD,[8] Carl E. Silver, MD,[9] Alessandro Rinaldo, MD, FRCSEd ad hominem, FRCS (Eng, Ir) ad eundem, FRCSGlasg,[10] Robert P. Takes, MD, PhD,[11] Alfio Ferlito, MD, DLO, DPath, FRCSEd ad hominem, FRCS (Eng, Glasg, Ir) ad eundem, FDSRCS ad eundem, FHKCORL, FRCPath, FASCP,IFCAP[10]

- prophylactic swallowing exercises
- avoidance of gastrostomy tubes
- **IMRT**

The potential benefit of swallowing sparing intensity modulated ra
to reduce swallowing dysfunction: An in silico planning comparati

Hans Paul van der Laan *, Miranda E.M.C. Christianen, Hendrik P. Bijl, Cornelis Schilstr
Johannes A. Langendijk

Radiotherapy and Oncology 10

$PTV_{95\%}$ = 98%
D_{max} SC=54 Gy, BS=60 Gy, n.II/chiasm=54 Gy
Plan $D_{max} \leq 77$ Gy, $V_{75Gy} \leq 2$ cm^3

The doses to the SWOARs were reduced according to the following order of priority:

1. minimising the superior-PCM D_{mean}
2. minimising the SG-larynx D_{mean}
3. minimising the middle-PCM D_{mean}
4. minimising the EIM V60

The mean dose in the parotid glands was not allowed to be higher with SW-IMRT than with ST-IMRT.

Table 2
Dose-volume data and normal tissue complication probabilities.

	ST-IMRT	SW-IMRT
PTV volumes (cm^3)		
PTV54	709 (452–1091)	
PTV70	229 (36–637)	
PTV coverage (%)		
PTV54, 95% dose/98% volume	100%	100%
PTV70, 95% dose/98% volume	100%	100%
Integral irradiated volumes (cm^3)		
V51.3 Gy (95% * 54 Gy)	1236 (586–1882)	1277 (666–1993)
V57.8 Gy (107% * 54 Gy)	496 (97–1153)	528 (110–1178)
V66.5 Gy (95% * 70 Gy)	300 (51–806)	308 (50–814)
Max dose (Gy)		
Integral	74.5 (72.5–75.6)	75.2 (73.2–76.2)
Spinal cord	48.6 (43.7–49.9)	48.8 (46.8–50.8)
Salivary glands mean dose (Gy)		
Parotid ipsilateral	43.2 (14.6–63.3)	43.3 (14.7–64.9)
Parotid contralateral	36.0 (19.0–60.1)	35.7 (19.2–59.8)
Submandibular ipsilateral	65.1 (51.3–71.1)	65.7 (51.9–72.1)
Submandibular contralateral	61.5 (48.0–70.4)	62.0 (49.2–71.4)
SWOAR mean dose (Gy)		
Superior PCM	61.0 (25.8–71.5)	56.3 (9.1–70.9)
Middle PCM	61.9 (49.2–71.6)	57.7 (31.2–70.9)
Supraglottic larynx	61.3 (45.5–71.1)	55.6 (26.2–70.4)
Volume receiving ⩾60 Gy (%)		
EIM	3.3 (0–100)	3.3 (0–100)
NTCP swallowing dysfunction (%)		
RTOG Grade 2–4	42 (7–61)	33 (2–58)
Problems swallowing solid food	34 (11–66)	26 (3–62)
Problems swallowing soft food	16 (2–47)	13 (1–44)
Problems swallowing liquid food	7 (2–12)	6 (1–12)
Choking when swallowing	6 (1–37)	5 (0–36)

Swallowing-sparing intensity-modulated radiotherapy for head and neck cancer patients: Treatment planning optimization and clinical introduction

Radiother Oncol 2013;107:282-7

Hans Paul van der Laan*, Agata Gawryszuk, Miranda E.M.C. Christianen, Roel J.H.M. Steenbakkers, Erik W. Korevaar, Olga Chouvalova, Kim Wopken, Hendrik P. Bijl, Johannes A. Langendijk

Table 2
Dose–volume data and normal tissue complication probabilities.

