Difficult Base of Tongue Cancer Cases: **MD Anderson Cancer Center**

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Head and Neck Radiation Oncology

2014

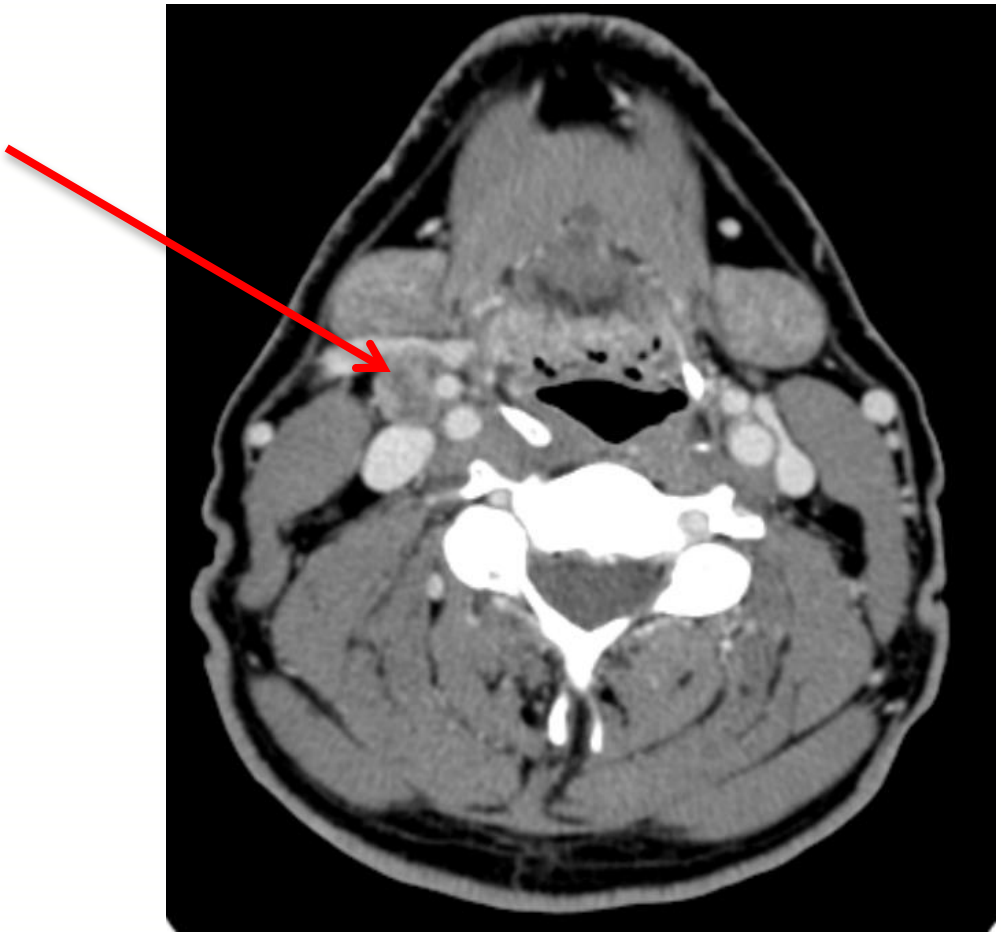
BOT Cases

- **Case 1**: Radiation therapy alone
- **Case 2**: Induction chemotherapy → chemoradiation therapy

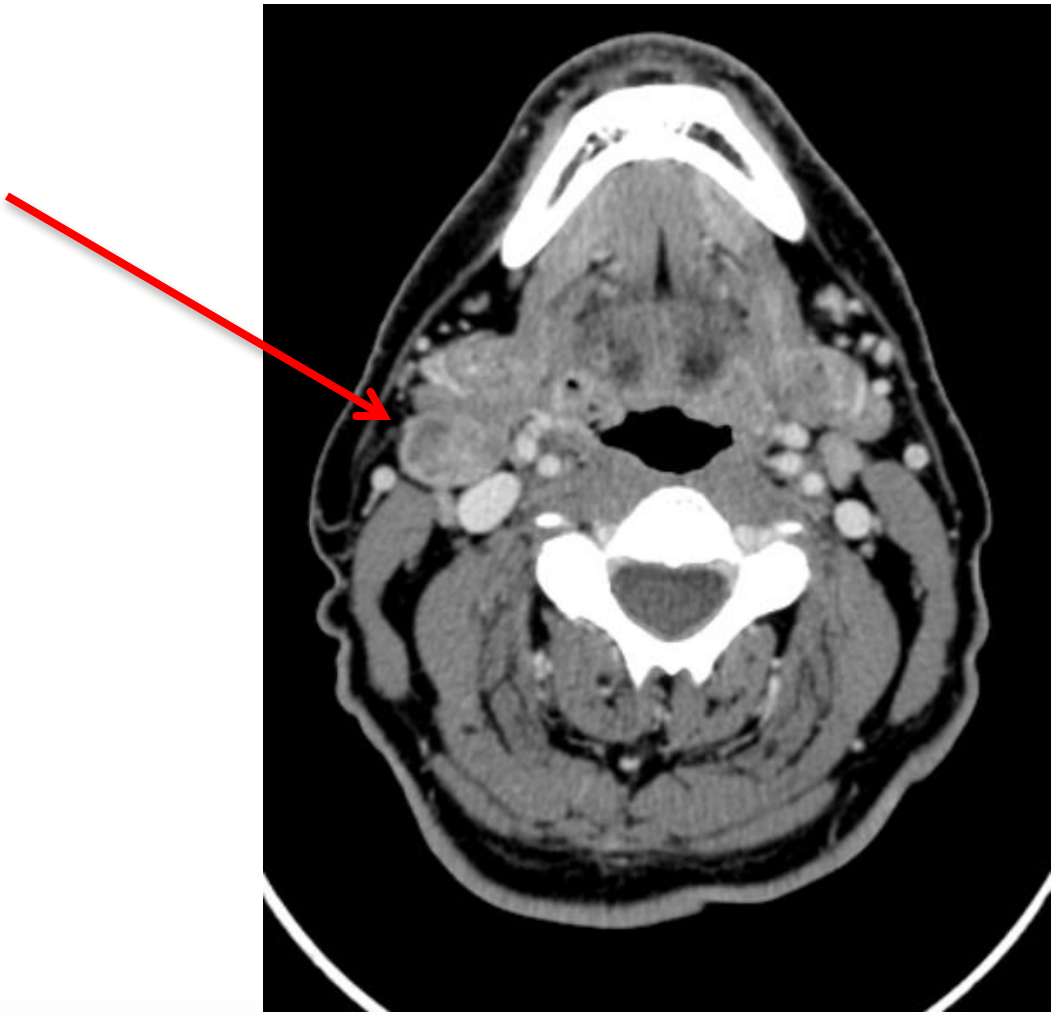
Case 1

- 60 year old male
- Several month history of right neck mass, no other symptoms
- FNA -> squamous cell carcinoma
- EUA and biopsy showed primary site to be right BOT, p16 positive
  - p16 positivity accepted as surrogate for HPV positivity for oropharynx cancer

CT neck



CT neck



Work-up

- H and P including H and N exam, mirror and fiberoptic exam
- Biopsy
- HPV testing
- Chest imaging
- CT with contrast and/or MRI with contrast of primary/neck
- Consider PET/CT for Stage II-IV
- Dental evaluation
- Nutrition, speech, swallow, audiogram as indicated
- EUA with endoscopy as indicated
- Preanesthesia studies
- Multidisciplinary evaluation

