Overview of IMRT in head and neck cancer

Jean Bourhis, MD PhD

- IGR, Villejuif & ESTRO -
How to improve the therapeutic index of radiotherapy?

**Balsitics (PTV, GTV)**  
**Biomodulation (CTV/ GTV)**

**Imaging**
- Multimodal / Motion
- Functional
Very high precision

RT 2D

RT 3D, conformational

IMRT

IGRT

Stereo radiotherapy

Cyberknife

Vero

Tomotherapy

Carbon 12

Protons

Particles

Cost / sophistication

Photons

Particles
Head & neck cancer

New

Molecular Targeted therapies

IMRT

EGFr targeting

Induction TPF

RT-CT

Amifostine

Altered fractionation

Hypoxia targeting

Proved

(EBM Level 1)
IMRT is increasingly used (2004....)

Mell LK, Cancer 2005;104:1296-303
IMRT in HNSCC

1) Better normal tissue protection

2) Dose escalation to the tumor

*Interesting since*: - Most relapses in the GTV - Dose effect relationship

3) Dose painting?
IMRT:

Increased dose conformality → Subsequent clinical benefit?
IMRT: increased dose conformality
IMRT > to more conventional RT in NPC ...
Carcinological results in NPC

**Table 1: Locoregional Control After IMRT for Head and Neck Cancer**

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients</th>
<th>Primary Site</th>
<th>RT</th>
<th>Follow-Up (months)</th>
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<tbody>
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<td></td>
<td></td>
<td></td>
<td>Definitive</td>
<td>Postoperative</td>
<td>Local (%)</td>
</tr>
<tr>
<td>Chao et al(^\text{19})</td>
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Abbreviations: IMRT, intensity-modulated radiotherapy; RT, radiotherapy; NPX, nasopharynx; OPX, oropharynx.

*Patients treated from 1994 to 2002; three-dimensional conformal radiotherapy was used before 1996, and IMRT thereafter.

Mendenhall W. JCO 2006

Tham et al *IJROBP* 2009, 195 pts…
Lin et al *IJROBP* 2009, 323 pts… etc…
NPC: unmet results before IMRT
(ex: Lee et al 2002)

- 67 patients

- 2/3 stage III / IV

- 70 Gy + IMRT + CDDP
IMRT ± Chemo for NPC
Progression-Free: Local & Regional

5-Y nodal control: 97%
5-Y primary tumor control: 94%

N = 87
Median FU = 30 months

Lee et al (UCSF), IJROBP, 53:1:12-21
Late radiation effects (Lee et al 2002, $N = 67$ pts)

- At 24 months: xerostomy
  - Grade 1 = 33%
  - Grade 0 = 67%

- Other late effects:
  - 20 grade 2
  - 7 grade 3
  - 1 grade 4
IMRT > to more conventional RT in other HNC …
# IMRT in HNSCC: Carcinological Results

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Mendenhall W. JCO 2006
Comparison IMRT vs Conventional 3D RT

Fig. 9. Frequency of Radiation Therapy Oncology Group (RTOG) Grade 0–2 xerostomia among patients with at least 20 months follow-up after concomitant boost radiotherapy (CBRT) or intensity-modulated radiotherapy (IMRT).
Example: a prospective multicentric study HNSCC with bilateral irradiation of the neck

(M Lapeyre)
Gortec study: survival and LRC (N = 93 pts)

- LRC: 59% stage III / IV
- Survival: 30% concomitant RT-CT
- Relapse: 9 (100% infield)
Gortec study: late xerostomia
(RTOG-EORTC)
# Saliva dysfunction as a function of parotid dose

<table>
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<th>Grade &gt;= 2</th>
</tr>
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## Controlateral parotid:

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<th>Mean dose &lt; 30 Gy</th>
<th>16 %</th>
</tr>
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<td>Mean dose &gt; 30 Gy</td>
<td>43 %</td>
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$p=0.05$
Importance of the other salivary glands: Sub-mandibular (Murdoch Kinch, IJROBP 2008)

Selective collection of stimulated saliva flow from Wharton’s ducts:

- Post-RT flow decreases with increasing mean dose: (1.2%)/Gy up to 39 Gy
- 2.2% increase flow time/month when mean dose <= 39 Gy
IMRT in HNC: beyond EBM level 3?

- Do we need it since we have converging EBM level 3?

