
بسم الله الرحمن الرحيم

Radiotherapy in cancer larynx

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Contents

- Introduction to RT
- Treatment Algorithm
- Technology
  - In early stage
  - Laryngeal preservation
  - PORT

http://scholar.cu.edu.eg/?q=ashrafhassouna

Publications

Bio

Classes

Images

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Professor of Radiation Oncology

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Bio

Biography | *Curriculum Vitae*

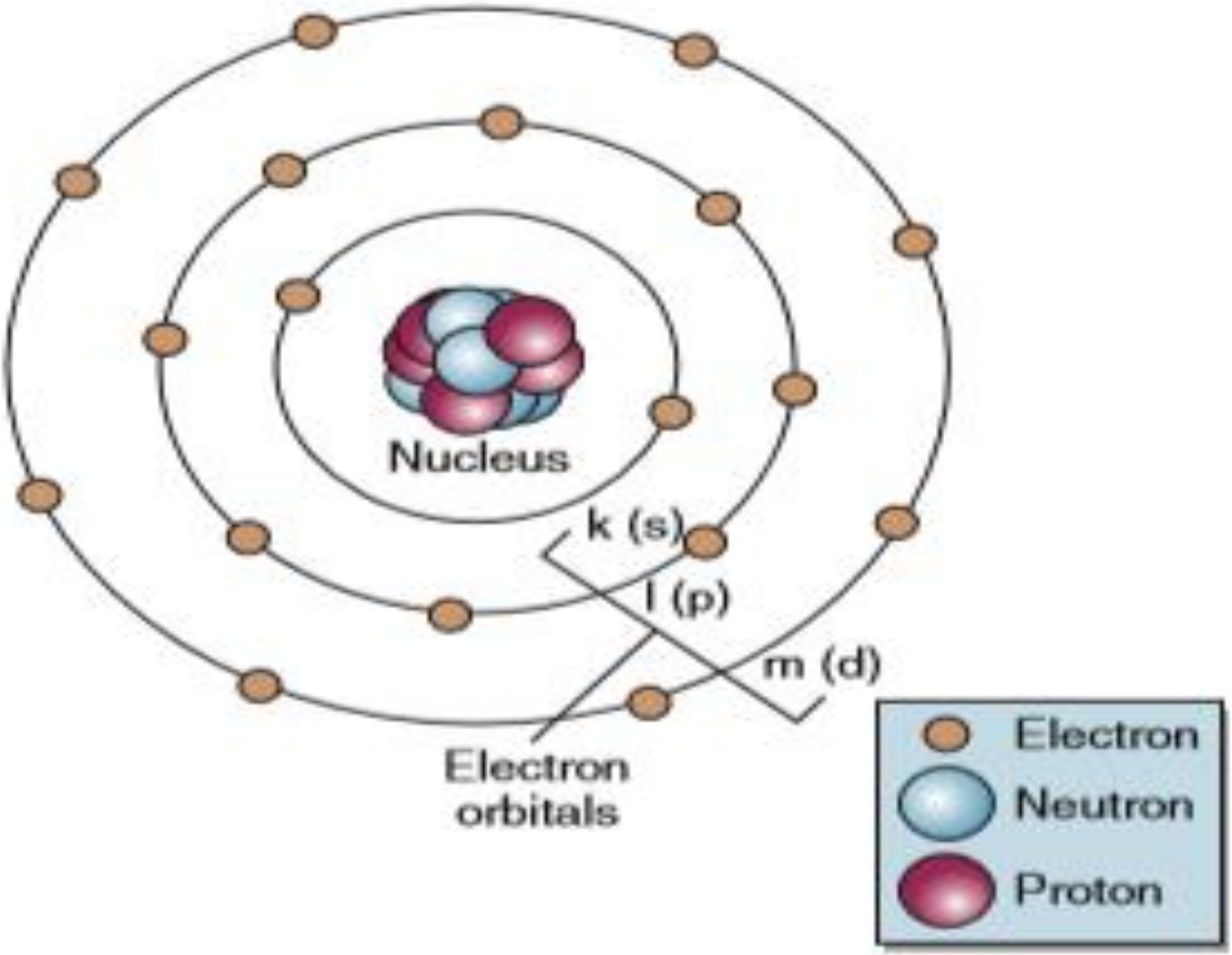
M.D.
in Radiation Oncology

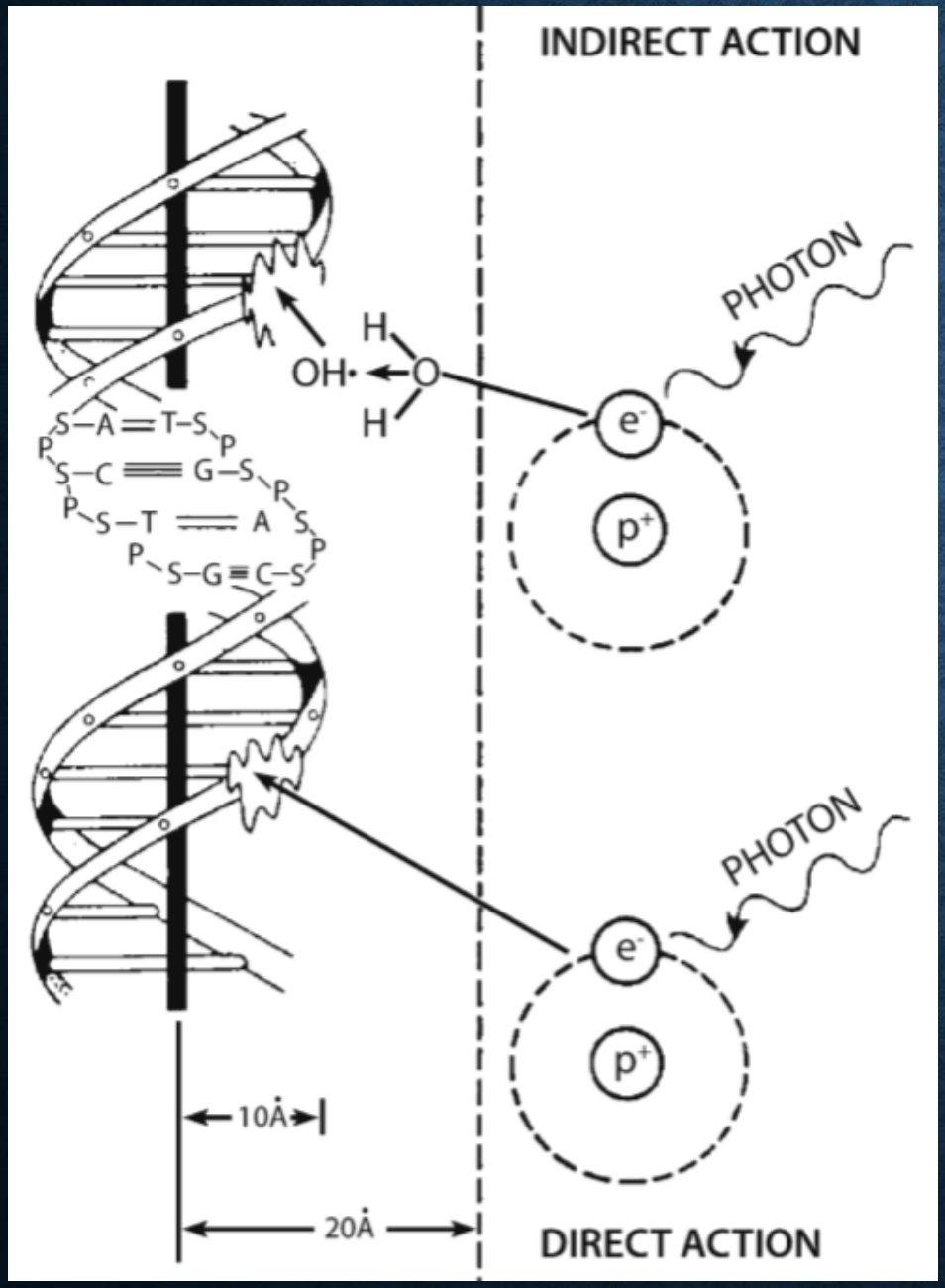
NCI, Cairo University,

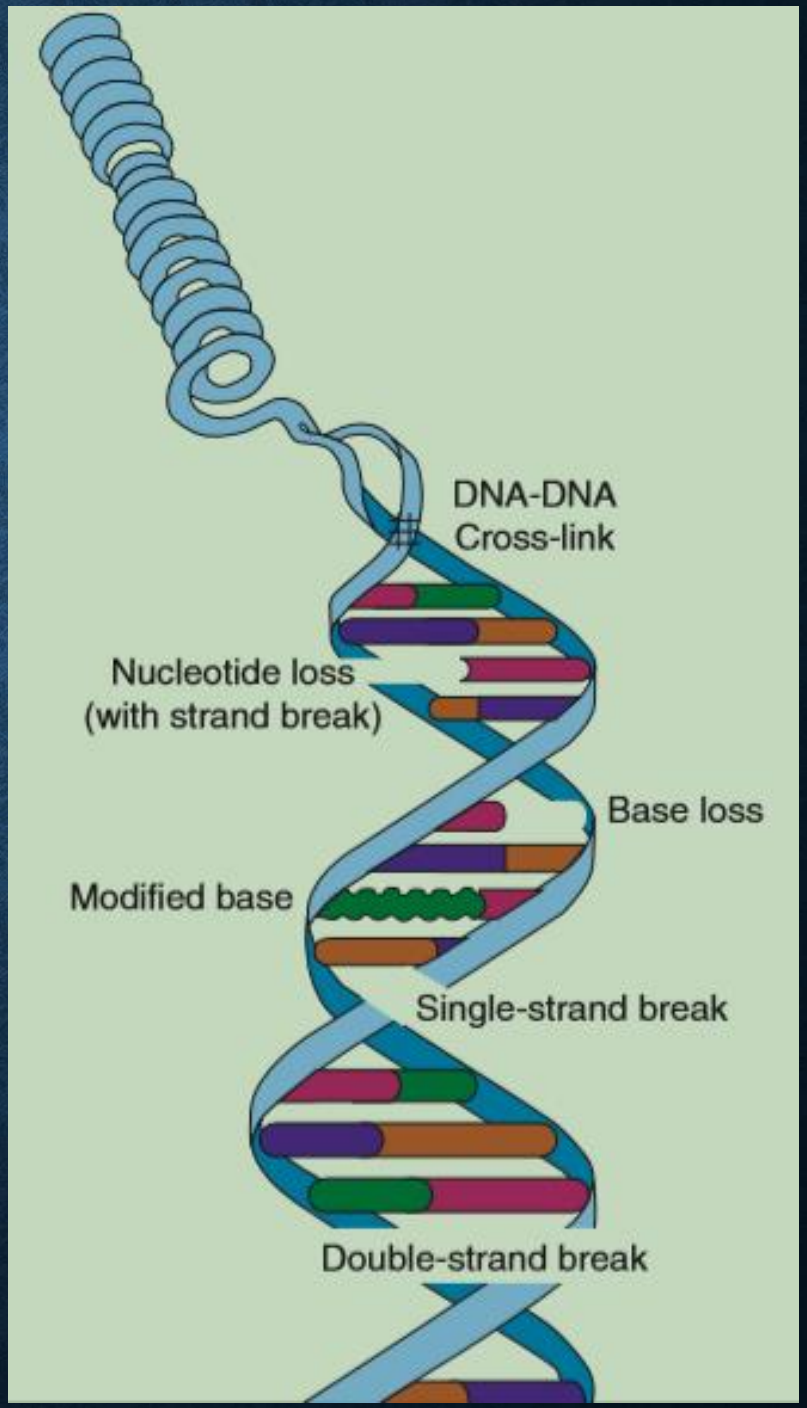
CAIRO UNIVERSITY

You Can Get This Presentation …. and… More

Contents


Nucleus
k (s)
l (p)
m (d)
Electron orbitals
Electron
Neutron
Proton


INDIRECT ACTION
PHOTON
H
OH·
O
H
e⁻
p⁺
S–A═T–S
P
S–C≡G–S
S–T═A
S–G≡C–S
PHOTON
e⁻
p⁺
10Å
20Å
DIRECT ACTION

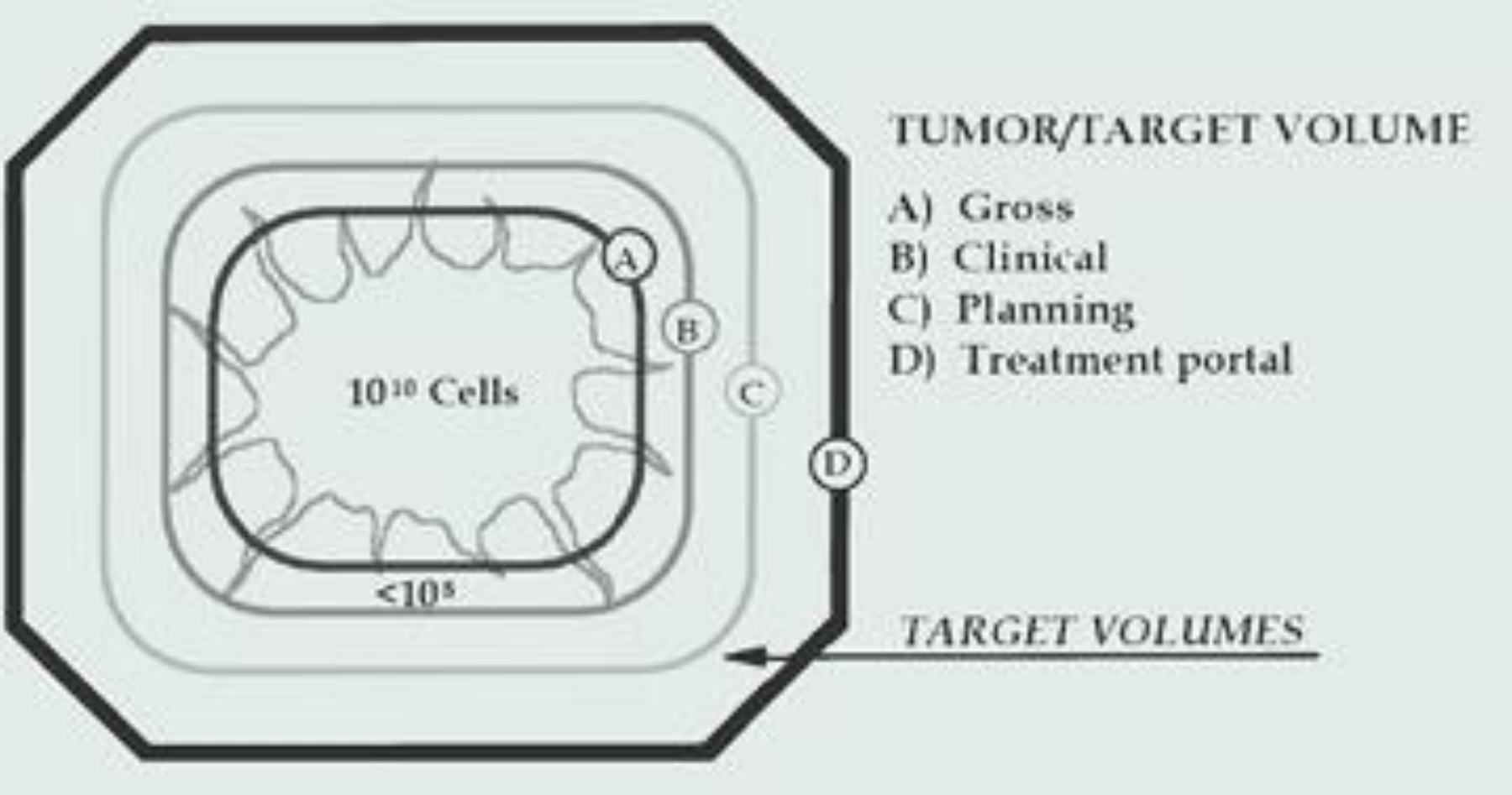

DNA-DNA
Cross-link
Nucleotide loss
(with strand break)
Base loss
Modified base
Single-strand break
Double-strand break