Case 1 – Treatment options

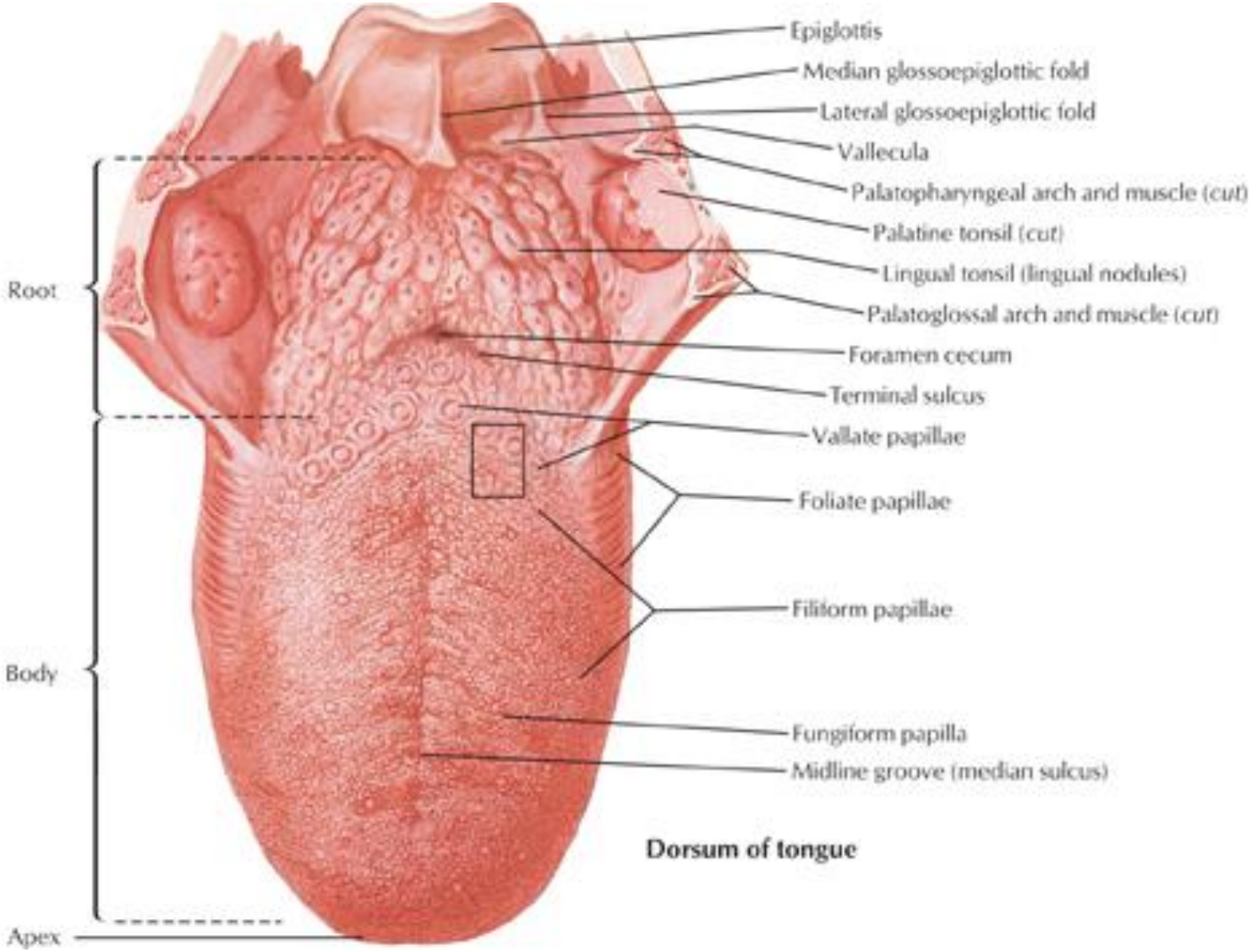
- **T1N2b** right base of tongue squamous cell carcinoma
- At MDACC, for T1-2, N0 – small N2b → we consider the following treatment options:
  - RT + systemic therapy
  - Definitive RT (small volume disease)
    - Post RT neck dissection if residual
  - Resection of the primary +/- ipsilateral or bilateral neck dissection
    - Post RT or CRT as indicated by pathology
  - Multimodal clinical trials

Case 1

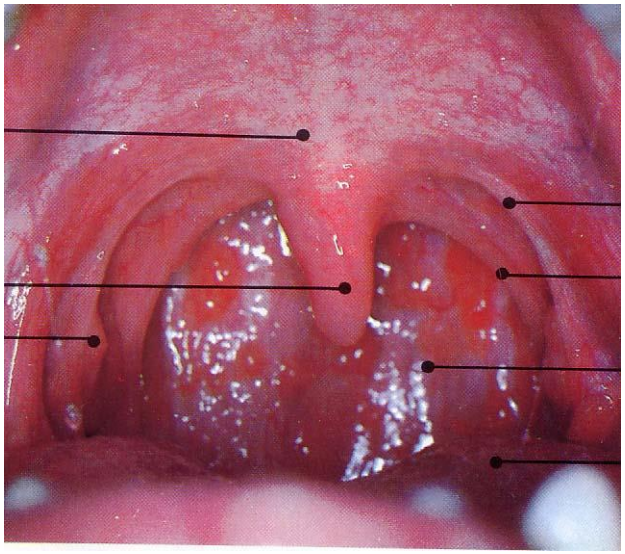
- T1N2b right base of tongue squamous cell carcinoma
- Treatment:
- IMRT to primary with margin and upper neck
  - 66 Gy in 30 fractions to primary and gross neck disease
  - 60 Gy for the involved neck (outside CTV1)
  - 54 Gy for contralateral neck and RP nodes
- Matched to low neck field at top of arytenoids:
  - 40 Gy in 20 daily fractions with larynx block
  - 10 Gy in 5 fractions with midline block
  - 10 Gy in 5 fractions for right neck boost LAO/RPO (node within 1cm of junction, but totally within IMRT fields)

Borders of Oropharnx

- Anterior: oral tongue
  - Circumvallate papillae separates oral and base of tongue
- Superior: hard palate/ soft palate junction
- Inferior: valleculae / hyoid bone
- Posterior: prevertebral muscles and vertebrae posterior to the pharyngeal wall


Epiglottis
Median glossoepiglottic fold
Lateral glossoepiglottic fold
Vallecula
Palatopharyngeal arch and muscle (cut)
Palatine tonsil (cut)
Lingual tonsil (lingual nodules)
Palatoglossal arch and muscle (cut)
Foramen cecum
Terminal sulcus
Vallate papillae
Foliate papillae
Filiform papillae
Fungiform papilla
Midline groove (median sulcus)
Root
Body
Apex
Dorsum of tongue

Anatomy



Slide courtesy: Shalin J. Shah, MD

OPX Staging

- T1: ≤ 2 cm
- T2: 2-4 cm
- T3: > 4 cm
- T4a: moderately advanced: invades larynx, extrinsic tongue muscles, medial pterygoid, hard palate
- T4b: very advanced: invades lateral pterygoid, lateral nasopharynx, skull invasion, carotid encasement

Staging

N1: single, ipsilateral, < 3 cm
N2a: single, ipsilateral, 3-6 cm
N2b: multiple, ipsilateral, < 6 cm
N2c: bilateral or contralateral, < 6 cm
N3: any > 6 cm

Stage I: T1N0
Stage II: T2N0
Stage III: T3N0 or T1-3N1
Stage IVA: T4aN0-1 or T1-4aN2
Stage IVB: T4b or N3
Stage IVC: M1

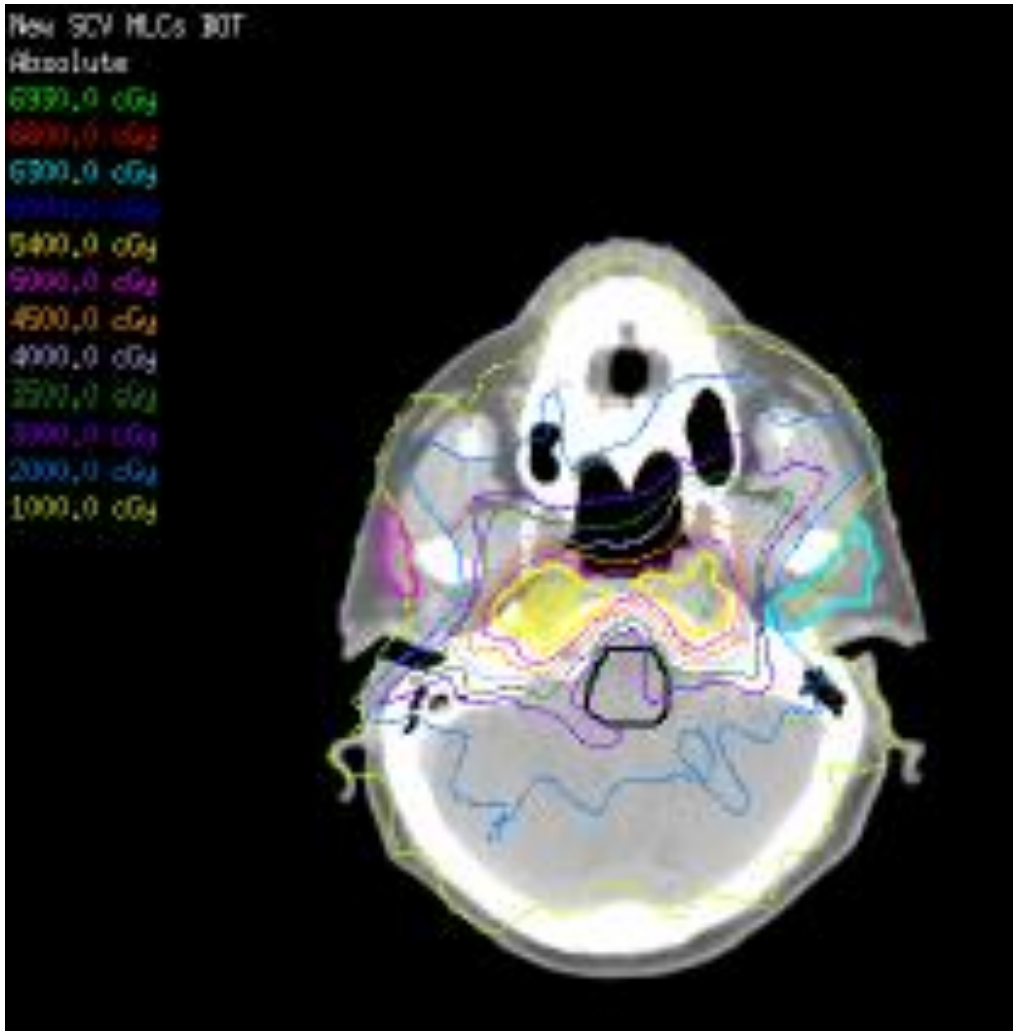
MDACC Management Options

In general, management options can be institution specific.

