General Principles of Head & Neck Radiotherapy

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Disclosure

- I have no financial disclosures or conflicts of interest with the presented material

Background

- Radiation: energy that travels through matter or space

- Electromagnetic radiation
  - radio waves, microwaves, light, UV, X rays, and gamma rays

- Ionizing radiation: sufficient energy to ionize atoms or molecules

- Gray (Gy) = Joule/kg = absorbed dose of energy
  - Sievert (Sv) = absorbed dose x a radiation weighting factor

Radiobiology for the Radiologist.
Hall and Giaccia. 7th edition

The 4 Rs of Radiobiology

- Repair of Sublethal Damage

- Re-assortment of cells within the cell cycle
  - Most sensitive in late G2/M phase

- Repopulation
  - Treatment with cytotoxic agent, including radiation, can lead to tumor cells dividing faster than before. Seen in H&N and cervical cancer

- Reoxygenation
  - Tumor hypoxia can lead to radio-resistance

Radiobiology for the Radiologist.
Hall and Giaccia. 7^{th} edition

Fractionation

- Standard Fractionation: 1.8 – 2 Gy per fraction, with 5 fractions per week, for 5 or more weeks.

- Hypofractionation: > 2 Gy per fraction
    - Moderate: 50 Gy in 20 fractions, 70 Gy in 28 fractions
    - SBRT: 50 Gy in 5 fractions

- Hyperfractionation: small fraction sizes, often given more than once a day, over the same duration as standard fractionation

- Accelerated fractionation: Course of radiation therapy is given over a shorter period of time

CT Simulation

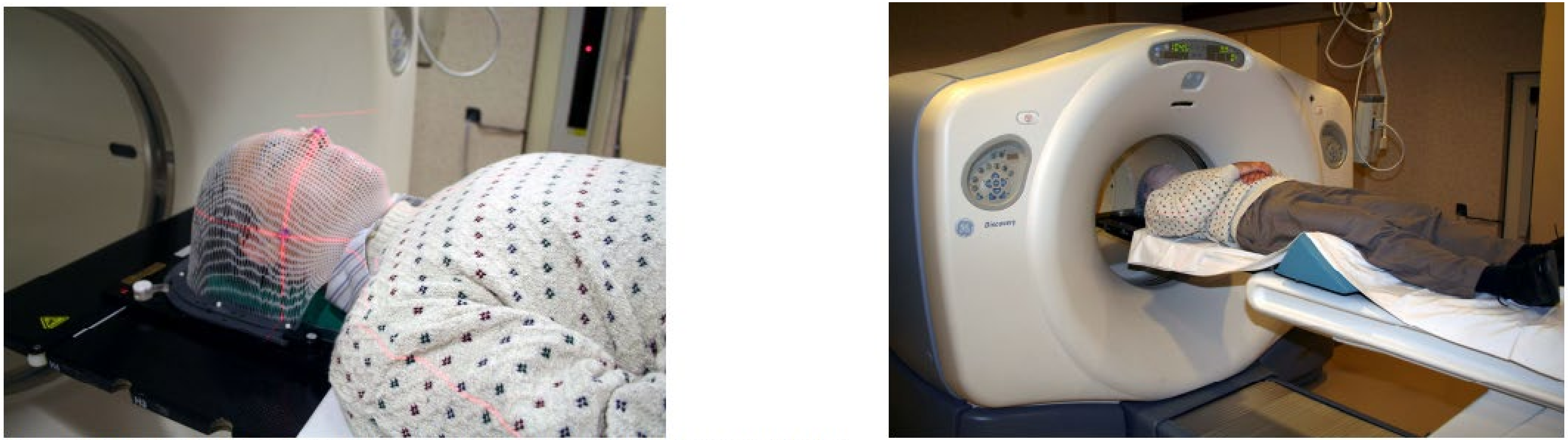


Figure B.2 Left: Patient alignment using lasers; Right: CT images acquisition.

IAEA-TECDOC 1588

Image-Guided Radiation Therapy (IGRT)