RT effects

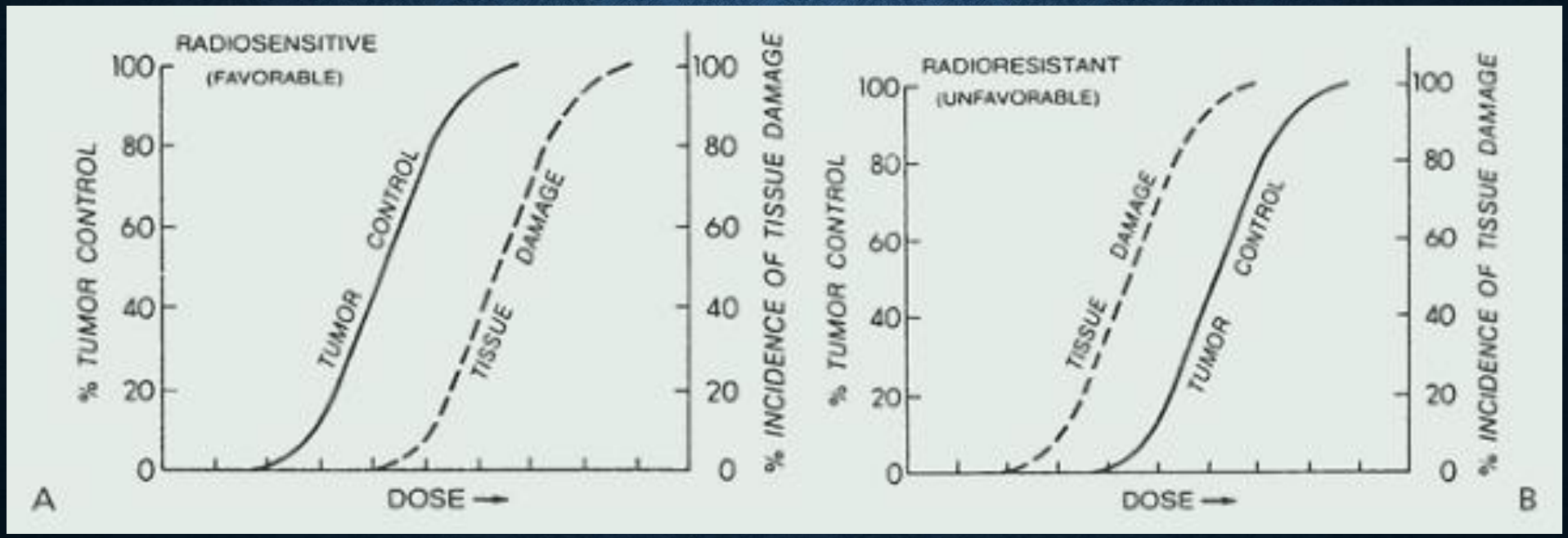
- Cell death
  - Tumour cell death
  - Normal tissue side effects

- Cell transformation
  - Teratogenesis
  - Carcinogenesis

Radiation Target volumes



Therapeutic Ratio



Conventional Fractionation

- 2Gy / Fraction
- 1 Fraction / Day
- 5 Days / Week

Altered Fractionation

- Hyperfractionation
- Hypofractionation
- Accelerated fractionation

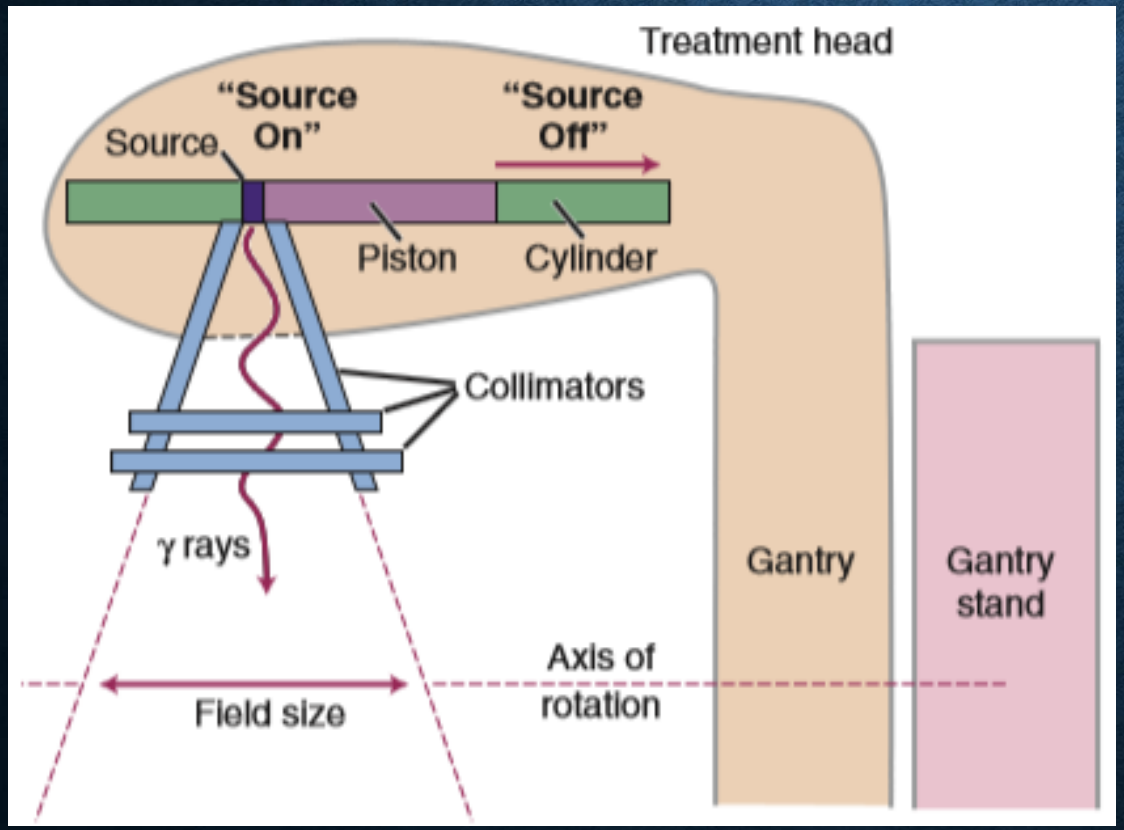
5Rs of Radiobiology

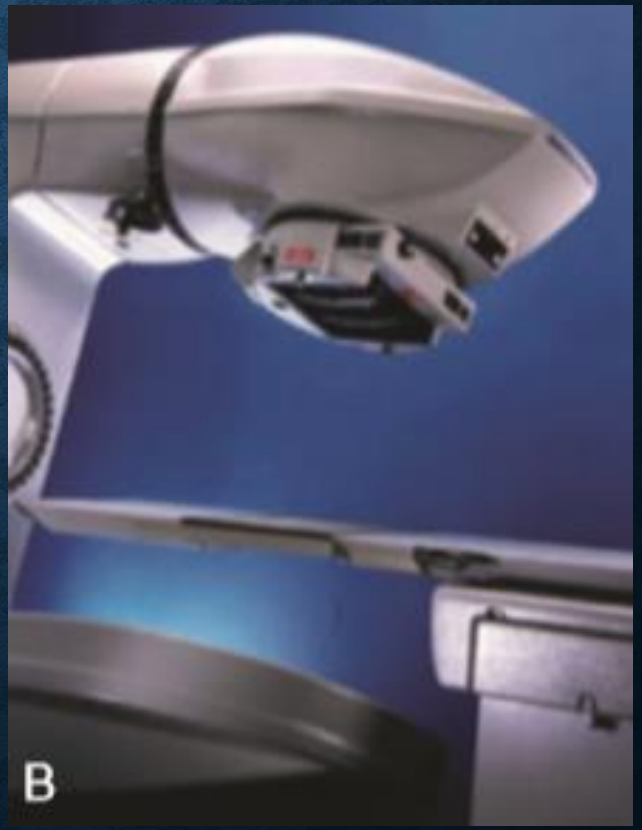
- Repair
- Repopulation
- Redistribution
- Reoxygenation
- Radiosensitivity

Doses

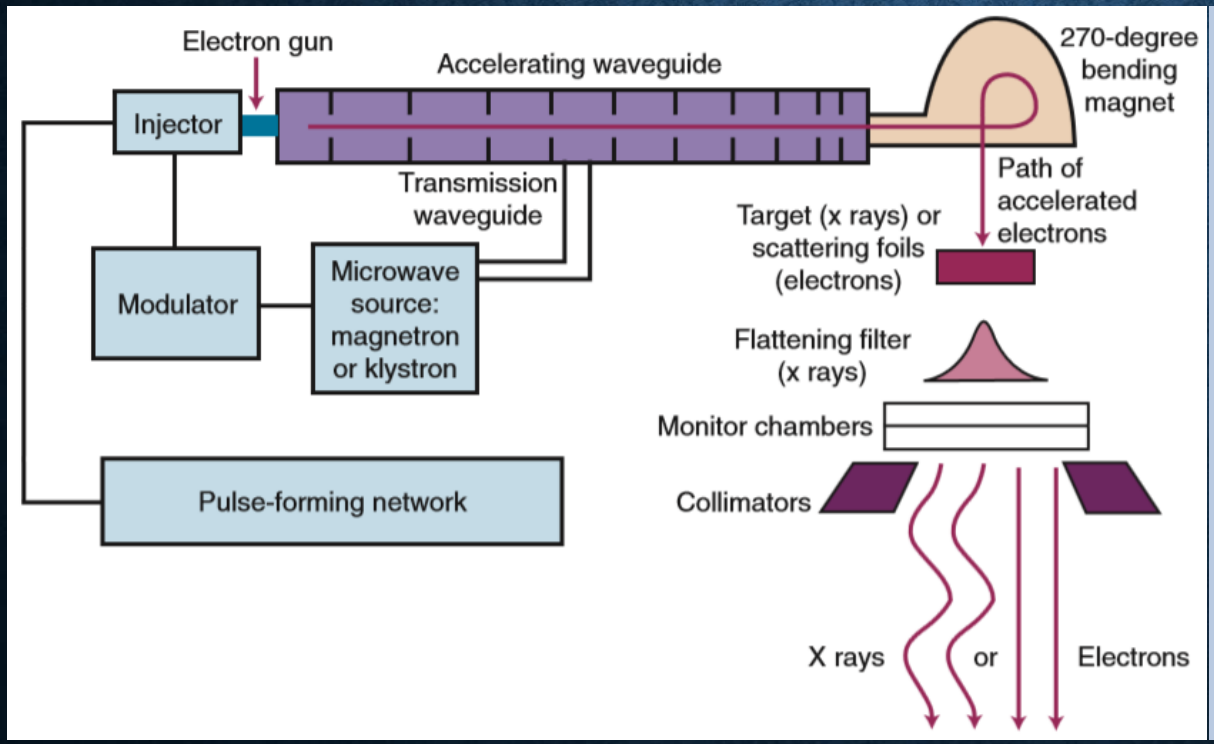
- Radical: 70Gy/35F/7W
- Adjuvant: 60Gy/30F/6W
- Palliative: 30Gy/10F/2W

Cobalt Machine

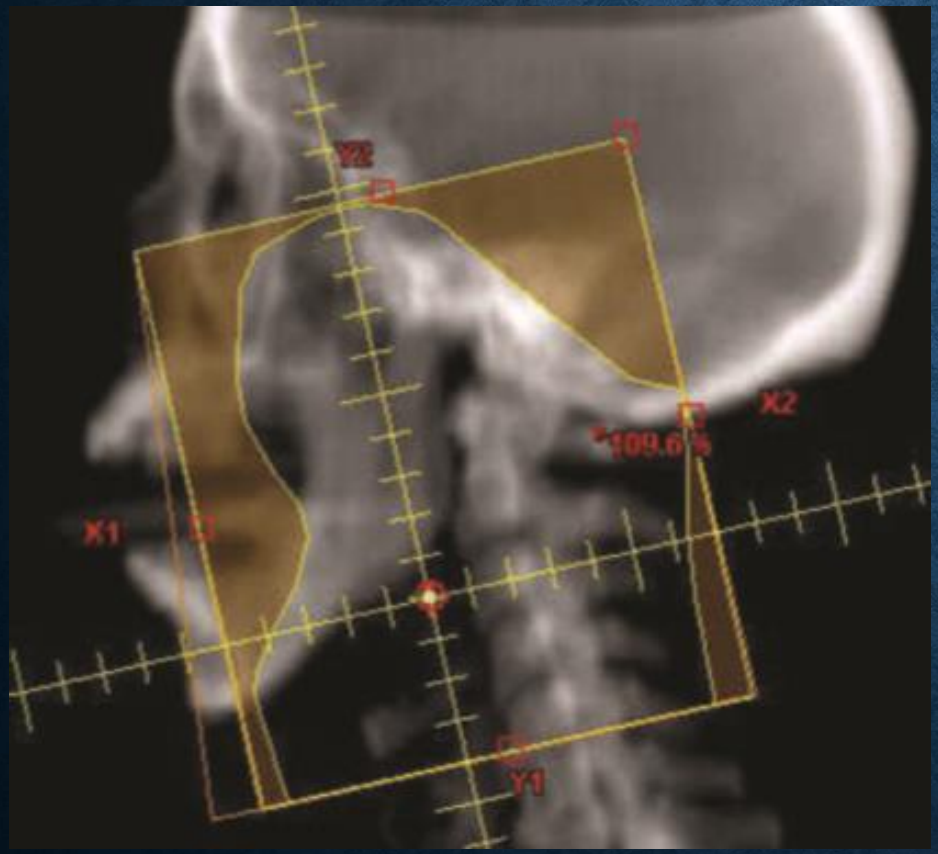


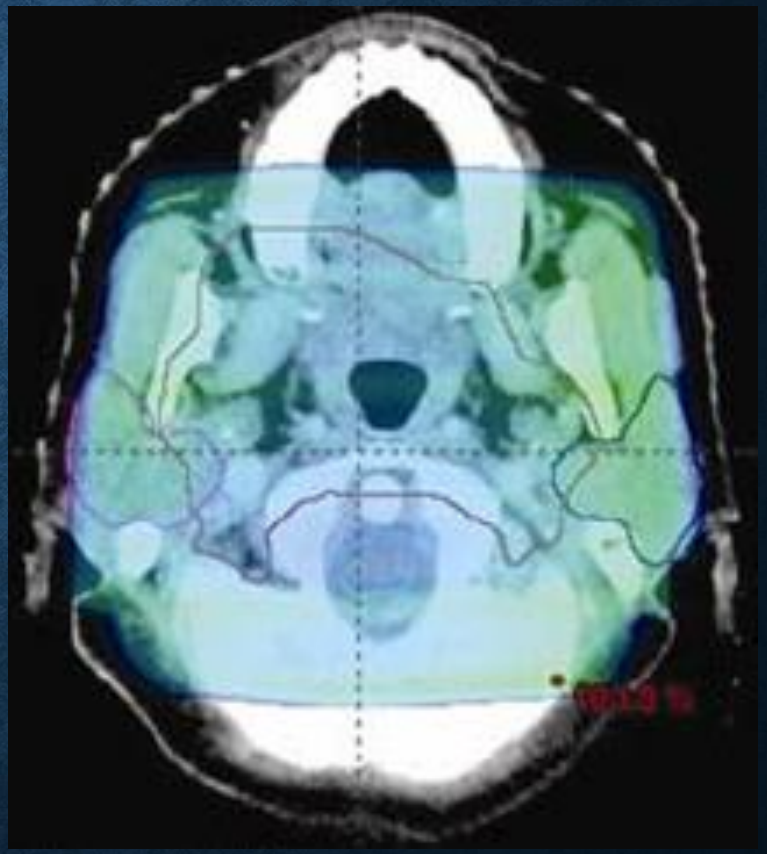


Linear Accelerator (Linac)