At MDACC, typically:

- Definitive radiation alone
  - T1-2N0-1 (small N2)
- Definitive chemoradiation
  - T2-T4N1-3
  - Cisplatin preferred; cetuximab 2nd line and being tested for equivalency to (RTOG); at MDACC cetuximab also used for small volume stage 3/4
- Induction chemotherapy followed by chemoradiation
  - N2c-3
  - In light of Paradigm and DECIDE negative trials, while induction is an option in NCCN guidelines, enthusiasm declining

Plan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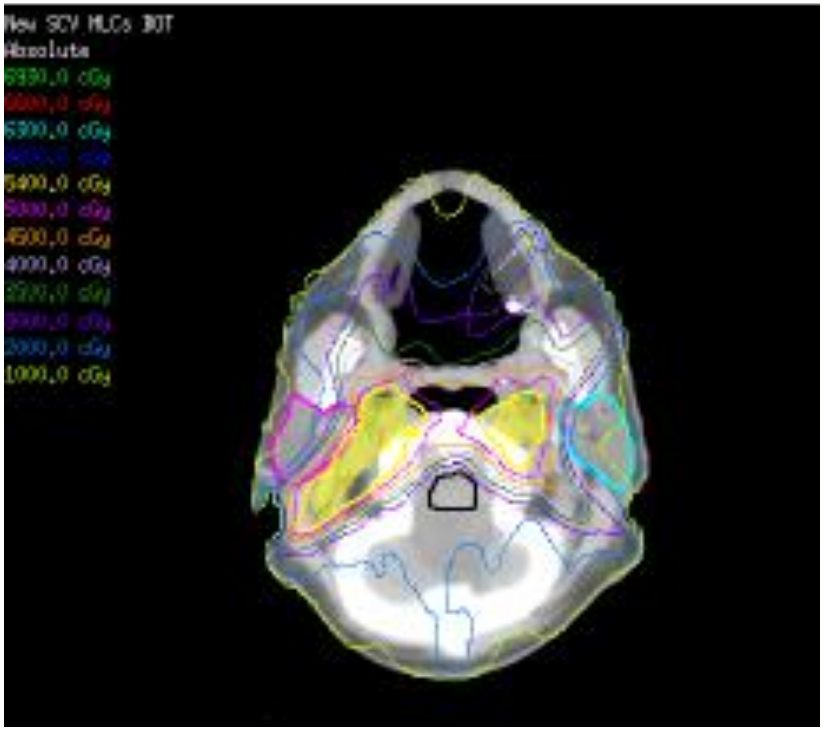
Plan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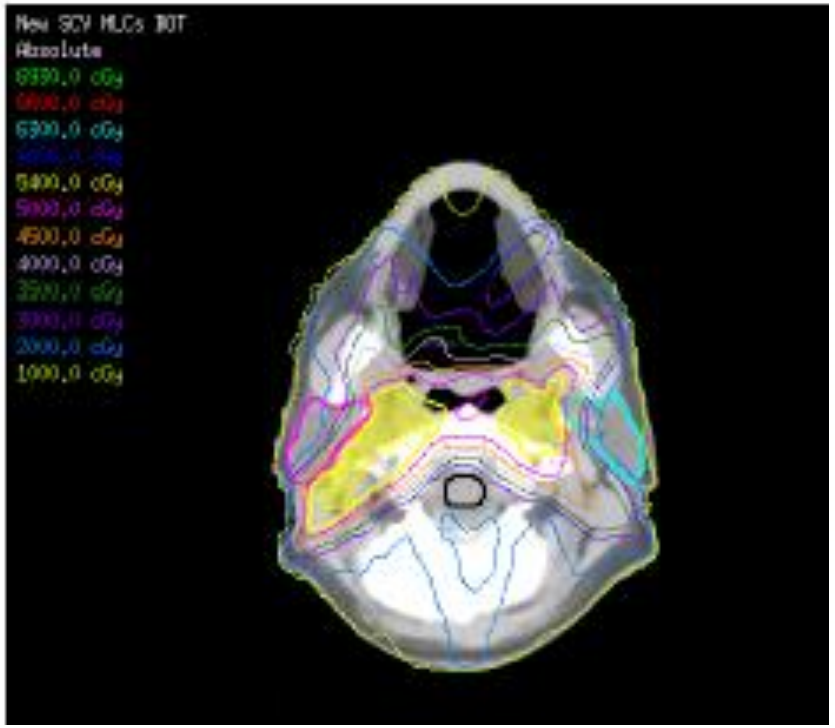