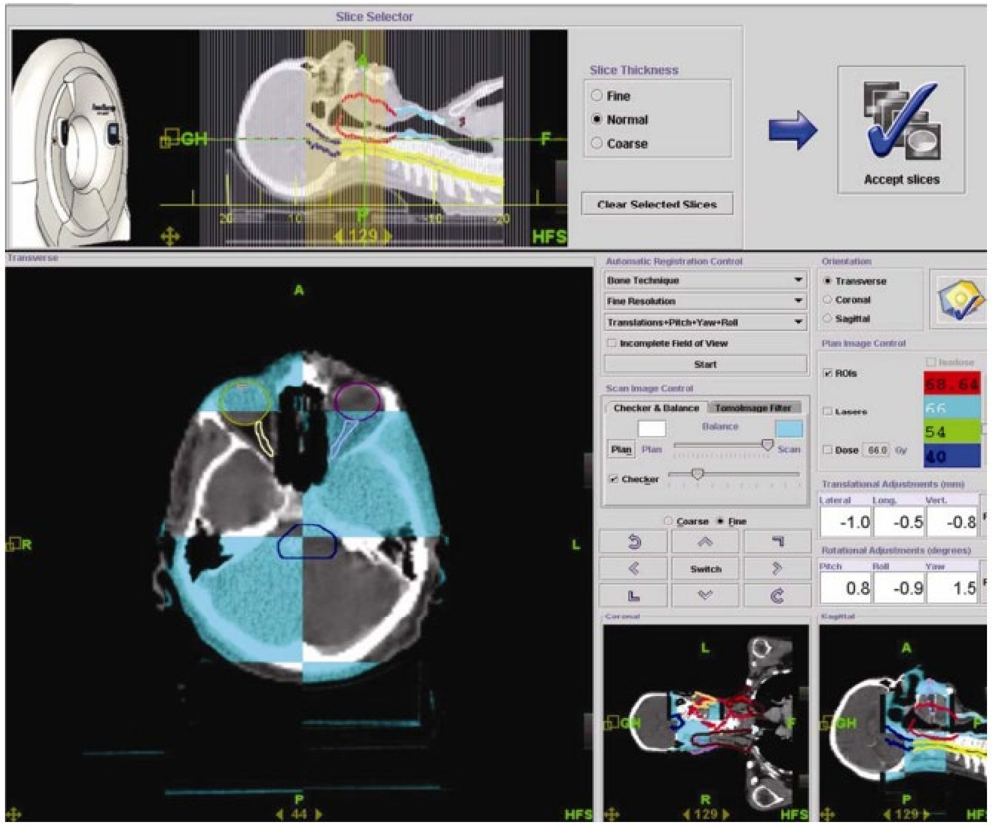
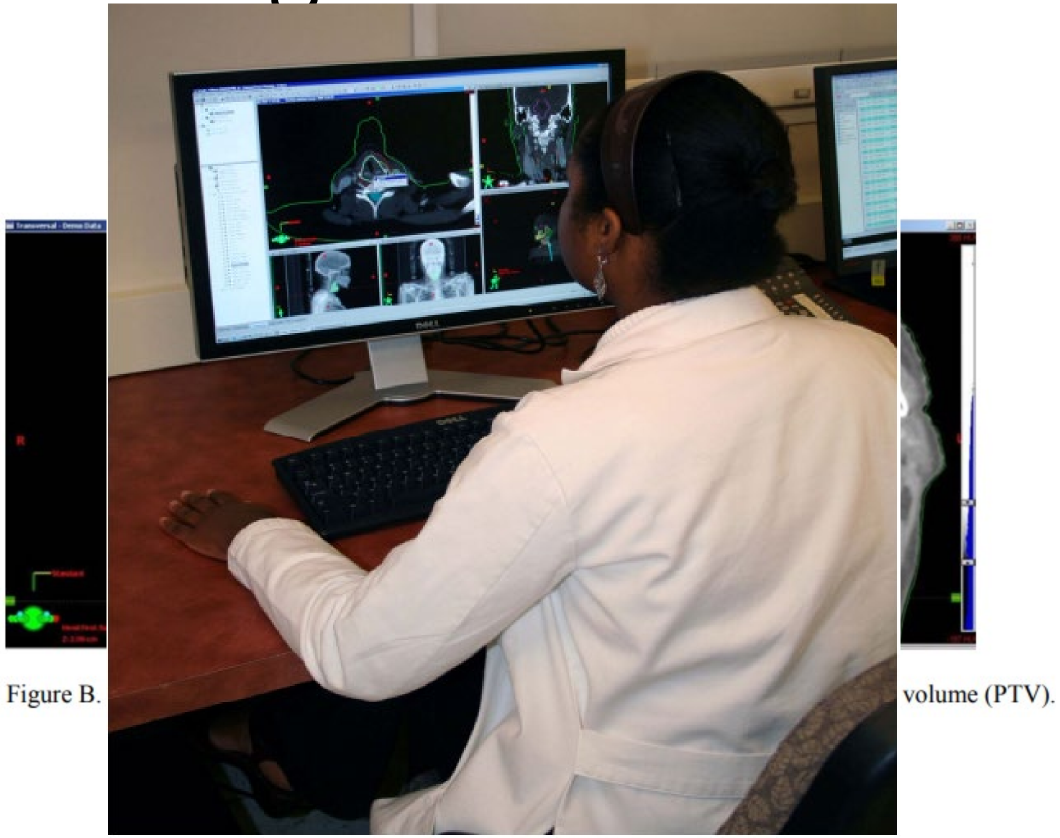


Fig. 6 Co-registration of planning kVCT (grayscale) with daily acquired MVCT images (light-blue) prior to delivery. Set-up errors in lateral, longitudinal, vertical directions (translational displacements) and rotational axis (roll) can be corrected by applying the shifts automatically

Tejpal et al. Indian J Surg Oncol 1(2):166–185.
2010. DOI: 10.1007/s13193-010-0030-x