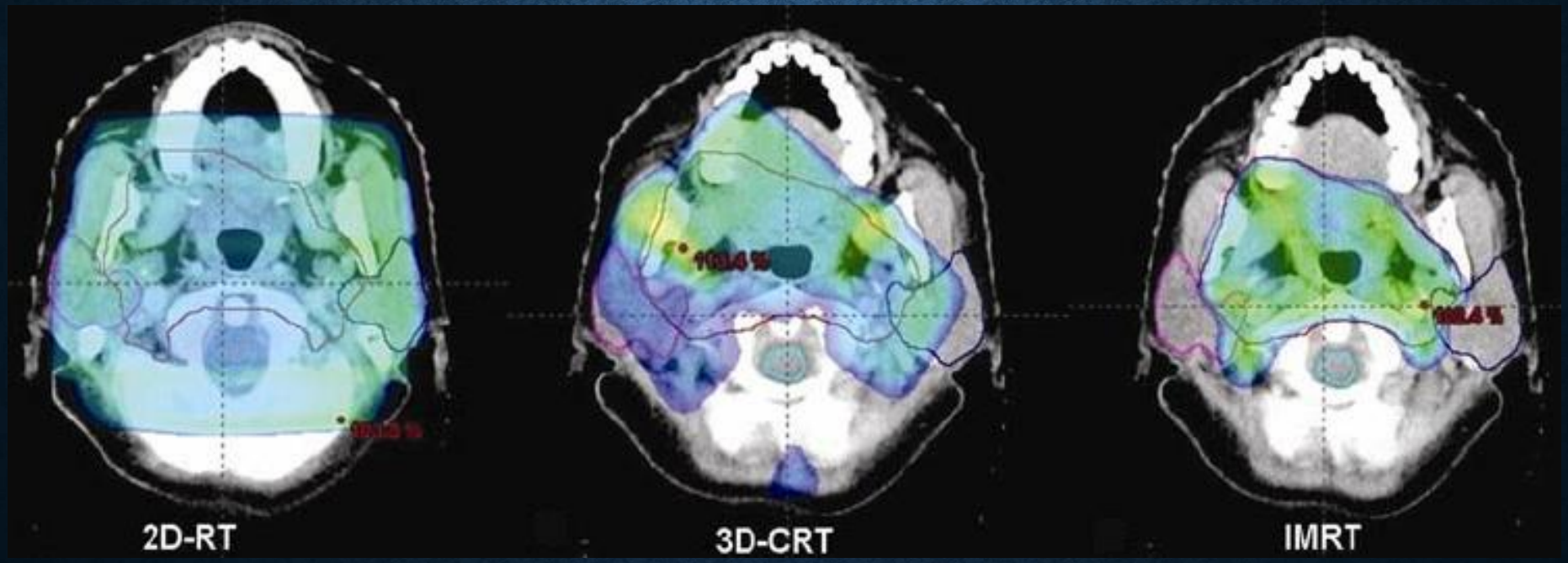


2D

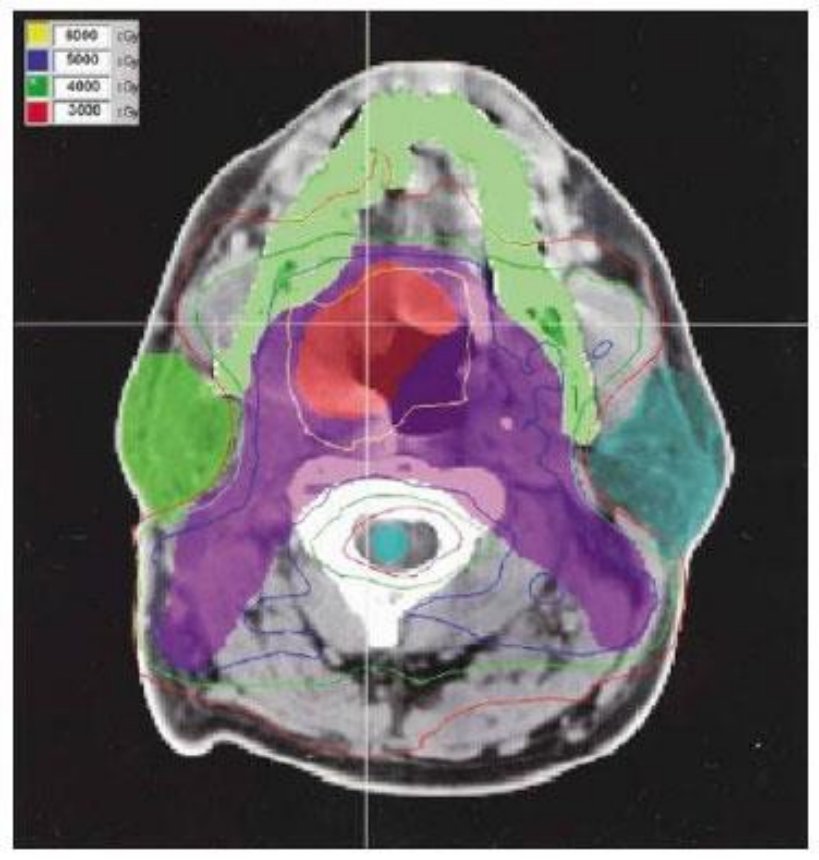


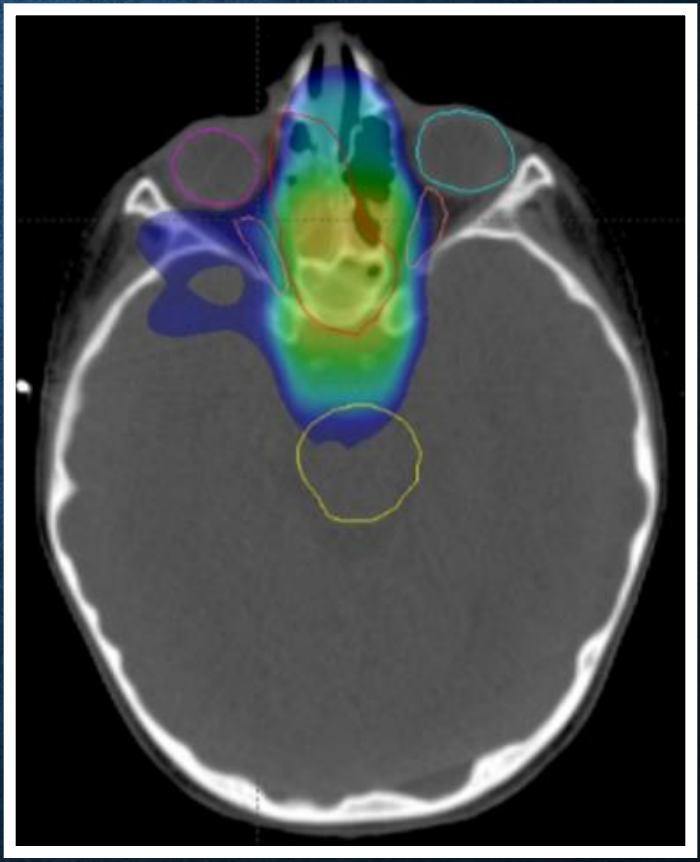


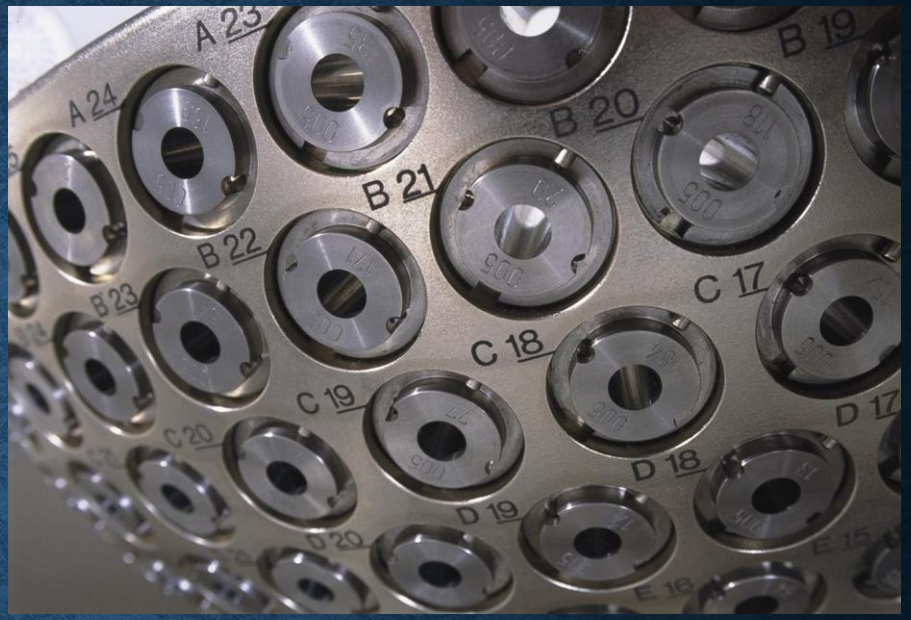
2D - 3D CRT - IMRT



IMRT







Gamma Knife

SRS

Cyberknife

SRS & SRT

Brachytherapy

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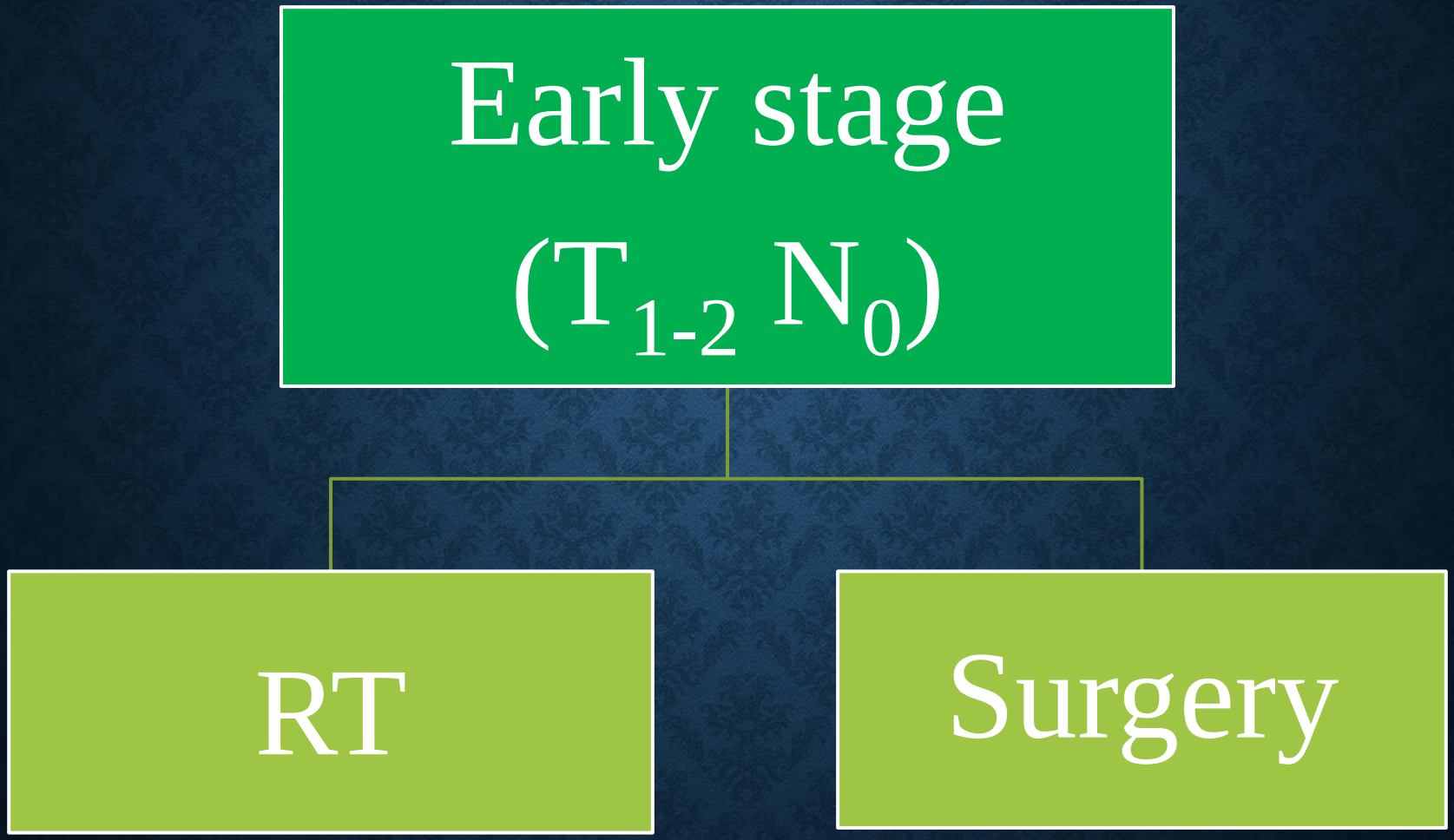
Summary

Indications for RT

- Radical in early stage ($T_{1-2}N_0M_0$)
- Laryngeal preservation protocol in $T_3N_+M_0$
- Postoperative RT: T3-4, N+, close margin, recurrence
- Postoperative CCRT in: ECE or +ve margin


Early stage
(T_{1-2} N_0)
RT
Surgery

T1-2 Glottic Ca

- RT vs Microsurgery
- RT preferred unless disease is very superficial
- Selected T2 (T2b: impaired cord mobility) may benefit from cisplatin/RT
- LC:
  - RT: T1 85:95%, T2 65:85%.
  - RT including salvage surgery: T1 ~ 95%, T2 ~ 90%.

Advanced Stage

(T_{3-4} or N_{+ve})

Combined Modality

* Surgery + PORT ± CT
* Preoperative CT then Surgery + RT

Organ preservation

* CCRT
* Induction CT then CCRT

Larynx preserving surgery

Palliation

Clinical Trials for Laryngeal Preservation

Study	No. of Patients (accrual period)	Site	Stage	Treatment	Response of Primary to Induction Chemotherapy	Larynx Preservation	Overall Survival
VALCSG	332 (1985-1988)	Larynx	III (57%)[a]	a) TL → RT	NA	NA	3-year, 5-year
Phase III[12]		SG (63%)	IV (43%)	b) PF × 3 → RT[b]	85% CR + PR	3-year, 62%[c]	a) 56%, 45%
		G (37%)				Composite end point	b) 53%, 42%
RTOG	547 (1992-2000)	Larynx	III (64%)[a]	a) PF × 3 → RT[b]	85% CR + PR	5-year, 10-year	5-year, 10-year[d]
91-11		SG (69%)	IV (36%)[e]	b) RT + P	NA	a) 71%, 68%	a) 58%, 39%
Phase III[13,14]		G (31%)		c) RT	NA	b) 84%, 82%[f]	b) 55%, 28%
						c) 66%, 64%	c) 54%, 32%
GORTEC	213 (2000-2005)	Larynx (46%)	III, IV	a) PF × 3 → RT[h]	59.2% CR + PR	3-year	3-year
2000-01		Hypopharynx (54%)		b) TPF × 3 → RT[h]	80% CR + PR	a) 57.5%	a) 60%
Phase III[11]					(P = .002)	b) 70.3% (P = .03)	b) 60%

Larynx preservation

Estimated long-term (>2 years) rates:

- Concurrent chemo-RT: 80-85%.
- Induction chemo → RT: 65-75%.
- RT alone: 60-70%.