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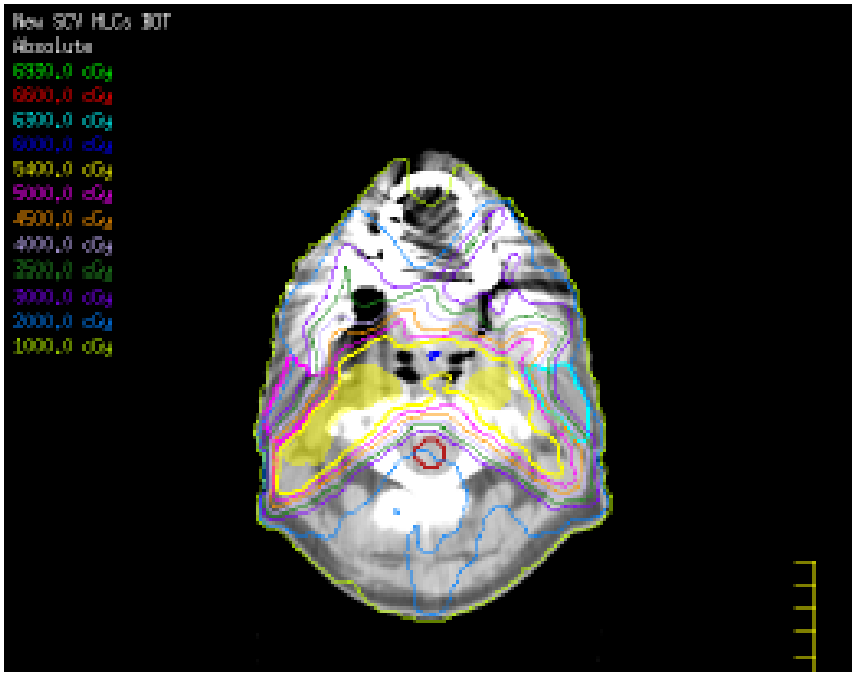
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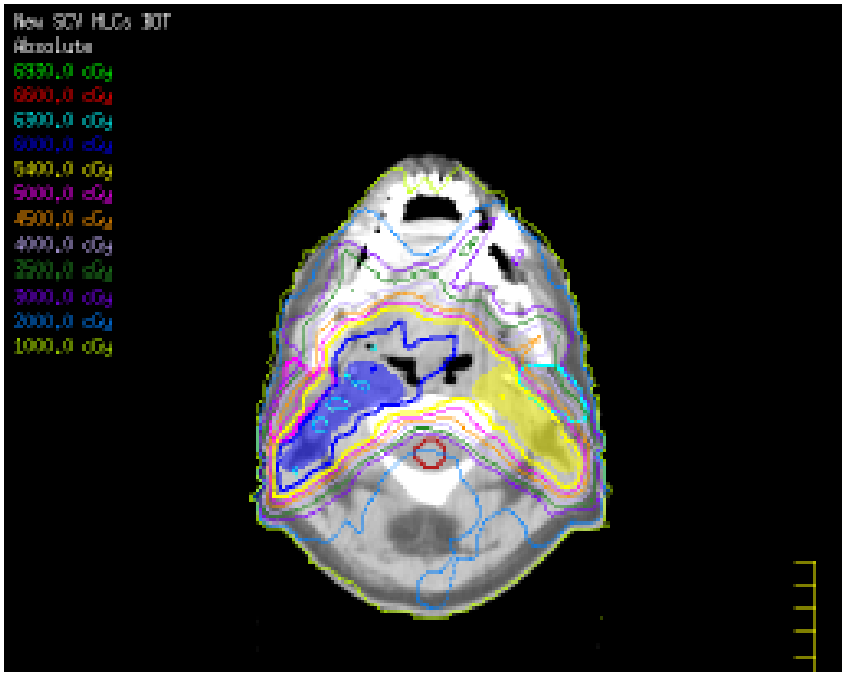
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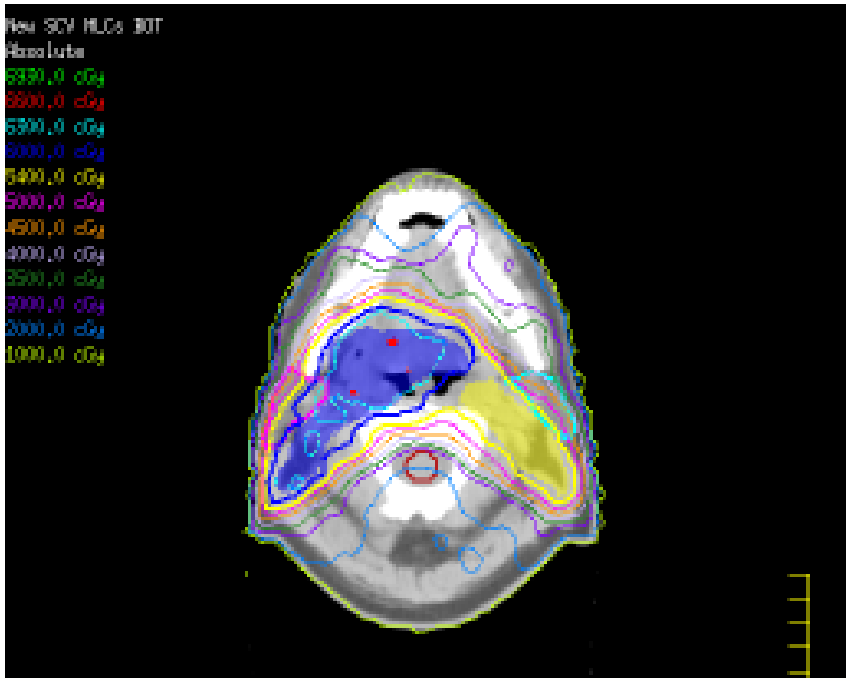
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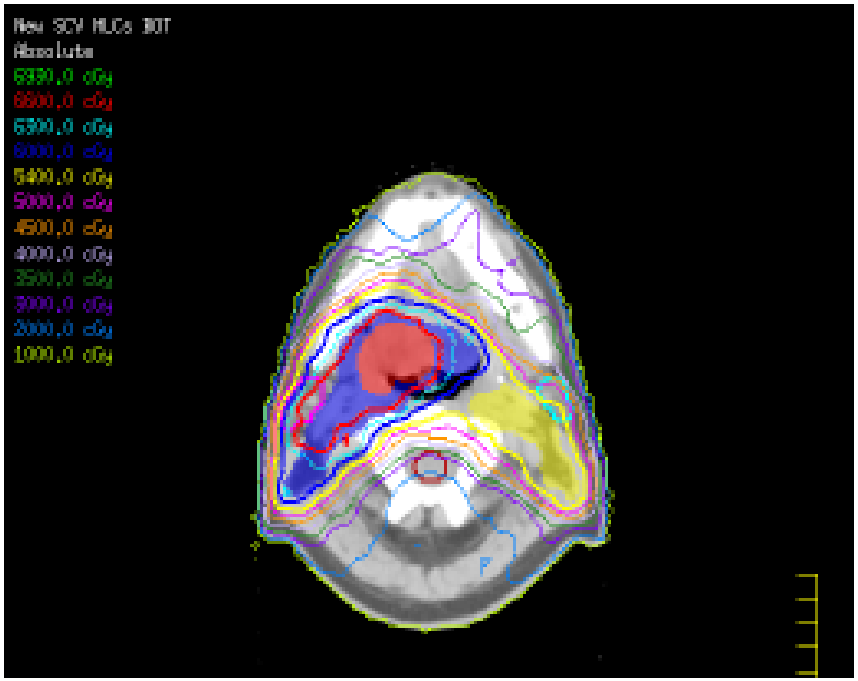
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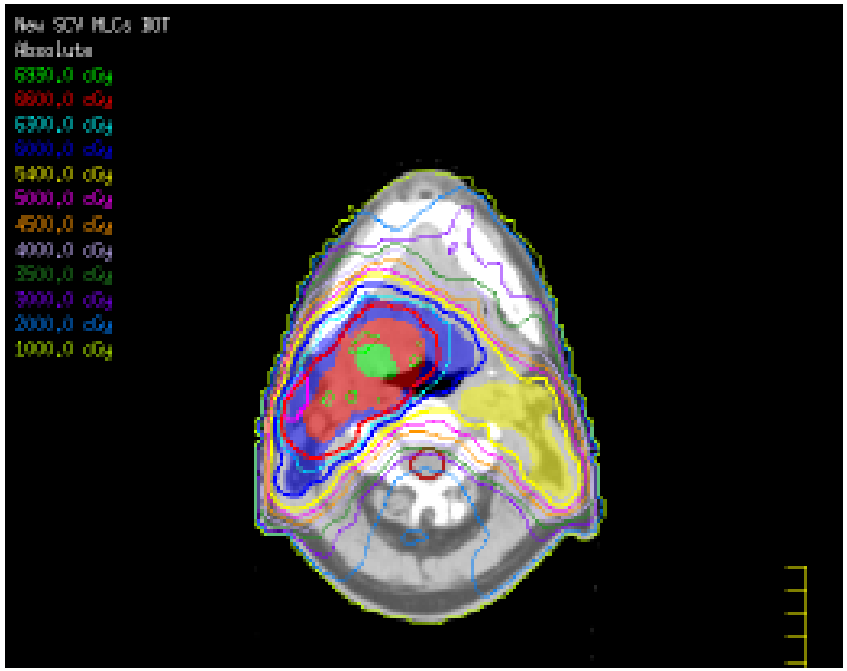
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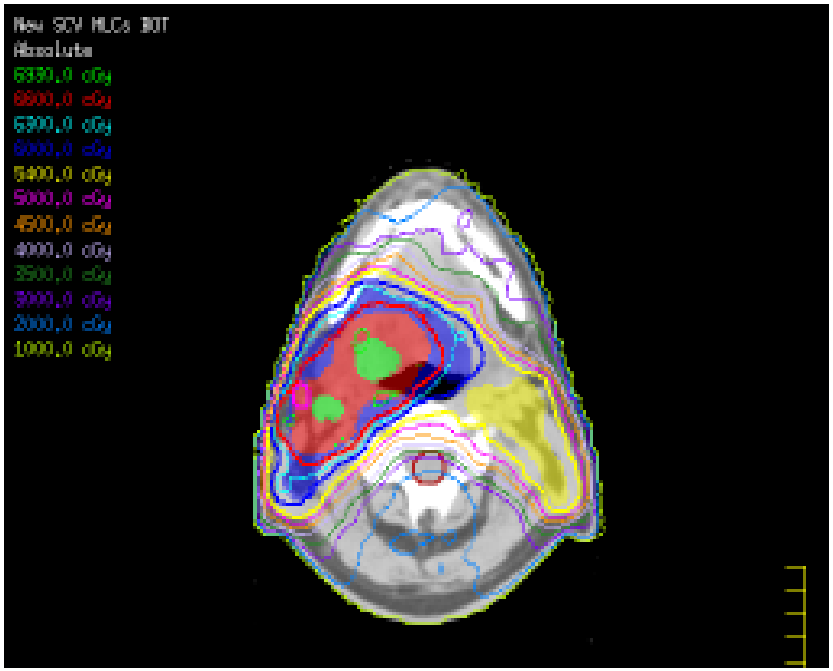
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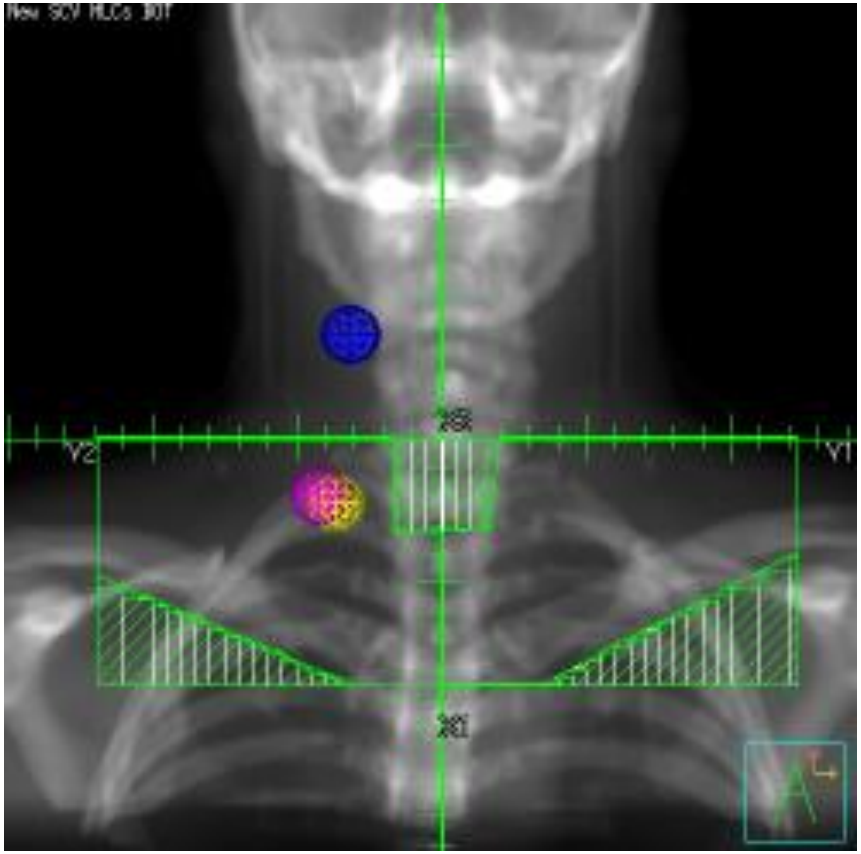