$n = 80$ (patients #21-100)	ST-IMRT	SW-IMRT	p-Value
Integral irradiated volume (cm^3) V95% PTV1	871 (68–1911)	895 (63–1911)	<0.001
Parotid glands mean dose (Gy)			
Ipsilateral	33.9 (0–69.9)	33.8 (0–69.9)	0.175
Contralateral	23.3 (0–53.4)	22.5 (0–54.2)	<0.001
SWOAR mean dose (Gy)			
Superior PCM	49.4 (1.6–70.4)	44.6 (1.5–69.6)	<0.001
Middle PCM	53.4 (9.2–71.9)	48.1 (4.2–70.3)	<0.001
Supraglottic larynx	55.8 (4.0–71.0)	51.0 (2.8–70.2)	<0.001
Volume receiving ⩾60 Gy (%)			
EIM	6.8 (0–92)	3.9 (0–58)	0.011
NTCP swallowing dysfunction (%)			
RTOG grade 2–4	29.6 (1.1–61.7)	23.5 (0.6–59.7)	<0.001
Problems swallowing solid food	25.0 (0.5–63.3)	19.5 (0.2–61.4)	<0.001
Problems swallowing soft food	10.3 (0.3–47.7)	8.6 (0.2–45.3)	<0.001
Problems swallowing liquid food	6.4 (0.1–12.7)	5.3 (0.1–12.0)	<0.001
Choking when swallowing	5.9 (0.1–36.8)	4.3 (0.1–16.9)	<0.001

Dose reductions with SW-IMRT were largest for patients who:

1. received bilateral neck irradiation
2. had a tumor located in the Lx, OPh, NPh or OC
3. had <75% overlap between SWOARs and PTVs.

$n = 80$	n	Mean NTCP reduction RTOG grade 2–4
Neck radiotherapy		
Local RT[a]	7	0.3% (0.3%)
Unilateral neck RT	17	4.3% (2.7%)
Bilateral neck RT	56	7.3% (3.9%)
Tumour location		
Larynx	25	6.6% (5.2%)
Hypopharynx[a]	9	2.3% (0.9%)
Oral cavity	6	8.3% (3.3%)
Oropharynx	23	7.6% (3.3%)
Nasopharynx	3	8.0% (0.5%)
Salivary-skin-other[a]	14	3.7% (2.5%)
Overlap SWOAR-PTV[b]		
0–25%	22	4.4% (3.3%)
26–50%	21	7.8% (4.1%)
51–75%	20	8.4% (3.0%)
>75%[b]	17	3.4% (3.9%)

SPINAL CORD

- ENDPOINT: CTCAEv3.0 G≥2 myelopathy/ spinal cord injury (≤3 yrs after RT, rarely <6 mos post-RT)
  pain, sensory/motor deficits, incontinence (loss of function)

- Factors effecting risk
  - age (vascular damage, ↑RT-sensitivity of developing CNS)
  - chemotherapy

- Time-dependent (partial) repair after full-course RT
  (evident ~6 mos post-RT → increases over 2 yrs)

SPINAL CORD

RECOMMENDED DOSE-VOLUME LIMITS

(QUANTEC, Kirkpatrick JP et al. IJROBP 2010)

Myelopathy risk

- conventional fx (2 Gy/day, full cord cross-section)
  50 Gy $\rightarrow$ 0.2%, 60 Gy $\rightarrow$ 6%, ~69 Gy $\rightarrow$ 59%

- stereotactic RadioSurgery (partial cord irradiation)
  13 Gy/single fx *or* 20 Gy/3 fx $\rightarrow$ <1%

- re-irradiation (conventional fx, 2 Gy/day, full cord cross-section)
  $\uparrow$ in SC tolerance for at least 25%/6 mos after RT

BRAIN STEM

- Manifestation: mos→yrs after RT
- Difficult to distinguish between toxicity and TU progression

RECOMMENDED DOSE-VOLUME LIMITS
(QUANTEC, Mayo C et al. IJROBP 2010)

- conventional fx (≤2 Gy/fx)

  limited risk: entire BS irradiation → 54 Gy
  smaller volumes (1-10 cc) → D_{max} 59 Gy

  markedly increased risk: D_{max} >64 Gy

- stereotactic RadioSurgery

  12.5 Gy/single fx → <5%

OPTIC NERVES & CHIASM

- RION, radiation-induced optic neuropathy
  = painless rapid visual loss (≤3 yrs after RT)

  vascular injury

  age
  chemotherapy, DM, hypertension ?