Median OAS: 4-6 years; no difference by therapy.

VA Larynx Trial (Wolf, NEJM 1991)

- 332 patients with stage III–IV ca larynx (T1N1 excluded), randomized to surgery + PORT (50–74 Gy) vs. induction cisplatin/5-FU × 2c (with a 3rd cycle if PR/CR) → RT (66–76 Gy). If < PR/CR then surgery → PORT.
- Larynx preservation at 2 years with induction CT 64%.
- No difference in 2-year OS (68%).
- Induction CT decreased DM, but higher LF (12 vs. 2%).
- Salvage laryngectomy was required for 56% of T4 patients.

RTOG 91–11
(Forastiere *NEJM* 2003, *JCO* 2013)

- 547 patients with advanced ca larynx (T2–3 or low-volume T4 [not invading through thyroid cartilage and <1 cm base of tongue invasion], or LN+) randomized to 3 arms: RT alone, CT → RT, or concurrent CT-RT (all 2/70 Gy). Induction CT was cisplatin/5-FU × 2c (with a third cycle if PR/CR, otherwise surgery). Concurrent CT was cisplatin × 3c.
- Over RT alone or induction CT, concurrent CT-RT improved 10-year larynx preservation (64 → 68 → 82%) and LRC (47 → 49 → 65%). Trend toward improved distant control with any CT (76 → 83 → 84%). No significant difference in 10-year OS (32 → 39 → 28%), although more late deaths unrelated to disease with concurrent CT-RT.

RTOG 91–11

Phase III clinical randomized trial for advanced ca larynx

	RT	CT → RT	concurrent CRT
• 10-year larynx preservation	64	68	82%
• LRC	47	49	65%
• Distant control	76	83	84%
• 10-year OAS	32	39	28%

GORTEC 2000-01 (Pointreau, JNCI 2009)

- 220 patients with locally advanced larynx/hypopharynx cancer randomized to 3c of TPF vs PF.
- If CR/PR and larynx mobility → RT. If no response → surgery + PORT.
- TPF improved overall response (59 → 80%) and 3-year larynx preservation (58→70%), but with more neutropenia.
- No difference in 3-year OS or PFS.

T3 Glottic Larynx: Treatment Approach

- Larynx preservation is the central concept.
- To be a candidate for larynx preservation, patient must have a functional larynx (able to breathe and swallow).

T4 Glottic larynx: Treatment Approach

- Is a "surgical disease" based on poor outcome of T4 cases in VA larynx trial.

- Beware of the trap of offering T4 patients larynx preservation with the idea of saving total laryngectomy for salvage

Not all recurrences can be salvaged

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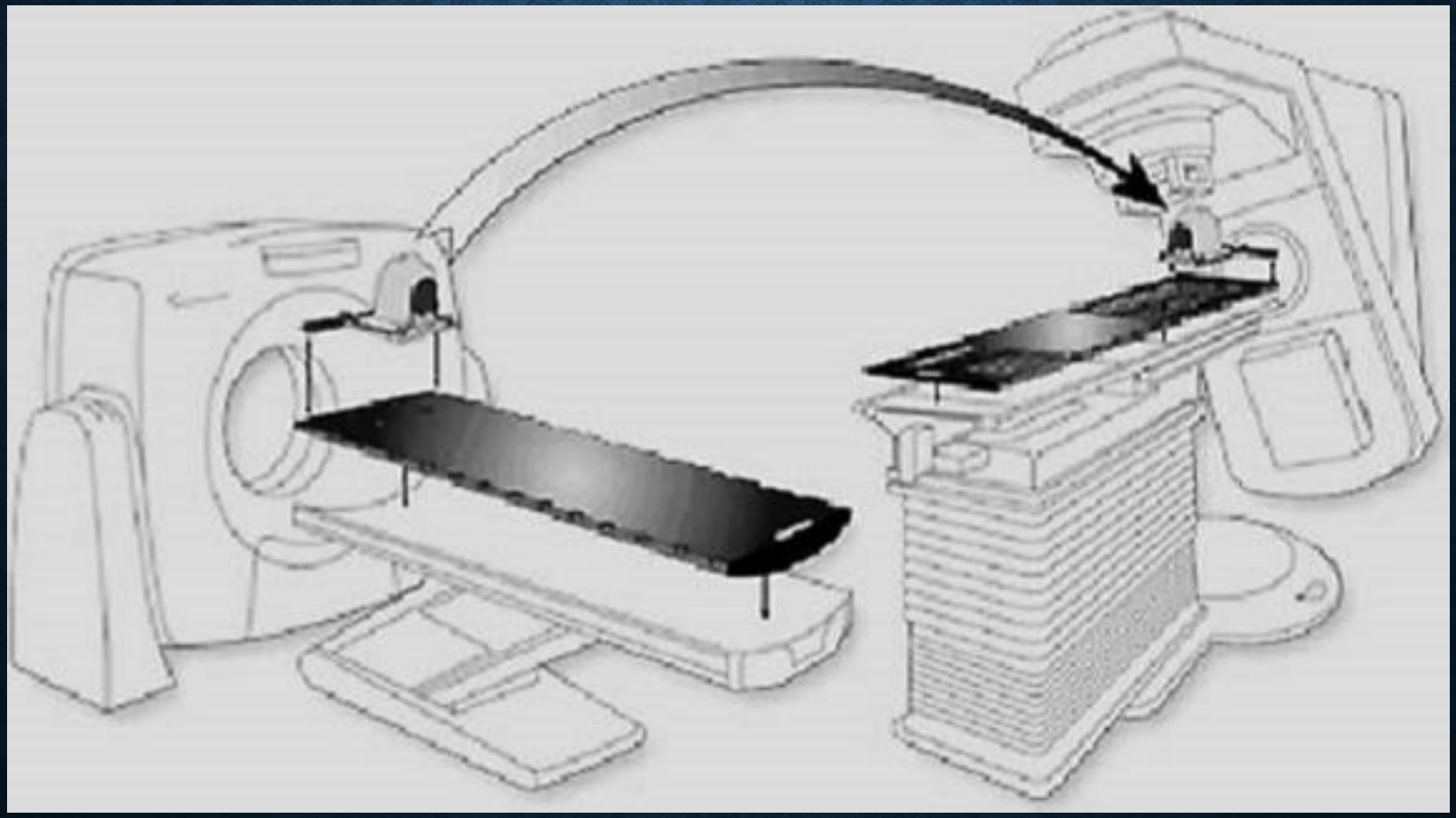
Head & Neck Cancer
AWARENESS

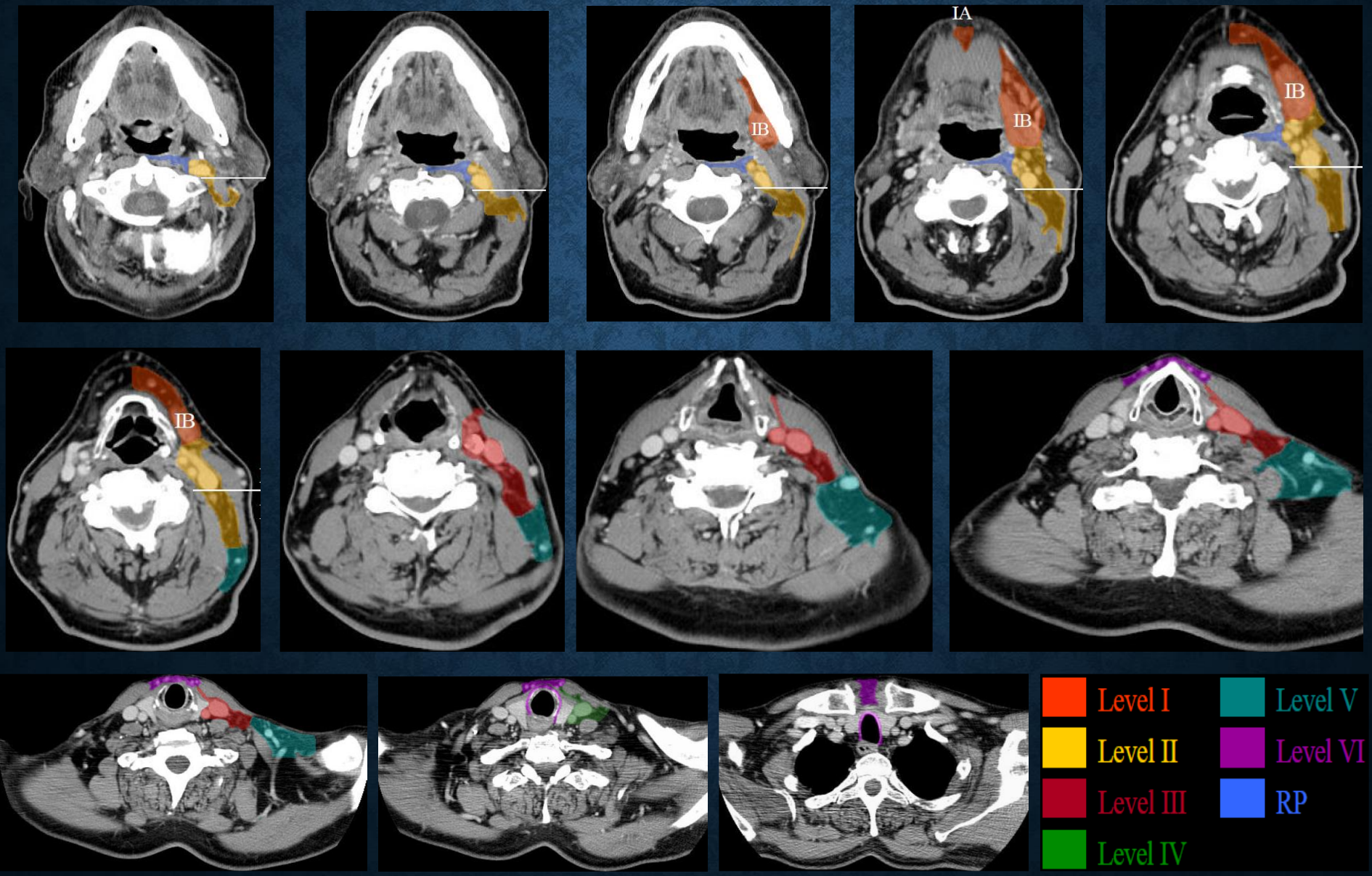
Position & Fixation

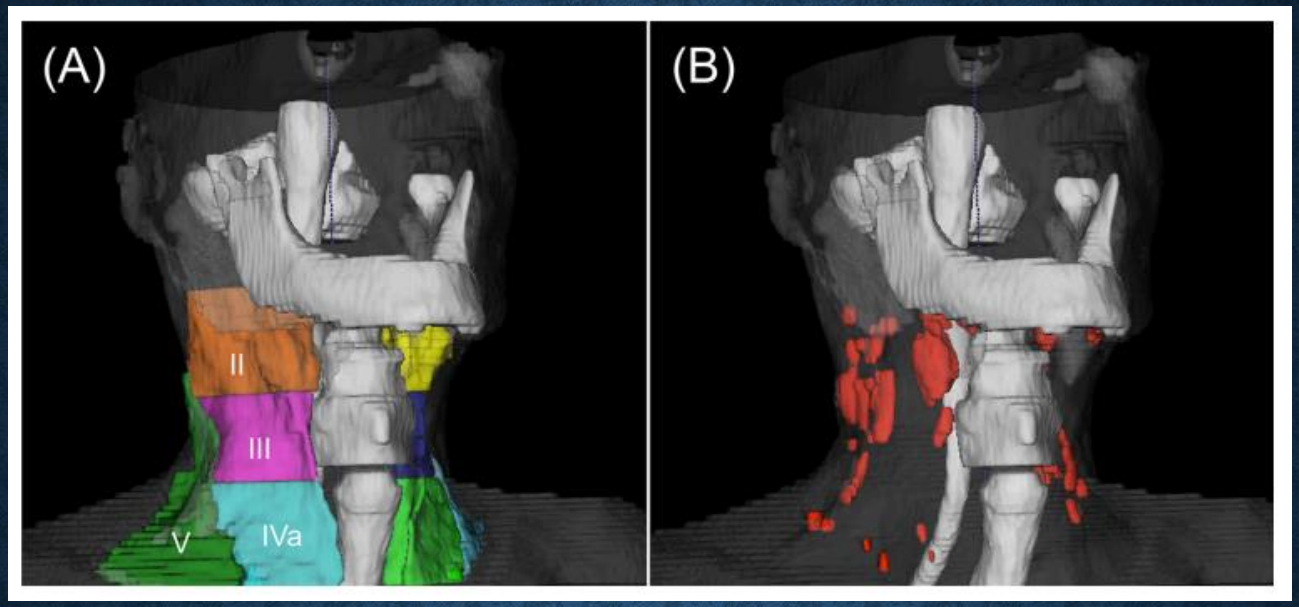
- Head & Neck shell
- Supine
- Neck extension

