Dosimetric analysis of the effect of MLC leaf width on parotid sparing for head and neck cancers treated using a simulataneous integrated boost IMRT technique.

Hasan Murshed, M.D., M.S.
Department of Radiation Oncology
The University of Alabama at Birmingham

Introduction

- Case presentation 1
  - recurrent nasal melanoma
- Case presentation 2
  - H&N SCCa
  - RT side effect - xerostomia
  - Minimizing side effects
  - WR 2721
  - IMRT
  - Other

- Compare conventional vs IMRT
- Biological model for complication probability
- Compare 5 mm vs 10 mm leaf width
- Conclusions/Future

Teh et al., 1999

- IMRT is a new technology in RT that delivers radiation precisely to the tumor while relatively sparing the surrounding normal tissues

- Combines two advance concepts to deliver 3D conformal radiation
  - inverse treatment planning with computer optimization
  - computer controlled intensity modulation of the radiation beam
- Potential advantages
  - to create multiple targets
  - multiple critical avoidence
  - new accelerated fractionation scheme

- Has potential in radiation oncology in the the 21st century
  - Can be used to spare parotid gland in HN cancer pts

The Oncologist 4:433-442, 1999

3D CRT vs IMRT - Case Presentation

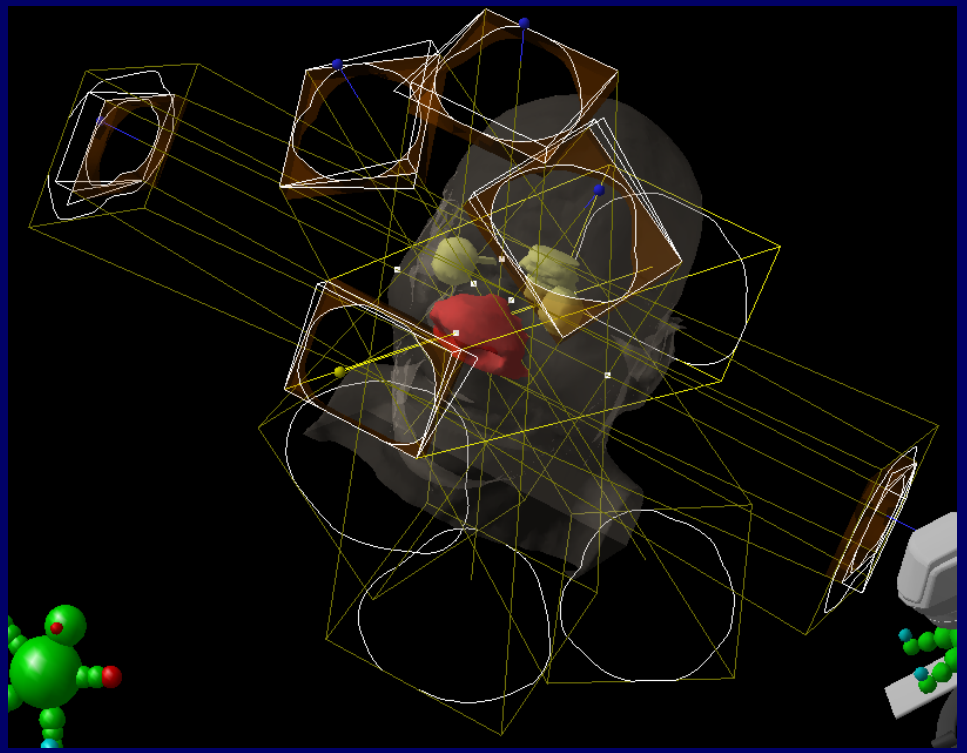
- 71 YOM
- H/O Malignant melanoma of the nasal cavity 1998
- S/p resection, s/p post op RT to 5000 cGy
- Now with recurrent melanoma at the nasal cavity, unresectable
- Symptomatic with breathing difficulty and bleeding
- Metastatic work up negative
- Chemotherapy failed to prevent progression

- **Referred for repeat radiation therapy.**

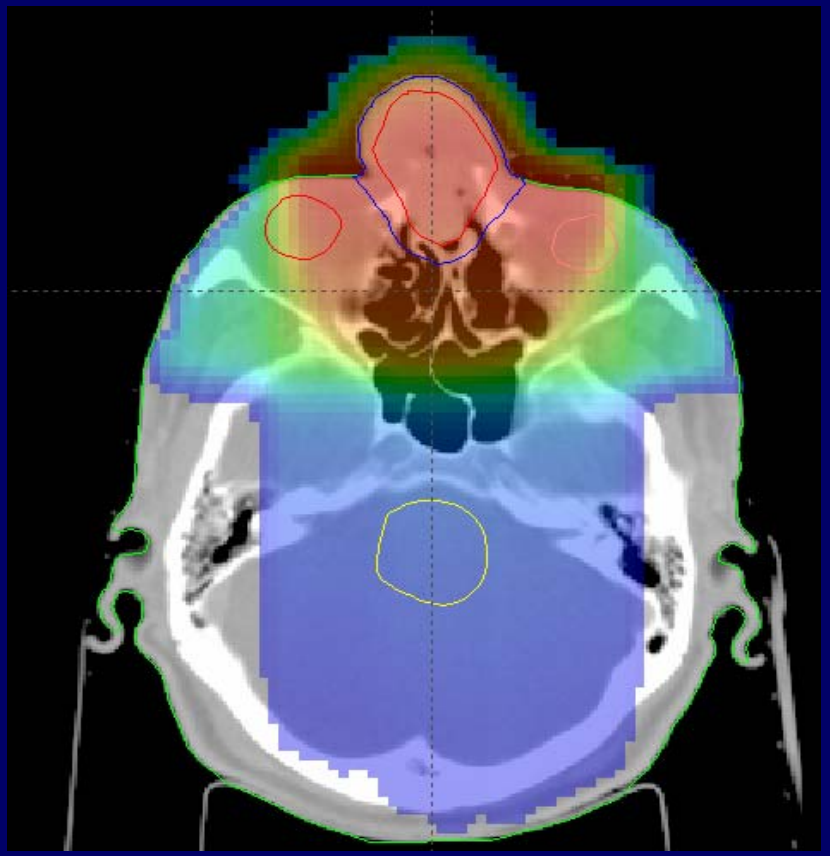
3D CRT vs IMRT - Case Presentation

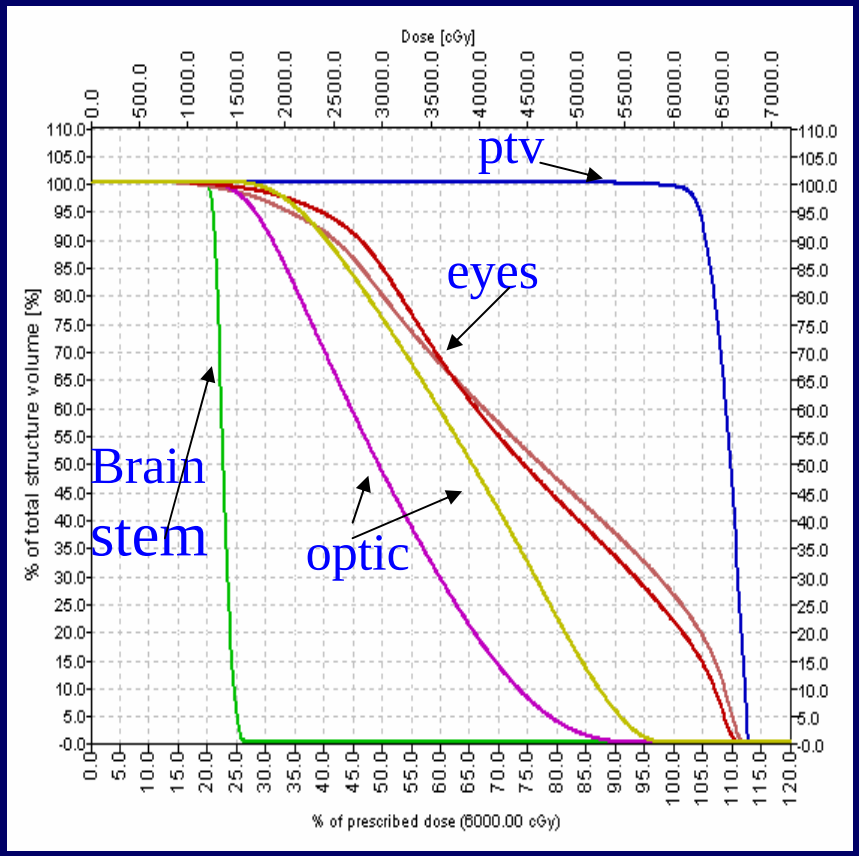
- **PROBLEMS**
  - Repeat radiation for recurrent melanoma
  - Critical structures - eyes, optic nerves, chiasm, brain stem
  - Coverage of PTV vs sparing of the critical structures

