Adjuvant external beam radiotherapy after therapeutic groin lymphadenectomy for patients at risk of nodal relapse: A dosimetric comparison of three-dimensional conformal and intensity modulated techniques

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Aim

Primary cutaneous melanoma is the third most common cancer in Australia[1]. Although most diagnoses are at an early stage whereby local therapy may be curative, regional disease in the draining lymph-node field remains a common site of relapse with median overall 5 year survival rates of 33% to 59% after treatment, depending on the burden of macroscopic nodal disease [2]. The mainstay of treatment for regional disease is therapeutic lymphadenectomy [3].

The role of adjuvant external beam radiotherapy has been controversial with data often limited to retrospective reviews [4] and phase II data [5,6] suggesting benefits in terms of local control but not necessarily survival. This was confirmed in the recently published randomised phase III [8] trial where there was an improvement in lymph-node field control with radiotherapy (48 Gy in 20 fractions), after therapeutic lymphadenectomy in high risk patients.

When these trials were designed, there were no standard guidelines for target volumes for the post-lymphadenectomy patient and treatment was based on the use of simple field arrangements for the three major node sites [7]. As technology improved treatment has evolved to individualised 3-dimensional conformal radiotherapy (3DCRT) with the use of multiple photons beams, often with similar arrangements, but with greater use of shielding in order to produce more conformal plans with greater avoidance of critical structures. Both acute and late toxicities are usually manageable with these techniques [6, 7]. However it is difficult, especially when treating the ilio-inguinal lymph-node basin, to obtain adequate target volume coverage while sufficiently sparing of organs at risk (OAR), particularly small bowel.

Newer technologies such as intensity modulated radiotherapy (IMRT) can provide improved coverage of the target volume while more adequately sparing OARs which should produce better outcomes for patients. This improved dosimetry has been shown at other target sites [9-13].

The aim of this study was to perform a comparative planning study in order to assess differences in dose distribution with 3DCRT and IMRT techniques for treating the ilio-inguinal lymph-node basin after therapeutic lymphadenectomy for melanoma.
Methods and materials

Study population.

The study consisted of 15 consecutive patients with macroscopic node positive, non-metastatic (stage IIIB or IIIC) melanomas involving the ilio-inguinal lymph-node basin for whom post-operative adjuvant radiotherapy was recommended by the melanoma multidisciplinary meeting. Five patients were the final patients treated with 3DCRT before a departmental switch to IMRT. The remainder were the initial patients treated with IMRT. The prescribed dose was 48 Gy in 20 fractions for all patients.

Radiotherapy simulation and planning.

Simulation was similar for all. Patients were positioned supine on the couch with the affected leg in a comfortable position with the hip slightly abducted and externally rotated, knee slightly flexed and leg immobilised in a vacuum bag. The scar and drain sites were marked with wire and a planning computed tomography (CT) scan performed from mid abdomen to at least 5 cm beyond the most inferior aspect of the scar. With reference to all available information, including operative notes, pathology reports and pre-operative imaging a high risk target volume (HRTV), representing the location of involved nodes was marked on the planning CT scan. A 1 cm isotropic expansion of the HRTV was made which was clipped to anatomical boundaries such as skin, muscle and bone if uninvolved. This was then expanded to the clinical target volume (CTV) by including the at risk lymph nodes; deep femoral, inguinal, obturator, internal and external iliac, as well as the surgical bed and a 3 cm margin around the scar (below the level of the inguinal ligament), and drain sites. Nodal volumes were identified using published guidelines [14]. A planning target volume (PTV) was produced by a 7 mm isotropic expansion on the CTV which was clipped to skin. To ensure adequate coverage of the skin within the CTV, 1 cm of wax bolus was placed on the skin surface within the CTV.

OARs were volumed on the CT plan for both IMRT and 3DCRT patients. These consisted of femoral necks (each as a separate structure), small bowel, bladder and external genitals. These were outlined according to guidelines from the Trans Tasman Radiation Oncology Group (TROG) research project TRP11.A protocol B studying the role of IMRT in the treatment of anal cancer [15]. Volumetric dose constraints were placed on OARs as shown in Fig. 1 on page 5. These were based on those stipulated in this research project. Given the altered dose and fractionation (54 Gy in 30 fractions for anal cancer) the constraints were modified in order to achieve an isoeffective biological equivalent dose (BED) for late normal tissues (#/# ratio 3) using the formula:

\[
\text{BED} = D \left[ 1 + \frac{d}{(\#/#)} \right]
\]
where $D$ is total dose and $d$ is dose per fraction [16].

For each patient optimised 3DCRT and IMRT plans were generated with prescriptions in accordance with International Commission on Radiation Unit 50 and 62 (3DCRT) and 83 (IMRT) guidelines.

Dose volume histograms were produced for each plan in order to allow direct comparisons of 3DCRT and IMRT plans for each patient.

The Wilcoxon signed-rank test was used to compare dose received to both target and OARs from each plan for individual patients.

Dosimetric parameters for comparison

Dose volume histograms (DVH) were produced for 3DCRT and IMRT plans for each patients. For individual patients dosimetric comparisons of 3DCRT and IMRT plans made for the parameters in Fig. 2 on page 6.

The homogeneity index (HI) should be less than 15 with lower values indicating a more homogeneous dose distribution [12]. Both the conformity index [13] and coverage index [12] give figures ranging from 0 to 1 with higher figures reflecting better conformailty and coverage.