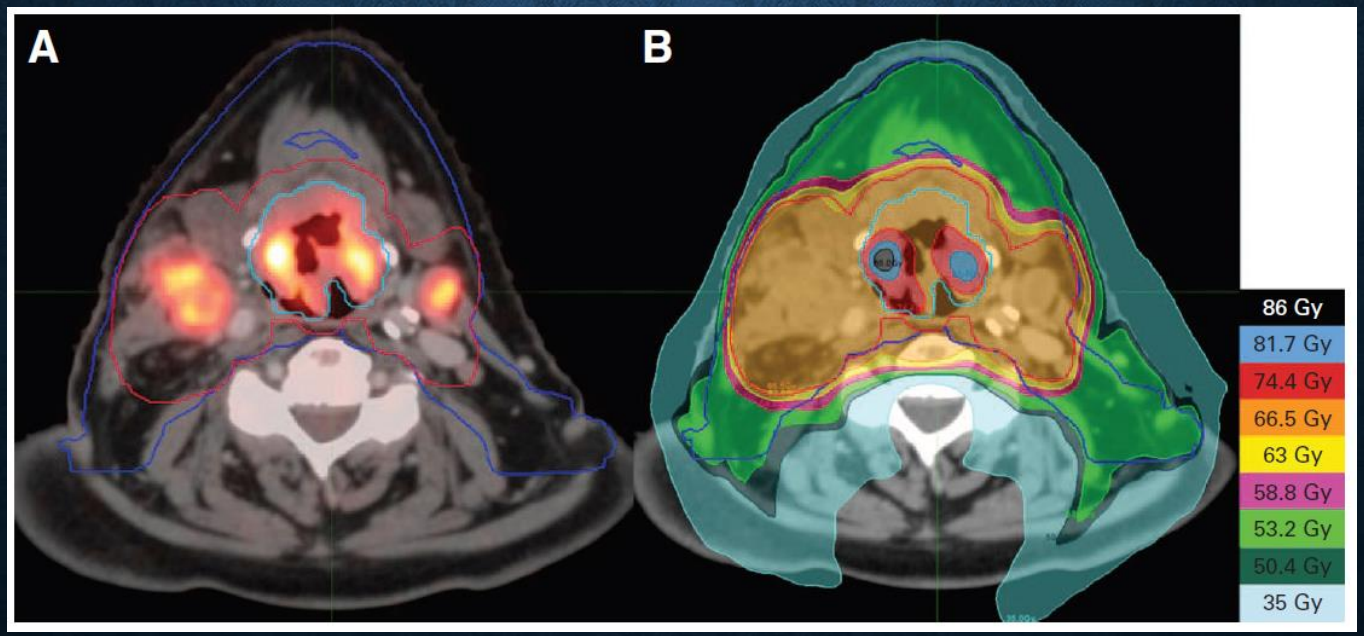
Simulation



Contouring

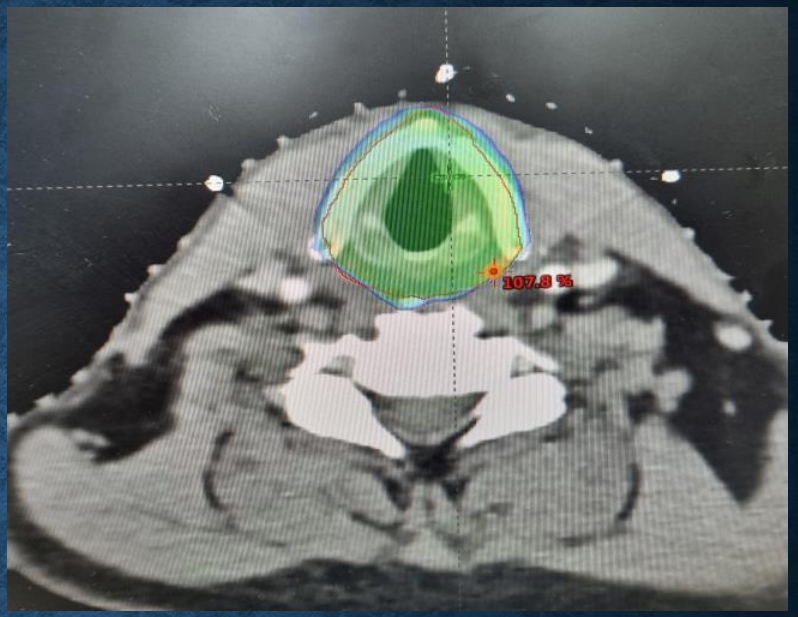

IA
IB
IB
IB
IB
Level I
Level II
Level III
Level IV
Level V
Level VI
RP

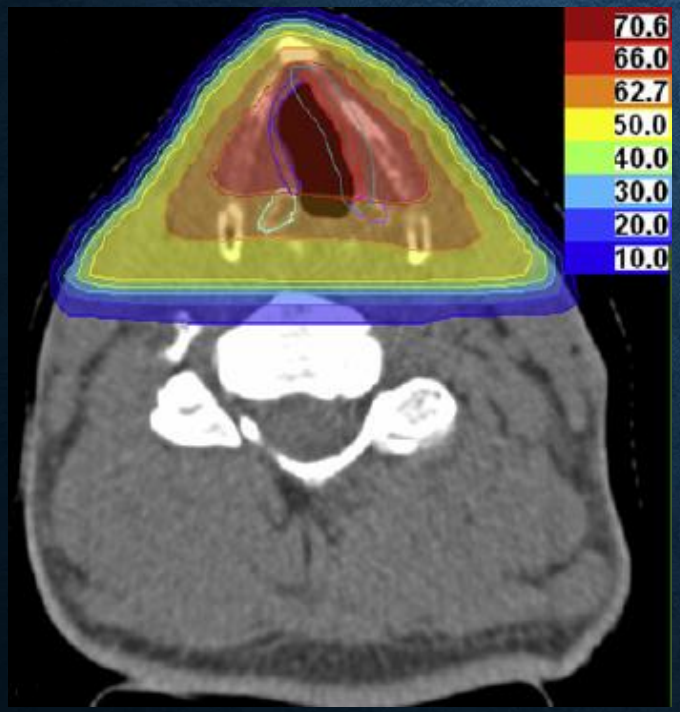

(A)
(B)
II
III
IVa
V

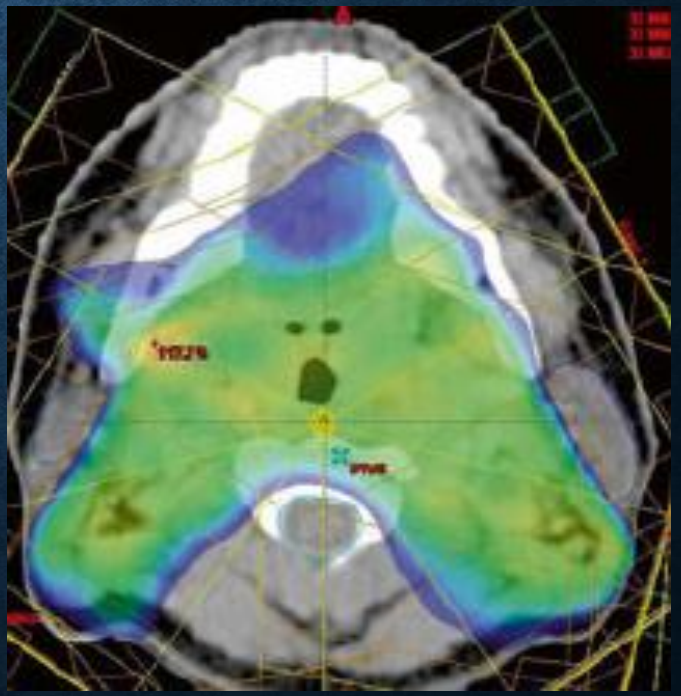

A
B
86 Gy
81.7 Gy
74.4 Gy
66.5 Gy
63 Gy
58.8 Gy
53.2 Gy
50.4 Gy
35 Gy

RT Plan

Acceptance







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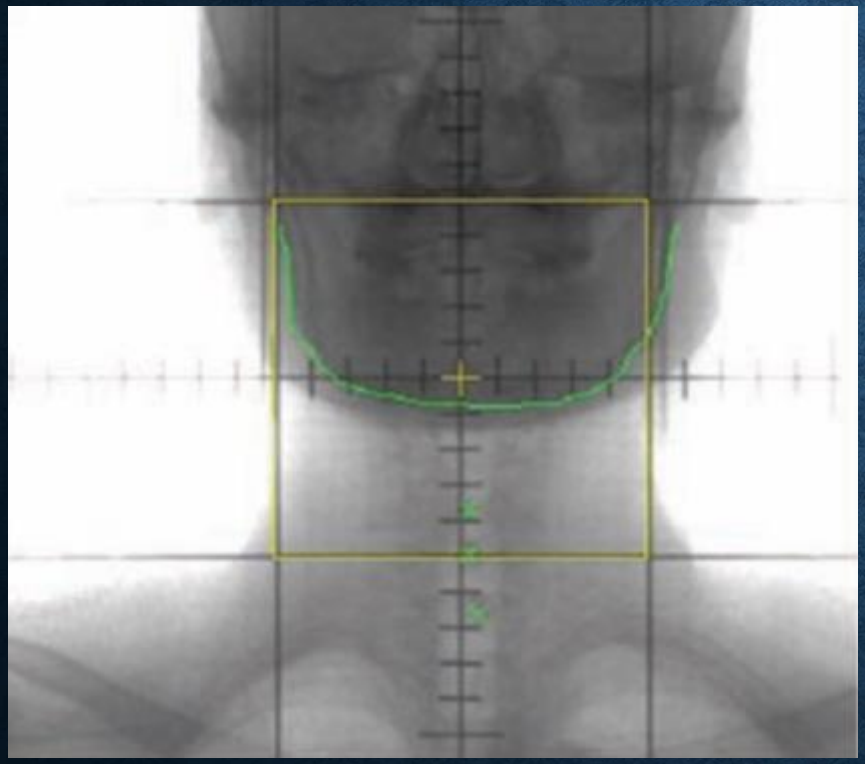
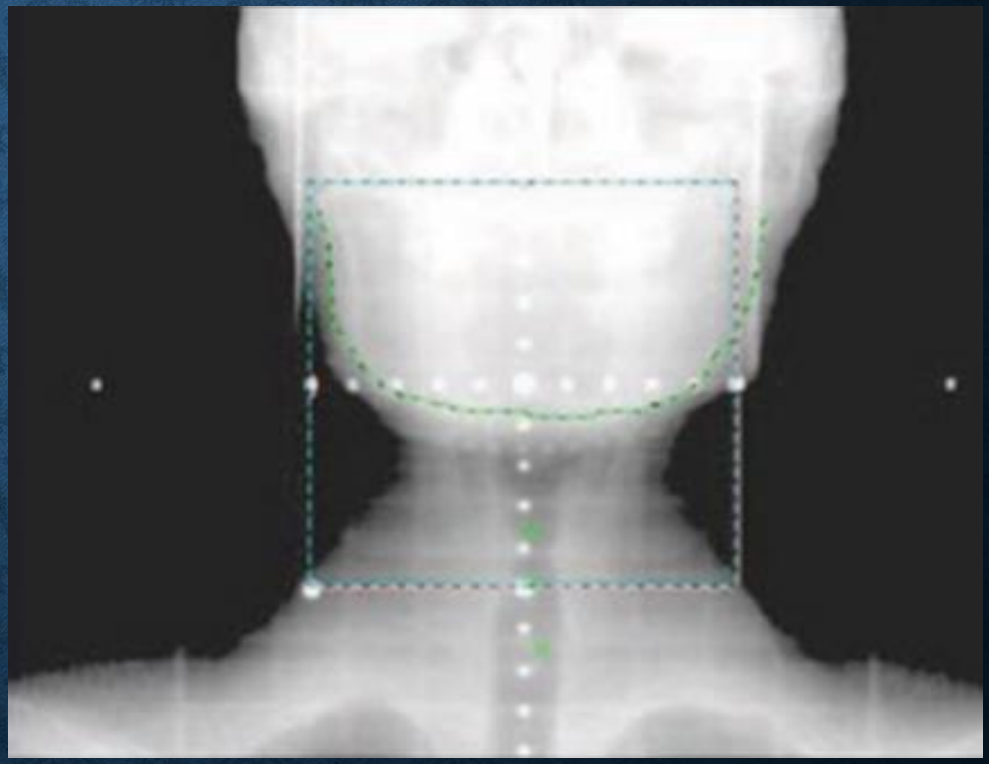
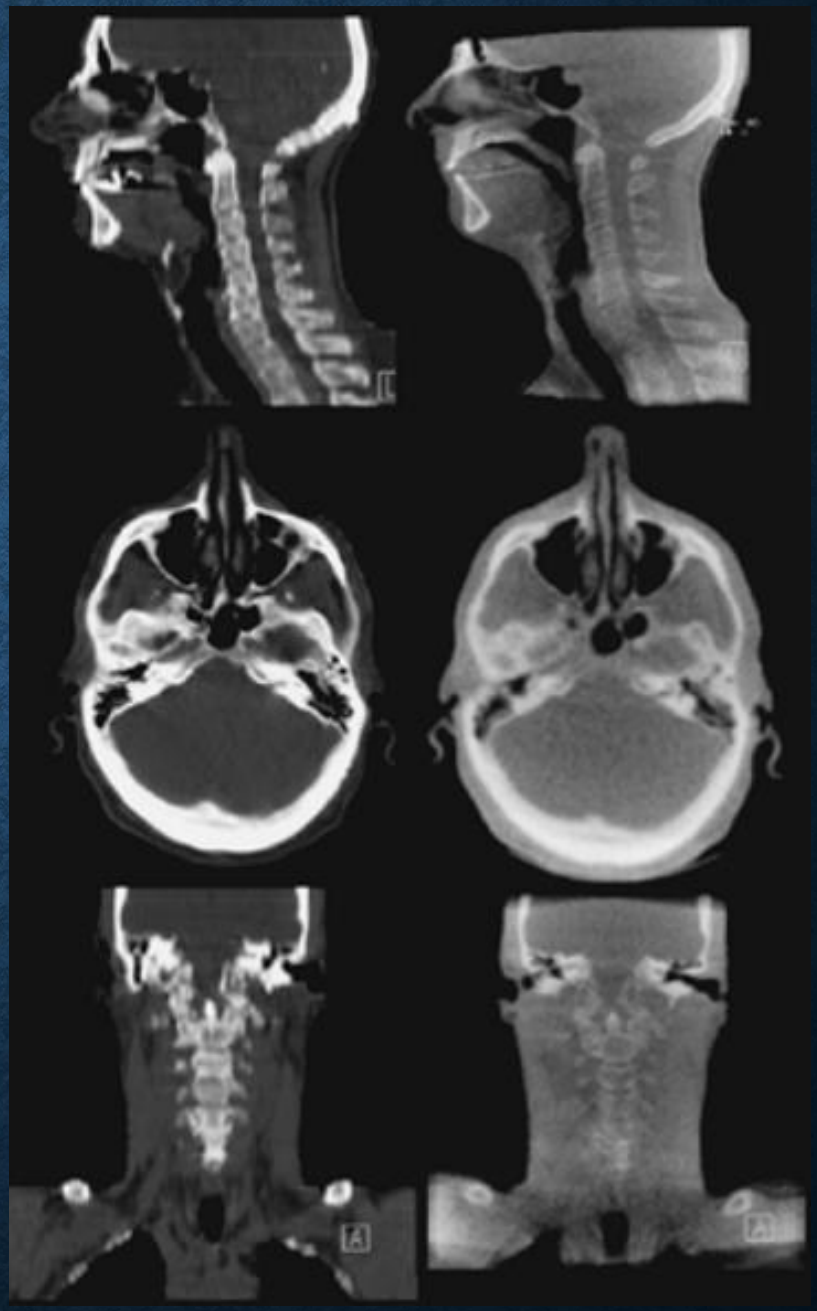


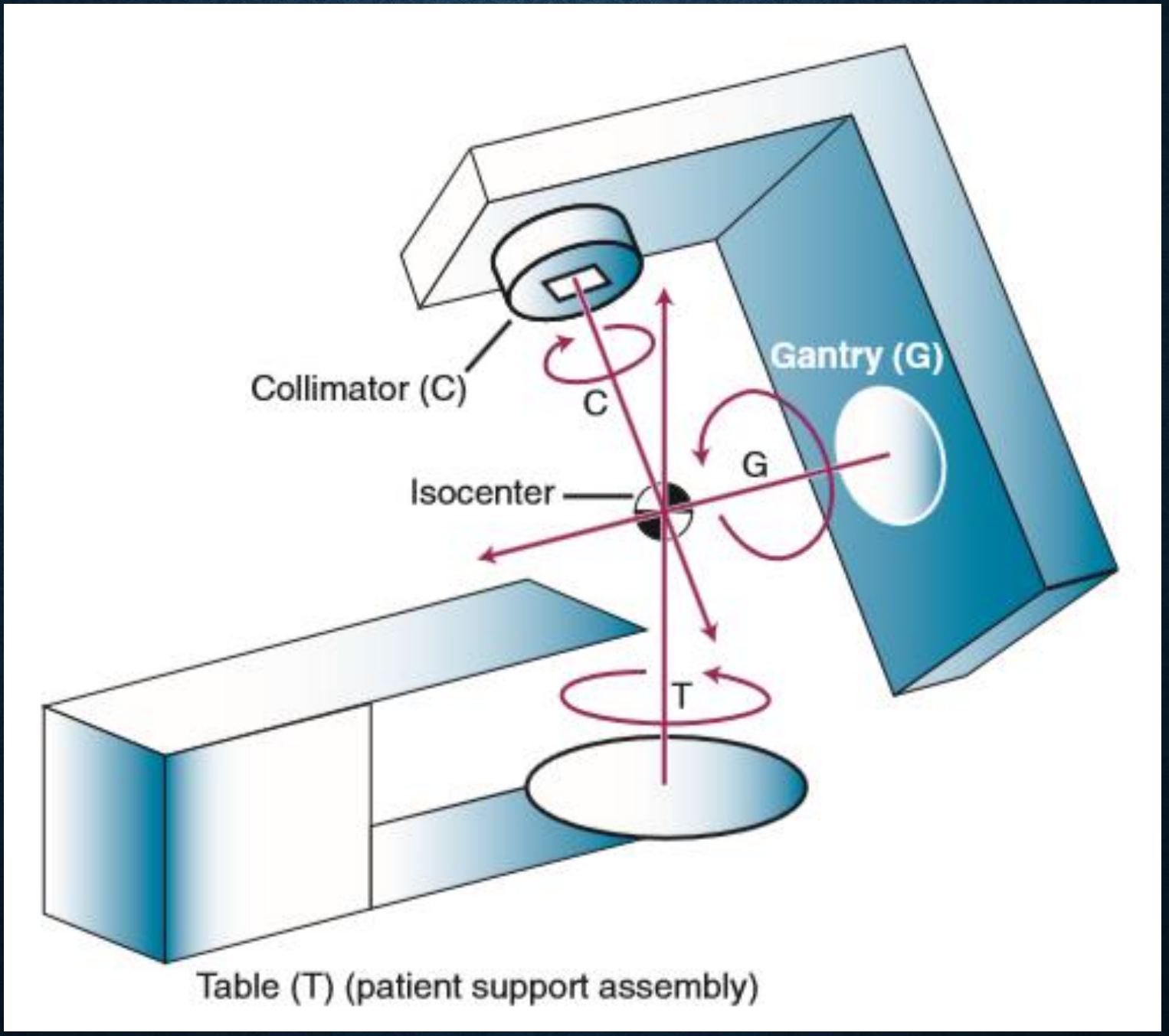


DRR

EPID

CBCT




Collimator (C)
C
Gantry (G)
G
Isocenter
T
Table (T) (patient support assembly)

Primary tumor CTV

- Microscopic tumour infiltration occurs within a distance of 0-10 mm from the edge of the GTV defined as the macroscopic tumour specimen.