3D CRT Beam Geometry

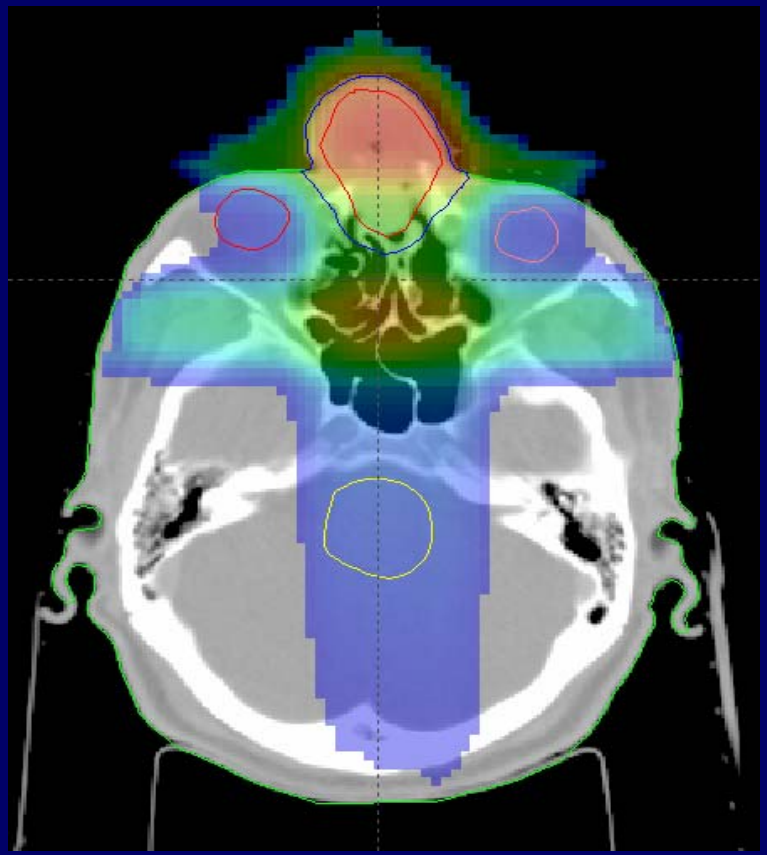


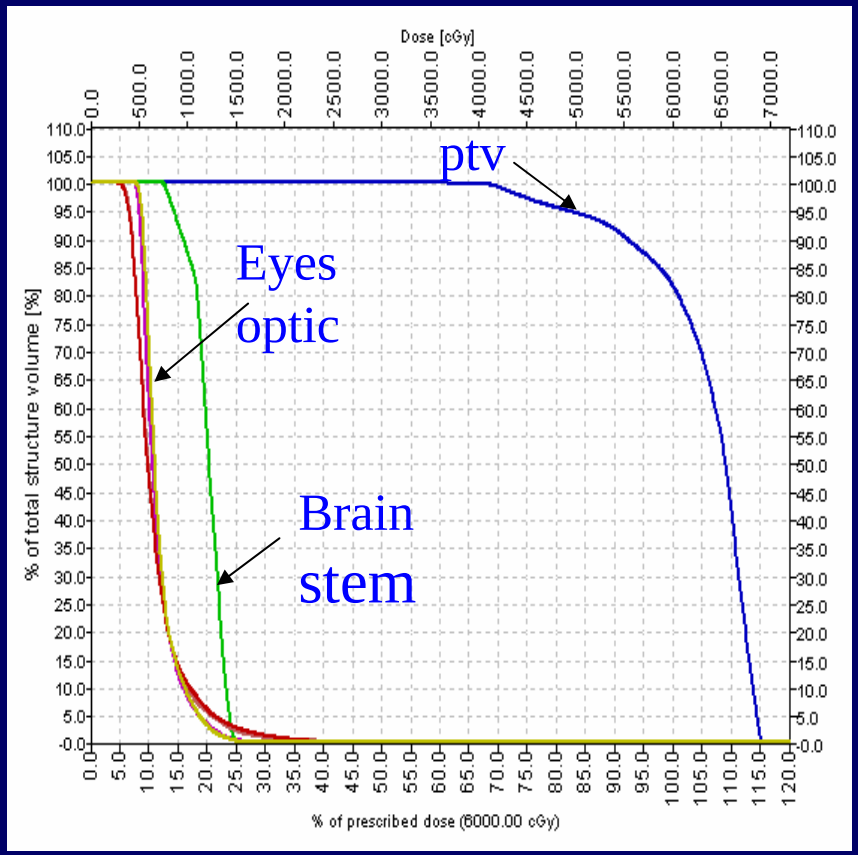
3D CRT - PTV coverage



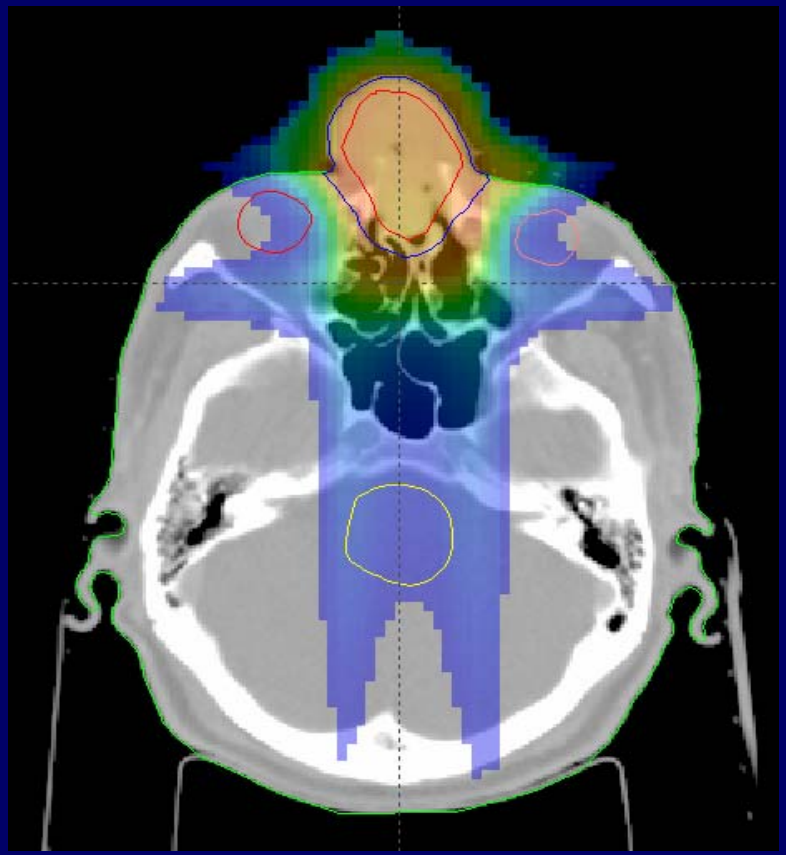


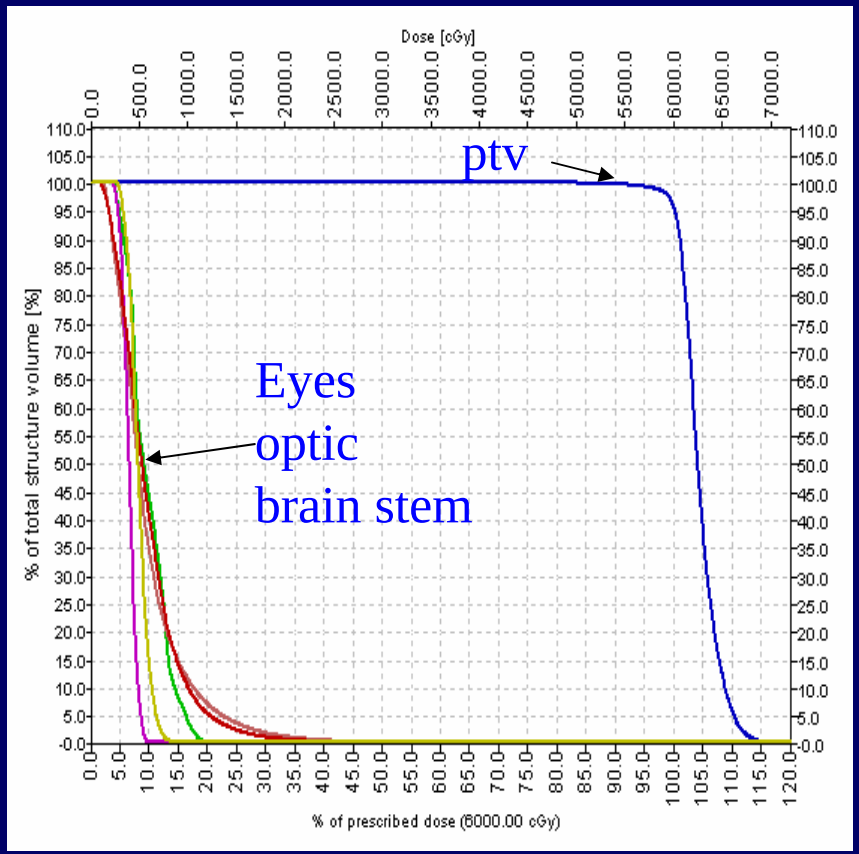
3D CRT - Critical organ sparing





IMRT




Dose [cGy]
ptv
Eyes
optic
brain stem
% of total structure volume [%]
% of prescribed dose (6000.00 cGy)

3D CRT vs IMRT

- IMRT made retreatment feasible of this recurrent nasal cavity melanoma to a therapeutic dose while maintaining the critical tissue tolerances.

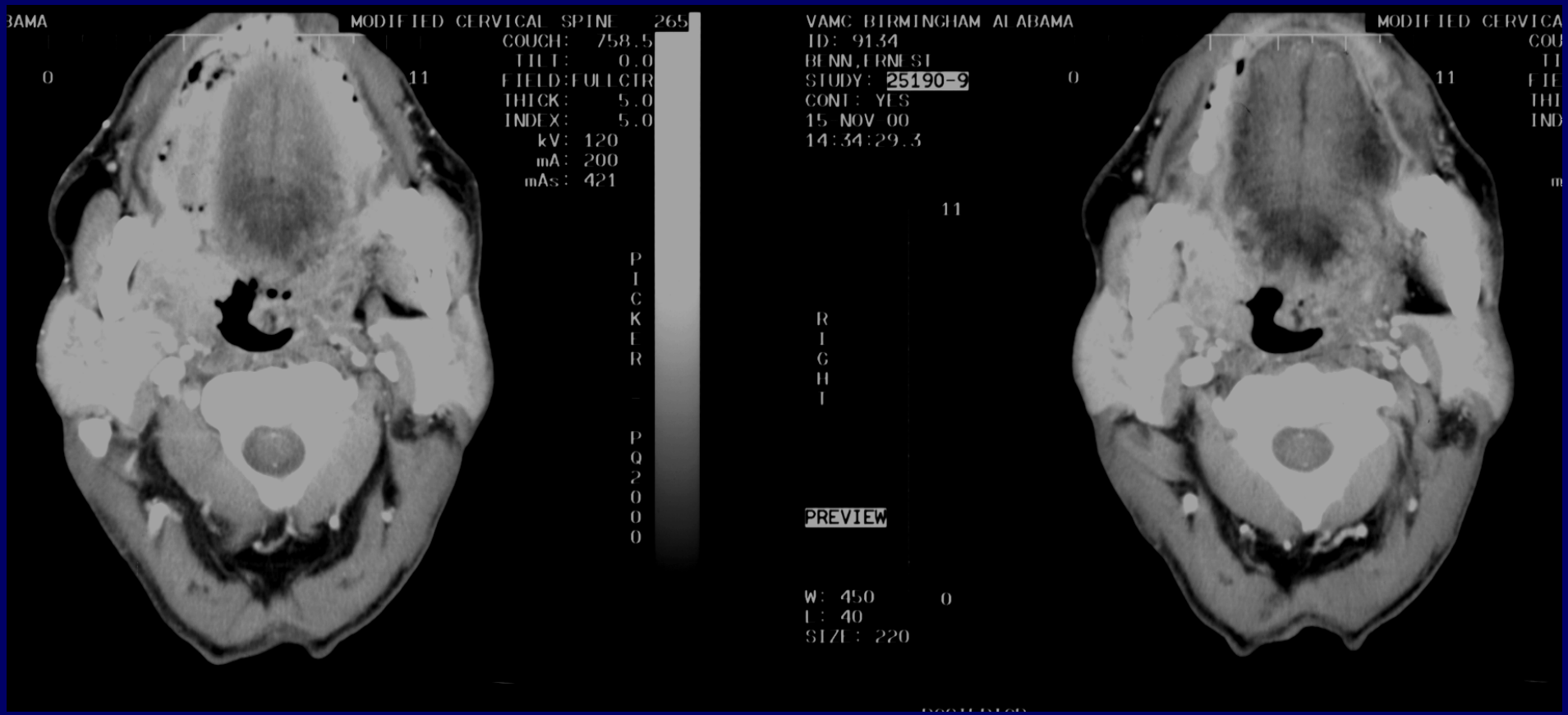
Case presentation

- 58 yom
- c/o dyphagia, odynopgagia, wt loss x4-5 m
- No SOB, ear pain, bleeding, paresthesia
- Current smoker, 40 PY smoke hx, occasional alcohol use
- P/E
  - no neck LN
  - a 3x4 cm ulcerative exophytic lesion of the rt retromolar trigone
- CT neck - large mass involving both tonsils, tongue, soft palate bilat, rt post triangle and lt parapharyngeal LN

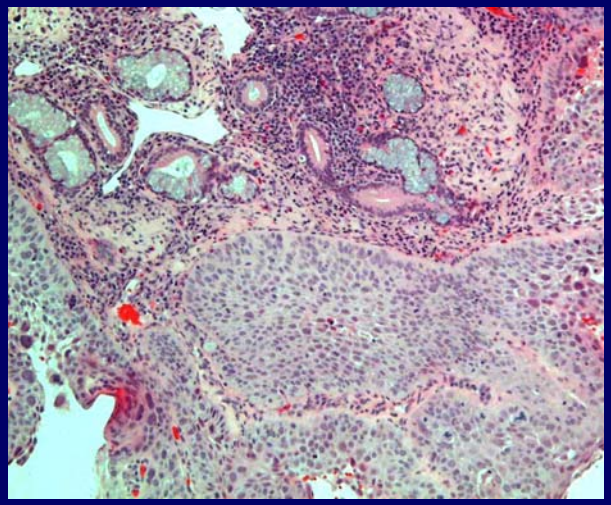
- Bx - moderately diff SCCa

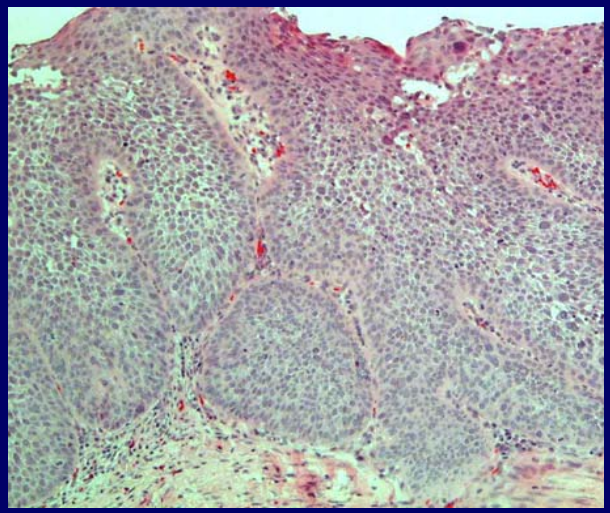
Case presentation/ CT

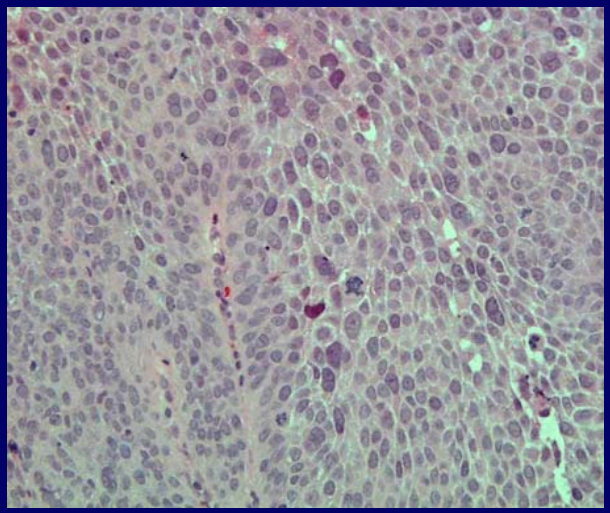
Case presentation/ CT



Case presentation/ Pathology







- Salivary glands
- Squamous cells
- Mitotic figure

Case presentation

- 58 yom, rt tonsil mod diff SCCa T4N2CM0, IVA
- Received concurrent chemoRT
- RT dose
  - primary : 200 cGy/fx to 7000 cGy
  - rt. post neck : 200 cGy/fx to 6000 cGy
  - lt. post neck : 200 cGy/fx to 5000 cGy
- Chemo - CDDP/5FU x4 cycles
- COT 3/01
- Last F/U on 5/01
  - clinically NED
  - most acute RT side effects resolved
  - continues to have dry mouth RTOG grade 2