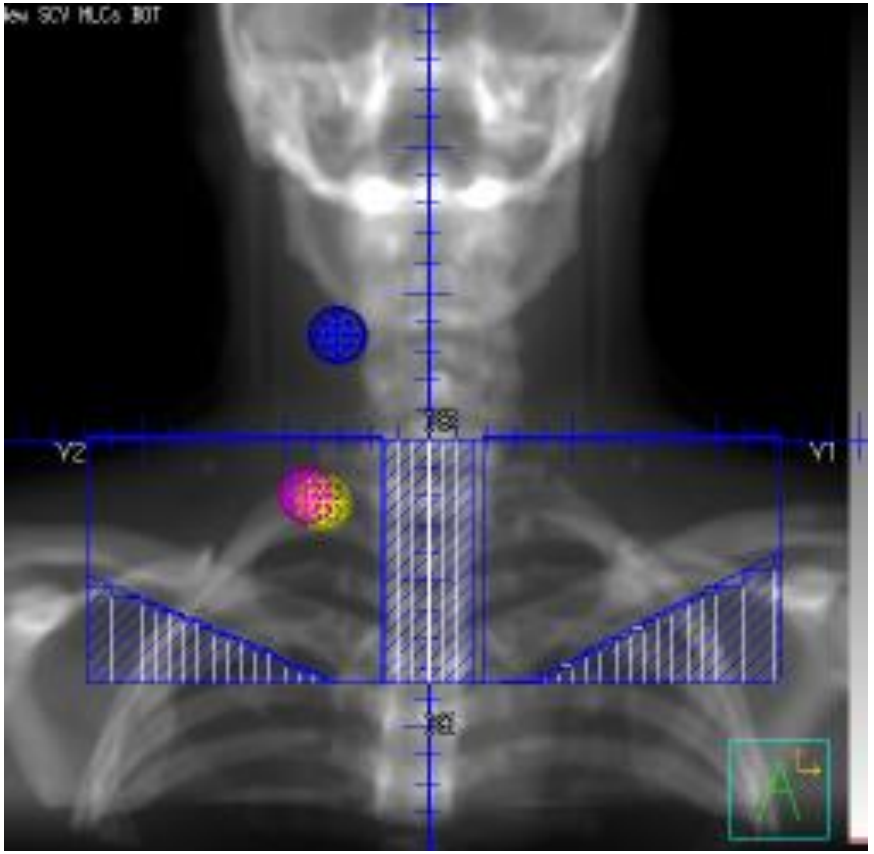

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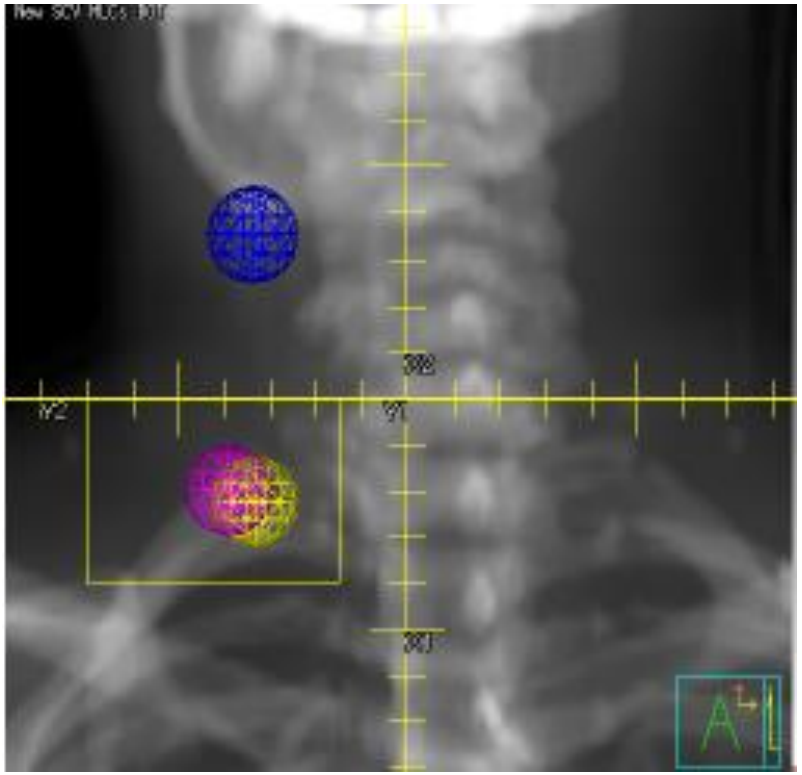

For discussion regarding whole field vs split field IMRT, please see “additional slides” at the end of the presentation


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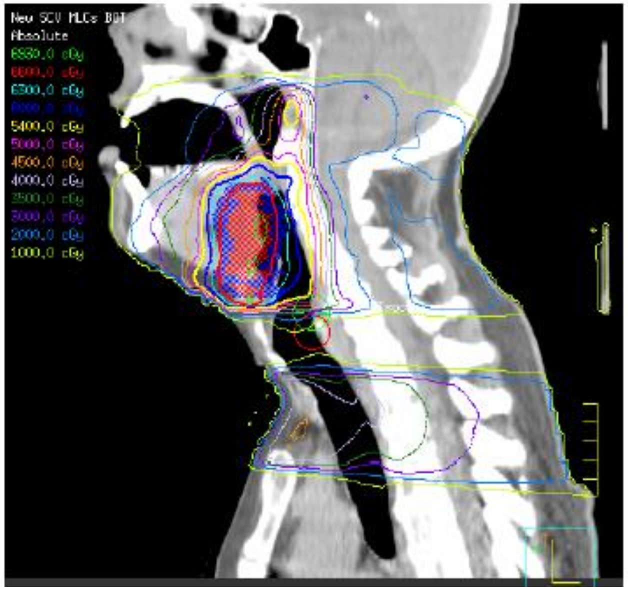
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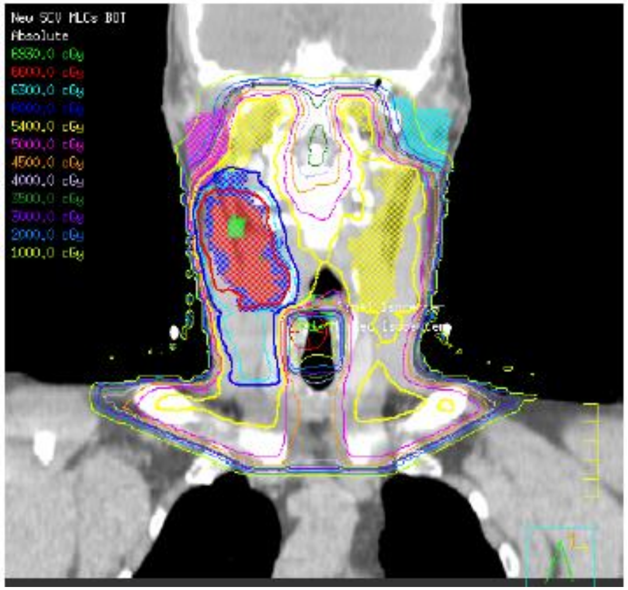
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Post-treatment restaging and re-evaluation

- H & P exam every 1-3 months for year 1; q2-4 months for year 2; q6 months until year 5, then yearly
- Consider baseline post-treatment imaging at 6-8 weeks after treatment (within 6 months), then as needed clinically (this practice may vary)
- Chest imaging as clinically indicated
- TSH q6-12 months if neck irradiated
- Speech/swallow, audiology, rehabilitation as needed
- Smoking cessation and alcohol counseling
- Dental re-evaluation as needed

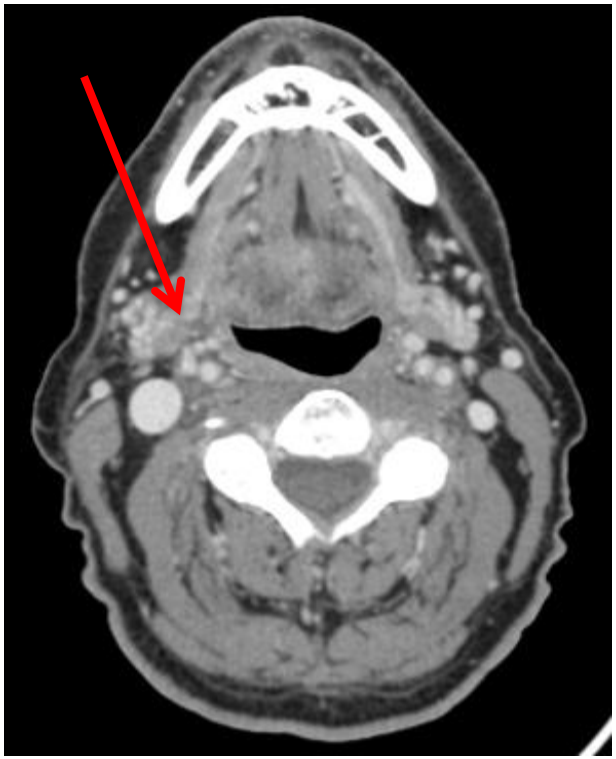
Post-treatment restaging and re-evaluation: PET/CT

- Consider PET/CT 8-12 weeks after finishing radiation therapy (approximately 12 weeks at MDACC)
- Re-evaluation for residual primary and cervical nodal disease

On Follow-up imaging…

Pre-treatment CT Neck

Post-treatment CT Neck



Post-treatment management

- If neck nodes remain enlarged or progressively increase in size, neck dissection may be required post-RT

Case 2

- 46 year old male
- Unhealing dental extraction
- Developed odynophagia, trismus, right sided jaw pain, right neck mass
- CT Head and Neck imaging obtained:

CT Head and Neck

CT Head and Neck

CT Head and Neck

CT Head and Neck

CT Head and Neck

CT Head and Neck Findings:

- Heavy involvement of the right tongue base with extension into the extrinsic tongue musculature
- Involvement laterally to the right retromolar trigone and mandibular gingiva (with mandibular destruction of an extensive nature)
- Extension upward to involve the tonsillopharyngeal wall and up into the nasopharynx
- Lateral extension through the parapharyngeal space and into the masticator musculature
- Extensive ipsilateral necrotic nodal metastases and several contralateral nodal metastases

Stage?