RECOMMENDED DOSE-VOLUME LIMITS
(QUANTEC, Mayo C et al. IJROBP 2010)

- conventional fx (≤2 Gy/fx)

  D_{max} <55 Gy → 0%
  55–60 Gy → 3–7%
  >60 Gy → >7–20%

- stereotactic RadioSurgery

  D_{max} <8 Gy → rare
  12–15 Gy → >10%

IMRT for Sinonasal Tumors Minimizes Severe Late Ocular Toxicity and Preserves Disease Control and Survival

Fréderic Duprez, M.D., Ph.D.,* Indira Madani, M.D., Ph.D.,* Lieve Morbée, BA,* Katrien Bonte, M.D.,† Philippe Deron, M.D.,† Vilmos Domján, M.D.,† Tom Boterberg, M.D., Ph.D.,* Werner De Gersem, Ir., Ph.D.,* and Wilfried De Neve, M.D., Ph.D.*

Int J Radiation Oncol Biol Phys, Vol. 83, No. 1, pp. 252–259, 2012

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Table 2 Dose–volume constraints for organs at risk

Organ at risk	Dose–volume constraint
Optic nerves and chiasm (PRVs)	$V_{60} < 5\%$*
Retina (PRV)	$V_{55} < 5\%$*
Lacrimal gland (PRV)	$D_{50} < 30$ Gy
Spinal cord (PRV)	$D_{50} < 45$ Gy and $V_{50} < 5\%$*
Brainstem (PRV)	$D_{50} < 50$ Gy and $V_{60} < 5\%$*
Parotid gland	$V_{27} < 50\%$
Mandible	$V_{70} < 5\%$

Table 4 Late toxicity

Adverse Event	Grade 0	Grade 1	Grade 2	Grade 3
Ocular				
Vision	48	23*	14*	1
Light sensitivity	59	17	10	0
Xerophthalmia	64	11	11	0
Tearing	21	30	25	10
Cornea erosion	78	8	0	0
Nonocular†				
Mucosal integrity	77	6	1	0

Table 8. Summary of studies reporting treatment outcome and late severe (grade 3) visual impairment after IMRT for sinonasal tumors

Investigator	Patients (*n*)	Histologic type*	Treatment	Median Dose (Gy)	Follow-up (mo)	Local control rate (y)	Overall survival rate (y)	Grade 3 visual impairment (*n*)
Claus *et al.* (8)	32	ADC (53)	S+IMRT or IMRT	70	15	NR	80% (1)	0
Duthoy *et al.* (9)	39	ADC (79)	S+IMRT	70	31	73% (2)	68% (2)	2
						68% (4)	59% (4)	
Combs *et al.* (22)	46	ACC (43.4)	S+IMRT or IMRT	64	16	85% (1)	96% (1)	0
						81% (2)	90% (3)	
Hoppe *et al.* (21)†	30		S+IMRT	60	23	NR	NR	0
Daly *et al.* (20)	36	SCC (33)	S+IMRT or IMRT	70	39	62% (2)	69% (2)	0
						58% (5)	45% (5)	
Chen *et al.* (19)‡	23		S+IMRT or IMRT	70	44	65% (5)	47% (5)	0
Dirix *et al.* (23)	25	ADC (68)	S+IMRT	60	27	81% (2)	88% (2)	0
Present study	84	ADC (64)	S+IMRT or IMRT	70	40	74.9% (3)	70.2% (3)	1
	N=315					70.7% (5)	58.5% (5)	

PERIPHERAL NERVES

- Mixed sensory & motor deficits (6 mos → yrs after RT)
  progressive vascular degeneration, fibrosis, demyelination

- Neuropathy/plexopathy <5% → 60 Gy (2 Gy/fx)
  Brachial plexus constraints on recent RTOG IMRT HNC protocols:
  - RTOG 0022, 0025, 1016 none specified
  - RTOG 0522 D_{max} ≤60 Gy
  - RTOG 0615 D_{max} ≤66 Gy
  - RTOG 0619 D_{max} ≤66 Gy, D_{05} ≤60 Gy
  - RTOG 0912 D_{max} ≤66 Gy to point source at least 0.03 cm^3
  - RTOG 1008 D_{max} <66 Gy if low neck involved, for others <60 Gy

  Robert RW, Radiat Oncol 2013;8:173

HEARING LOSS (EAR)