Statistics

Estimated New Cancer Cases and Deaths by Sex for All Sites, United States, 2000*

	Estimated New Cases			Estimated Deaths		
	Both Sexes	Male	Female	Both Sexes	Male	Female
All Sites	1,220,100	619,700	600,400	552,200	284,100	268,100
Oral cavity & pharynx	30,200	20,200	10,000	7,800	5,100	2,700
Tongue	6,900	4,500	2,400	1,700	1,100	600
Mouth	10,900	6,500	4,400	2,300	1,300	1,000
Pharynx	8,200	5,900	2,300	2,100	1,500	600
Other oral cavity	4,200	3,300	900	1,700	1,200	500

- 60, 400 new cases of H&N cancer in USA
- 15, 600 deaths in 2000
- Most pts will undergo RT and may experience toxic side effects.
  - Early - fatigue, skin changes, mucositis, loss of appetite
  - Late - xerostomia, tissue necrosis

American Cancer Society 2000

Xerostomia

- Xerostomia is the prominent long term RT side effect in the H&N ca pts, dependent on
  - radiation field
  - radiation dose
  - initial volume
  - function of salivary gland

1. Severe radiation-induced mucositis.

Figure 2. Effects of radiation-induced xerostomia.

- Irradiated salivary glands show
  - acinar atrophy and chronic inflammation

- Permanent xerostomia affects QOL, causing
  - dental caries, difficulty chewing, swallowing, speaking, increased incidence of oral candidiasis and reflux esophagitis

Xerostomia

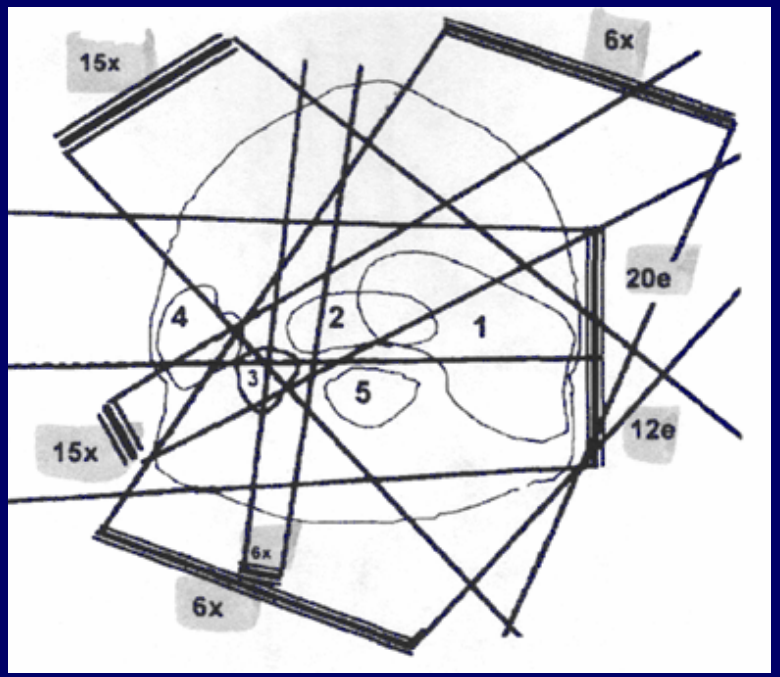
- The goals of treating xerostomia are to
  - improve comfort
  - maintain mucosal integrity
  - prevent infection
  - sustain nutrition
  - ensure dental preservation.

- Treatments
  - siologogues - pilocarpine
  - radioprotectant - WR 2721
  - parotid sparing radiation - 3D/IMRT technique
  - Others - surgery, acupuncture

Eisbruch et al., 1996

- Reported on 15 H&N ca pts, prospectively treated using 3D planning
- Designed radiation fields that would treat target, sparing the parotid gland
  - GTV=gross tumor/LN, CTV=GTV+1cm, PTV=CTV+0.3cm
  - Secondary PTV=LN at risk+0.3cm
  - Typically 7-8 beams were needed
  - Including photons/electron beams

- Salivary gland function was assessed
  - By sialometry
  - subjective questionnaire



Int J Radiat Oncol Biol Phys 36:469-480, 1996

Eisbruch et al., 1996

- Results
  - the spared gland mean average dose 21 ± 8 Gy
  - The nonspared gland mean average dose 58 ± 5 Gy
  - The flow rate from spared gland reduced to 50% of the baseline
  - The flow rate from the nonspared gland remained nonmeasurable
  - 3 months after RT 40% no, 13% mild/mod, 33% high xerostomia

- Conclusion
  - Partial parotid gland sparing is possible by 3D planning for HN ca pts
  - Most pts treated had no or mild xerostomia

Int J Radiat Oncol Biol Phys 36:469-480, 1996

Mohan et al., 1999

- New fractionation strategy for clinical trials/routine use of IMRT of HN ca pts
  - Simultaneous integrated boost (SIB) designed to simultaneously deliver different dose levels to different tissues of the HN region in a single treatment session
  - Superior dose distribution, more efficient, no electron/s'clav field

Table 4. Nominal doses corresponding to normalized total doses*

Target	NTD (Gy)	Nominal dose in 25 fractions (Gy)	Nominal dose/fx for 25 fractions (Gy)	Nominal dose in 30 fractions (Gy)	Nominal dose/fx for 30 fractions (Gy)	Nominal dose in 35 fractions (Gy)	Nominal dose/fx for 35 fractions (Gy)
Electively treated nodes	50.0	50.0	2.00	54.0	1.80	57.9	1.65
Regional disease	60.0	55.9	2.24	60.0	2.00	64.0	1.83
Primary	70.0	61.7	2.47	65.9	2.20	70.0	2.00
Primary	80.0	67.4	2.69	71.7	2.39	75.9	2.17
Primary	90.0	73.0	2.92	77.5	2.58	81.8	2.34

* Isoeffect calculations utilized $\alpha/\beta = 20$ and doubling time = 4 days.

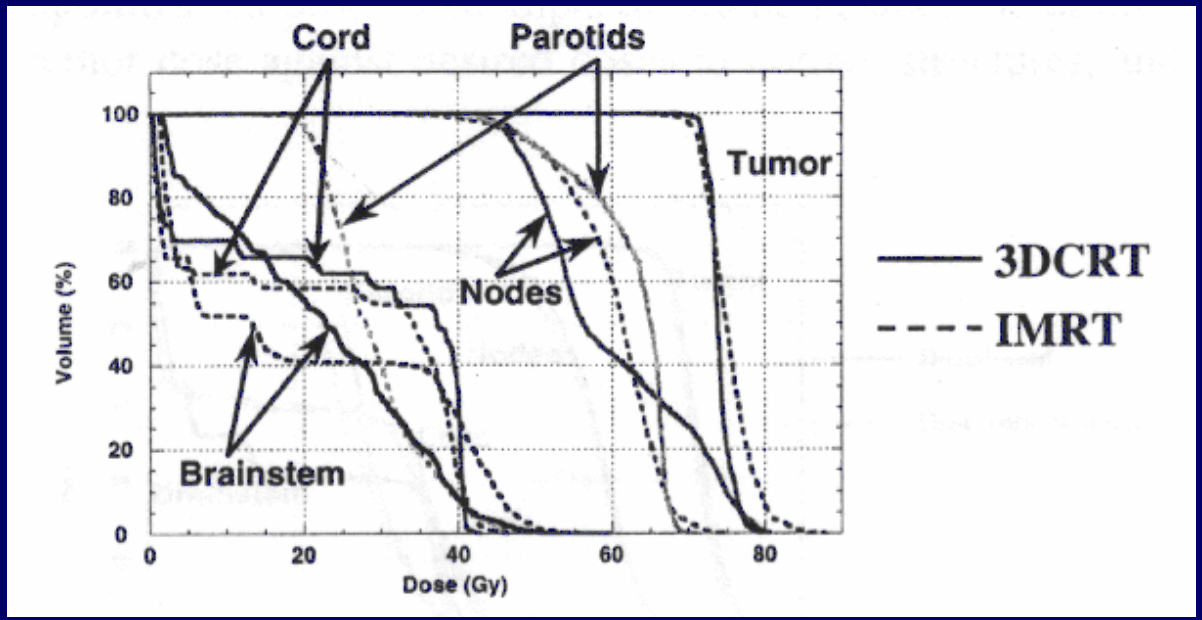
Int J Radiat Oncol Biol Phys 46:619-630, 2000

Wu et al., 1999

- Investigated the potential of IMRT to achieve adequate sparing of parotids and to escalate nominal and/or biologically effective dose
- Four HN pts
  - T2-T4 N0-N3 dz
  - GTV=gross dz
  - elective irradiation=all LN I-IV
  - post neck/s'clav in IMRT
- IMRT
  - 9 coplanar beams/equiangular spacing
  - MLC sliding window technique
  - SIB fractionation
    - 70 Gy/2.5 Gy to the tumor
    - 50.4 Gy/1.8 Gy to the LN

Int J Radiat Oncol Biol Phys 46:195-205, 2000

Wu et al., 1999

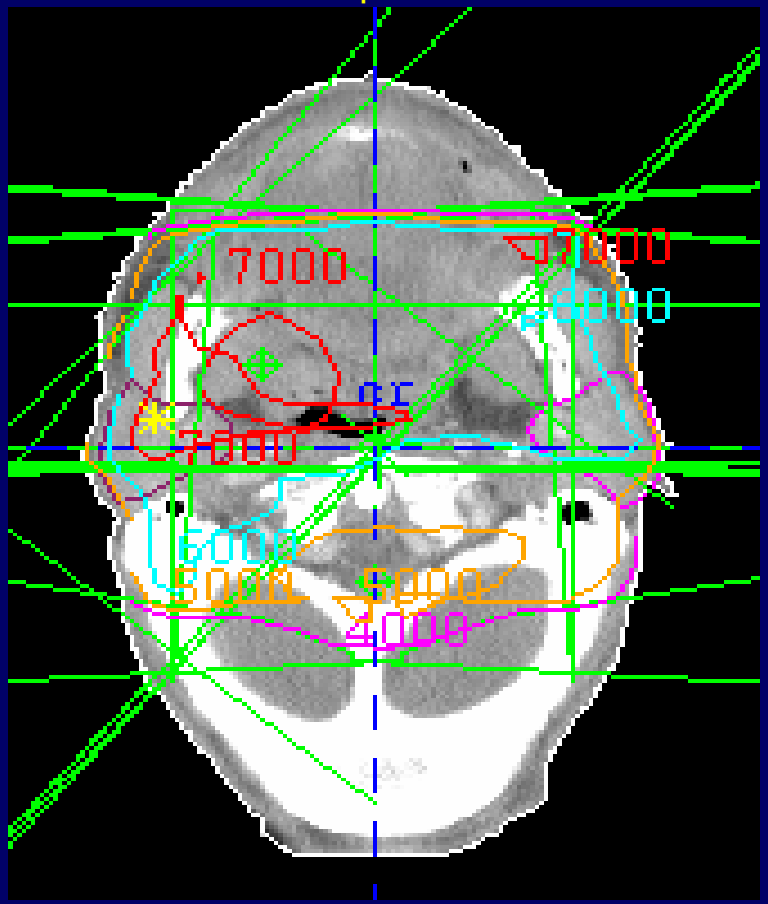


- Conclusion: compared with 3D, IMRT reduced parotid dose while allowing dose escalation