AJCC Stage Descriptions

- T4a - invades larynx, **deep/extrinsic muscles of the tongue**, medial pterygoid, hard palate, or mandible
- T4b - invades lateral pterygoid, pterygoid plates, **lateral nasopharynx**, skull base, or encases carotid

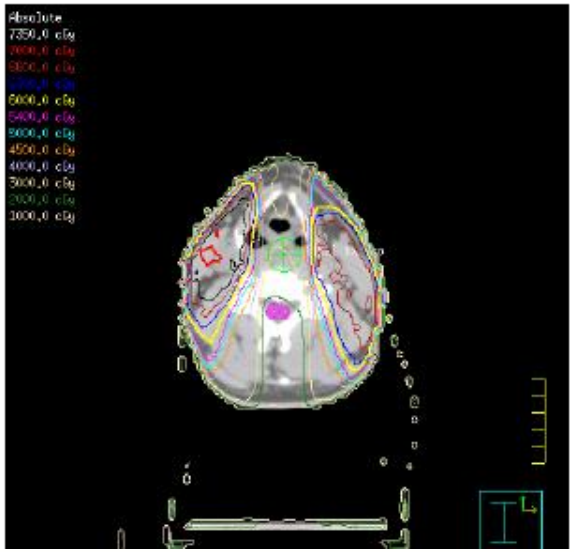
Stage: T4bN2c

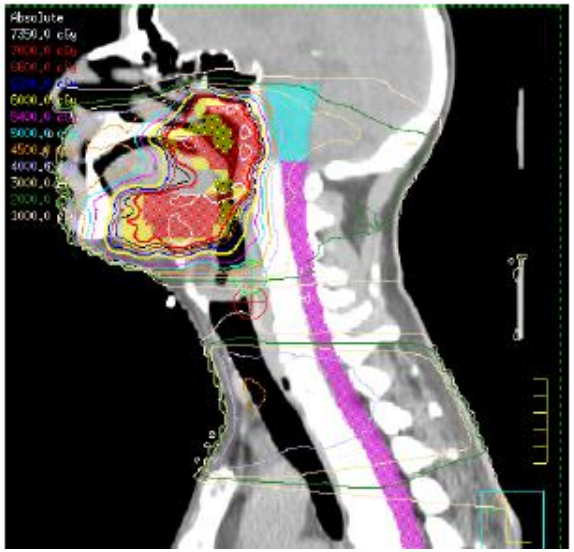
- Treatment options:
  - For N2-3 disease:
    - Concurrent chemoradiation
    - Induction chemotherapy followed by RT or chemoradiation
    - Surgery for primary and neck
    - Multimodality clinical trials
- For discussion of chemoradiation and induction chemotherapy, please see the discussion section at the end of the presentation

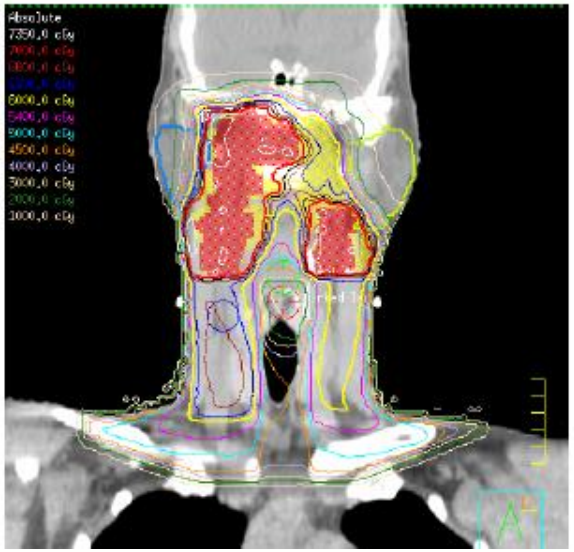
Chemoradiation treatment plan

- Radiation treatment
  - 70 Gy in 33 fractions to gross disease and areas of previous gross disease
  - 60 Gy in 33 fractions to at risk areas
  - Matched to low neck field:
  - 40 Gy in 20 daily fractions with larynx block
  - 10 Gy in 5 fractions with midline block
  - 10 Gy in 5 fractions for right neck boost LAO/RPO
  - 6 Gy in 3 fractions right low neck boost

Plan – see contouring file for full set of contours







On Follow-up…

Before

After

Before

After

Before

After

Before

After

Before

After

Thank you!

- Dr. Adam S. Garden
  - Professor
  - Department of Radiation Oncology
  - University of Texas MD Anderson Cancer Center

Additional Slides

- Split field vs whole field IMRT
- Induction chemotherapy

What's the advantage of whole-field vs split-field IMRT?

Int. J. Radiation Oncology Biol. Phys., Vol. 63, No. 4, pp. 1000–1005, 2005
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ELSEVIER

doi:10.1016/j.ijrobp.2005.03.069

CLINICAL INVESTIGATION **Head and Neck**

INTENSITY-MODULATED RADIATION THERAPY (IMRT) OF CANCERS OF THE HEAD AND NECK: COMPARISON OF SPLIT-FIELD AND WHOLE-FIELD TECHNIQUES

Bouthaina Dabaja, M.D., Mohammad R. Salehpour, Ph.D., Isaac Rosen, Ph.D., Sam Tung, M.S., William H. Morrison, M.D., K. Kian Ang, M.D., Ph.D., and Adam S. Garden, M.D.

Department of Radiation Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX

Background: Oropharynx cancers treated with intensity-modulated radiation (IMRT) are often treated with a monoisocentric or half-beam technique (HB). IMRT is delivered to the primary tumor and upper neck alone, while the lower neck is treated with a matching anterior beam. Because IMRT can treat the entire volume or whole field (WF), the primary aim of the study was to test the ability to plan cases using WF-IMRT while obtaining an optimal plan and acceptable dose distribution and also respecting normal critical structures.
Methods and Materials: Thirteen patients with early-stage oropharynx cancers had treatment plans created with HB-IMRT and WF-IMRT techniques. Plans were deemed acceptable if they met the planning guidelines (as defined or with minor violations) of the Radiation Therapy Oncology Group protocol H0022. Comparisons included coverage to the planning target volume (PTV) of the primary (PTV66) and subclinical disease (PTV54). We also compared the ability of both techniques to respect the tolerance of critical structures.
Results: The volume of PTV66 treated to >110% was less in 9 of the 13 patients in the WF-IMRT plan as compared to the HB-IMRT plan. The calculated mean volume receiving >110% for all patients planned with WF-IMRT was 9.3% (0.8%–25%) compared to 13.7% (2.7%–23.7%) with HB-IMRT ($p = 0.09$). The PTV54 volume receiving >110% of dose was less in 10 of the 13 patients planned with WF-IMRT compared to HB-IMRT. The mean doses to all critical structures except the larynx were comparable with each plan. The mean dose to the larynx was significantly less ($p = 0.001$), 18.7 Gy, with HB-IMRT compared to 47 Gy with WF-IMRT.
Conclusions: Regarding target volumes, acceptable plans can be generated with either WF-IMRT or HB-IMRT. WF-IMRT has an advantage if uncertainty at the match line is a concern, whereas HB-IMRT, particularly in cases not involving the base of tongue, can achieve much lower doses to the larynx. © 2005 Elsevier Inc.

Oropharynx cancer, Whole-field technique, Half-beam technique.

Conclusions

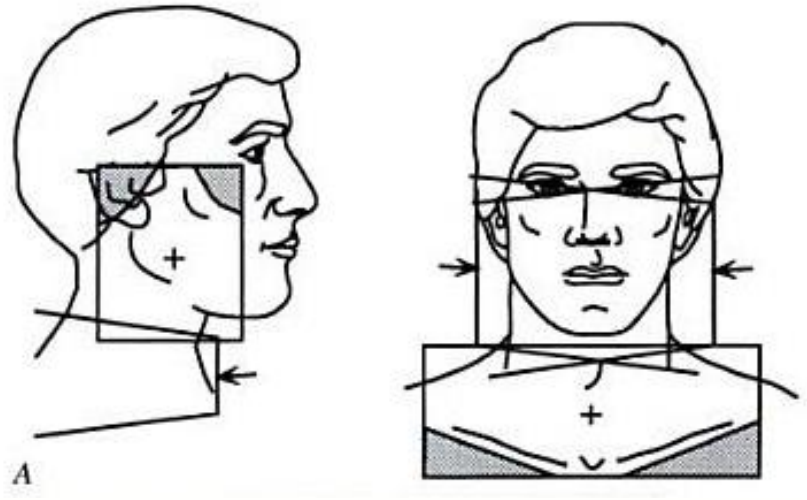
- Half Beam-IMRT (i.e. split-field):
  - Shorter duration to treat 1-4 minutes
  - Gives lower dose to larynx for OP high tumors
  - Gives 362 less MU ($p<0.001$)
- Whole Field -IMRT:
  - Less heterogeneity
  - Less match line uncertainty
- No difference in planning times