Target Delineation



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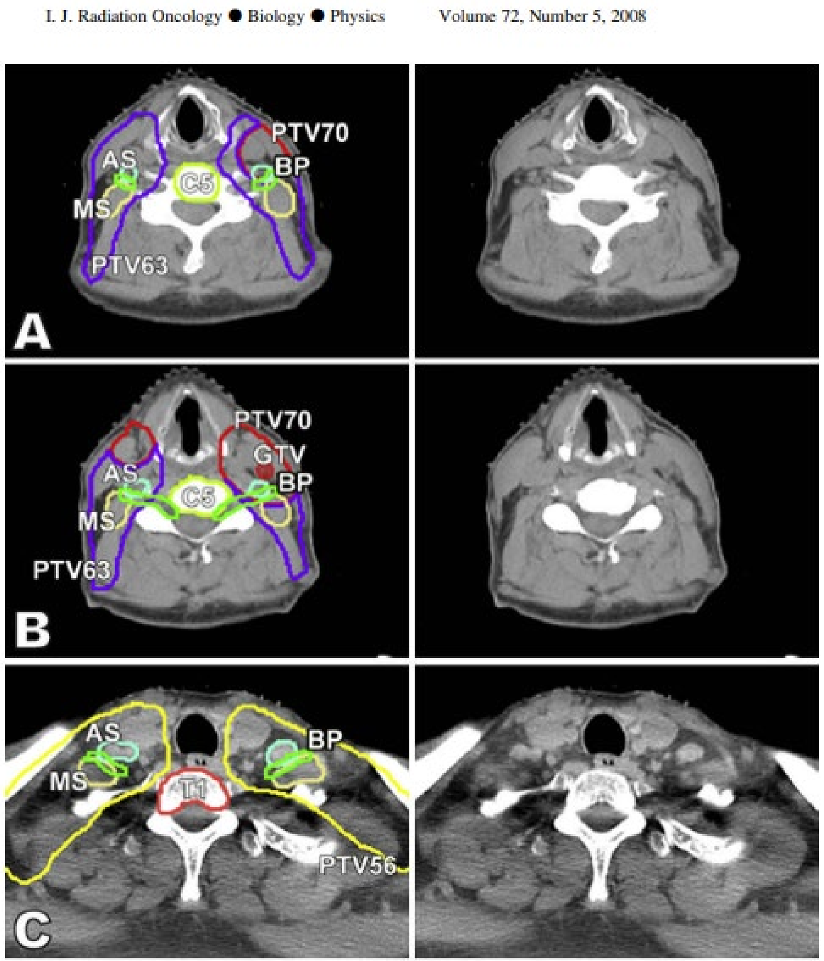
Brouwer et al. Consensus Delineation Guidelines for Head and Neck OARs. Radiotherapy and Oncology, 2015-10-01, Volume 117, Issue 1, Pages 83-90

Radiation Planning for Head and Neck Cancer

- Perfect World
  - Full dose to the tumor
  - No dose to adjacent critical structures

Radiation Planning for Head and Neck Cancer

- 30-35 fractions
- Gross tumor: 70 Gy
- +SM and/or ENE: 66 Gy
- Operative Bed: 60 Gy
- At risk lymph nodes: 54-63 Gy*