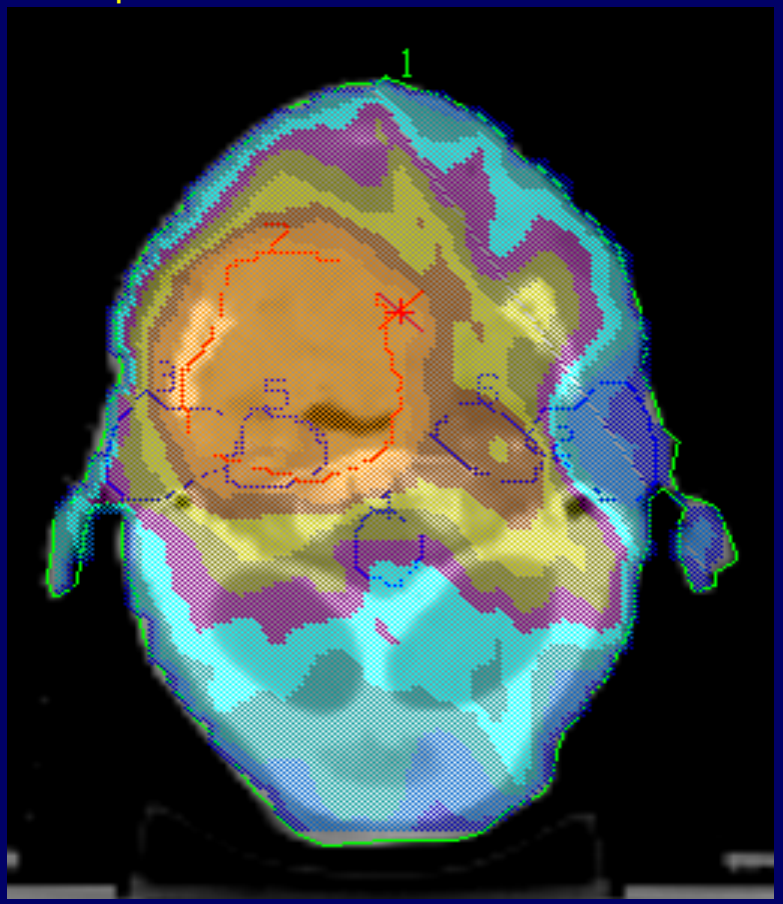
Int J Radiat Oncol Biol Phys 46:195-205, 2000

Compare conventional vs IMRT

- Case 1
- conventional plan

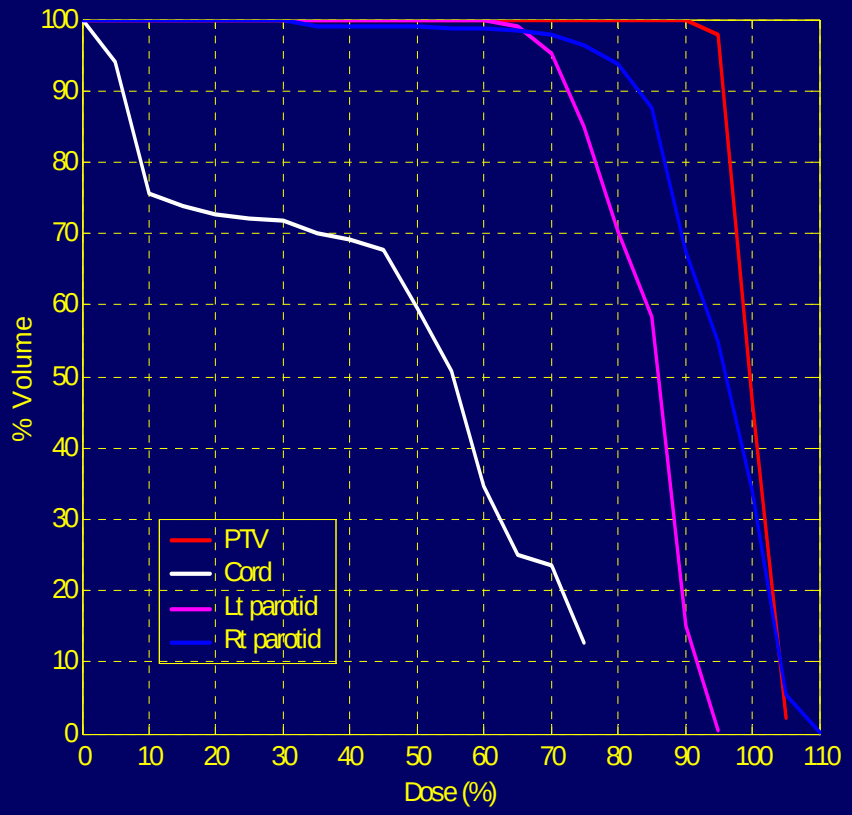


IMRT plan

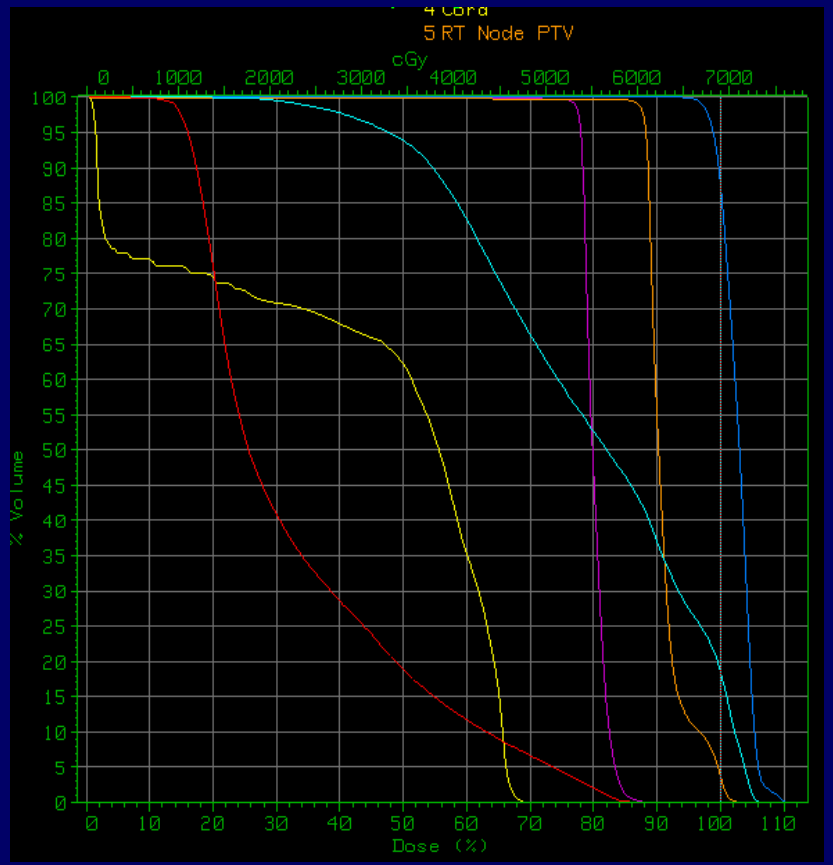


Compare conventional vs IMRT

- Conventional 3 fld RT DVHs



- 120 leafs SIB IMRT DVHs



Eisbruch et al., 1999

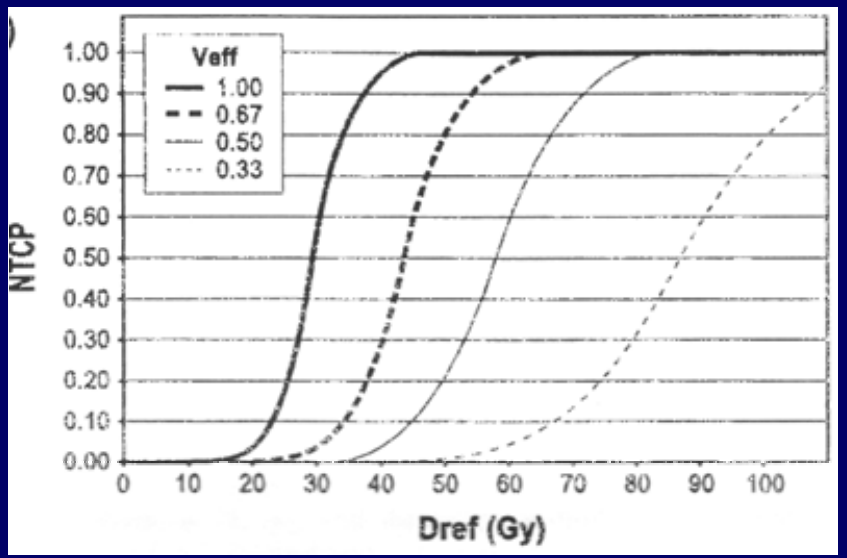
- 88 HN ca pts treated with parotid sparing 3D/static IMRT, the mean dose and partial parotid volumes receiving specified doses were determined, the nonstimulated/stimulated saliva flow rates were measured
- These data were then fitted into a NTCP model by Lyman, to find the parameters to quantify the probability of severe RT late effects
- The Lyman model uses four parameters to represent the NTCP of an organ irradiated with uniform dose to a partial volume
  - TD50, n, m, Vref

Int J Radiat Oncol Biol Phys 45:577-587, 1999

Eisbruch et al., 1999

- Results @ 12 m post RT
  - unstimulated saliva flow rate 15% of the baseline
  - stimulated saliva flow rate 56% of the baseline
  - threshold for unstimulated/stimulated saliva mean dose 24 Gy/26 Gy

- The model predicted severe complication accurately in 35/37 cases



Int J Radiat Oncol Biol Phys 45:577-587, 1999

Eisbruch et al., 1999

- Conclusion
  - NTCP model can predict complication probability, which is a function of dose/volume
  - A planning goal of parotid gland mean dose of $\leq$ 26 Gy, is needed to retain parotid gland function

Int J Radiat Oncol Biol Phys 45:577-587, 1999

Clinical Data

authors	nuber of pts	spared gland mean dose (Gy)	spared gland saliva flow (ml/min)	CR (%)	LC (%)	OS 4 yrs (%)	Xerosto gr 0/1 (%)	xerosto gr 2 (%)
Eisbruch et al 1996	15	21 +/- 8	0.5				53	33
Butler et al 1999	20	21		95			55	45
Sultanem et al 2000	35	29			100	94	65	35
Chao et al 2001	27	30 +/- 9	0.6				corrl	corrl

Comparison of MLC Leaf Width

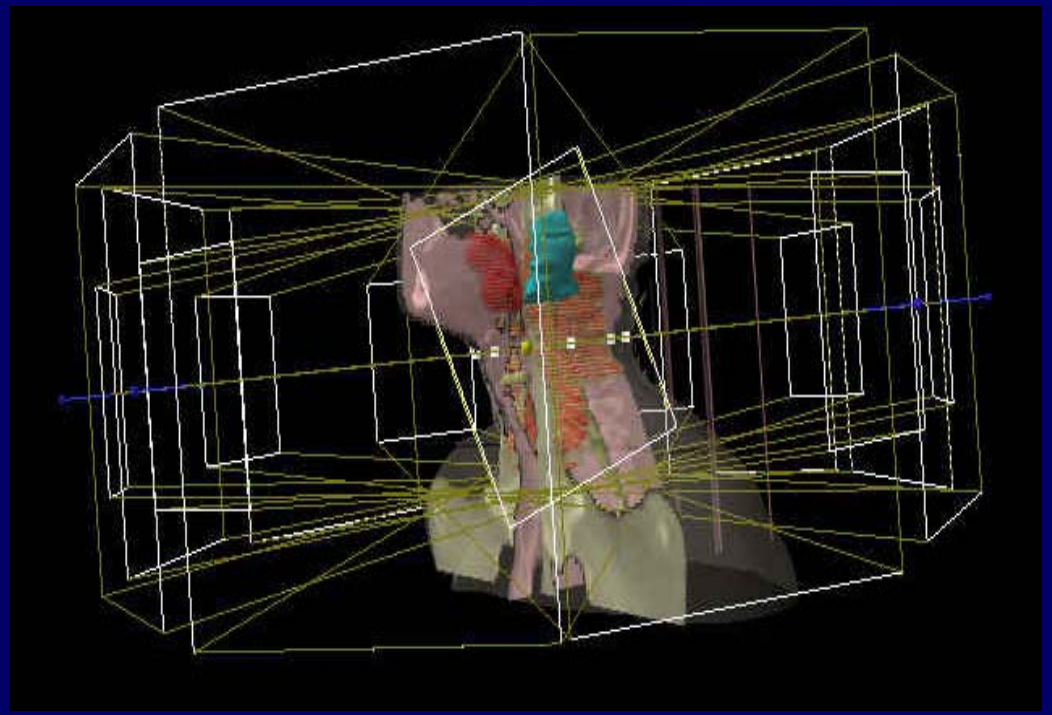
- Purpose: to examine the effect of the MLC leaf width on parotid sparing for HN ca patients
- SIB IMRT technique
- Delivery
  - Sliding window MLC
  - 5 mm vs. 10 mm leaf width
- End points
  - Physical dose distribution
  - Predicted NTCP