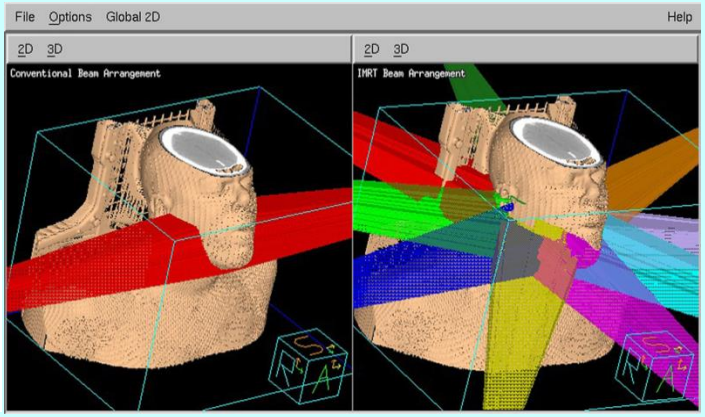
- sensorineural hearing loss (SNHL, cochlea/n.VIII damage)
  = clinically sign.↑ in bone conduction threshold at .5-4 kHz
  (key human speech frequencies, pure-tone audiometry)

  age (>50 yrs), pre-RT hearing, post-RT otitis media, chemotherapy

Threshold dose to COCHLEA for SNHL cannot be determined → SUGGESTED DOSE-VOLUME LIMITS:

QUANTEC, Bhandare N et al. IJROBP 2010

- conventional fx: D_{mean} ≤45 Gy (more conservatively ≤35 Gy)
- stereotactic RadioSurgery: 12–14 Gy
- hypo-fx (for vestibular schwannomas):
  21–30 Gy in 3–7 Gy/fx (over 3–10 days)



BEAM PATH TOXICITIES TO NON-TARGET STRUCTURES DURING INTENSITY-MODULATED RADIATION THERAPY FOR HEAD AND NECK CANCER

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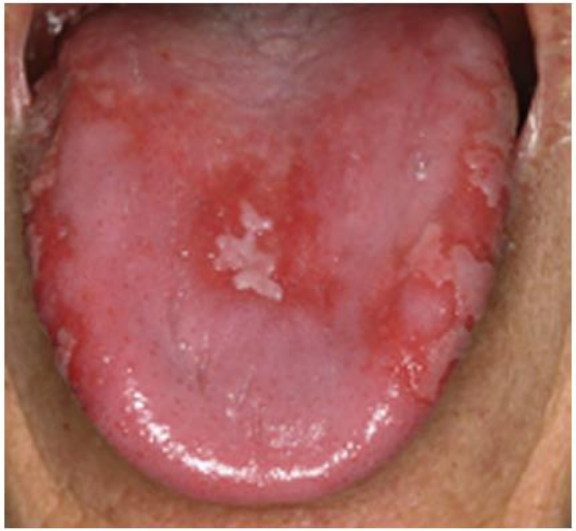


Fig. 4. Results of intensity-modulated radiotherapy ''hot spots'' on oral tongue mucositis.