- What is the evidence?
IMRT in early stage NPC: a randomized trial

(Pow et al, IJROBP 2006, Hong Kong)

NPC
T2, N0-N1
N = 51

70 Gy (2D)

70 Gy

IMRT
Early stage NPC salivary flow (catheter 15’) N = 51 (Pow et al IJROBP 2006)

DFS = 88% at 1 year
Improved QOL

(>25% recovery / baseline)
A randomized trial of IMRT in HNC

(C. Nutting, ASCO 2009)

HNC R

70 Gy (2D/3D)

70 Gy IMRT
Impact of intensity-modulated radiotherapy on health-related quality of life for head and neck cancer patients: Matched-pair comparison with conventional radiotherapy.

Comparison in 2 groups of patients

- 67 patients 3D
- versus
- 67 patients IMRT

Matched analysis

(QLQ C30 & QLQ-H&N35)
### Results: 7 scores in favor of IMRT

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>RTE conv</th>
<th>IMRT</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>Score pain</td>
<td>33,5 [28,5]</td>
<td>21,5 [25,0]</td>
<td>0,01</td>
</tr>
<tr>
<td>Score deglutition</td>
<td>35,1 [26,2]</td>
<td>23,0 [25,6]</td>
<td>0,01</td>
</tr>
<tr>
<td>Score eating in public</td>
<td>38,2 [31,8]</td>
<td>26,9 [30,3]</td>
<td>0,03</td>
</tr>
<tr>
<td>Score teeths</td>
<td>34,9 [40,0]</td>
<td>19,5 [30,6]</td>
<td>0,02</td>
</tr>
<tr>
<td>Score mouth opening</td>
<td>48,3 [37,7]</td>
<td>28,8 [31,9]</td>
<td>0,001</td>
</tr>
<tr>
<td>Score dry mouth</td>
<td>83,1 [25,5]</td>
<td>57,2 [33,2]</td>
<td>&lt;0,0001</td>
</tr>
<tr>
<td>Score sticky saliva</td>
<td>76,6 [30,1]</td>
<td>47,1 [34,7]</td>
<td>&lt;0,0001</td>
</tr>
</tbody>
</table>
### Prevalence of severe symptoms:

<table>
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<th>Item</th>
<th>RTE conv</th>
<th>IMRT</th>
<th>Odds ratio adjusted</th>
<th>p</th>
</tr>
</thead>
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<tr>
<td>Q31: mouth pain</td>
<td>35,8</td>
<td>19,4</td>
<td>3,58</td>
<td>0,02</td>
</tr>
<tr>
<td>Q32: pain other</td>
<td>36,4</td>
<td>16,7</td>
<td>3,35</td>
<td>0,04</td>
</tr>
<tr>
<td>Q37: deglutition</td>
<td>56,1</td>
<td>34,8</td>
<td>2,76</td>
<td>0,02</td>
</tr>
<tr>
<td>Q40: mouth aperture</td>
<td>45,5</td>
<td>21,2</td>
<td>2,60</td>
<td>0,02</td>
</tr>
<tr>
<td>Q41: dry mouth</td>
<td>83,6</td>
<td>56,7</td>
<td>3,17</td>
<td>0,04</td>
</tr>
<tr>
<td>Q42: sticky saliva</td>
<td>80,3</td>
<td>47,5</td>
<td>3,16</td>
<td>0,02</td>
</tr>
<tr>
<td>Q49: difficulties to eat</td>
<td>43,3</td>
<td>23,9</td>
<td>2,68</td>
<td>0,03</td>
</tr>
</tbody>
</table>
IMRT in HNSCC: some questions

Improved xerostomia: which patients will benefit?

SIB? Contouring? QA?

IMRT in re-irradiation (Sulman et al, IJROBP 2009, 78 patients)

Dose escalation?

Dose effect relationship

Most of the relapses in the GTV
Simultaneous integrated boost

2.35 Gy / fraction up to 70 Gy

1.7 Gy / fraction up to 54 Gy
Alternative to the SIB: 2 plans

2 Gy / fraction up to 50 Gy + 20 Gy in PTV2
SIB: potential advantages

- More conformal
- Only one planning
- No Junctioning
- Superior equivalent biological dose
  Higher in the GTV
  Lower for the CTV (need to compensate)
IMRT in HNC: dose escalation?