Comparison of MLC Leaf Width

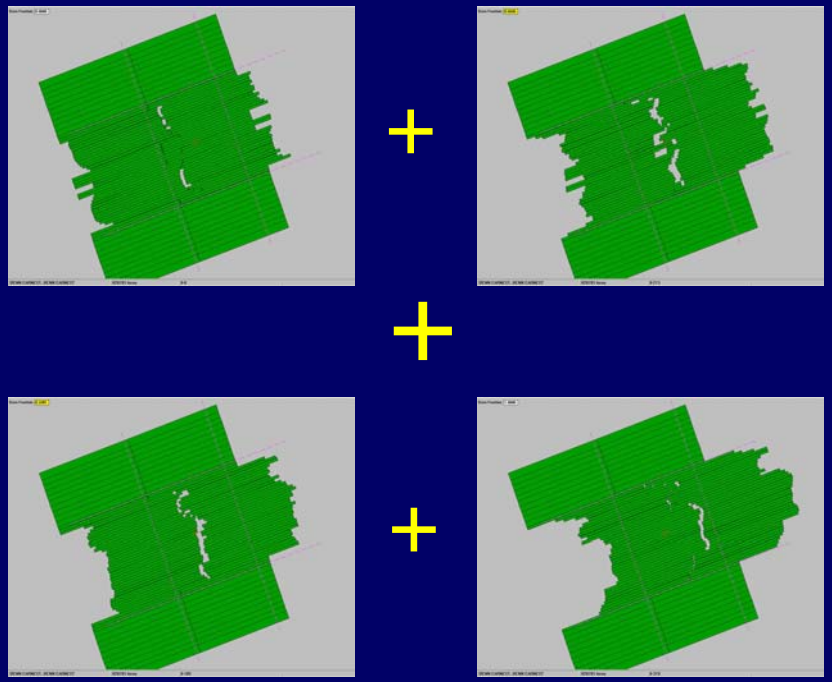
- HN ca pts with T2-T4 N0-N2c selected for planning
  - PTV1 = gross dz/enlarged LN + 1.0 cm + 0.3 cm
  - PTV2 = LN at risk + 0.3 cm
- Defined in a single plan for 30 fractions using 6 MV photons
  - PTV1 dose 2.3 Gy/fx to 69 Gy
  - PTV2 dose 1.8 Gy/fx to 54 Gy
  - Planning goal was to restrict contralateral parotid gland mean dose < 26 Gy

Comparison of MLC Leaf Width

- 9 equidistance coplanar beams were used
- 2 inverse plans were generated for each pt, one for each MLC (5 vs 10 mm)
- Leaf motions generated
- Beam fluence computed



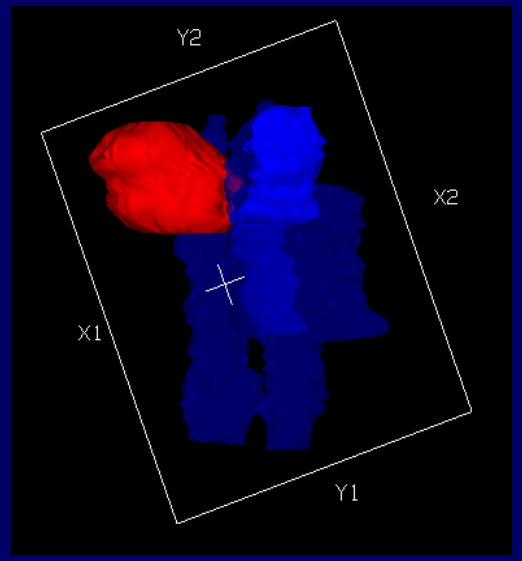
Comparison of MLC Leaf Width



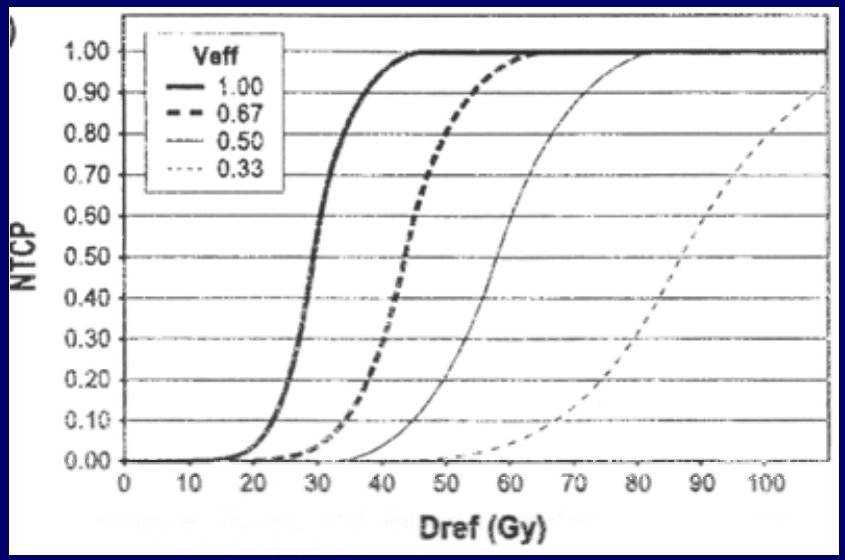
Primary PTV

Parotid

Nodal PTV



Comparison of MLC Leaf Width



- Because of differences observed in physical dose to the parotid gland an NTCP model based upon clinical parameters of Eisbruch et al was used for comparison

Comparison of MLC Leaf Width

		average mean doses		
MLC	**PTV1**	**ipsi PTV2**	**cont PTV2**	**spinal cord**
width	**dose (Gy)**	**dose (Gy)**	**dose (Gy)**	**dose (Gy)**
5 mm	71.0 (69.8-73.3)	61.9 (59.6-63.4)	55.6 (55.1-55.9)	34.8 (29.5-39.6)
10 mm	71.7 (70.8-73.4)	62.0 (59.4-63.2)	55.8 (55.7-55.9)	34.9 (30.8-40.3)

- Results
  - Both MLC leaf widths maintained target volume coverage
  - Critical organ dose goal

Comparison of MLC Leaf Width

	average mean doses	
MLC width	**spared parotid dose (Gy)**	**NTCP of parotid (%)**
5 mm	21.0 (19.9-22.9)	8.2 (5.5-14.2)
10 mm	22.3 (19.9-24.9)	13.7 (4.9-25.2)

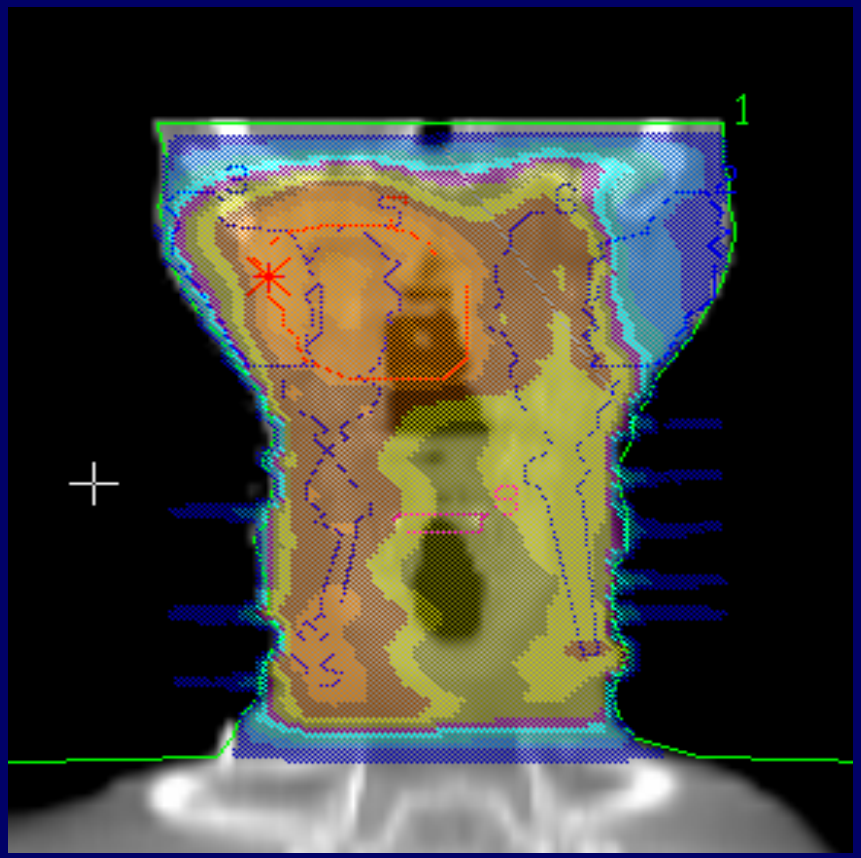
- Results
  - Both MLC leaf (5 mm, 10 mm) spared the contralateral parotid glands
  - Predicted complication probability was 5% better with 5 mm leaf width

Comparison of MLC Leaf Width

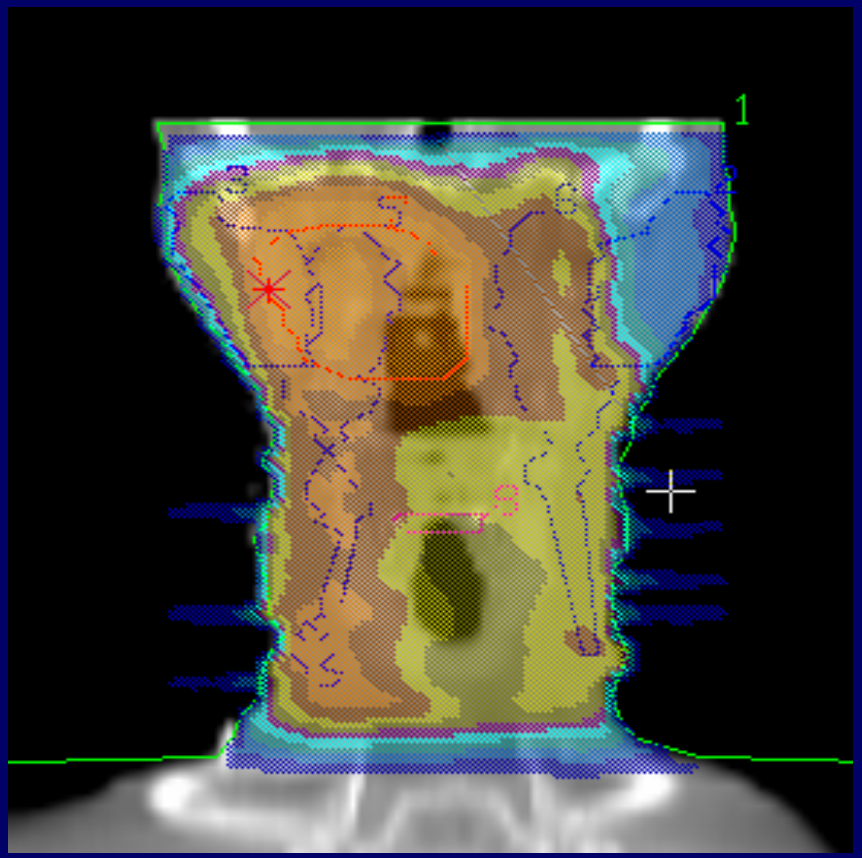
- Conclusion
  - The goal of parotid sparing was met for all levels of case complexity using either 5 mm or 10 mm leaf width
  - NTCP estimates suggested a modest reduction in xerostomia using smaller leaf width