Hall et al. 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. IJROBP 2008

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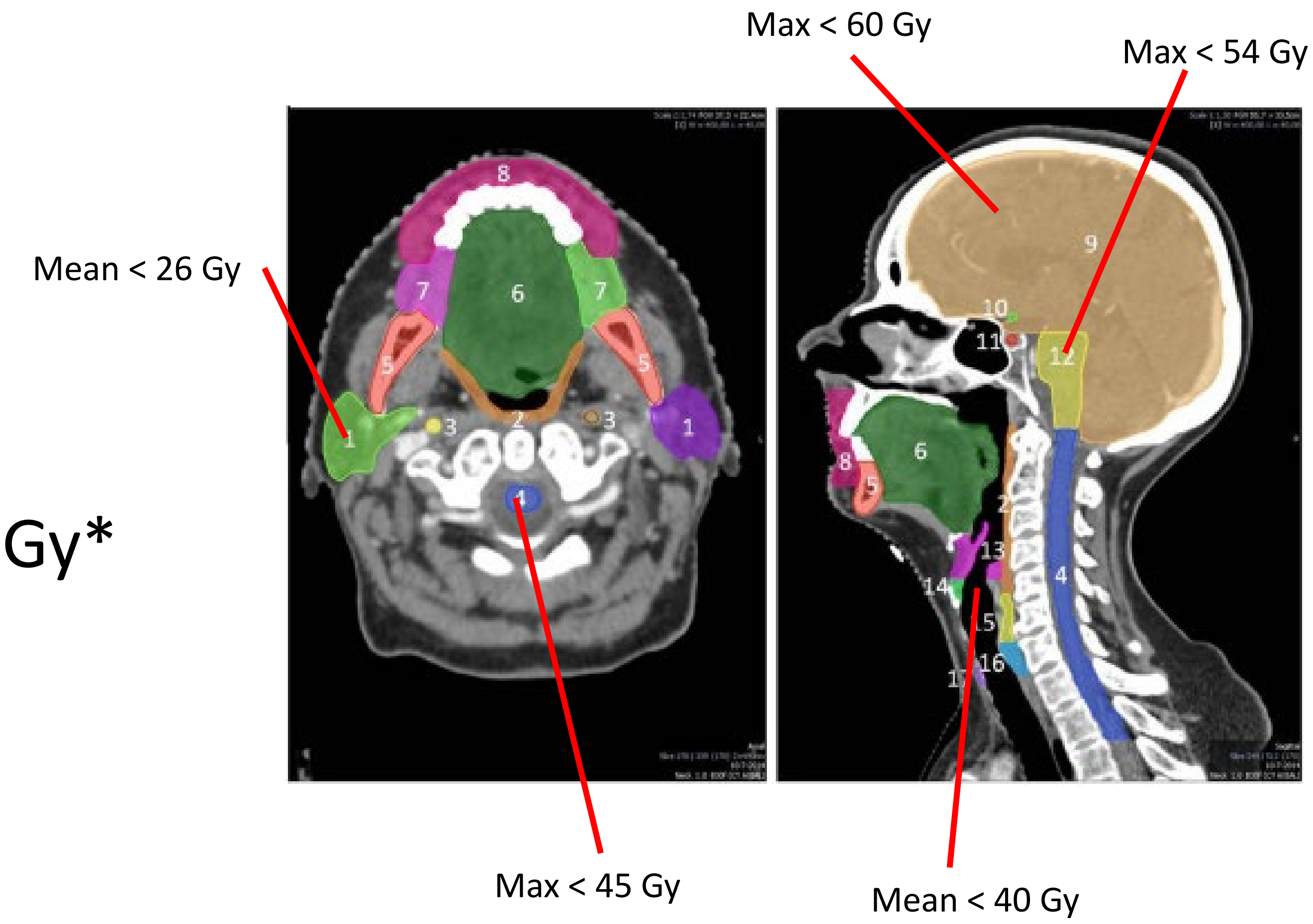


Brouwer et al. Consensus Delineation Guidelines for Head and Neck OARs. Radiotherapy and Oncology, 2015-10-01, Volume 117, Issue 1, Pages 83-90

Radiation Techniques

- 2D Radiotherapy
- 3D Conformal
- Intensity modulated radiotherapy (IMRT)
  - Step and Shoot
  - VMAT
- Proton

