Proton therapy for cancer: the evidence and the ethical and juridical considerations

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Proton therapy is a form of radiation therapy that allows for more precise delivery of higher doses to deeper structures within the body. We undertook a systematic review to assess whether this therapeutic potential of proton therapy translates into improved cancer control or reduced radiation induced complications.

**Methods**

Studies were identified in Medline 1966-2005 with a defined search strategy. Studies were included that reported >3 months follow up of clinical outcomes for patients treated with proton therapy (>50 patients included for adults and >10 for children).

**Results**

Children with intracranial or paracranial tumor

Five small non-controlled case series were identified (1-6) that reported results from proton therapy in a total of 100 children with different intracranial or paracranial tumors.

- **Proton therapy allowed for delivery of higher radiation doses than conventional radiotherapy**
- **Heterogeneity in indication and intervention impedes further synthesis of overall and disease-free survival**
- **Complications reported were hormone deficiency and neuropsychological impairment**

Eye tumors

Most eye tumors are managed by surgery (eye removal) or radiation therapy. One RCT (7), two cohort studies (8,9) and multiple publications from four case-series were included (10-13). The RCT and cohort studies suffer from methodological limitations and do not allow for conclusions.

- **5-year overall survival ranged from 70-95% and 5-year disease-free survival was 85-96% in different case series**
- **The affected eye was retained in 90% of patients 5 years after treatment**
- **50% of patients reported satisfactory visual capacity 3-5 years after treatment**
- **Complications reported were glaucoma, radiation maculopathy, cataract amongst other**

Prostate cancer

Prostate cancer treatment is associated with significant morbidity, and at present there appears to be no curative treatment for localised prostate cancer. One RCT (19,20) and several case-series were included (21-24).

- **No conclusion regarding overall and disease-free survival can be drawn**
- **Patients treated with higher doses reported more complications (rectal bleeding, urethral stricture)**

**Summary of findings**

The overall synthesis of findings from proton therapy studies was limited by the heterogeneity in population, indication and intervention. Proton therapy allow for delivery of higher radiation doses compared with conventional radiation therapy, but whether this translates into improved survival or acceptable side effects remains unknown.

Knowing that more than 30 000 patients have been treated with proton therapy, and that new treatment facilities are popping up, there should be an ethical duty to conduct scientifically valid trials to allow for comparison of proton therapy with conventional radiation therapy.

**Chordomas and chondrosarcomas**

Management of chordomas and low grade chondrosarcomas at the base of the skull is complex, due to the close proximity to critical neurological structures. One RCT (14) and several case-reports have been published (15-18).

- **Proton therapy allowed for delivery of higher radiation doses than conventional radiotherapy**
- **Heterogeneity in population and intervention does not allow for conclusions regarding overall or disease-free survival**
- **Complications reported were hormone deficiency and neuropsychological impairment**

**Ethical issues**

Proton therapy may offer a therapeutic option for patients with certain malignancies, but neither individual studies nor the overall synthesis of these studies allows for conclusions regarding the clinical effectiveness of proton therapy.

**Juridical issues**

The juridical implications are considered within the national legal context, although some issues might be of cross-national relevance.

- **referrals for and reimbursement of treatment conducted in another nation**
- **follow up of treatment associated complications**

**Diagnosis**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Publications identified</th>
<th>Publications included</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children with CNS tumour</td>
<td>7</td>
<td>6</td>
<td>N&lt;10 (n=1)</td>
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<tr>
<td>Head and neck cancer</td>
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<td>11</td>
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<td>Eye cancer</td>
<td>56</td>
<td>48</td>
<td>N&lt;50 (n=12) Endpoint (n=3)</td>
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<td>Prostate cancer</td>
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<td>Bone cancer</td>
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<td></td>
<td>N&lt;50 (n=1)</td>
</tr>
</tbody>
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**Table 1** Publications identified, included and reason for exclusion

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References


(23) Rossi CJ. Conformal proton beam therapy of prostate cancer-update on the Loma Linda University medical center experience. Strahlenther Onkol 1999; 175 Suppl 2:82-84.