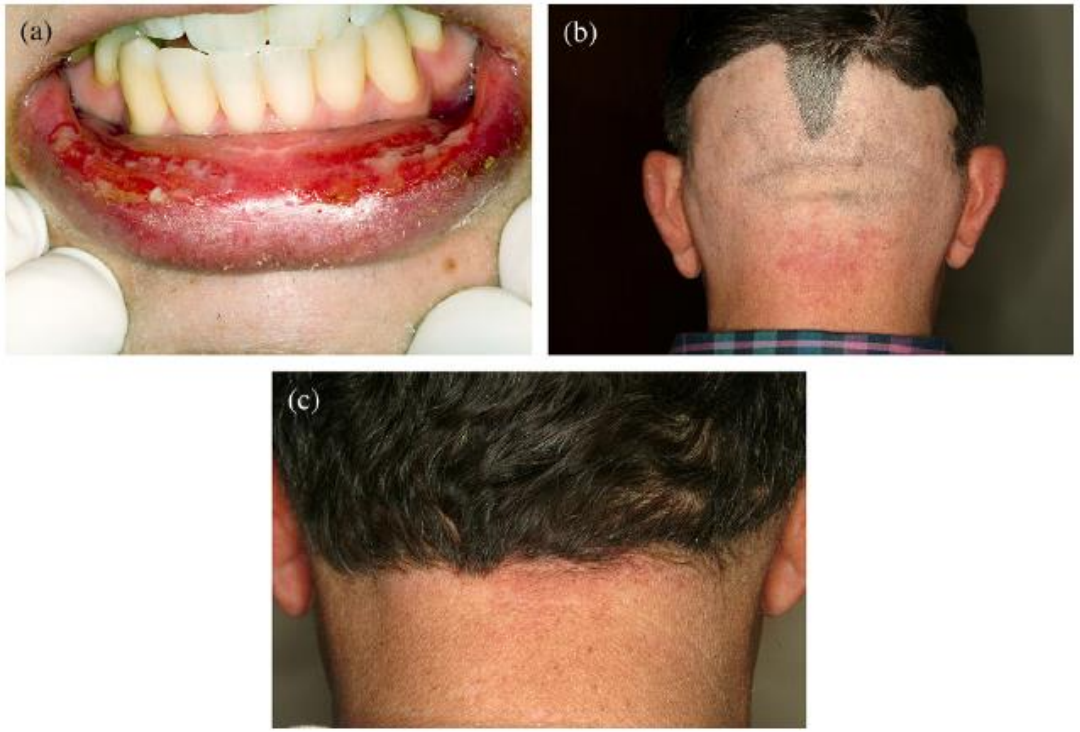
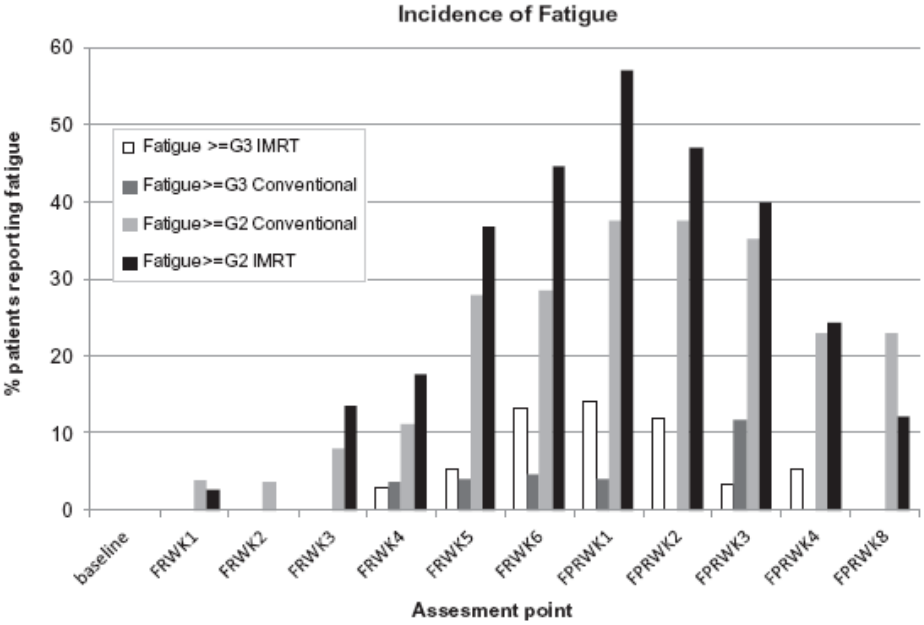


Fig. 3. (a) Anterior oral mucositis during intensity-modulated radiotherapy (IMRT). (b) Occipital scalp epilation after IMRT. (c) Scalp hair subsequent regrowth, same patient.

Dosimetric explanations of fatigue in head and neck radiotherapy: An analysis from the PARSPORT Phase III trial