- While it is recognized that a “5+5 mm margin” may not encompass 100% of tumour extensions, the benefit of further widening the margin around the GTV-P must be balanced against the increased risk of RT induced morbidity.

Target Volumes (Radical)

- GTV:

  Gross tumor (primary or LN)

- CTV_{70}:

  GTV + 5 mm margin

- CTV_{60}:

  CTV_{70} + remaining larynx + high risk LN regions

- CTV_{54}:

  Low risk LN regions

LN CTV in Ca Larynx

For early-stage

- Glottic: nodal RT is not indicated.
- Subglottic or supraglottic: nodal RT is indicated.

For advanced stages:

- Include levels II through IV.
- Include level V for any N+ or extension to the BOT. Include retropharyngeal nodes if extension to pharyngeal wall (possibly glossopharyngeal sulcus) or BOT. Consider level VIb nodal coverage for hypopharyngeal extension

Dose & Fractionation

- Radical
  - 66-70 Gy / 33-35 F/ 7 W
- Adjuvant
  - 60 Gy / 30 F / 6 w (-ve margin)
  - 66Gy / 33 F / 6.5 w (+ve margin)

Yamazaki, IJROBP 2006

- 180 patients with T_1N_0 glottic ca randomized to 60Gy/30f (if ≤2/3 TVC involved) or 66 Gy (if >2/3 TVC involved) vs. 56.25-63 Gy (2.25Gy/f).
- Higher fraction size improved 5-year LC (77 → 92%), but not CSS (97 vs. 100%) or toxicity.

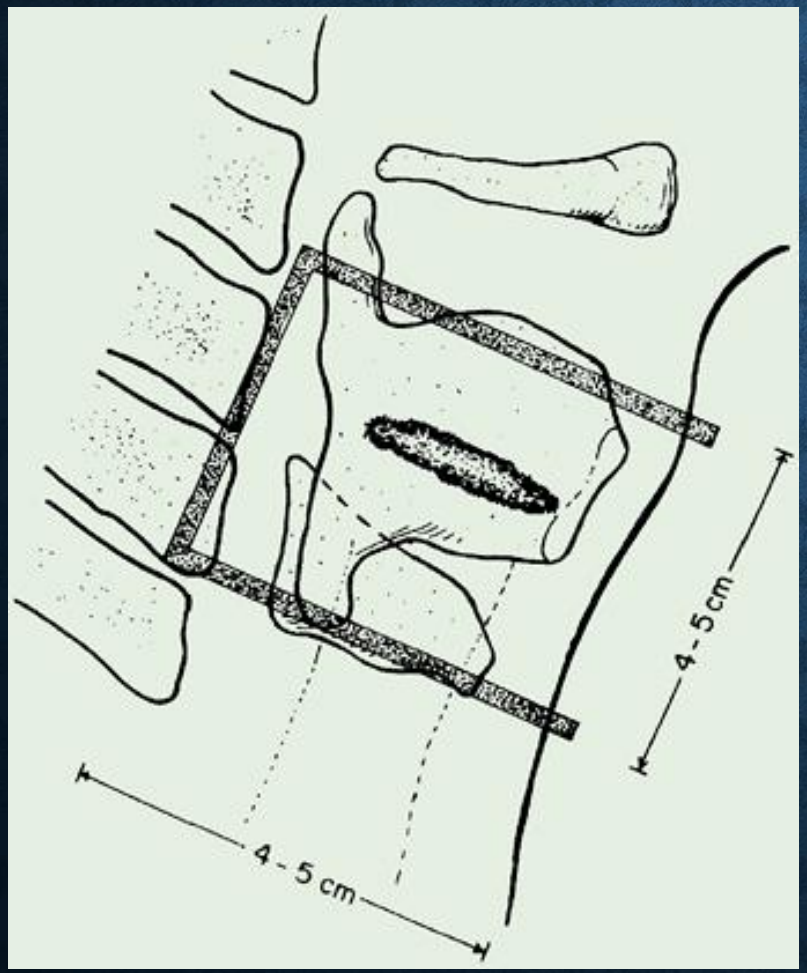
Hypofractionation in Early Glottic Ca

(2.25 Gy/f)

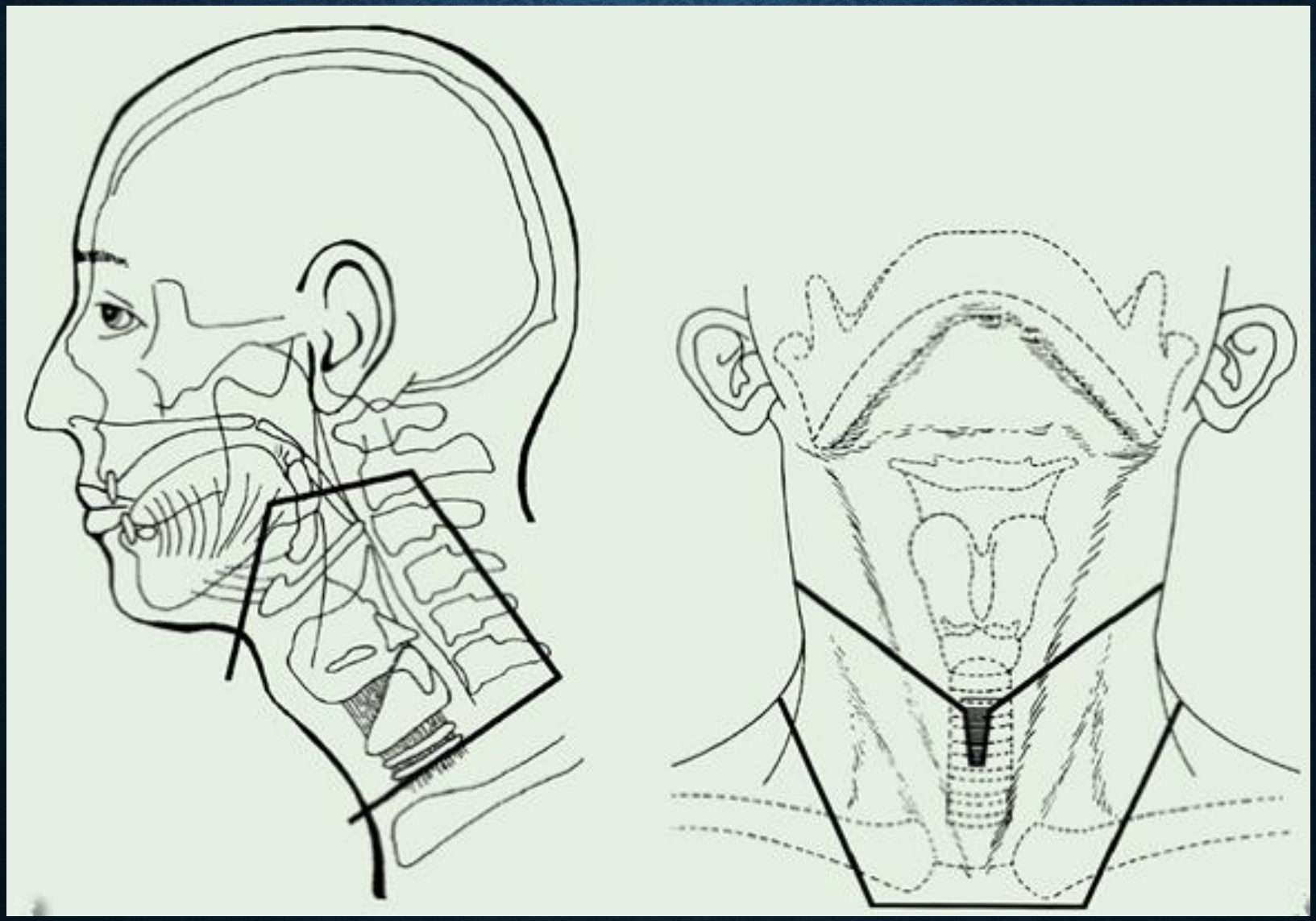
- Tis : 58.5 Gy / 26f / 5w
- T_1N_0 : 63 Gy / 28f / 6w
- T_2N_0 : 65.25 Gy / 29f / 6w

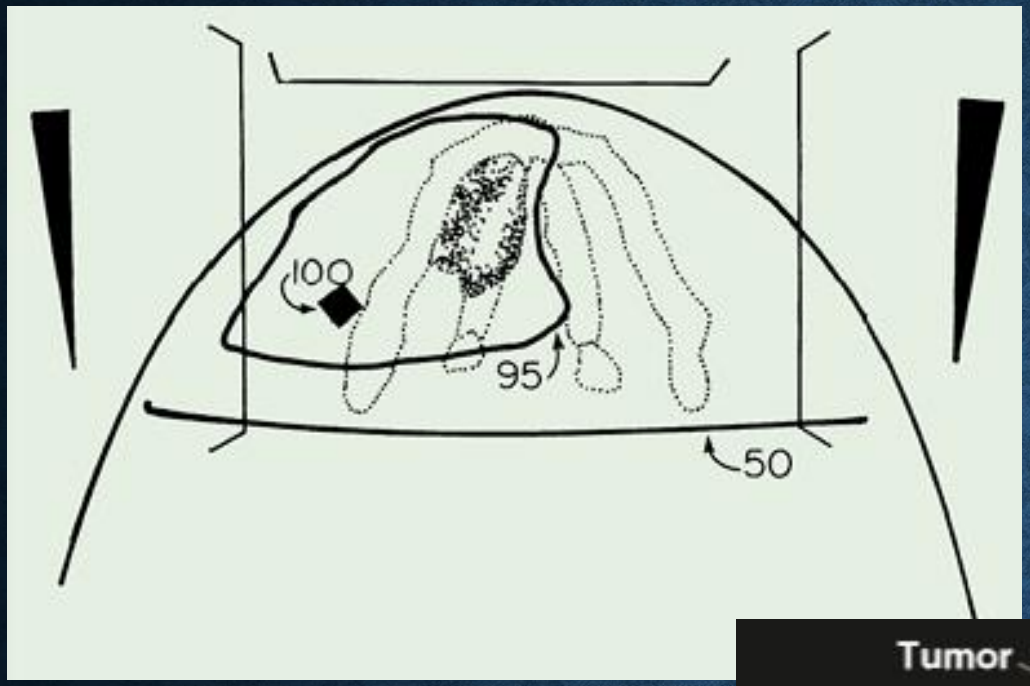
- 55Gy / 20 f / 4 w (2.75 Gy/f)
- 50Gy / 16 f / 22 d (3.125 Gy/f)

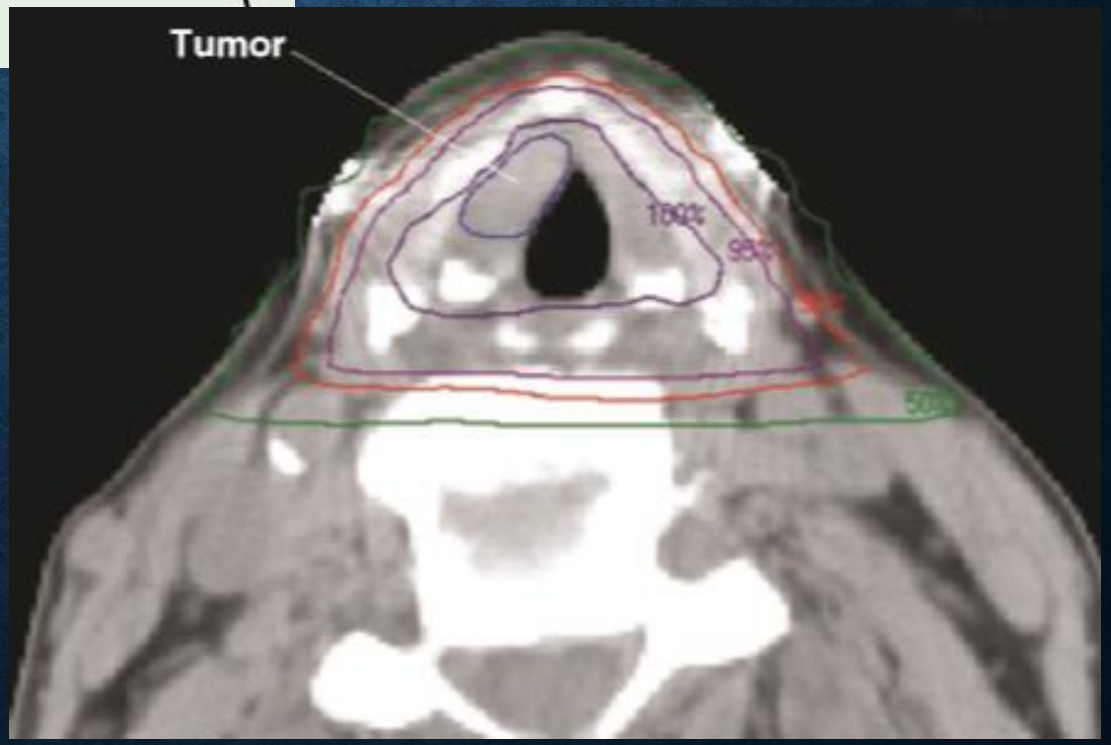
T_1 Glottic ca (2D Planning)



