General Principles of Radiotherapy

In

Head & Neck Cancers

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The Silent Tsunami

**HNSCC** (Head & Neck Squamous Cell Carcinoma)

Accounts for about 4,50,000 cases worldwide
By 2020, incidence double

20% of cancer burden - 1,50,000 new cases in 2000 in India*

Oral Cancers

TMH - 12% of all new cases annually (1800)
> 75 % present with advanced disease

*GLOBOCAN-IARC, Lyon 2000*
HNSCC CANCER

Patterns of failure

- Loco regional failure: 75 - 90 %
- Distant Mets: 05 - 10 %
- Second Primary: 10 - 20 %
HNSCC CANCER

Multidisciplinary Team

Surgical Oncologist
Radiation Oncologist
Medical Oncologist
Medical Physicists
Radiotherapy Technologist
Dentistry / Prosthodontics
Speech and Swallowing therapy
Physical Medicine & Rehabilitation
Social Services
Role of radiotherapy

- Radical: External beam
- Brachytherapy: Interstitial
  Intraluminal
- Concurrent chemo-radiotherapy
- Adjuvant
- Palliative
What is radiotherapy?

The use of ionising radiation in the treatment of malignant and benign conditions

Aim of radiotherapy

Deliver tumoricidal doses to the disease limit dose to surrounding normal structure to tolerance
General Management Guidelines: HNSCC Cancers

AIM

Highest loco-regional control

Anatomical with functional Preservation

• **Stage I / II** disease - Single modality (Surgery or RT)

• **Stage III / IV** disease – Combined modality
  
  *Surgery + RT (in most patients)
  *Chemotherapy + RT in selected patients
Basis of fractionation in radiotherapy can be understood today in terms of the principles of

- **Repair** of sublethal damage
- **Reassortment** of cells within the cell cycle
- **Repopulation**
- **Reoxygenation**
- **Inherent radiosensitivity**
RADIOThERAPY

High tumour control, high risk of complications

Low risk of complications, low tumour control

Medium tumour control, medium risk of complications
RADIOTHERAPY
PROCESS

Patient Immobilization → Diagnostic Imaging → Contour Target Volume and Normal Structure → Select Beam Geometry and Energy

Forward or Inverse Plan Optimization → Plan Evaluation & Approval

Set up Simulation

Treatment Planning

Verification and QA

Machine Quality Assurance → Patient Dose Verification → Patient Position Verification → Patient Set up → Patient Treatment
RADIOTHERAPY PROCESS
Radical Radiotherapy

**Indications**
- Early stage disease
- Inoperable (medical contra-indications)
- Surgery is morbid

- Combination of EBRT + Brachytherapy
- EBRT alone
- Radical Brachytherapy
Radical Radiotherapy

Volume:

- 70-80 Gy
- 66-70 Gy
- 45-50 Gy
Tissue compensator

Conformal block
ELECTRONIC PORTAL IMAGING
Conventional fractionation

1.8 - 2 Gy/ fr
One fraction per day
5 days a week
Altered Fractionation Schedules

Biologic Rationale:

a) the fraction size is the dominant factor in determining late effects, and the overall time has little influence

b) by contrast, the fraction size and overall treatment time both determine the response of acutely responding tissues
Accelerated treatment

- approx. conventional total dose

- conventional fraction number

- overall time is approx. halved (since two fractions are given)

- Intent- to reduce repopulation in rapidly proliferating tumours.
Hyperfractionation

- to further separate the early and late effects
- overall treatment time 6-8 wks
- two fractions / per day
- number of fractions are doubled to 60-80
- dose per fraction - decreased
- Intent - further reduce late effects while achieving the same or better tumour control and the same or slightly increased early effects.
Altered Fractionation- In conclusion

Modification of dose per fraction, total dose based on tumor kinetics in an attempt to increase therapeutic ratio
Criteria for brachytherapy

- Accessible
- <3 cm in size
- Away from bone
- No nodal disease
INTERSTITIAL BRACHYTHERAPY FOR CARCINOMA OF TONGUE
DISTRIBUTION OF TONGUE IMPLANT
Intraluminal brachytherapy for cancer nasopharynx
Prophylaxis

Pre-treatment

- Dental prophylaxis:
  - Extraction
  - Scaling

- Application of fluoride gel
Adjuvant Radiotherapy

Indications

T3, T4 primary
High grade
Infiltration of soft tissues/ muscle/ bone
Perineural invasion
Lymphovascular emboli
Cut margin positive/ close
Thickness
Recurrent disease
Multiple nodes
Perinodal extension
Adjuvant Radiotherapy