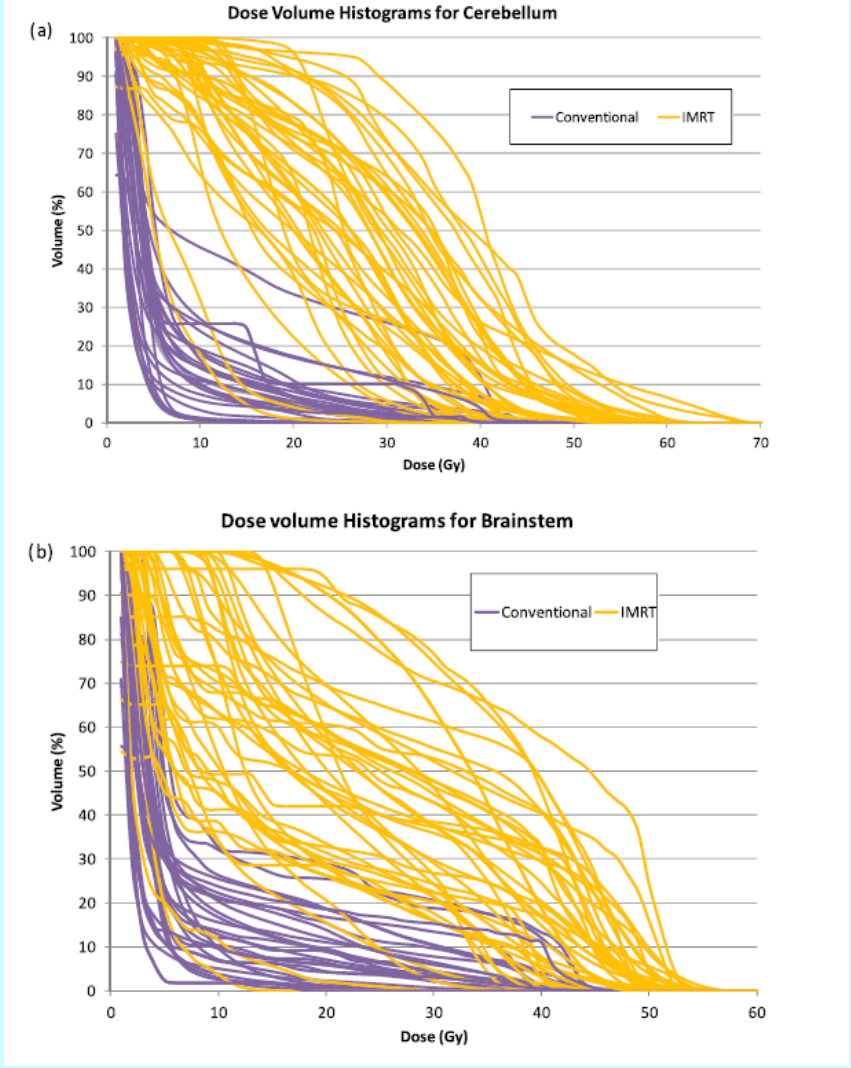
Radiotherapy and Oncology 104 (2012) 205–212

Sarah L. Gulliford [a,*], Aisha B. Miah [b], Sinead Brennan [c], Dualta McQuaid [a,b], Catharine H. Clark [d,e], Mike Partridge [a], Kevin J. Harrington [a,b], James P. Morden [a], Emma Hall [a], Christopher M. Nutting [a,b]



Conclusion

A statistically significant increase in ⩾G2 acute fatigue was observed in the IMRT cohort of the PARSPORT trial. The evidence presented here suggests that the increase may be related, at least in part, to the dose received by the posterior fossa, brainstem and cerebellum. These results apply to patients whose treatment was not confounded by the addition of concomitant chemotherapy.



Dose-volume constrains (targets, critical structures)

GTV, CTV	OR $V_{100\%}$ >95 % OR $V_{93\%}$ >99 %	OR > 95% of volume on 100% dose OR >99% of volume on 93% dose
PTV-buildup	$V_{95\%}$ >98 %	>98% of volume on 95% dose
Spinal cord	$V_{EQD\ 45Gy}$ <1 cm^3 AND EQD_{max} <50 Gy	max 1 cm^3 of volume on **equivalent dose** >45 Gy AND max **equivalent dose** <50Gy
Brainstem	$V_{EQD\ 54Gy}$ < 1 cm^3	max 1% of volume on **equivalent dose** >54 Gy
Parotid glands	OR D_{mean} <26 Gy OR $D_{50\%}$ <30 Gy	mean dose < 26 Gy OR 50% of volume on <30 Gy
Chiasm, optic nerves	EQD_{max} <54 Gy	max **equivalent** dose <54 Gy
Eye bulb	OR D_{max} <50 Gy O D_{mean} <35 Gy	OR max dose <50 Gy OR mean dose <35 Gy
Retina	D_{max} <50 Gy	max dose <50 Gy
Lens	$V_{10\ Gy}$ <1 %	max 1% of volume on >10 Gy
Mandible	$V_{70\ Gy}$ <1 cm^3	max 1 cm^3 of volume on >70 Gy
Hypophysis	$V_{65\ Gy}$ <1 %	max 1% of volume on >65 Gy
Temporal lobes	D_{max} >70 Gy AND $V_{65\ Gy}$ <1 %	max dose >70 Gy AND max 1% of volume on >65 Gy
Larynx	D_{mean} <60 Gy	mean dose <60 Gy
Constrictor muscles	D_{mean} <60 Gy	mean dose <60 Gy
Oral cavity	D_{max} <50 Gy	max dose <50 Gy
Lips	D_{max} <50 Gy	max dose <50 Gy
Temporomandibular joint	$V_{75\ Gy}$ <1 %	max 1% of volume on >65 Gy
Inner ear	D_{mean} <50 Gy	mean dose <50 Gy