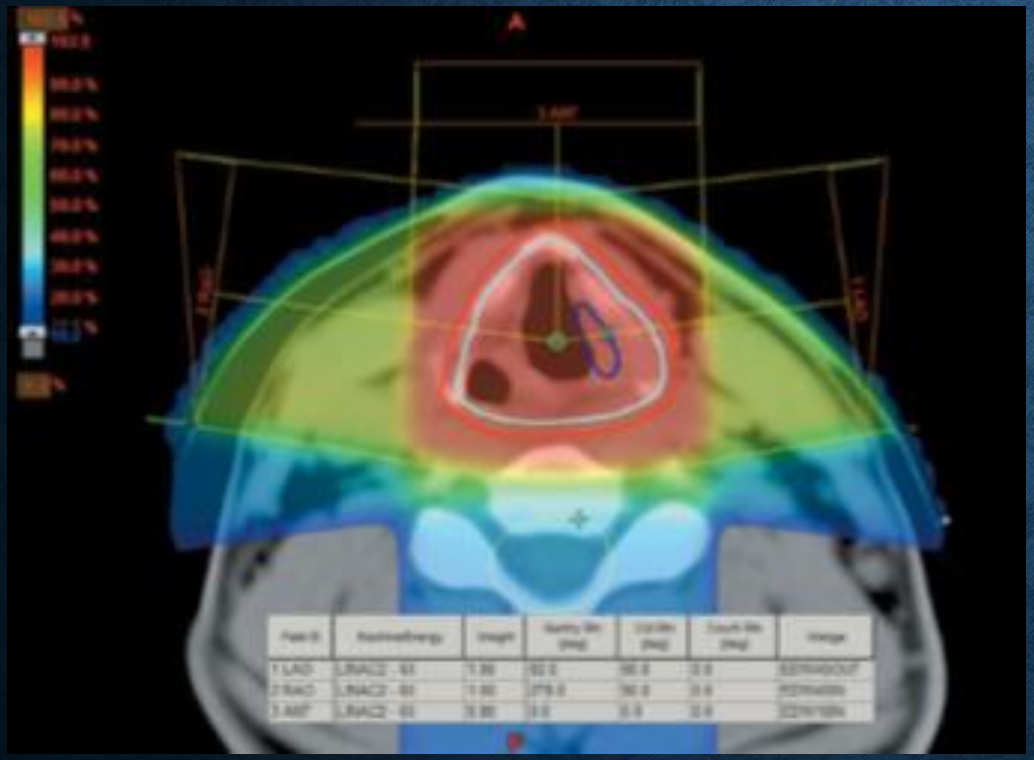
T3-4 glottic ca (2D planning)

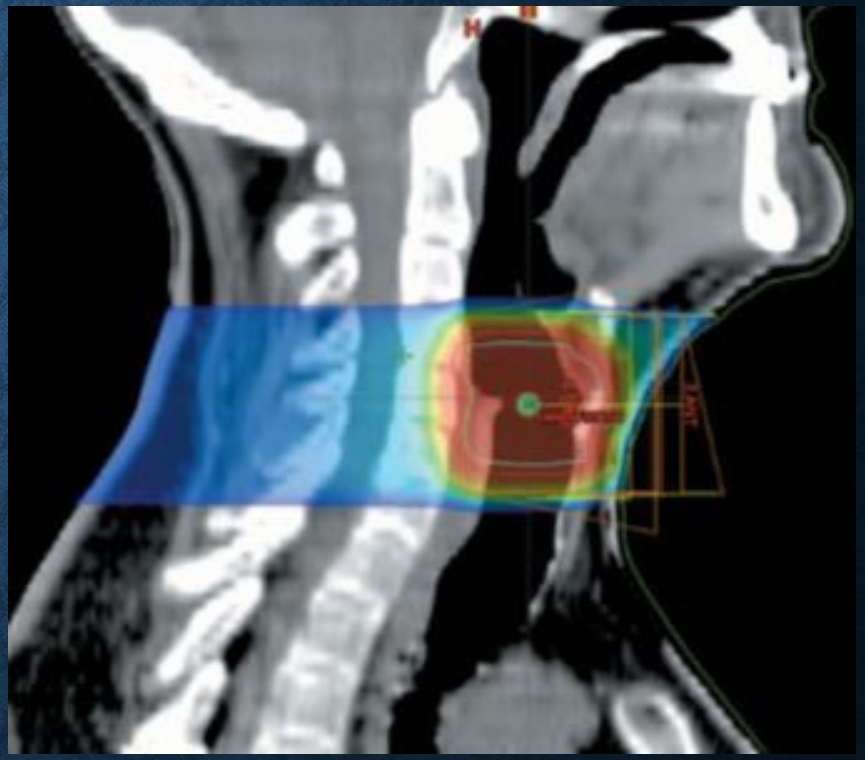



100
95
50


Tumor

CRT for T_{1a} of the left glottis with three beams



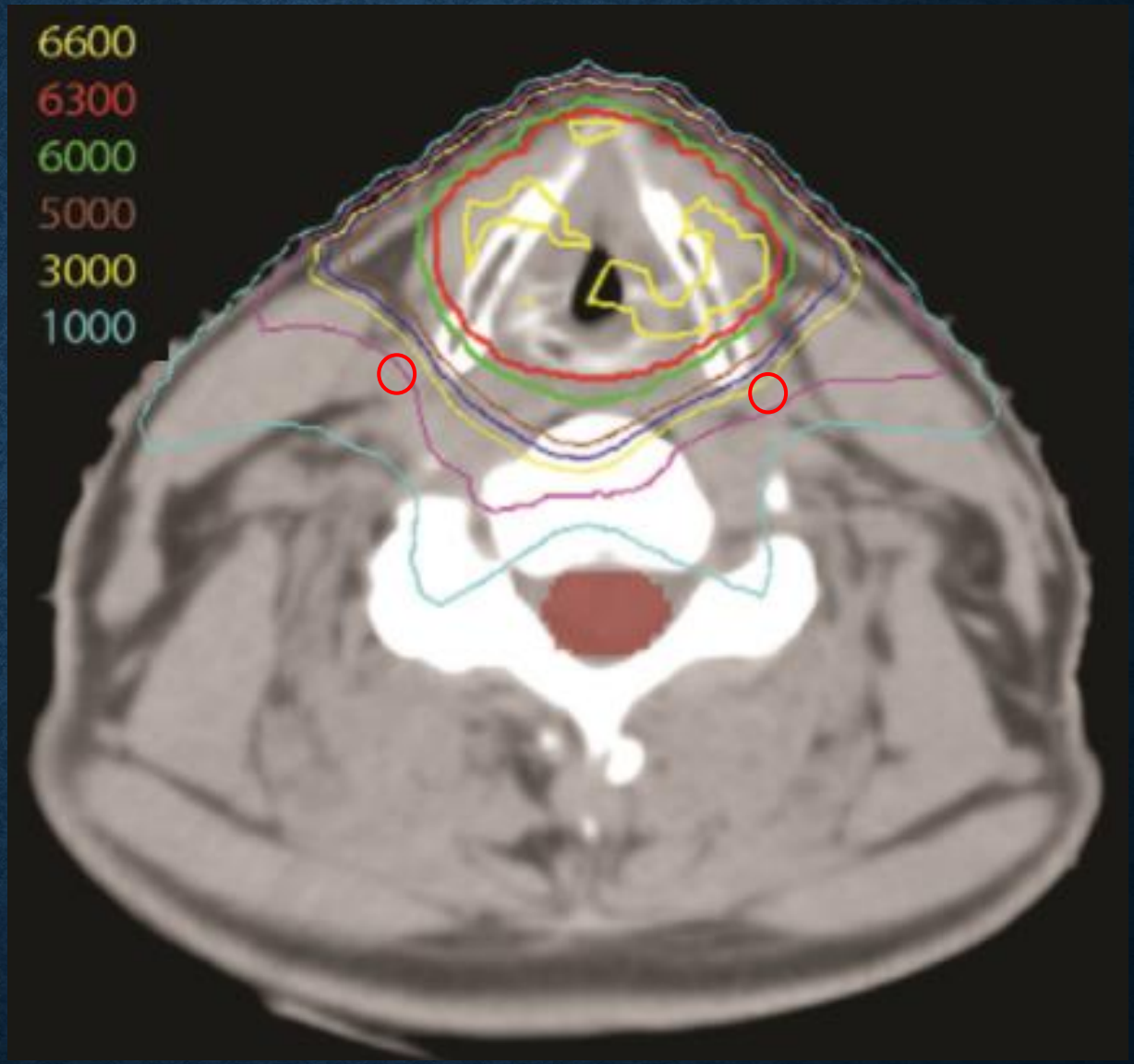


Superior border: mid-body of the hyoid bone.

Inferior border: inferior margin of the cricoid cartilage.

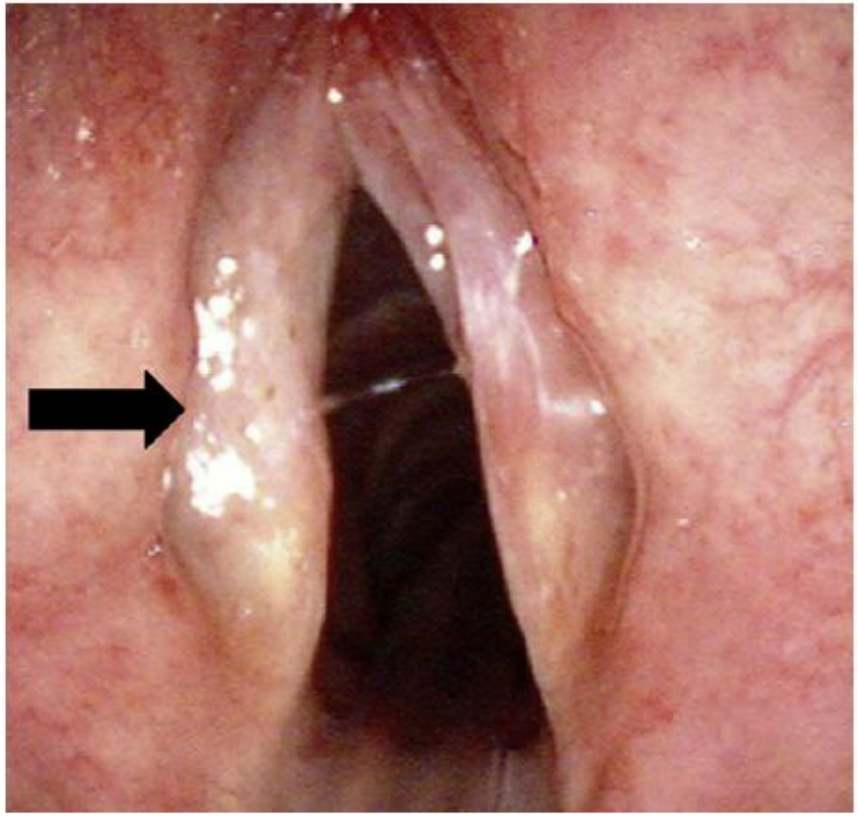
Carotid Sparing

IMRT

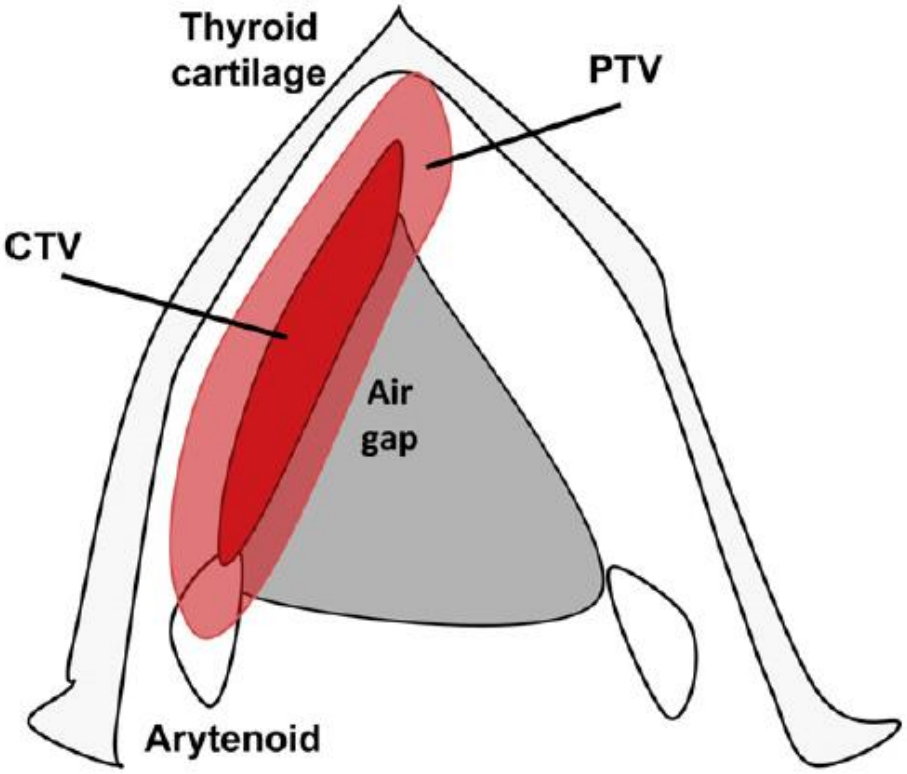


Three-field IMRT for T1 glottic cancer
Dose: 63 Gy / 28 f
30Gy isodose line at the anteromedial edges of the carotids

