



# **Protons for Head and Neck Cancer** William M Mendenhall, M.D.



#### **Protons for Head and Neck Cancer**

#### **Potential Advantages:**

- Reduce late complications via more conformal dose distributions
- Likely to be the major advantage of protons for sites where they would be advantageous



#### **Potential Advantages:**

- Dose-escalation to improve local-regional control
  - Unlikely to occur because dose-escalation, even with more conformal treatment volumes, will likely result in increased late complications



#### **Protons for Head and Neck Cancer**

#### **Potential Disadvantages:**

- Depending on daily variability, air cavities may cause dose distributions to be less predictable compared with photons
- Increased skin reactions
- Overly conformal dose distributions may result in marginal misses that would likely not be salvaged



#### **<u>Reduce Late Complications</u>**:

- Paranasal sinuses, nasal cavity, nasopharynx, minor salivary gland carcinomas involving skull base, skin cancer with clinical perineural invasion
- Protons alone or combined with IMRT to reduce risk of visual and CNS complications



#### **Protons for Head and Neck Cancer**

#### **Reduce Late Xerostomia\_:**

- Oropharynx
- IMRT plus proton boost
- Reduce dose to salivary gland(s) to  $\leq 26$  Gy



#### **Protons for Head and Neck Cancer**

# **Protons Unlikely to be Beneficial :**

- Oral Cavity
- Larynx
- Hypopharynx
- Thyroid



#### Ca Oropharynx – Concomitant Boost 72 Gy





### Ca Oropharynx – Concomitant Boost 72 Gy

95% PTV receives prescription dose, 99% PTV receives 93% of prescription dose, and 20% PTV receives <110% of prescription dose

Tumor coverage	Photon IMRT	Protons
95% of PTV 5400/7200	7320 (101.6%)	7178 (99.7%)
99% of PTV 5400/7200	7221 (100.3%)	6975 (96.7%)
20% of PTV 5400/7200	7722 (107.3%)	7243 (106%)
Brain stem (0.1 c.c.)	5020	2685
Spinal cord (0.1 c.c.)	4400	546
Contralateral parotid	2529	1482
(mean dose ≤ 2600)		
Contralateral submandibular gland	6928	6148
(mean dose ≤ 2600)		



#### **Protons for Head and Neck Cancer**

#### "Where's the Beef?"

- Supposition that protons will be advantageous based on comparative dosimetry
- Limited long-term outcome data including variable primary sites, histologies, de novo vs. recurrent, etc...
- There's not much "beef"!





#### Nasal Cavity and Paranasal Sinus Ca

### **University of Florida**

- •1964 2005
- •109 patients
  - Definitive RT, 56 patients
  - •Surgery and RT, 53 patients
  - Altered fractionation, 96 patients (88%)

• Median follow-up on living patients, 9.4 years (range, 2.0 to 35.9 years)

•5 NED patients (5%) lost to follow-up from 4.9 years to 16.6 years



#### **Nasal Cavity and Paranasal Sinus Ca**

#### **University of Florida 5-yr Outcomes**

<u>Outcome</u>	<u>T1 – T3</u>	<u>T4</u>	<u>Overall</u>		
Local control	82%	50%	63%		
	<u>I-III</u>	<u>IV</u>	<u>Overall</u>		
DMFS	91%	75%	81%		
CSS	81%	52%	62%		
OS	71%	45%	55%		

Mendenhall et al, unpublished

### **Nasal Cavity and Paranasal Sinus Ca**

#### **University of Florida – Severe Complications**

- Definitive RT 9 (16%) of 56 patients:
  - Ipsilateral blindness (6)
  - Bilateral blindness (1)
  - Maxillary ORN (1)
  - Fatal post-op meningitis after salvage CFR (1)
- Surgery and RT 13 (25%) of 53 patients:
  - Ipsilateral blindness (3)
  - Post-op infection (1)
  - Graft failure (1)
  - Frontal bone ORN (1)
  - Frontal lobe necrosis (1)
  - Intracranial bleed (1)
  - Post-op meningitis (1)
  - Bilateral blindness (1)
  - Fatal infected bone flap (1)



#### Melanoma Maxillary Sinus





# **Paranasal Sinus Cancer**

#### **Massachusetts General Hospital**

- 91 patients carcinoma, 82 patients; sarcoma, 9 patients
  - Median dose 73.6 Gy (range, 59.4 and 77.8 Gy)
  - Median proportion of proton dose 49% (range, 23% to 84%)
  - -87% treated with accelerated hyperfractionated RT
  - 35% received adjuvant chemotherapy
  - Median follow-up, 45 months



### **Paranasal Sinus Cancer**

#### Massachusetts General Hospital 5-yr Outcomes (91 patients)

<u>Outcome</u>	<u>Percentage</u>
Local control	82%
Ultimate local control	86%
DMFS	75%
DFS	52%
OS	58%

Patel & Delaney, PPO Supplement, 2008



#### **Paranasal Sinus Cancer**

#### Massachusetts General Hospital (91 patients)

RT Complication	<u>Number of</u> <u>Patients</u>
Frontal/temporal lobe injury on MR	4 patients
Soft tissue or bone necrosis	2 patients