Comparison of MLC Leaf Width

- Coronal color wash
- 5 mm leaf

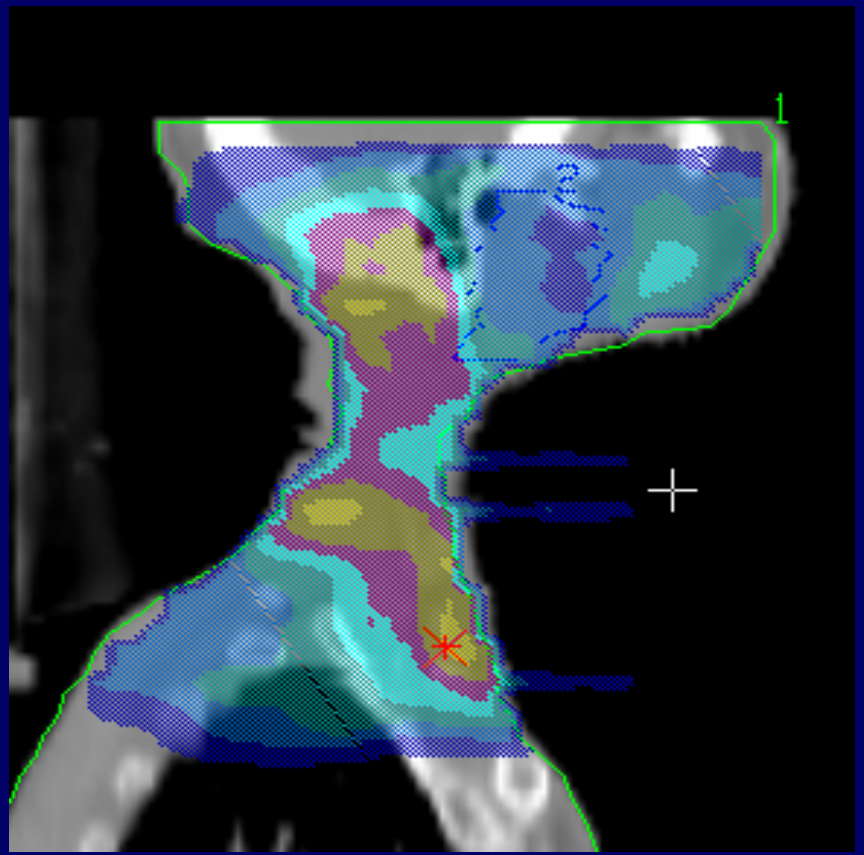


- 10 mm leaf

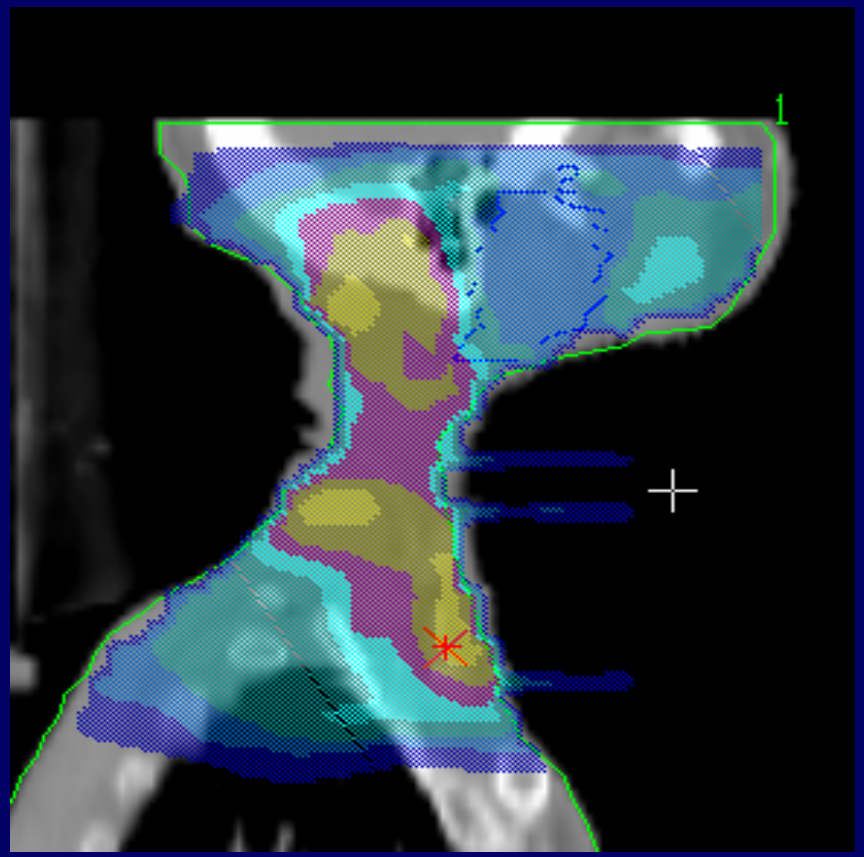


Comparison of MLC Leaf Width

- Sagittal color wash
- 5 mm leaf

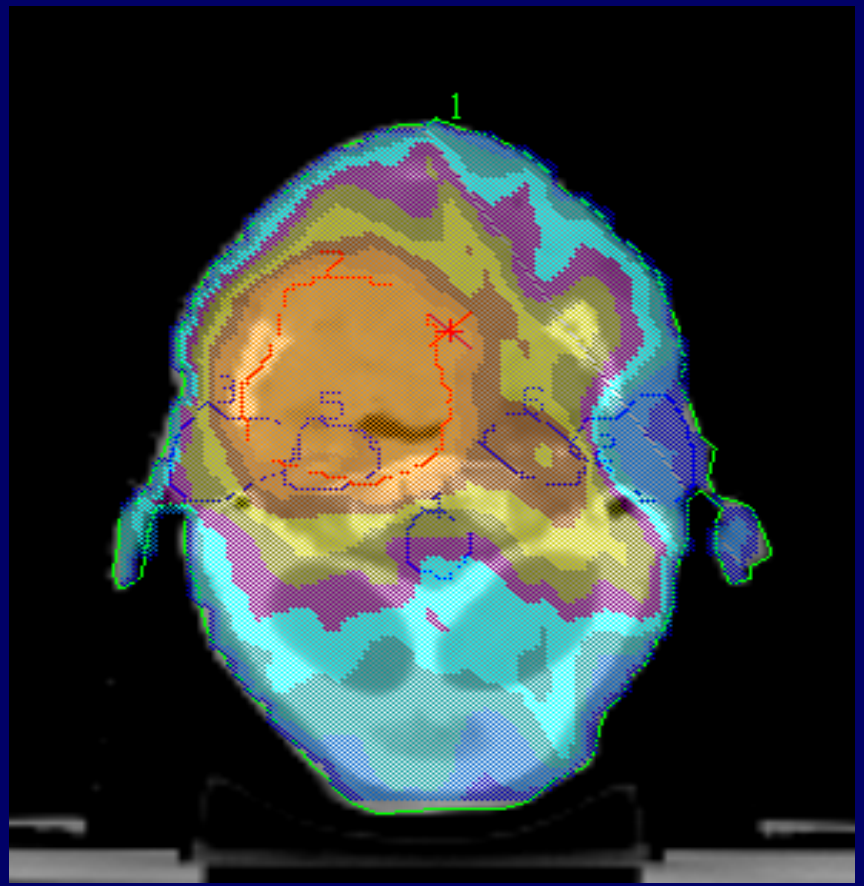


- 10 mm leaf

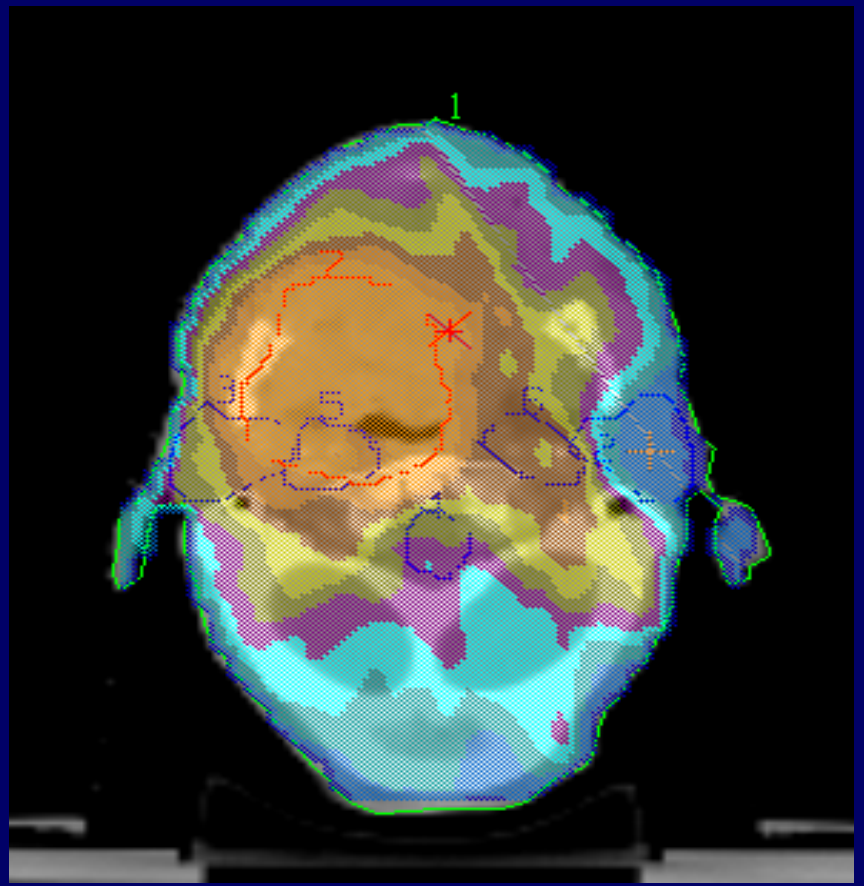


Comparison of MLC Leaf Width

- Transverse color wash
- 5 mm leaf



- 10 mm leaf

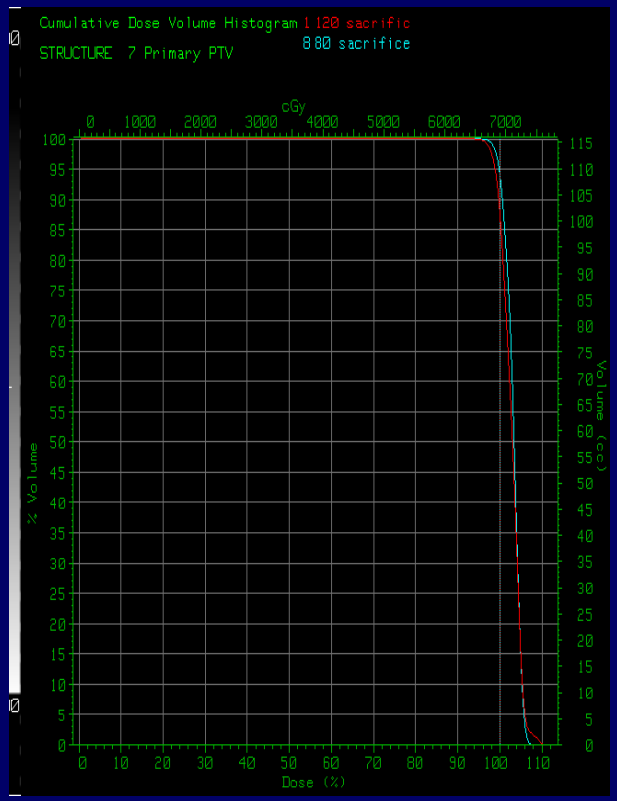


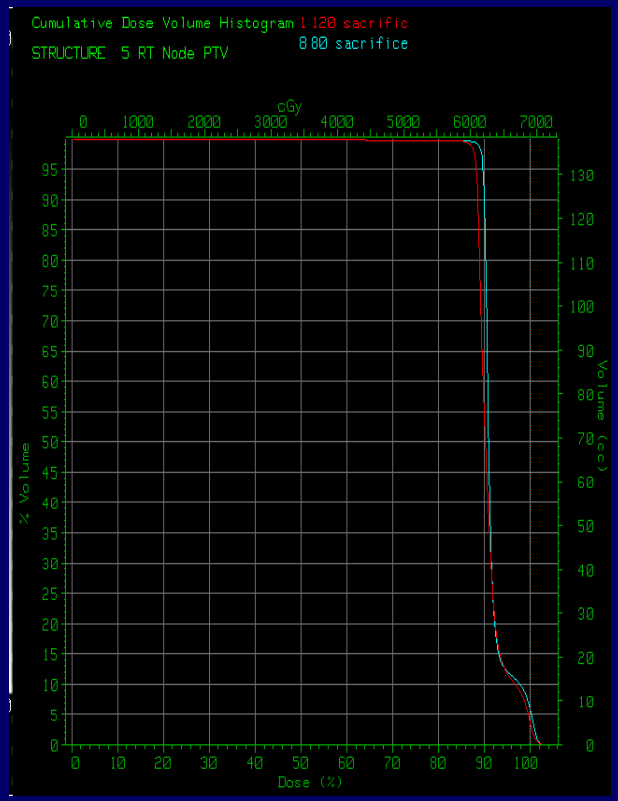
Comparison of MLC Leaf Width

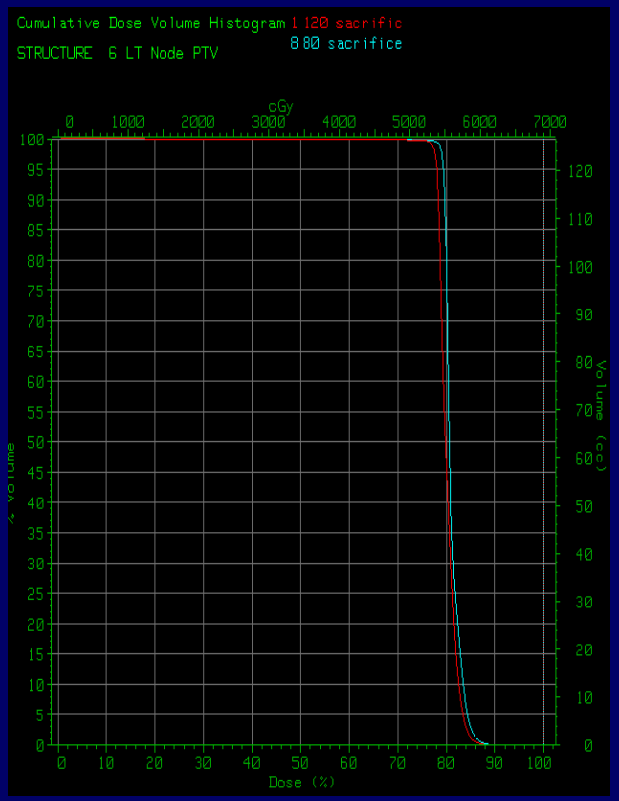
- PTV DVHs
- PTV1

Rt PTV2

Lt PTV2

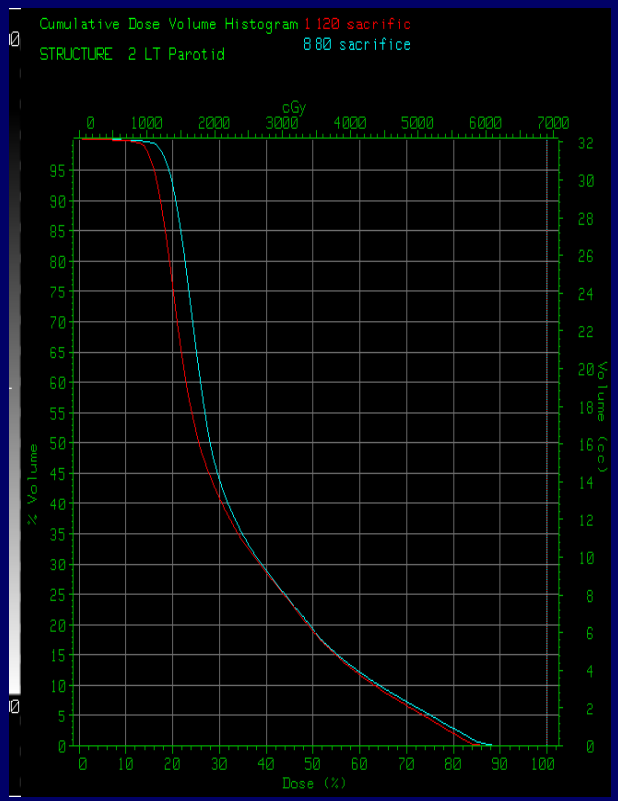






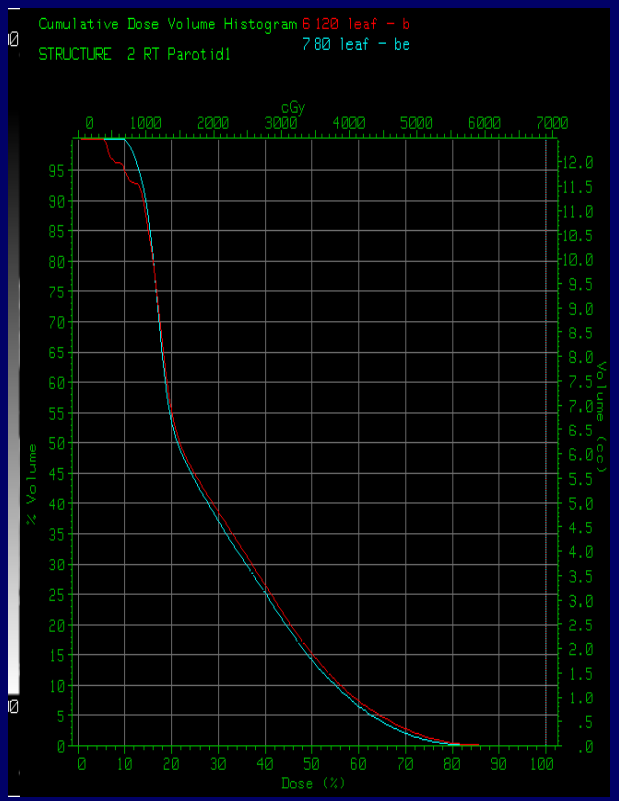
Comparison of MLC Leaf Width

- Parotid gland DVHs
- Case 1

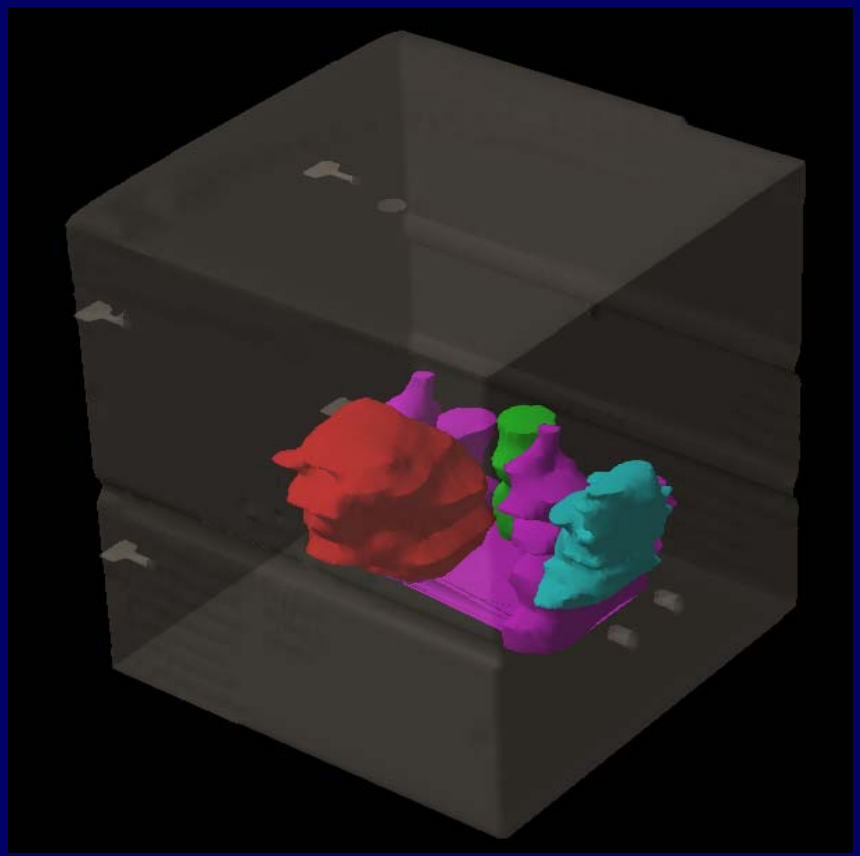


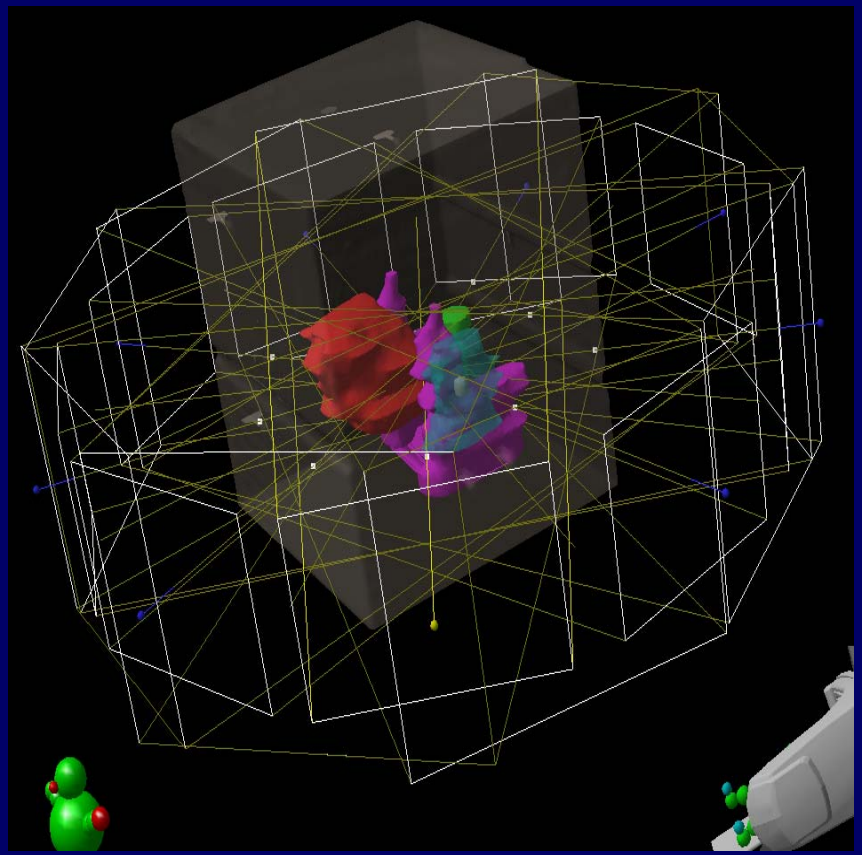
- Case 2

- Case 3

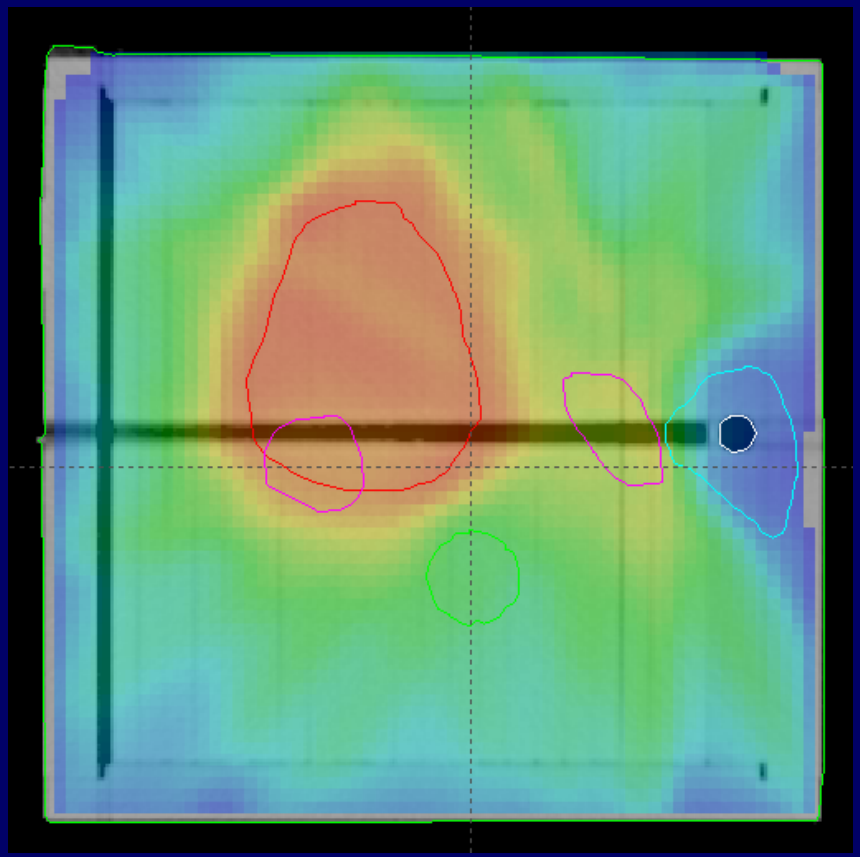


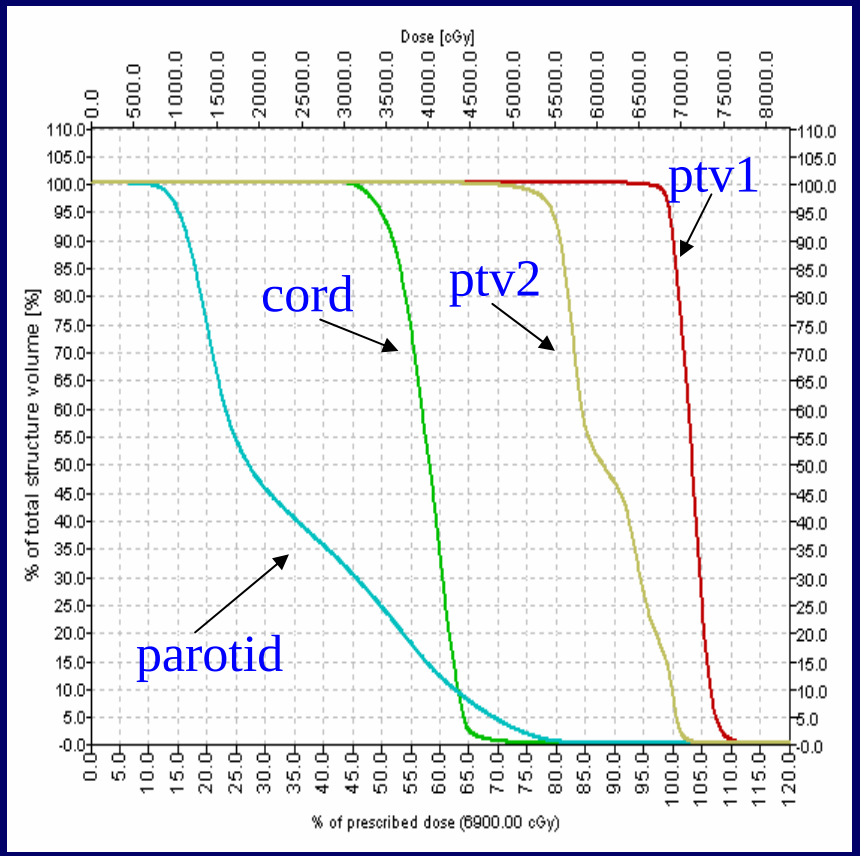
Phantom measurement



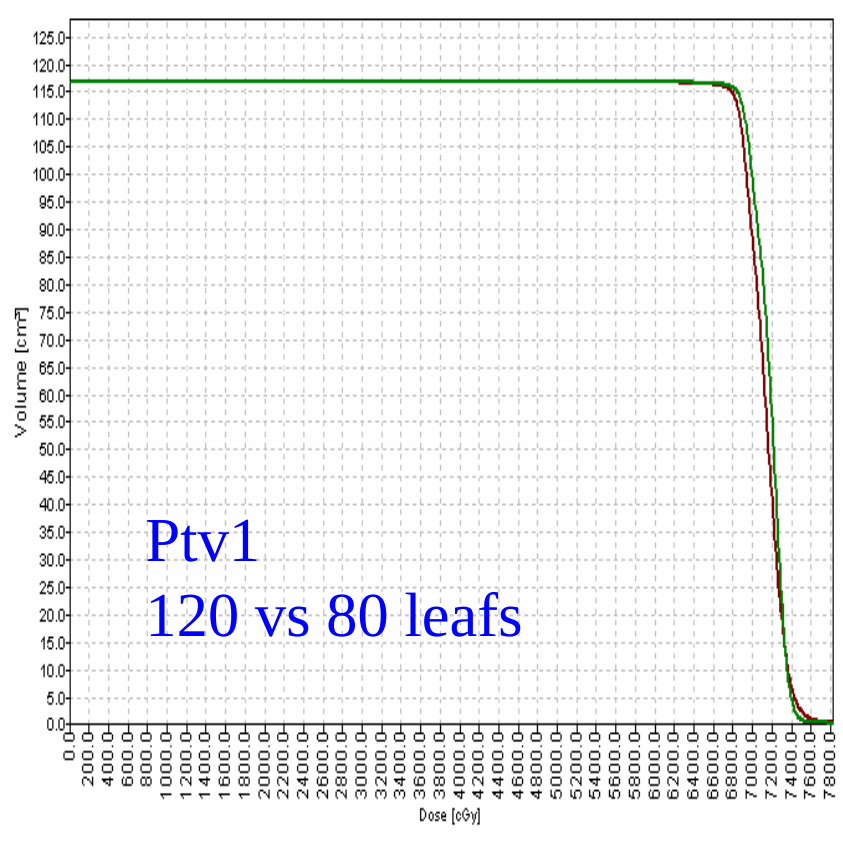


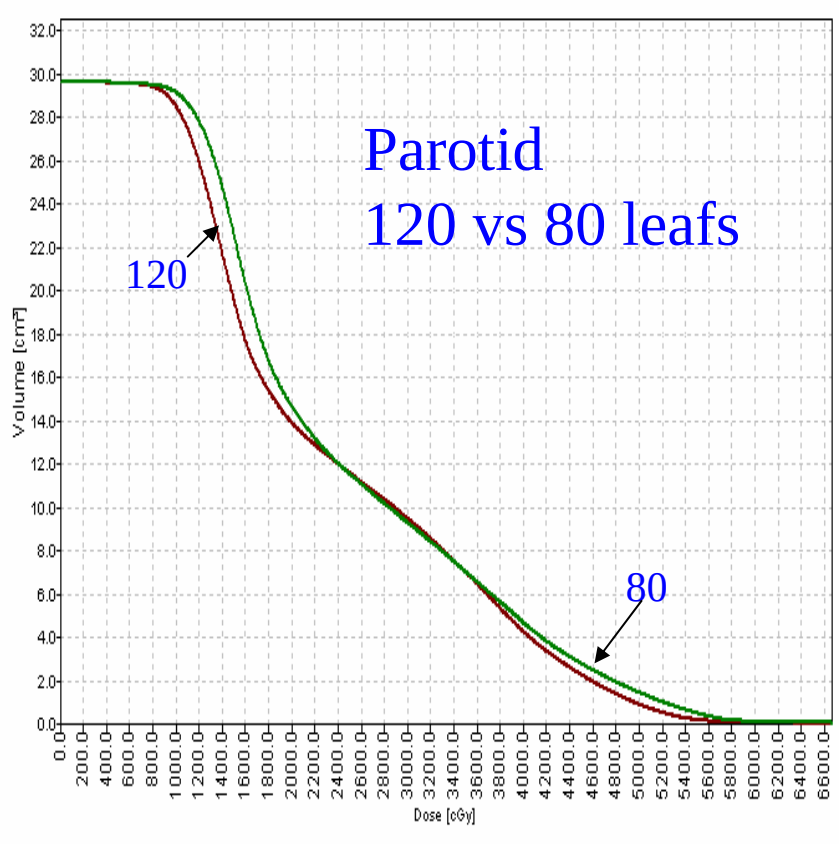
Phantom measurement





Phantom measurement





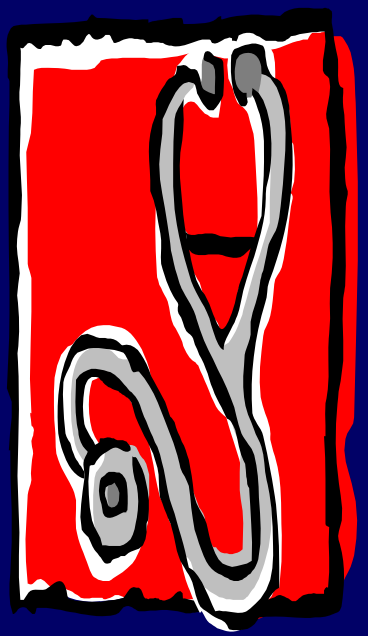