Single vocal cord irradiation by IMRT

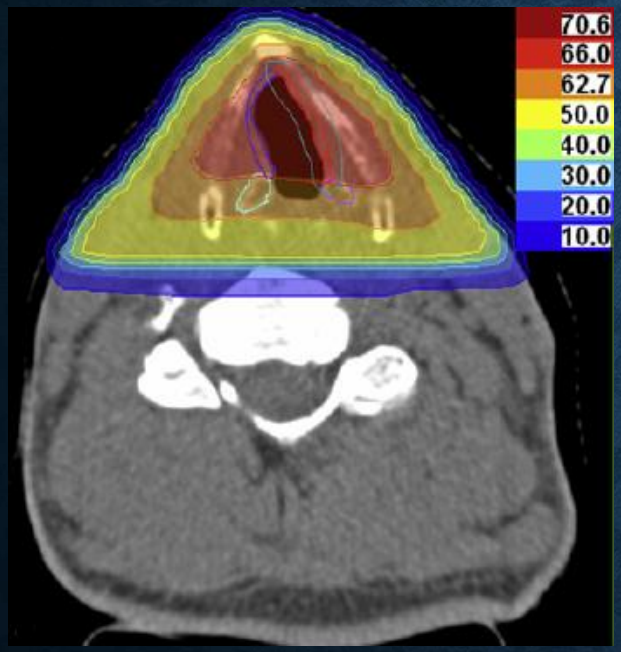


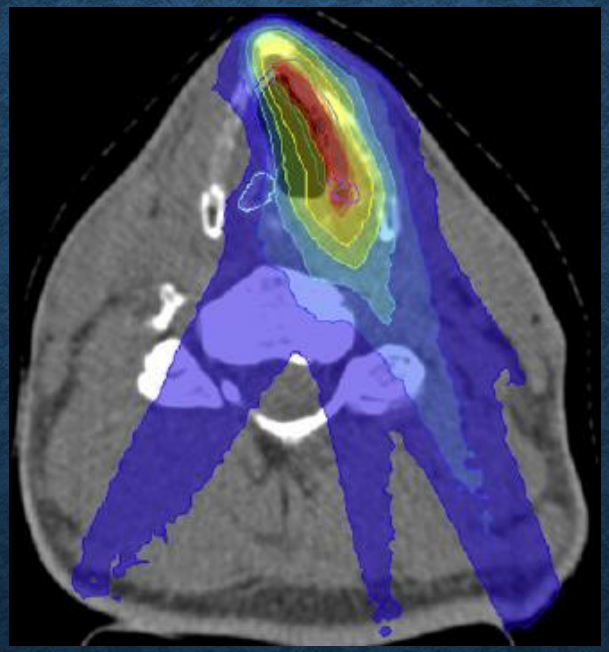
Tumor on left vocal cord

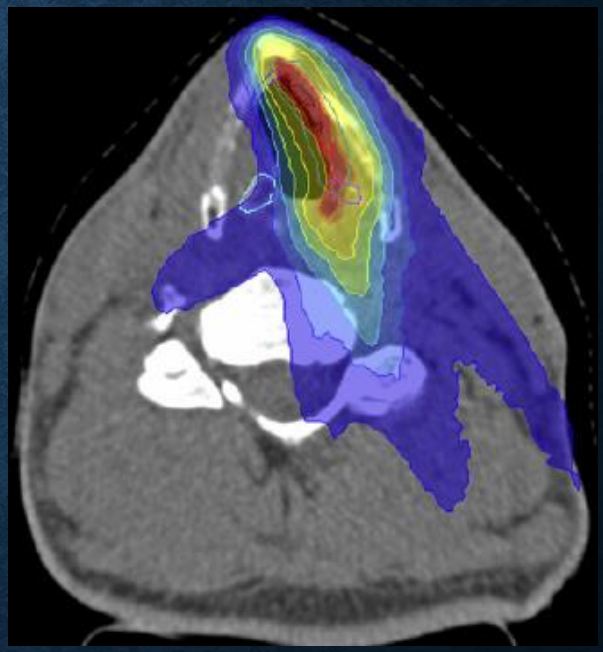


CTV and PTV

IMRT reduced contralateral vocal cord dose







Conventional

Coplanar IMRT

Non-coplanar IMRT

66Gy

39Gy

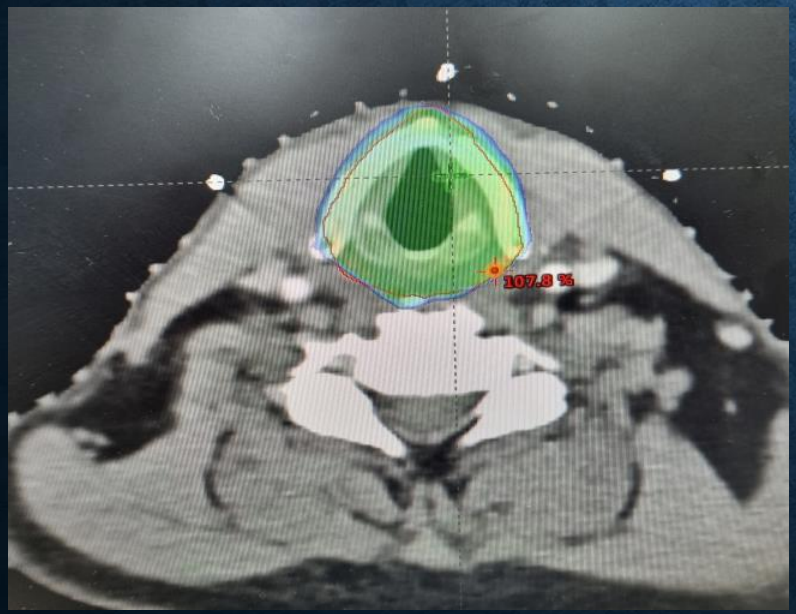
36Gy

Contralateral vocal cord dose

T1aN0 Glottic Cancer

Randomisation
1:1

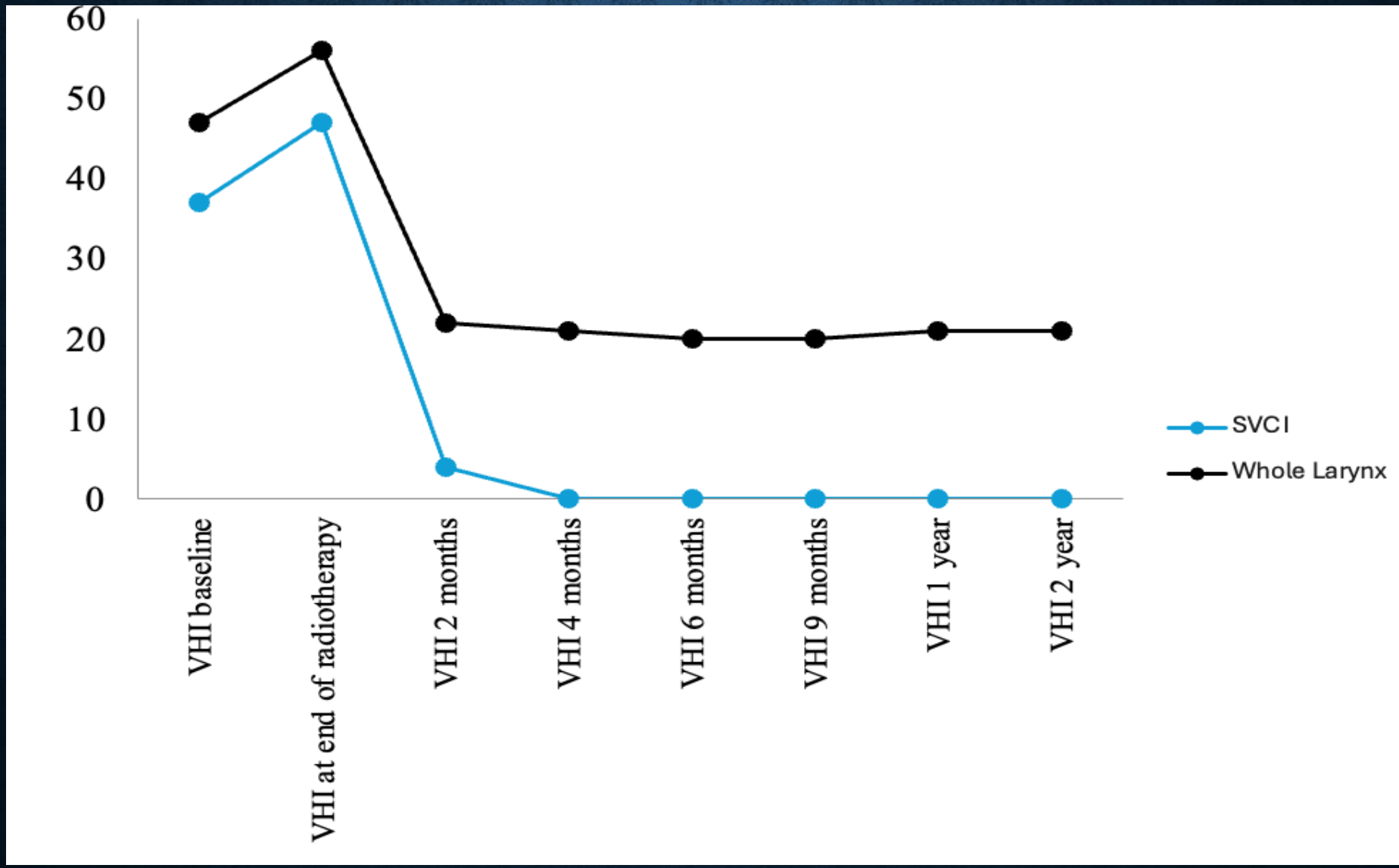
Arm A (Standard arm)
Whole larynx
63Gy/28F

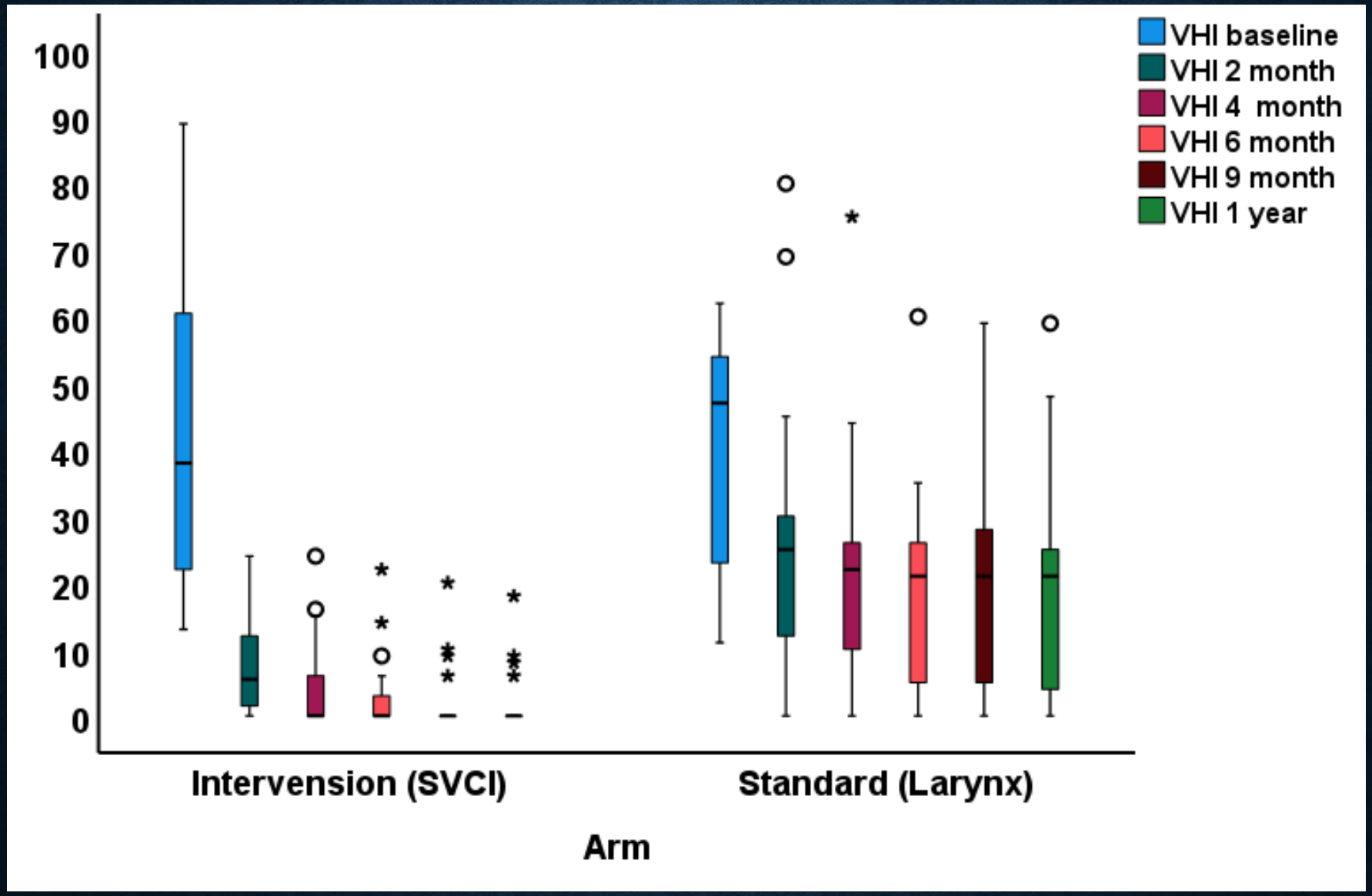


Arm B (experimental)
SVCI
58Gy/16F

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

Target Volumes (post-operative)

CTV66:

Very high risk regions (+ve margin)

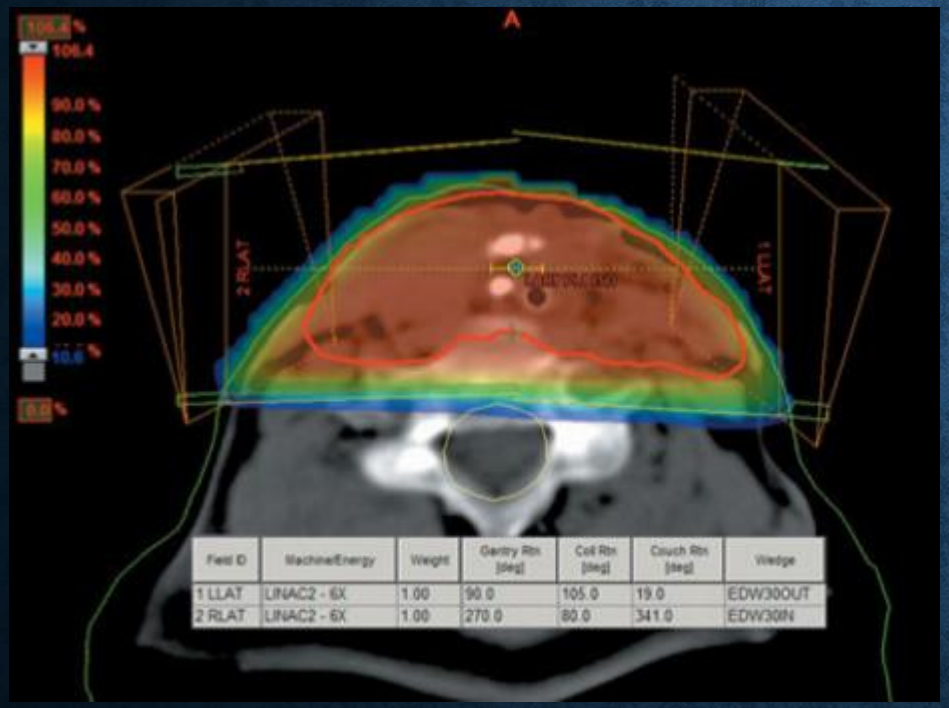
CTV60:

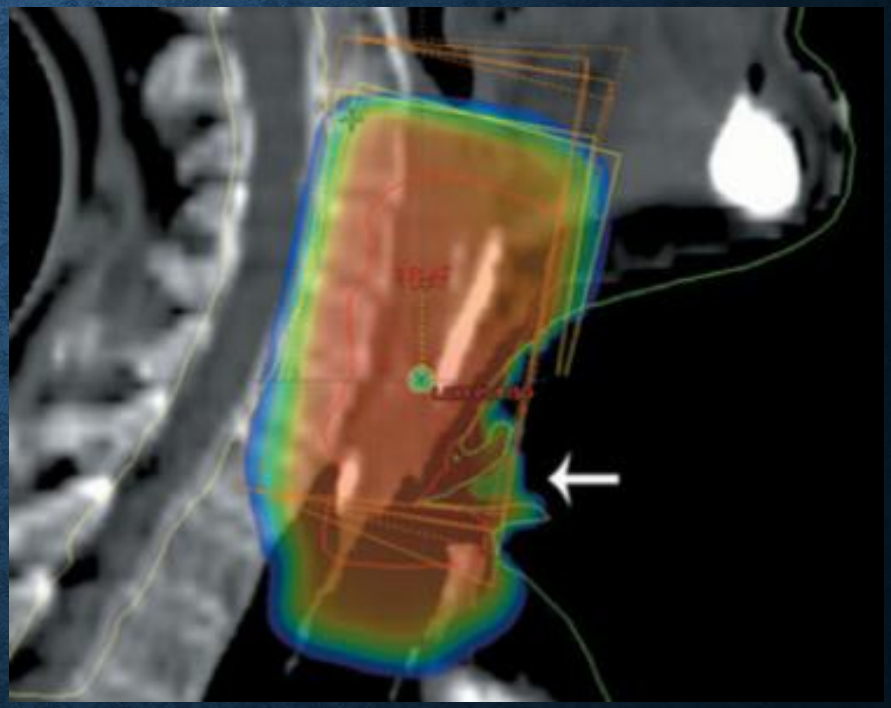
Tumor bed + 1 cm margin + High risk LN regions

CTV54:

Low risk LN regions

Adjuvant RT for a pT_4N_0 laryngeal tumor





Tissue planes are difficult to define in the postoperative setting.

The stoma (arrowed) included within the treated volume.

RT Adverse Events

Time

- Early (acute)
- Late (chronic)

- Skin
- Mucosa
- Spinal cord
- Parotid


Thank You

http://scholar.cu.edu.eg/?q=ashrafhassouna

Publications

Bio

Classes

Images

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