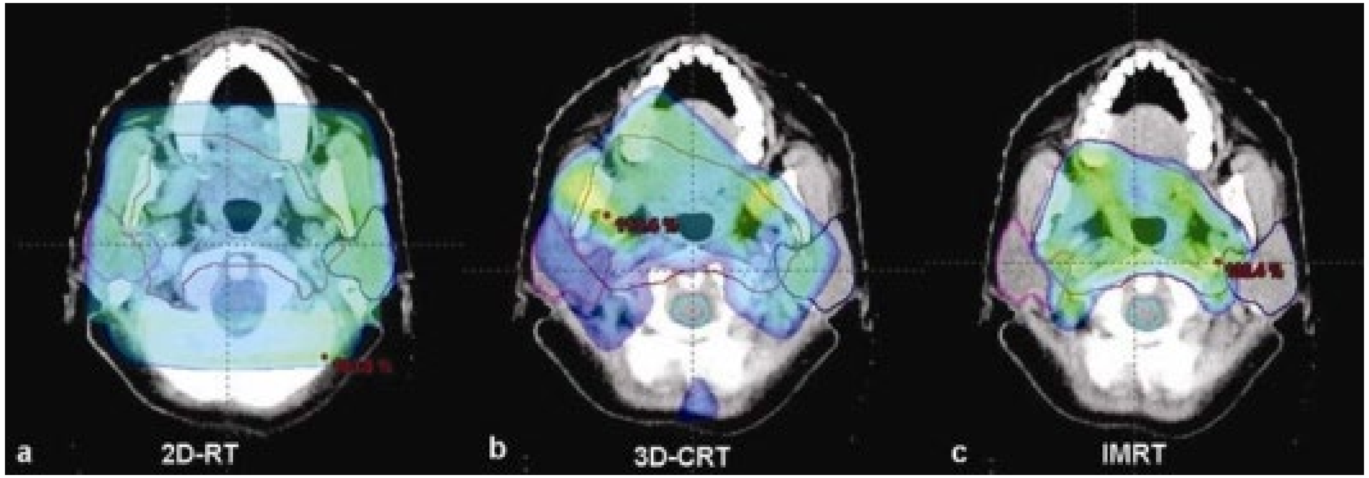


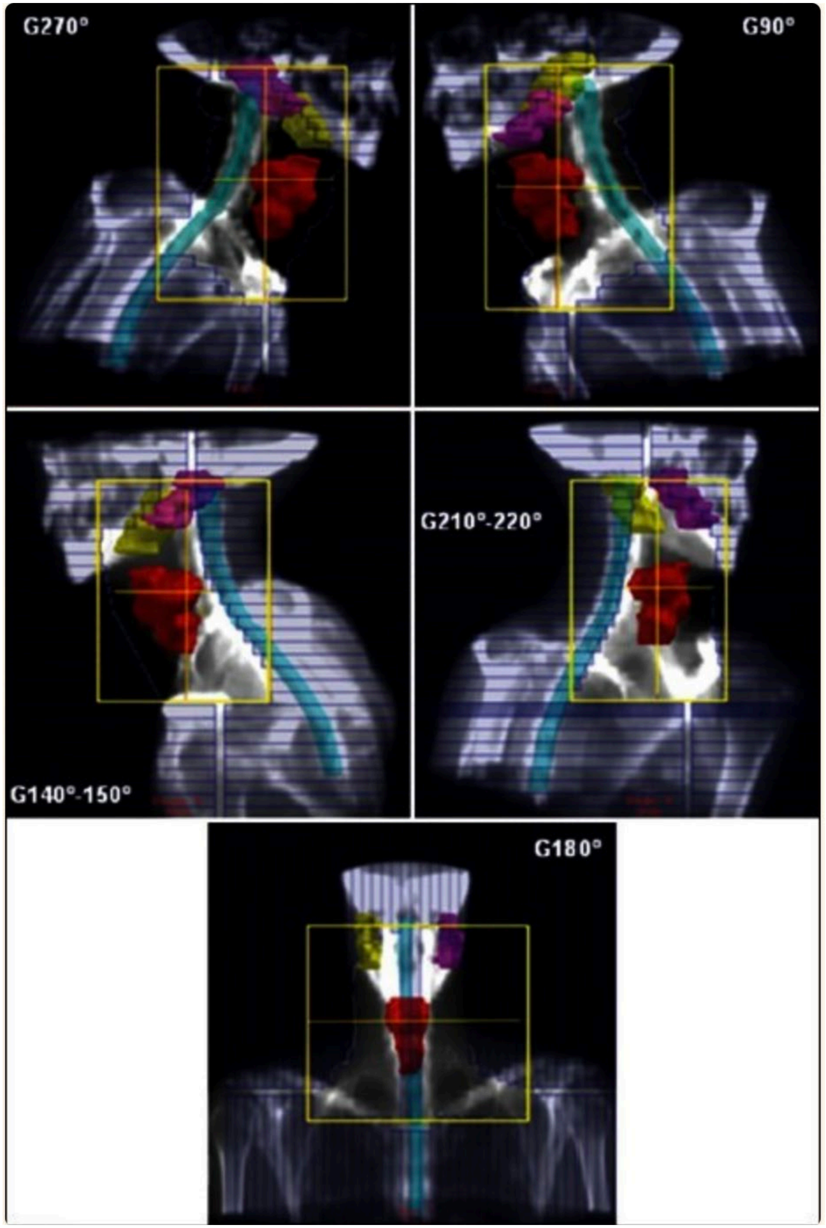
Fig. 1 Axial planning CT slice showing typical dose-wash of (a) conventional radiotherapy (2D-RT); (b) 3D-CRT; and (c) IMRT plan for head-neck cancer. Note the progressive high-dose conformation to the target volume and sparing of surrounding normal structures

Tejpal et al. Indian J Surg Oncol 1(2):166–185.
2010. DOI: 10.1007/s13193-010-0030-x

3D Conformal Radiation

IAEA definition

- the design and delivery of radiotherapy plans based on 3-D image data with treatment fields individually shaped to treat only the target tissue



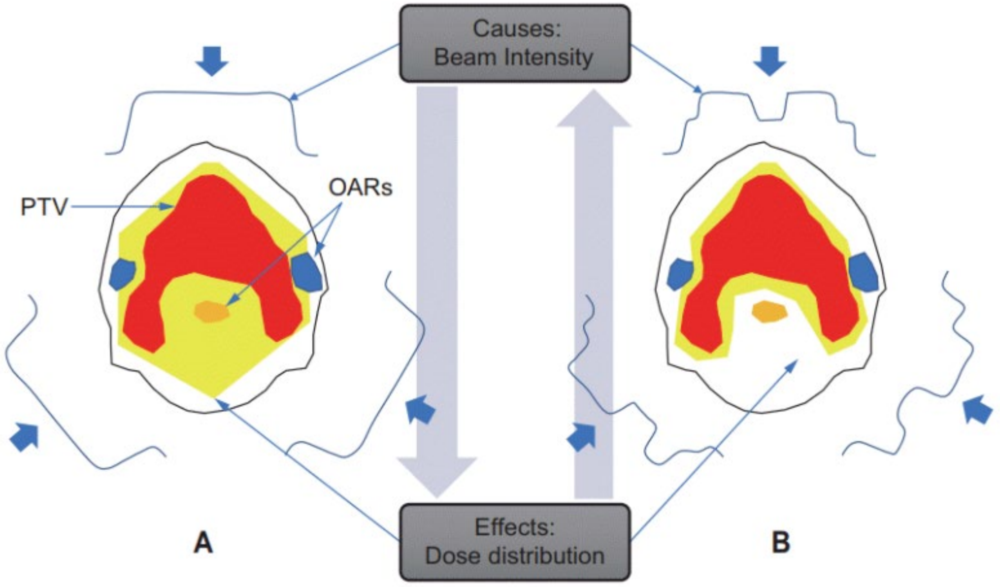
Herassi et al J Med Phys. 2013 Apr;38(2):98-105.
doi: 10.4103/0971-6203.111331.