Phantom measurement

MLC leaf width	Mean ion chamber dose (cGy)	
	Plan	**Measurement**
5 mm (120 leaves)	55.7	73.5
10 mm (80 leaves)	61.7	79.5
Diff	6 **(-10%)**	6 **(-9%)**

- Difference between the 5 mm vs 10 mm measured data agrees with the difference of the Helios planning data.
- 120 leaf plan delivers about 9% less dose than the 80 leaf plan.

Conclusion

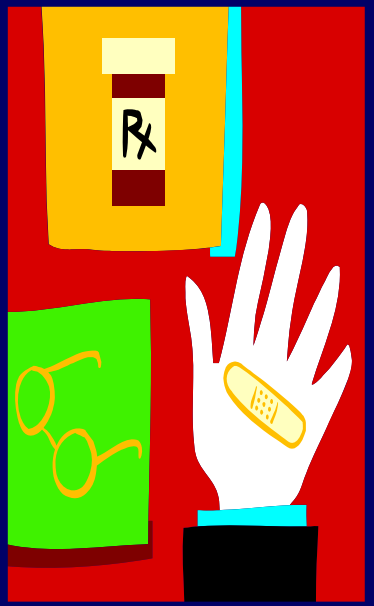
- Xerostomia is a significant problem for HN cancer pts receiving radiation therapy
- Managements of xerostomia includes salivary gland stimulant, radioprotector, surgical removal of the gland, acupuncture, 3D/IMRT technique



Conclusion

- IMRT significantly spares the contralateral parotid gland and avoids xerostomia for HN cancer pts
- IMRT dose distribution is more conformal when given as SIB, more efficient and may be biologically more effective
- A mean parotid gland dose < 26 Gy should be the planning target dose

Conclusion



- While both 5 mm and 10 mm width MLC spared the contralateral parotid gland, the NTCP estimates suggested a modest reduction of xerostomia using smaller leaf width, in selected cases