(Kwong et al, IJROBP 2006)

- 50 pts T3-4

- Dose (mean) to the GTV = 79.5 Gy

- Median follow-up 25 months, failure rate:
  \[ T = 4 \; ; \; N = 2 \; ; \; M = 2 \]

- Conclusion = feasible
Dose escalation with IMRT in HNSCC …

An ongoing randomized trial with / wo IMRT

(GORTEC 2004-01)

Oropharynx + OC
Stage II-IV with R

70 Gy + CDDP
IMRT 75 Gy + CDDP

Hypothesis = IMRT 75 Gy more efficient & less toxic ?
N = 67 pts
IMRT in HNC:

Importance of the RT-QA ...contouring
Contouring

- **GTV**: Endoscopy
  - CT-Scanner
  - MRI
  - CT-PET

- **CTV (prophylactic)**?
IMRT:

Importance of ...contouring

Pharynx constrictor muscles...
International survey : T2 Tonsil

Primary Tumor

Neck Node

Harari 2004
Samples:
Elective CTV Designs

Harari 2004
Outcome of radiotherapy in HNC:

Importance of the RT-QA … RT plan verification
LR Failure according to RT deviations yes / no (N=820)

(Dany Rishin, Lester Peters et al ASCO 2008)

Estimated percentage locoregional failure-free

No deviation

Deviation

2P < 0.0001

Years following end of radiotherapy

compliant plan by TMC
no adv impact
adv impact
IMRT in HNC:

Importance of the RT-QA
**QA**
de chacun des faisceaux d'intensité modulée du patient sur fantôme parallélépipède au Clinac et exploitation des résultats (mesure de la dose absolue par chambre d'ionisation et de la dose relative par film).

**QA**
de la distribution de dose cumulée pour l'ensemble des faisceaux d'intensité modulée du patient sur fantôme cylindrique et/ou anthropomorphe au Clinac et exploitation des résultats.

Measure on film

Calculation on TPS
IGR: position verification before each fraction

50’ (initial)

20’
Control / DRR
Do we need **daily** verifications? *(Pelhivan et al Acta Oncol 2008)*

20 patients with HNC treated by IMRT (Institute Gustave Roussy)

Portal verifications at each session: isocentre and comparison to DRR Ant-post; right / left; head / foot directions

**Results**:

Significant Deviation > 5-6 mm needing correction = 20% of cases

- **If portal every day with correction**: Margin CTV to PTV = 3 mm
- **If portal less frequent (any)**: Margin CTV to PTV = 6 mm
IMRT, next steps:

Further improvement of precision needed … and achievable.
New tools for radiation delivery:

Image guided RT

Adaptive RT

Dose Guided RT
Adaptive Radiotherapy - Anatomic and set-up Changes
19 CT Scans over 47 Days

Patient Immobilized with Acquaplast Mask

Barker et al. *IJROBP* 59:960-970, 2004 (MDACC); Lei Dong et al. (MDACC)
IMRT to Dose-guided-RT Innovations

CT (or Multimodality) + MVCB, kVCB, or CT
**Tomotherapy**

**Avantages**
- Source in rotation – no junction
- IMRT highly conformal
- Controle of position of soft tissues
- Simplicity

**Inconvenients:**
- Duration (>=30 mn)
- preparation/optimisation
- Diffuse low dose irradiation
Pilot Study for:

Dose painting based on hypoxia images

A. PET - $^{18}$FMISO
B. Fused $^{18}$FMISO FDG
C. $^{18}$FMISO profile

Lee, Schoder, Nehmeh, Humm et al.
MSKCC
IMRT in HNC: summary

- Better conformality / 3D, & increasingly used +++

- Steep dose gradient: need for clinical validation in locally advanced disease

- Very promising & converging results in HNC (EBM 2-3):
  - Few LR recurrence
  - Less late toxicity

- Learning curve / Re-inforced QA needed ++
• MV cone beam CT (Pouliot et al, USA)

MV CB CT:
1. Patient setup
2. Dose calculation
3. DGRT: exit dosimetry

1. Repositioning the patient: CT / CBCT
2. Calculation of the dose:
   comparaison of dose distribution between CT and MVCBCT

3. DGRT: reconstruction of the dose received and visualisation on the MVCBCT
Image Guided RT

1. In room CT
2. Cone Beam CT (CB CT)
   • kV CB CT
   • MV CB CT
3. MV CT (Tomotherapy)