Intensity Modulated Radiotherapy

- IAEA: dose plan and treatment delivery that is optimized using inverse planning techniques for modulated beam delivery
- Incorporates 3D planning (using 3-dimensional imaging for target planning)

Intensity Modulated Radiotherapy

- Forward planning: beams are placed first and the dose is subsequently calculated.
  - Energy (6MV vs 18MV),direction, size, shape, angle
- Inverse planning: optimum beam distribution is determined by minimizing/ maximizing objective functions (dose to normal tissue and target volumes)

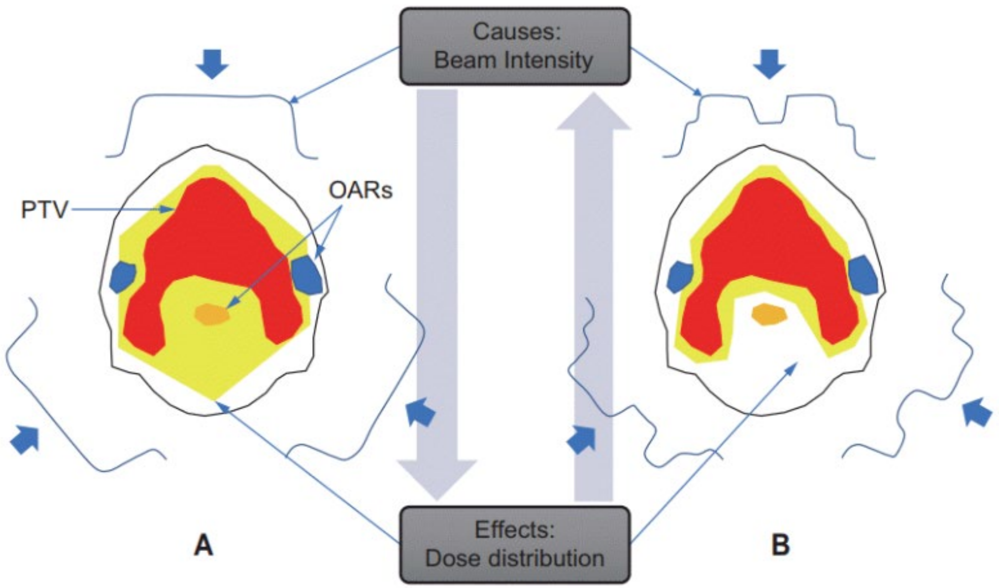


Cho. Radiation Oncology Journal 2018; 36(1): 1-10.
DOI: https://doi.org/10.3857/roj.2018.00122

Chui, Spirou Med Dosim. 2001. doi: 10.1016/s0958-3947(01)00069-3.

What do you gain with IMRT?

- Plans look better
- Increases treatment planning times
- Longer treatment times
- Higher risk of geographical miss?
- Does this lead to better tumor control? Less side effects?



Cho. Radiation Oncology Journal 2018; 36(1): 1-10.
DOI: https://doi.org/10.3857/roj.2018.00122

PARSPORT Trial – Lancet Oncology 2011

- Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial
- T1-4,N0-3,M0 pharyngeal squamous cell carcinoma
- n=94, Randomized 1:1 to conventional radiotherapy or IMRT
- Results
  - 12 months, grade 2 or worse xerostomia was significantly lower in the IMRT group (38% vs 74%, p=0.0027)
  - At 24 months: no significant differences were seen between randomized groups in non-xerostomia late toxicities, locoregional control, or overall survival

Nutting et al. Lancet Oncology 2011.
DOI:https://doi.org/10.1016/S1470-2045(10)70290-4

Three-dimensional conformal radiotherapy (3D-CRT) versus intensity modulated radiation therapy (IMRT) in squamous cell carcinoma of the head and neck: A randomized controlled trial

- n=60, T1-3,N0-2b SCCa of opx, lnx, hpx to 3D vs IMRT
- Primary endpoint: G2+ acute salivary toxicity

- Significantly less G2+ with IMRT (59% v 89%)
- IMRT also had less late xerostomia and subcutaneous fibrosis
- No difference in LRC or OS

T. Gupta et al. Radiotherapy and Oncology 104 (2012) 343–348

Retrospective Studies

- Decreased PEG tube dependence at 1 year with IMRT compared to 3D CRT
  - *Lohia et al. JAMA Otolaryngol Head Neck Surg. 2014;140(4):331-337. doi:10.1001/jamaoto.2013.6777*
- Decreased grade 3 or greater mucositis and skin toxicity
  - *Ghosh et al. J Clin Diagn Res. 2016. doi: 10.7860/JCDR/2016/21457.8583*

Why does this guy keep talking about the dentist?