**Volume**
Primary + one station beyond involved nodes

**Dose**
56 - 60 Gy/ 28 - 30 fr/ 5-6 weeks
Radical RT (TMH): 568 PTS. \textit{Clin Oncol 2006}

5-yr Local Control: 53%

Local Control vs stage

Stage I
Stage II
Stage III
Stage IV

p=0.0000

Local Control vs primary site

Larynx
Hypopharynx
Oropharynx
Oral cavity

p=0.0028

Local Control vs RT dose

RT dose $\geq$ 66 Gy
RT dose < 66 Gy

p=0.0015
Radical RT (TMH): 568 PTS. \textit{Clin Oncol 2006}

5-yr DFS: 41%

DFS vs stage

DFS vs primary site

DFS vs RT dose

DFS vs RT dose

RT dose ≥ 66 Gy

RT dose < 66 Gy

Stage I

Stage II

Stage III

Stage IV

Larynx

Oral cavity

\(p=0.0000\)

\(p=0.0984\)

\(p=0.0017\)
Post-operative Radiotherapy

Indications:

• T3/4 STAGE
• HIGH GR HISTOLOGY
• CUT MARGIN + OR CLOSE
• LVI/PNI

• NODE POSITIVE
• PNE
Post-op RT (TMH) 368 Pts.: J. Surg Oncol 2005

5-yr Local control: 79%

Local control vs Primary site

Local control vs PNE

Local control vs stage

Larynx

Oral cavity

Path stage I-II

Path stage III-IV

PNE negative

PNE positive

p=0.9852

p=0.0046

p=0.6811

p=0.0046
Post-op RT (TMH) 368 Pts. *J. Surg Oncol* 2005

5-yr DFS: 56%

DFS vs primary site

Oropharynx \( p = 0.0412 \)
Larynx
Hypopharynx
Oral cavity

DFS vs PNE

\( p = 0.0005 \)

PNE Negative
PNE positive

DFS vs Path stage

\( p = 0.9001 \)

AJCC Path Stage I-II
AJCC Path Stage III-IV
CONFORMAL RADIOTHERAPY

• Enhanced conformation allows for greater dosages of radiation to reach the target volume (conformal shaping)

• While minimizing the dose delivery to surrounding normal tissues (conformal avoidance)
Improving Efficacy of Irradiation

• Physical Dose Escalation
  – Better target definition/delineation
  – Better radiation delivery

• Biological Dose Escalation
  – Altered Fractionation Schemes
  – Radiation and Chemotherapy
  – Selective Tumor Radiosensitization
  – Bio reductive drugs Tirapazamine
  – EGFR Inhibitors
technology
<table>
<thead>
<tr>
<th>Investigators</th>
<th>No. of Trials</th>
<th>No. of pts.</th>
<th>Relative Risk of Death (RT / CT + RT)</th>
<th>Absolute Benefit</th>
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<tr>
<td></td>
<td>Period</td>
<td></td>
<td>Neo</td>
<td>Conc.</td>
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<tr>
<td>Stell (1992)</td>
<td>28</td>
<td>4292</td>
<td>1.09 (NS)</td>
<td>0.71</td>
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<td></td>
<td>(before 1991)</td>
<td></td>
<td>p=0.02 (NS)</td>
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<td>Munro (1995)</td>
<td>54</td>
<td>7828</td>
<td>0.83 p=0.01</td>
<td>0.56 p&lt;0.001</td>
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<td>(1963-1993)</td>
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<tr>
<td>El Sayed (1996)</td>
<td>42</td>
<td>5079</td>
<td>0.95 (NS)</td>
<td>0.78 p&lt;0.005</td>
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<td>(1963-1993)</td>
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<td>MACH NC (1998)</td>
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<td>0.95 (NS)</td>
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<td>(1965-1993)</td>
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<td>Browman (2001)</td>
<td>18</td>
<td>3192</td>
<td>0.83 p&lt;0.0001</td>
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Meta-analyses

• 6 Meta-analyses addressing the status of chemotherapy in HNC
• Only 1 is IPD based (MACH-NC)
• 5 favour the addition of chemotherapy
• Concomitant Platinum based chemotherapy appears most beneficial WHILE neo-adjuvant and adjuvant chemotherapy provide no advantage
• Concomitant chemoradiotherapy increases survival
• Morbidity not yet quantified
Head and Neck Intergroup Trial R91-11

- Abstract ASCO 2002
- 576 patients
- RT alone VS Three-weekly Platinum VS NACT (Platinum + 5FU)
- No Survival Difference =76% (5 yr)
- Larynx preserved in 66% of concurrent arm VS 58% in NACT arm VS 52% in RT arm
Points to Ponder

• Chemoradiotherapy and Altered fractionation (concomittant boost and hyperfractionation) may provide improvement in control and survival -

• Are they feasible?
• Which is better?
• What is the optimum combination and sequencing?
Factors

- Type of radiation
- Dose per fraction
- Time between fractions
- Total dose delivered
- Irradiated volume
- Anatomic structures exposed
Effects of Radiotherapy

- Skin
- Mucosa
- Salivary glands
- Spinal cord
- Teeth
Palliative radiotherapy

**Symptoms:**
- Bleeding
- Fungation
- Pain

**Volume:**
- Gross disease with min margins

**Dose:**
- $8\text{Gy}/1\text{fr}$ or $20\text{Gy}/5\text{fr}$ or $40\text{Gy}/16\text{fr}$