Conclusion/ F/U on pt.

- Last F/U on 5/01 - clinically NED, most of his acute RT side effects resolved, continue to have dry mouth RTOG grade 2
- The parotid sparing SIB IMRT planning might have reduced the chance of xerostomia in our pt

RTOG H-0022

- Phase I/II study of conformal/IMRT for T1-T2 N0-N2 oropharyngeal ca pts
  - to assess feasibility of adequate target coverage and sparing of the major salivary gland
  - to determine rate and pattern of LRF
  - to determine acute and late side effects

- PTV1 = gross tumor+1-2 cm+0.5 cm, PTV2 = LN at risk+0.5 cm
  - PTV1 = 2.2 Gy/fx to 66 Gy, PTV2 = 1.8 Gy/fx to 54 Gy, a boost 4-6 Gy to gross tumor is optional, QD 5d/wk, 6-6.5 wks
  - salivary gland dose = less than 26 Gy/ 50% gland less that 30 Gy

- Accrual target is 64 pts - needed to reduce xerostomia by 50%, LRC 65%

Acknowledgement

- I am grateful for the helpful support of all my colleagues at the Department of Radiation Oncology, UAB at Birmingham. I would like to thank

  R. A. Popple, Ph.D

  J. Duan, Ph. D

  J. A. Bonner, M. D.

  Mark Hyatt, C. M. D

  J. B. Fiveash, M. D.

The END