University of Michigan, uniform policy:

- extracting high risk, periodontally involved and non restorable teeth
- fluoride supplements
- guards to reduce electron backscatter off metal restorations

- *Ben-David et al. IJROBP 2007. doi: 10.1016/j.ijrobp.2006.11.059*

Ben-David et al. IJROBP 2007

- Particular attention to teeth to receive > 50 Gy
- Teeth with mobility, significant pocketing, advanced recession, furcation involvement (periodontal disease causing bone damage) are extracted.
- non-restorable caries, or caries that extended to the gum line, teeth with large, compromised restorations with significant periodontal attachment loss (pocketing >5 mm), and those with severe erosion or abrasion were extracted
- Start of RT was delayed at least 14 days after extraction to allow healing.

Ben-David et al. IJROBP 2007

- Mandible Dose
  - Max < 72 Gy
- Dental Guards
  - Heavily restored with metallic restorations were provided trays made from polyvinyl siloxane putty to reduce electron backscatter off the metal into adjacent soft tissue.
- Patient education
  - Daily high concentrated fluoride (1.1% neutral sodium fluoride)
    - Trays or tooth paste

Proton Therapy

Bragg Peak

Leeman et al. Lancet Oncol 2017

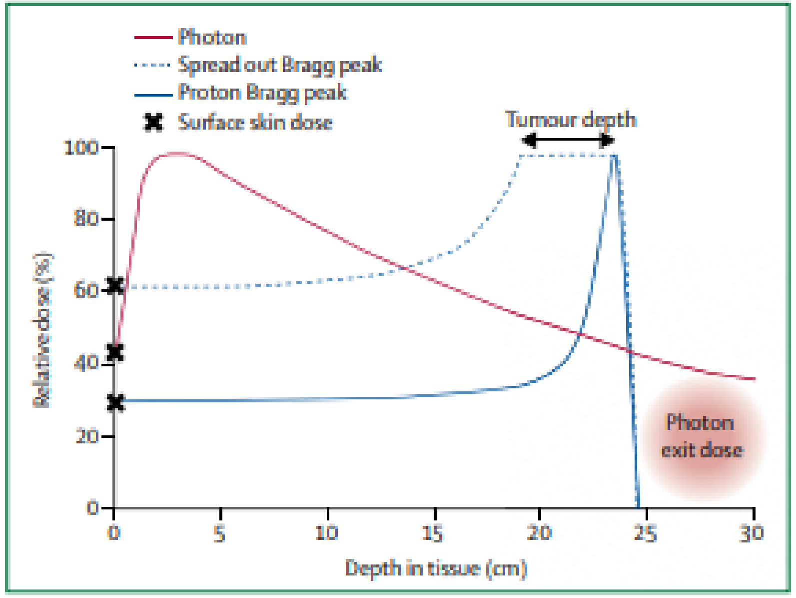


Figure 1: Depiction of depth-dose curves for photon and proton beams
The proton Bragg peak allows for elimination of exit dose. The modulated proton beam results in a spread out Bragg peak with loss of skin-sparing.

McGowan, Lomax et al. Br J Radiol 2013

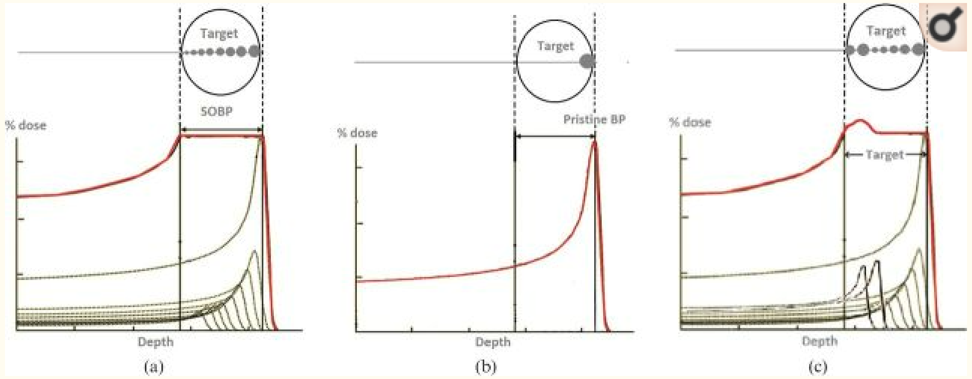


Figure 1

Schematic of Bragg peak delivery along a single profile through a target. (a) A flat spread-out Bragg peak (SOBP) is achieved by placing spots with increasing weights throughout the target to produce a uniform field, as used in passive scattering and single-field uniform dose. (b) Only the most distal single pristine Bragg peak (BP) is used for distal-edge tracking. (c) Optimally weighted spots are positioned throughout the volume to achieve fields with non-uniform doses for three-dimensional intensity-modulated particle therapy.

