Clinical Evidence & Indications for Head & Neck IMRT

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2D Conventional Radiotherapy

- Conventional radiotherapy uses uniform beams to create a treatment volume around a target
  - Beams flatness is an important parameter

- Simple field arrangements

- Uniformly irradiate both the target and the surrounding normal tissues.

- May include the use of shaped blocks to shield normal structures
3D Conformal Radiotherapy

- Multiple fields, including oblique and non-coplanar fields
- Varying weightage and wedges.
- Shaped blocks
  - Cerrobind
  - Multi-Leaf Collimators (MLC).
- CT-based 3D planning
Intensity Modulated Radiotherapy

• The basis of IMRT is the use of intensity-modulated beams that can provide two or more intensity levels for any single-beam direction and any single-source position.

• MRT treatment plans are able to generate concave dose distributions and dose gradients with narrower margins than those allowed using traditional methods especially suitable for treating complex treatment volumes and avoiding close proximity organs at risk.
Types of IMRT

• Forward planned IMRT
  – basically a form of complex 3DCRT using field-in-field technique.

• Inverse planned IMRT
  – requires Inverse Treatment Planning (ITP) software.
  – Set dose constraint on all important structures
  – Software calculates beam parameters
Advantage of IMRT

- Increased conformality may permit escalated tumor doses without increasing normal tissue toxicity and thus may improve local tumor control
  - Potential to improve cancer control rates, from possible dose escalation
- Decreased exposure to surrounding normal tissues, potentially reducing acute and late radiation toxicities.
  - Improved quality of life for patients
  - Reduced medication cost from short & long term effects
- Better dose homogeneity in the target may also improve local tumor control by avoiding underdosing within the tumor and decrease toxicity by avoiding overdosing
Disadvantages of IMRT

• Much more widespread distribution of low doses within parts of the body which would be spared with conventional treatments
  – Low dose effects have contributed to unexpected lung toxicity
  – Possible increased risk of second cancers occurring decades after treatment

• Beam on time is longer and there is increased leakage from the machine head and collimator

• Longer contouring and planning times
  – also less intuitive hence verify manually is more difficult
Evolution of Treatment planning with multiple beams
D1 = Low cures, No complications
D2 = Moderate cures, minimal complications
D3 = High cures high complications
30 studies, including 3 RCTs comparing IMRT with conventional RT/3DCRT
  - Of the 3 RCTs, 2 are small studies on Nasopharyngeal cancer.
  - The 3rd is the PARSPORT study from UK on oro-hypopharyngeal and laryngeal cancers.
Meta-analysis of IMRT

- Pow et al (n=51): Stage II NPX: 2DRT vs IMRT:
  - IMRT significantly increased xerostomia-related but not overall HRQoL.

- Kam et al (n=60): Stage I & II NPX: 2DRT vs IMRT:
  - IMRT significantly reduced the clinician assessed grade 2-4 xerostomia at both 6 weeks and 12 months
Overall, an estimated 30% of cancer patients can benefit from IMRT.
Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial

Christopher M Nutting, James P Morden, Kevin J Harrington, Teresa Guerrero Urbano, Shreerang A Bhide, Catharine Clark, Elizabeth A Miles, Aisha B Miah, Kate Newbold, MaryAnne Tanay, Fawzi Adab, Sarah J Jefferies, Christopher Scrase, Beng K Yap, Roger P A’Hern, Mark A Sydenham, Marie Emson, Emma Hall, on behalf of the PARSPORT trial management group*

Summary
Background Xerostomia is the most common late side-effect of radiotherapy to the head and neck. Compared with conventional radiotherapy, intensity-modulated radiotherapy (IMRT) can reduce irradiation of the parotid glands. We assessed the hypothesis that parotid-sparing IMRT reduces the incidence of severe xerostomia.
# PARSPORT Trial - Demographics

<table>
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<th>Conventional radiotherapy (n=47)</th>
<th>IMRT (n=47)</th>
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<tbody>
<tr>
<td>Mean age at randomisation (years)</td>
<td>57.3 (10.2; 37.5-82.8)</td>
<td>59.5 (9.2; 44.1-77.1)</td>
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<tr>
<td>Number of women</td>
<td>12 (26%)</td>
<td>14 (30%)</td>
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<td>WHO performance status</td>
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<tr>
<td>0 (89%)</td>
<td>42</td>
<td>41 (87%)</td>
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<td>1 (11%)</td>
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<td>Tumour site</td>
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<td>40 (85%)</td>
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<td>Hypopharynx</td>
<td>7 (15%)</td>
<td>7 (15%)</td>
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<tr>
<td>Tumour stage</td>
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<tr>
<td>T1 (13%)</td>
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<td>6 (13%)</td>
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<tr>
<td>T2 (57%)</td>
<td>27</td>
<td>22 (47%)</td>
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<tr>
<td>T3 (23%)</td>
<td>11</td>
<td>16 (34%)</td>
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<td>T4 (6%)</td>
<td>3</td>
<td>3 (6%)</td>
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<tr>
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<td>N0 (34%)</td>
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<td>23 (49%)</td>
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<tr>
<td>N1 (19%)</td>
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</tr>
<tr>
<td>N2a (15%)</td>
<td>7</td>
<td>2 (4%)</td>
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</tr>
<tr>
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<td>1 (2%)</td>
</tr>
<tr>
<td>N3 (6%)</td>
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<td>0</td>
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<tr>
<td>AJCC* stage</td>
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</tr>
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<td>1 and 2</td>
<td>8 (17%)</td>
<td>15 (32%)</td>
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<td>3 and 4</td>
<td>39 (83%)</td>
<td>32 (68%)</td>
</tr>
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</table>