Also generated were figures relating to the percentage of PTV volumes receiving 105%, 100%, 95% and 90% of the prescribed dose ($V_{PTV_{105}}, V_{PTV_{100}}, V_{PTV_{95}},$ and $V_{PTV_{90}}$ respectively); as well as minimum ($D_{Min}$) and maximum ($D_{Max}$) doses to the PTV and the doses covering 1%, 2%, 5%, 10%, 50%, 90%, 95%, 98% and 99% of PTV volume ($D_{1-PTV}, D_{2-PTV}, D_{5-PTV}, D_{10-PTV}, D_{50-PTV}, D_{90-PTV}, D_{95-PTV}, D_{98-PTV}$ and $D_{99-PTV}$ respectively).

Dose delivery to OAR was compared by assessing each DVH with regard to the parameters in Fig. 1 on page 5.

Statistical analysis

The Wilcoxon signed-rank test was used to compare dose received to both target and OARs from each plan for individual patients. A $p$ value of <0.05 was taken as the level of significance.

Images for this section:
<table>
<thead>
<tr>
<th>Organ at risk (OAR)</th>
<th>Dose Constraint</th>
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<tbody>
<tr>
<td>V25 Gy &lt; 350 cc</td>
<td></td>
</tr>
<tr>
<td>V32 Gy &lt; 150 cc</td>
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<tr>
<td>V45 Gy &lt; 40 cc</td>
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<td>V48 Gy &lt; 1 cc</td>
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<td>Small bowel</td>
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<td>V36 Gy &lt; 35%</td>
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<td>V42 Gy &lt; 5%</td>
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<td>Femoral head</td>
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<td>(Left and right as separate structures)</td>
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<td>V18 Gy &lt; 50%</td>
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<td>V25 Gy &lt; 35%</td>
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<td>V36 Gy &lt; 5%</td>
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<td>External genitalia</td>
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<td>V32 Gy &lt; 50%</td>
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<td>V36 Gy &lt; 35%</td>
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<td>V45 Gy &lt; 5%</td>
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<tr>
<td>Bladder</td>
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**Fig. 1:** Organs at risk (OAR) and target dose constraints

**Homogeneity Index (HI):**

\[ \frac{(D_{2.5\text{PTV}} - D_{98\text{PTV}})}{D_{\text{prescription-PTV}}} \times 100\% \]

Ideally should be less than 15

**Conformity Index (Conni):**

\[ \frac{TV_{\text{ref}}}{TV} \times \frac{TV}{TV_{\text{ref}}} \]

0 ≤ Conni ≤ 1 with 1 being ideal figure

**Coverage Index (CovI):**

\[ \frac{TV_{\text{ref}}}{TV} \]

0 ≤ CovI ≤ 1 with 1 being ideal figure

**D2.5PTV:** Dose (Gy) covering 2% volume of PTV

**D98.PTV:** Dose (Gy) covering 98% volume of PTV

**D_{\text{prescription-PTV}}:** Prescribed Dose to PTV (Gy)

**TV:** Target volume (cm³) – i.e. PTV volume

**TV_{\text{ref}}:** Target volume (cm³) receiving reference (i.e. prescription) dose

**V_{\text{ref}}:** Volume (cm³) covered by reference dose

**Fig. 2:** Dosemetric parameter used to evaluate plan
Results

Representative DVHs (Fig. 3 on page 7 and Fig. 4 on page 8) as well as CT slices from an optimised IMRT (Fig. 5 on page 9) and 3DCRT (Fig. 6 on page 9) plans are shown.

Conformality index was improved by the use of IMRT; median 0.649 (range 0.476-0.808) vs 0.442 (0.288-0.605); W=2, p<0.05 for IMRT and 3DCRT respectively. No difference was seen in the homogeneity index; median 10.92 (7.65-28.67) vs 11.17 (8.96-26.69); W=31, p>0.05.

Median dose to the bowel closest to the target volume was significantly less for IMRT. D1cc, 10cc and 40cc were 48.5Gy vs 49.7Gy; 47.8Gy vs 49.0Gy and 45.8Gy vs 48.2Gy for IMRT and 3DCRT respectively. W values 14, 2 and 10; p<0.05 for all.

Also reduced with IMRT was dose to the ipsilateral femoral neck; median V43.2Gy, 3.9% (0.1-22.0%) vs 43.2% (12.4-68.5%), W=0, p<0.05; and median V36Gy, 29.5% (14.8-42.3%) vs 61.1% (40.4-100%), W=0, p<0.05 for IMRT and 3DCRT respectively.

Images for this section:
Fig. 3: DVH from typical patient showing dose to planned target volume (PTV) and organs at risk (OAR) for both intensity modulated radiotherapy (IMRT) - triangle - and 3 dimensional conformal radiotherapy (3DCRT) - square.
Fig. 4: DVH from typical patient showing dose to planned target volume (PTV) and organs at risk (OAR) for both intensity modulated radiotherapy (IMRT) - triangle - and 3 dimensional conformal radiotherapy (3DCRT) - square.

Fig. 5: Cross sectional CT slice with overlying isodose lines from typical 3 dimensional radiotherapy (3DCRT) plan

Fig. 6: Cross sectional CT slice with overlying isodose lines from typical 3 dimensional radiotherapy (3DCRT) plan
Conclusion

A homogenous coverage of the target volume can be achieved with both IMRT and 3DCRT (homogeneity index <15). However, the use of IMRT appears to allow superior conformality of dose to the target volume while relatively sparing (and potentially reducing the risk of toxicity to) adjacent OARs such as the bowel and femoral neck.

Personal information

References


following nodal surgery in malignant melanoma-Trans Tasman Radiation Oncology Group (TROG) Study 96.06. Radiother Oncol 2006;81:136-142