Leeman et al. Lancet Oncol 2017

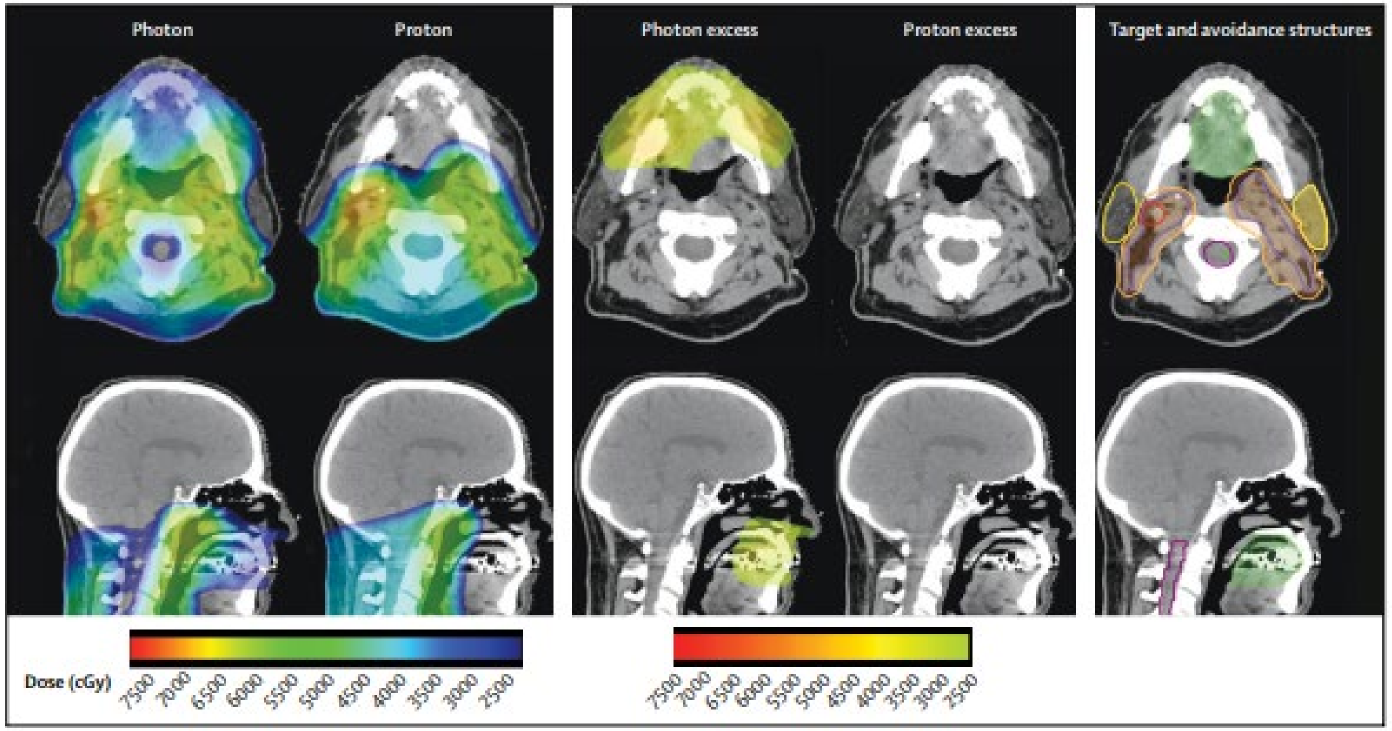


Figure 5: Postoperative radiation plans for a patient with squamous cell carcinoma of the left tonsil after transoral robotic surgery
Photon and proton plans are shown as well as plan differences showing excess dose with photon and proton techniques. Minimum dose shown is 2500 cGy. Better sparing of the anterior oral cavity is achieved with intensity modulated proton therapy. Target and avoidance structures are displayed. Green=oral cavity. Yellow=parotid glands. Magenta=spinal cord. Blue=clinical target volume (60 Gy). Orange=planning target volume (60 Gy). Red=planning target volume (70 Gy).

HN004: 2022 ASTRO

- Phase II, stage III-IV squamous cell carcinoma of the larynx, hypopharynx, oral cavity, oropharynx and selected stage I-II p16+ oropharynx with a contraindication to cisplatin.
  - Assigned 2:1 to receive durvalumab or cetuximab + 70 Gy in 35 fractions over 7 weeks
- Primary endpoint: PFS
- Closed early following interim futility analysis, with 2y PFS 51% for durvalumab vs 66% for cetuximab.
- 2y LRF 32% with durvalumab vs 15% with cetuximab

Mell LK, Torres-Saavedra P, Wong S, et al. Radiotherapy with durvalumab vs. cetuximab patients with locoregionally advanced head and neck cancer and a contraindication to cisplatin: phase II results of NRG-HN004. Presented at the 2022 American Society of Radiation Oncology Annual Meeting; San Antonio, TX; October 23-26, 2022. Abstract LBA02. Accessed October 24, 2022.

Thank You