Figure 3: Mean EORTC HN35 dry mouth subscale score changes from baseline

PARSPORT – LR Recurrence Free

Hazard ratio 1.53 (95% CI 0.63 to 3.70)

3D RT - 80%

IMRT - 78%

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Findings 47 patients were assigned to each treatment arm. Median follow-up was 44.0 months (IQR 30.0–59.7). Six patients from each group died before 12 months and seven patients from the conventional radiotherapy and two from the IMRT group were not assessed at 12 months. At 12 months xerostomia side-effects were reported in 73 of 82 alive patients; grade 2 or worse xerostomia at 12 months was significantly lower in the IMRT group than in the conventional radiotherapy group (25 [74%; 95% CI 56–87] of 34 patients given conventional radiotherapy vs 15 [38%; 23–55] of 39 given IMRT, p=0.0027). The only recorded acute adverse event of grade 2 or worse that differed significantly between the treatment groups was fatigue, which was more prevalent in the IMRT group (18 [41%; 99% CI 23–61] of 44 patients given conventional radiotherapy vs 35 [74%; 55–89] of 47 given IMRT, p=0.0015). At 24 months, grade 2 or worse xerostomia was significantly less common with IMRT than with conventional radiotherapy (20 [83%; 95% CI 63–95] of 24 patients given conventional radiotherapy vs nine [29%; 14–48] of 31 given IMRT, p<0.0001). At 12 and 24 months, significant benefits were seen in recovery of saliva secretion with IMRT compared with conventional radiotherapy, as were clinically significant improvements in dry-mouth-specific and global quality of life scores. At 24 months, no significant differences were seen between randomised groups in non-xerostomia late toxicities, locoregional control, or overall survival.
IMRT planning can be done conventionally by applying and adjusting beamlets from a chosen direction.

This approach is used to achieve a homogenous dose in selected patients with breast cancer. It is a simpler technique and is called forward planned IMRT.

One small trial compared 2D RT vs IMRT using field in field technique.
Breast radiotherapy – 2D vs Simple IMRT

Fewer patients in the simple IMRT arm developed suboptimal overall cosmesis (OR, 0.68; 0.48 -0.96; \( P \) .027) or skin telangiectasia (OR, 0.58; 0.36 to 0.92; \( P \) .021).

5-year LRR rates
- Control - 2.56%
- IMRT - 1.35% (\( P \).36).

5-year OS rates
- Control - 92.5%
- IMRT - 91.7%.

Mukesh BM et al JCO Vol 31 NO: 36 Dec 20 2013
Indications for IMRT

- If the reduction of xerostomia and improved quality of life are the main outcomes of interest, then IMRT is the recommended treatment for all nasopharyngeal, oropharyngeal, hypopharyngeal, laryngeal, oral cavity, and unknown primary cancers where lymph node regions requiring inclusion in the treatment volume would result in irreparable damage to salivary function if 2D EBRT or 3D EBRT were used due to their inability to maintain salivary doses within their tolerance limits (<26 Gy mean dose).
Indication for IMRT

• If blindness is to be minimized or avoided, IMRT is indicated in the definitive or adjuvant RT setting for nasal and paranasal sinus cancers or other sites where the disease is juxtaposed to the optic apparatus.
The H&N Multi-disciplinary team

- Cancers of the head and neck are relatively rare and should be managed by specialists as part of a multidisciplinary team.

- The team should include:
  - radiologist
  - pathologist
  - specialist head and neck cancer surgeons
  - clinical oncologist
  - restorative dentist
  - clinical nurse specialist
  - speech and language therapist
  - dietitian.
Summary

- There is a lack of level III evidence on the advantage of IMRT over conventional RT in terms of improved local control and overall survival
  - small trial focusing on side-effects and QOL have shown some advantage
- H&N cancer are ideally treated with IMRT due to the many OAR in close proximity with the PTV
  - IMRT can be recommended for all sites except T1N0 ca larynx based on improved dosimetry
- We await publication of more trials in the H&N area
Thank you
Intensity modulated radiotherapy (IMRT) is currently under development in UK cancer centres. No randomised controlled evidence was identified comparing outcome following IMRT with that following conventionally delivered radiotherapy for patients with head and neck cancer. Case series were identified which describe the use of IMRT to reduce radiation toxicity, particularly xerostomia (see section 6.7.2) and its use in re-irradiation following tumour recurrence (see section 9.2).