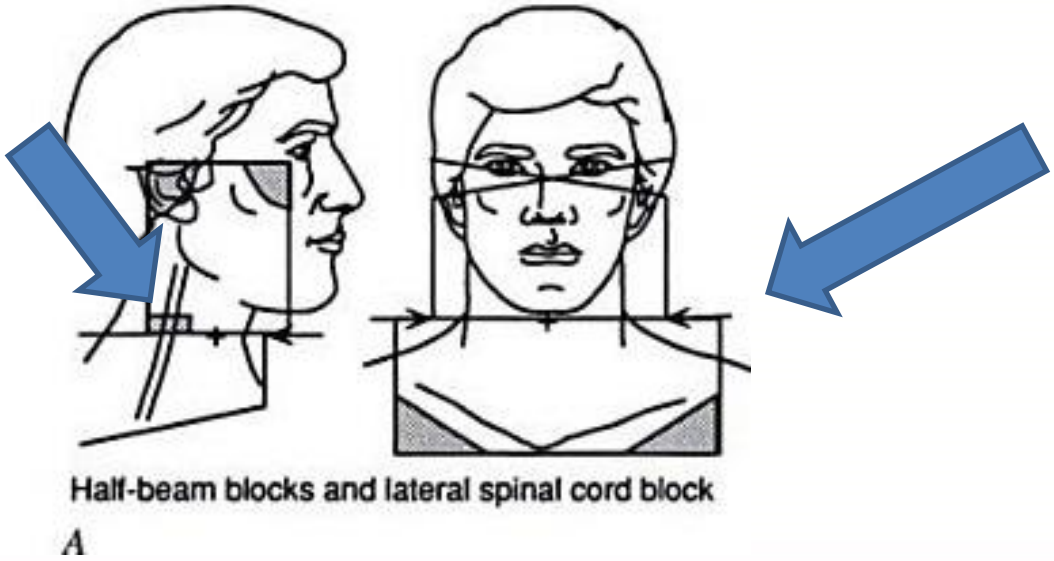
- Older study – newer planning systems may allow lower doses to larynx and esophagus
  - Newer delivery systems for whole field may allow for faster treatments with less MU such as VMAT

Recommendations

- HB-IMRT if:
  - Primary tumor ≥ 1.5cm above arytenoid
  - Recommend a composite for dosimetry at junction splits nodal disease
- WF-IMRT if:
  - Primary tumor near larynx

Courtesy of Lauren Layer





- Conventional technique with 2 opposed lateral fields for primary and nodes and single AP field for lower neck with safety block at matchline to protect overdose to cord.

Chemoradiation therapy

TAX 323

- Phase III multi-institutional trial
- 358 pts with unresectable Stage III-IV H&N cancer (46% OPX)
  - Induction PF (Cisplatin 100 mg/m^2, Fluorouracil 1000 mg/m^2) -> RT (66-74 Gy, SFx or HFx)
  - TPF (Docetaxel 75 mg/m^2, Cisplatin 75 mg/m^2, Fluorouracil 750 mg/m^2) -> RT (66-74 Gy, SFx or HFx)
- 3 yr OS 14.5 mos. (PF) vs. 18.8 mos. (TPF) (p=.02)
- Median PFS 8.2 mos. (PF) vs. 11 mos. (TPF) (p=.007)

Vermorken JB et al., 2007

RTOG 00-22

- Single arm prospective trial
- cT1-2N0-1, small cN2 pts with oropharyngeal cancer
- 69 patients from 14 institutions
- 66 Gy/ 60 Gy/ 54 Gy in 30 fractions using IMRT
- Split field technique allowed
- 2- year LR 9%, 2 yr OS 95.5%
- 2- year LR 50% in major under- dose variations (<90% of PTV66 covered by 66 Gy isodose line)

Eisbruch A et al., 2010

RTOG 90-03

- Multi- institution four arm randomized trial
- 1073 patients with Stage III- IV oral cavity, oropharynx (60%), supraglottic larynx or Stage II-IV BOT, hypopharnx
- Arms:
  - SF 70 Gy in 35 fx @ 2 Gy/ fx qd
  - HF 81.6 Gy in 68 fx @ 1.2 Gy bid
  - AFX-S 67.2 Gy in 42 fx @ 1.6 Gy bid w 2 wk break after 38.4 Gy
  - AFX- CB 72 Gy total; 54 Gy in 30 fx @ 1.8 Gy qd + 18 Gy in 12 fx @ 1.5 Gy concurrent bid boost

Fu KK et al., 2000

RTOG 90-03

	SFX	HFX	AHFX-S	AFX-C
Endpoint	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Local-Regional Failure *	59.1 (52.8, 65.5)	51.2 (44.8, 57.7)	57.8 (51.4, 64.1)	51.7 (45.2, 58.2)
Distant Metastases	29.4 (22.5, 36.2)	28.6 (22.0, 35.3)	26.8 (20.2, 33.3)	26.5 (20.2, 32.9)
Disease-Free Survival	21.2 (16.1, 26.2)	30.7 (25.0, 36.4)	26.6 (21.3, 31.9)	28.9 (23.3, 34.4)
Overall Survival	29.5 (23.8, 35.1)	37.1 (31.1, 43.2)	30.8 (25.2, 36.4)	33.5 (27.7, 39.3)
Cause-Specific Survival	42.9 (36.3, 49.4)	45.5 (39.1, 51.9)	40.9 (34.6, 47.3)	43.4 (36.9, 50.0)

116 **Long Term Outcomes of RTOG 90–03: A Comparison of Hyperfractionation and Two Variants of Accelerated Fractionation to Standard Fractionation Radiotherapy for Head and Neck Squamous Cell Carcinoma**

A. Trotti,[1] K.K. Fu,[2] T.F. Pajak,[3] C.U. Jones,[4] S.A. Spencer,[5] T.L. Phillips,[2] A.S. Garden,[9] J.A. Ridge,[7] J.S. Cooper,[8] K.K. Ang[9]

Although not statistically significant

EORTC 22791

- Multi- institution two arm randomized trial
- 356 pts withT2-T3, N0-N1 oropharyngeal cancer (excluding BOT)
- CF of 70 Gy in 35 fxs vs. HF of 80.5 Gy in 70 fxs using 1.15 Gy bid
- HF LC 59% vs. CF LC 40%, p=.007
- Trend to OS benefit (p=.08)

Horiot JC et al, 1992

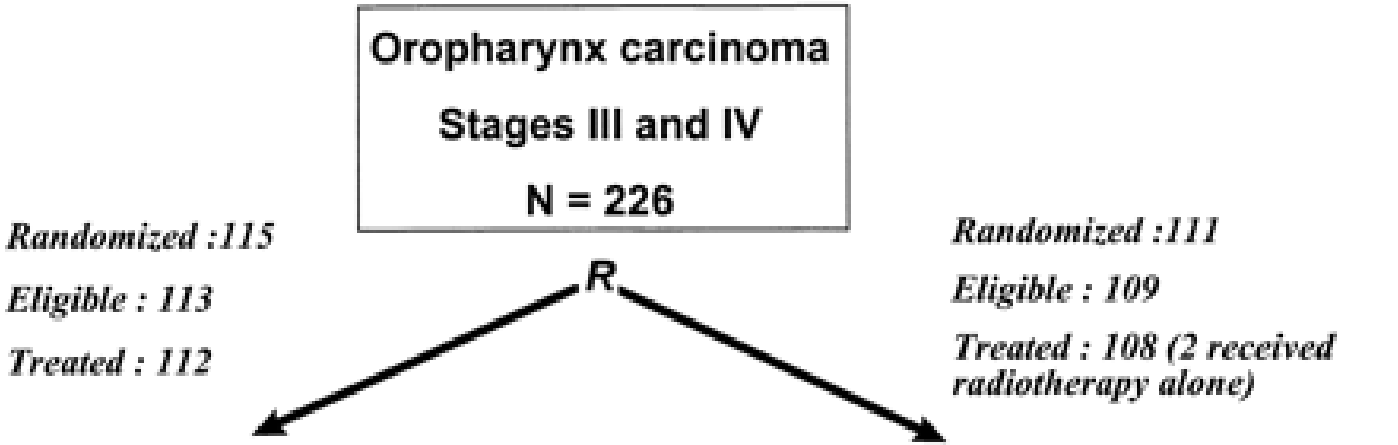
Chemoradiation?

What if the patient was dispositioned to chemoradiation, given the N2 neck disease? What would your dose/fractionation be?

Doses with chemoradiation at MDACC

- Radiation treatment
  - 70 Gy in 33 fractions to gross disease and areas of previous gross disease (very mild hypofractionation)
    - Alternative strategies include
      - 66 Gy in 33 fx
      - 70Gy in 35 fx
  - 60 - 63 Gy to intermediate risk areas
  - 55 -57 Gy to low risk areas