Patel & Delaney, <u>PPO Supplement</u>, 2008



#### Esthesioneuroblastoma

#### Proton Beam, NCI, Chiba, Japan

- 14 patients (1 previously irradiated)
- 1999 2005
- 65 Co<sup>60</sup> Gy equivalent at 2.5 Gy<sub>E</sub>/Fx
- Median follow-up, 40 months

Nishimura et al. IJROBP 68: 758, 2007



#### Esthesioneuroblastoma

#### NCI, Chiba, Japan N=14 patients

<u>5-year outcomes</u>	<u>Percentage</u>
Local control	84%
RFS	71%
Overall survival	93%
	Nishimura et al. IJROBP 68: 758. 200



#### Esthesioneuroblastoma

#### NCI, Chiba, Japan N=14 patients

- 1 patient with Kadish stage C tumor "liquorrhea" of skull base (STN?)
- No other grade 3 4 complications

Nishimura et al. IJROBP 68: 758, 2007



### Adenoid Cystic Carcinoma Head and Neck

# **University of Florida**

- 101 de novo patients
- 1966 2001
- T<sub>1</sub> T<sub>3</sub>, 57 patients; T<sub>4</sub>, 44 patients
- Surgery and RT, 59 patients; RT alone, 42 patients
- Median follow-up, 6.6 years (range, 0.4 30.6 years)



#### Adenoid Cystic Carcinoma Head and Neck

#### **University of Florida**

<u>Group</u>	<u>5-year local control</u>		
$T_1 - T_2$	92%		
$T_3 - T_4$	64%		
Overall	77%		
T <sub>4</sub> - RT alone	44%		
T <sub>4</sub> - Surgery and RT	93%		

Mendenhall et al. <u>Head Neck</u> 26: 54, 2004



#### Adenoid Cystic Carcinoma Head and Neck

#### **University of Florida** (N=110 patients)

<b>Complications</b>	Number of Patients
Ipsilateral blindness	6
Bilateral blindness	0
ORN requiring surgery	3
Permanent PEG	1
Oral antral fistula	1
Fatal meningitis after salvage surgery	1
Fatal hemorrhage after reconstructive surgery for tracheal stenosis	1
	Mendenhall et al. Head Neck 26: 54, 2004



# **Skull Base Adenoid Cystic Ca**

#### Massachusetts General Hospital

- 23 de novo patients
- 1991 2002
- Biopsy alone, 48%; subtotal resection, 39%; gross total resection, 13%
- Median follow-up on living patients, 64 months
- Median dose, 75.9 cobalt Gy equivalent



# **Skull Base Adenoid Cystic Ca**

# Massachusetts General Hospital 23 patients

5-year local control	93%
5-year DMFS	62%
5-year overall survival	77%

Pommier et al. Arch. Otolaryngol. 132: 1242, 2006



# **Skull Base Adenoid Cystic Ca**

#### Massachusetts General Hospital 23 patients

- No grade 5 visual complications; 1 grade 4 retinopathy
- 7 chronic seizure disorders controlled with meds
- One fistula with CSF leak and meningitis



# **Oropharyngeal SCCA**

#### Loma Linda

- 29 patients, stage II IV
- 1991 2002
- 75.9 GyE / 45 FX / 5.5 weeks
- Follow-up, 2 to 90 months

Slater et al. <u>IJROBP</u> 62: 494, 2005



# **Oropharyngeal SCCA**

#### Loma Linda

<u>5-year outcomes</u>	<u>Percentage</u>
Local control	88%
Neck control	96%
Local-regional control	84%
Late grade 3 toxicity	3/29 patients (10%)
No ORN	

Slater et al. <u>IJROBP</u> 62: 494, 2005



# **Oropharyngeal SCCA**

<u>Series</u>	No. of <u>patien</u> <u>ts</u>	<u>%</u> <u>T4</u>	<u>% St</u> <u>IV</u>	5-year <u>local</u> <u>control</u>	5-year local <u>regional</u> <u>control</u>	Late <u>complications</u>
Loma Linda	29	21%	<b>62</b> %	88%	84%	10%
UF – Tonsil	503	17%	<b>61</b> %	79%	73%	12%
UF – BOT	333	21%	75%	82%	77%	<b>16</b> %
Slater et al. <u>IJROBP</u> 62: 494, 2005 Mendenhall et al. <u>AJCO</u> 29: 32, 2006 Mendenhall et al. <u>AJCO</u> 29: 290, 2006						



# Conclusions

- Protons probably most useful for tumors involving skull base to reduce CNS and visual complications and possibly improve local control
- Hyperfractionated to reduce visual complications
- May be useful in oropharygeal cancer to reduce late effects, particularly xerostomia – decrease parotid dose to less than median 26 Gy





Do not be too conformal!

If you can miss with IMRT, you can miss with protons!

RAPID COMMUNICATION

RECURRENCE IN REGION OF SPARED PAROTID GLAND AFTER DEFINITIVE INTENSITY-MODULATED RADIOTHERAPY FOR HEAD AND NECK CANCER

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