GORTEC 94-01



Radiotherapy Alone

2 Gy/f, 5f/w

Total tumor dose = 70 Gy

Radiotherapy+Chemotherapy

Same radiotherapy regimen +

3 cycles of chemotherapy with

carboplatin : 70 mg/m²/d and

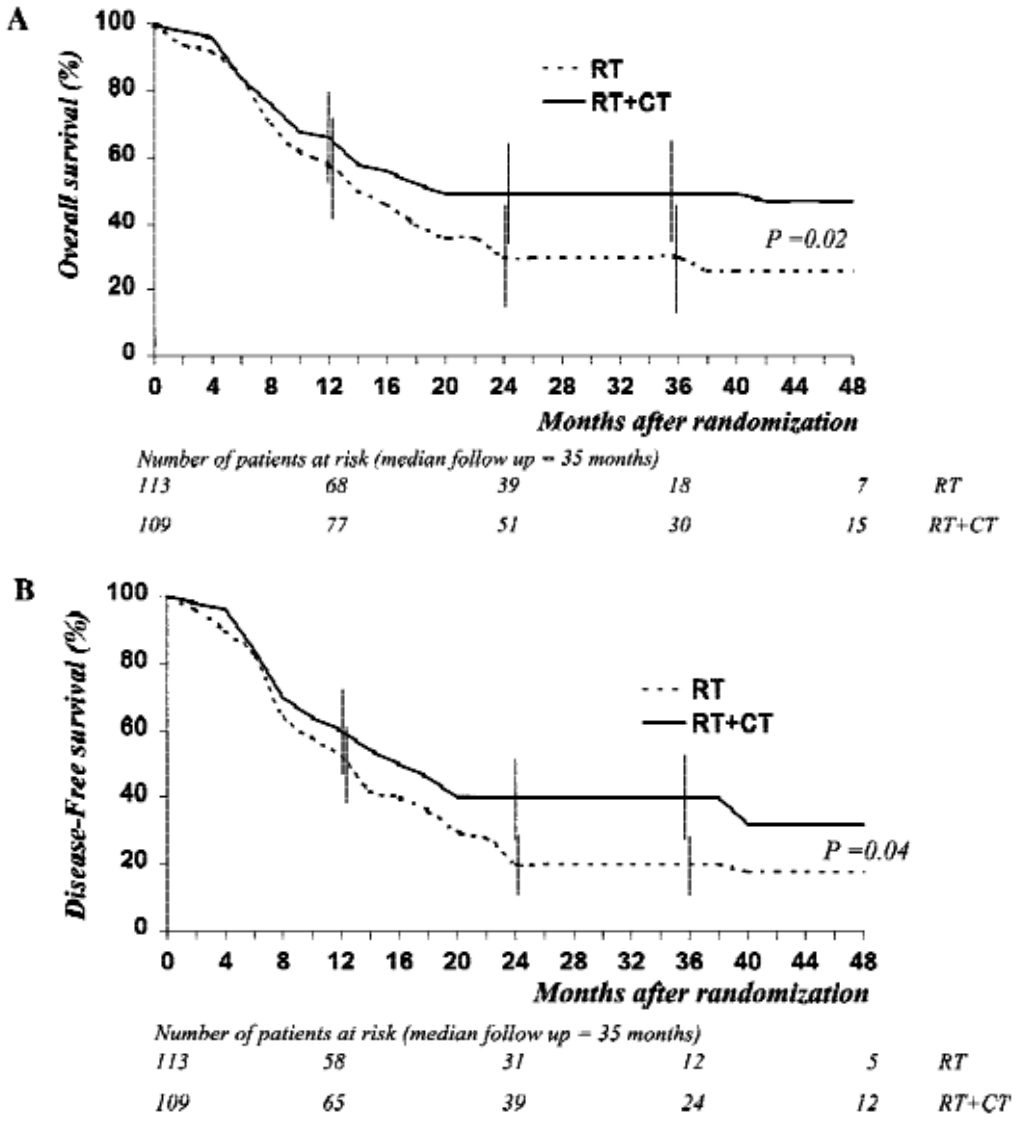
5-fluorouracil : 600 mg/m²/d CI on

days 1 to 4, 22 to 25, 43 to 46

Calais G et al., 1999

GORTEC 94-01

- 3 yr OS 51% vs. 31%
- DFS 30% vs. 14%
- LC 66% vs. 42%



Calais G et al., 1999

Intergroup trial

- Multi- institutional Phase III trial
- 295 pts with unresectable Stage III- IV head and neck cancers (55% oropharynx)
  - Arm A: RT alone to 70 Gy in 35 fxs
  - Arm B: CRT to 70 Gy in 35 fxs with concurrent Cisplatin
  - Arm C: Split course RT to 30 Gy with concurrent Cis/ 5FU then 30-40 Gy if unresectable
- 3 yr OS 23% Arm A vs. 37% Arm B (p=.014) vs. 27% Arm C
- DFS 33% Arm A vs. 51% Arm B (p=.01)vs. 41% Arm C

Adelstein DJ et al., 2003

RTOG 01-29

- 743 patients with Stage III-IV head and neck cancer (60% oropharynx)
  - AFX- CB 72 Gy/ 42 Fx/ 6 wk + Cisplatin 100 mg/m2 q 3 wks
  - SFX 70 Gy/ 35 Fx/ 7 wk + Cisplatin 100 mg/m2 q 3 wks
- OS 59% (AFX) vs. 56% (SFX) (p=0.18)
- DFS 45% (AFX) vs. 44% (SFX) (p=0.42)
- LRF 31% (AFX) vs. 28% (SFX) (p=0.76)
- DM 18% (AFX) vs. 22% (SFX) (p=.06)

LB 2 **A Phase III Trial to Test Accelerated Versus Standard Fractionation in Combination with Concurrent Cisplatin for Head and Neck Carcinomas (RTOG 0129): Report of Efficacy and Toxicity**

K. Ang[1], T. Pajak[2], R. Wheeler[3], D. Rosenthal[1], F. Nguyen-Tan[4], C. Lu[1], H. Kim[5], R. Axelrod[6], C. Silverman[7], R. Weber[1]

[1]M.D. Anderson Cancer Center, Houston, TX, [2]RTOG, Philadelphia, PA, [3]Huntsman Cancer Institute, Salt Lake City, UT, [4]CHUM Hopital Notre Dame, Montreal, QC, Canada, [5]Wayne State University Medical Center, Detroit, MI, [6]Thomas Jefferson University Hospital, Philadelphia, PA, [7]University of Louisville, Louisville, KY

Induction Chemotherapy

TAX 324

- Phase III multi-institutional trial
- 502 pts with unresectable Stage III-IV H&N cancer (52%) OPX
  - TPF (Docetaxel 75 mg/m2, Cisplatin 100 mg/m2, Fluorouracil 1000 mg/m2) -> CRT (70-74 Gy, SFx) and Carboplatin(AUC < 1.5)
  - Induction PF (Cisplatin 100 mg/m2, Fluorouracil 1000 mg/m2) -> CRT (70-74 Gy, SFx) and Carboplatin(AUC < 1.5)
- Median OS 70.6 mos. (TPF) vs. 34.8 mos. (PF) (p=.014)
- Median PFS 38.1 mos. (TPF) vs. 13.2 mos. (PF) (p=.007)

Lorch JH et al., 2011

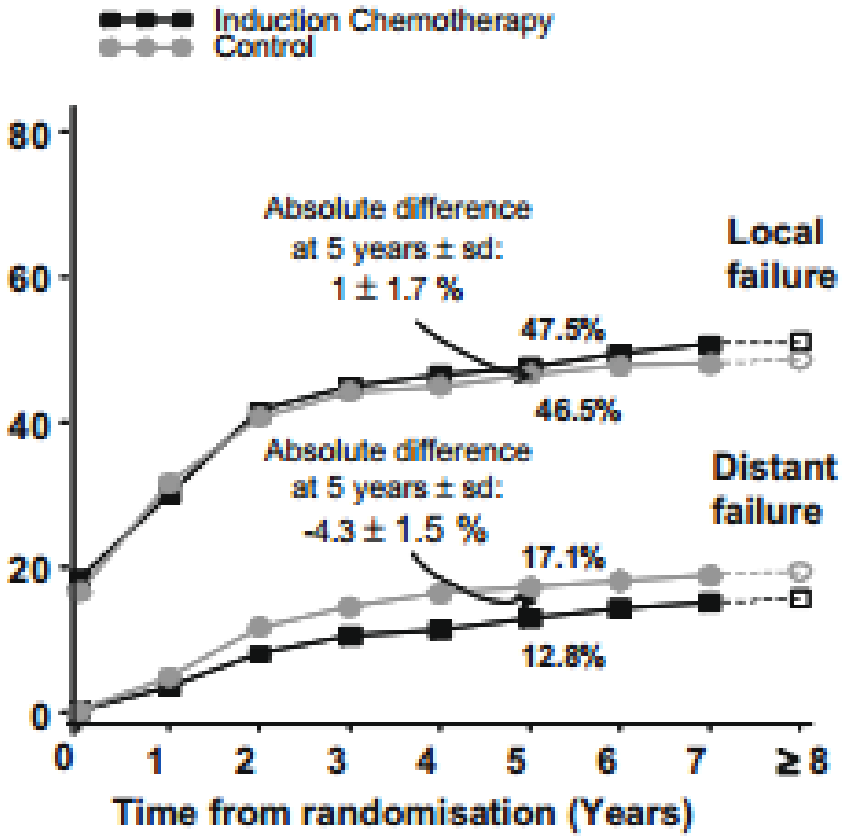
PARADIGM Trial

- Phase III multi-institutional trial
- 145 patients with Stage III-IV head and neck cancer (OPX 55%)
  - TPF (Docetaxel 75 mg/m2 D1, Cisplatin 100 mg/m2 D1, Fluorouracil 1000 mg/m2 D1-4) x3 -> CRT (weekly Docetaxel at 20 mg/m2 and 72 Gy with ACB 1.8/ 1.5 Gy fx's or weekly Carboplatin (AUC 1.5) and 70 Gy in 35 fx's)
  - CRT to 72 Gy with ACB 1.8/ 1.5 Gy fx's with Cisplatin 100 mg/m2 on D1 and D 22
- 3 yr PFS 67% (IC) vs. 69% (CRT) (p=0.82)
- 3 yr OS 73% (IC) vs. 78% (CRT) (p=0.77)

Haddad R et al., 2013

Meta-analysis of chemotherapy in head and neck cancer

- Meta-analysis of 93 trials of 17,346 patients from 1965 to 2000
- Overall, absolute benefit of 4.5% at 5-years with the addition of chemo
- Absolute benefit of 6.5% at 5 years for concomitant chemo.
- Decreasing effect of chemo with age



Pignon JP et al., 2009

Some Future Directions

- ECOG 1308:
  - Phase II trial of induction chemotherapy followed by reduced dose radiation to 54 Gy with cetuximab in patients with clinical complete response at the primary site
  - Stage III or IV HPV+ OPXSCC
- RTOG 1016
  - Concurrent chemoradiation (Cisplatin) vs. Cetuximab and radiation in patients with HPV + OPXSCC