Contact radiotherapy-Who?

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Background

Local treatment for early low rectal cancer is still controversial but gaining popularity as it avoids major surgery and permanent stoma formation. ACPGBI guidelines (2007) recommend local excision only for pT1 low risk rectal cancer less than 3 cm. However, patients must be fit for general anaesthesia and not all patients especially the elderly are fit for surgery. The alternative option is to use contact (Papillon) radiotherapy.

The treatment is given in 4-5 fractions every 2 weeks. The total tumour dose given is between 110-150Gy. Contact radiotherapy delivers radiation directly on to the tumour with a small margin. Therefore, the volume of normal surrounding tissue irradiated is limited and this reduces radiation toxicity. Moreover, delivery of radiation at two weekly intervals allows time for normal tissues to recover while tumour is being destroyed layer by layer at each treatment. Low energy radiation (50Kv) penetrates only a few millimetres and the deeper normal tissues are not affected. Therefore, a very high dose of radiation can be delivered to the tumour without affecting the normal tissues situated only a few millimetres beneath it. The response to treatment can be assessed after 2 fractions when most radiosensitive tumour can no longer be seen or palpated. If the response is satisfactory, the treatment is continued for a further 2 fractions using a reduced volume and lower radiation dose.
Case selection is very important. Rectal tumours should be accurately staged prior to treatment. Patients with suspicious lymph nodes should be excluded as contact radiotherapy does not treat mesorectal lymph nodes. If there is uncertainty about the status of lymph nodes external beam radiotherapy or preferably chemoradiotherapy should be offered in addition to contact radiotherapy. In properly selected cases cure rate over 90% can be achieved. Local recurrences can occur usually within the first 2-3 years. This can be salvaged by radical surgery in selected cases and close follow up is necessary during this high risk period. The risk of distant relapse for early rectal tumour is very low (<5%).

Introduction

Rectal cancer is a common malignancy with 13,000 new cases diagnosed in the UK each year [1]. The number of cases presenting with early rectal cancer has increased from 8% to 30%. It is likely to increase further with the introduction of colorectal screening in the UK [2]. The ageing population is also increasing in the UK and by 2020 half the population will be above the age of 70 years. It is important to realise that mortality and morbidity from radical surgery increases with advancing age. Thirty day mortality increases from 5% to >25% in patients above the age of 90 years [3]. Associated medical co-morbidity increases the risk further. In a recent publication, thirty percent of cases with early low rectal cancers were offered APER [4]. Therefore, an alternative treatment with contact radiotherapy, which is safe and effective, should be considered especially for elderly patients with early low rectal cancer.
**Materials and Methods**

Pre treatment staging is important but one must realise the limitations of presently available radiological methods. In addition to MRI, endorectal ultrasound should be carried out to evaluate local extent of the tumour and to exclude the possibility of suspicious lymph node spread. Again, this is operator dependant. Radiation treatment is given using 50 KV X-ray machines (Papillon RT50). Due to superficial nature of the radiation dose falls to 50% at 5 mm and to 10% at 20mm. Therefore, deeply infiltrating tumours are not suitable for Papillon treatment.

**Selection criteria for radical contact radiotherapy**

1. Histologically proven rectal adenocarcinoma less than 3 cm.
2. Well to moderately well differentiated tumours
3. Mobile exophytic tumour.
4. Rectum tumour situated below 12cm
5. No evidence of suspicious lymph nodes.
6. No evidence of confirmed distant spread.
7. Patient must agree for long term follow up.

**Exclusion criteria**

1. Anal adenocarcinoma
2. Poorly differentiated tumour
3. Lympho-vascular invasion
4. Infiltrating ulcerative tumours
5. Deep fixity to underlying structures
After careful selection and staging, if the rectal tumour is suitable for contact radiotherapy the patient is admitted overnight for bowel preparation. Patients who prefer to have the treatment as out patient are given instructions for bowel preparation with ‘Relaxit’ enemas at home. A low residue diet for 2-3 days prior to treatment helps.

On the day of treatment, further micro-enemas are given to clear the bowel. The patient is treated in prone jack knife position. Rigid sigmoidoscopy is carried out to check the tumour size and position. The treatment applicator is inserted using local anaesthetic gel to treat the tumour with a 5mm margin. GTN cream is applied to help relax the sphincter muscles. A radiation dose of 30Gy is given initially. The procedure is repeated after 2 weeks when a further radiation dose of 30Gy is given. Before the 3rd application if the tumour is still palpable then it is highly unlikely that the tumour will respond solely to contact radiation. External beam radiation or preferably chemoradiation is given using either oral capecitabine 850mg /m2 (or) 5FU infusion 1G/m2 concurrently with radiotherapy 45Gy in 25fractions over 5 weeks. The dose of chemotherapy and radiotherapy is modified as necessary depending on the patient’s age and general condition. The tumour usually regresses well with only superficial ulceration or small residual nodule. This area is resected using TEM or local transanal excision to establish pathological complete remission in patients who are fit for short anaesthesia.

**Multi-modality treatment for more advanced tumours.**

Radiological staging for small rectal tumours is unreliable especially if they are low and differentiation between T1 with early T2 or even early T3 (T3a) tumours are not always possible. Patients not fit for radical surgery or those who refuse surgery (if it involves
permanent stoma) could be offered external beam chemoradiotherapy initially and response assessed after 4-6 weeks. Some tumours respond well and can be downstaged to ypT0 or ypT1. In such cases, a contact radiotherapy boost of 60-80 Gy can be offered to improve local control. Any small residual tumour or scarred area should be excised either by TEM or full thickness local excision to establish pathological complete response. The patient should be fully aware that this is not a standard treatment and that there is a higher risk of recurrence for which they would need radical salvage surgery [5]. Close follow up is essential. Clinical examination, repeat endoscopy, biopsy of suspicious areas and radiology (MRI, EUS) is carried out 3 monthly in the first 2 years and 6 monthly up to 5 years. Late recurrences can occur and annual follow-up beyond 5 year is recommended [6].

**Results**

Radiotherapy alone will sterilise 5% of patients with radiation dose of 40Gy (2Gy per fraction) or its radiobiological equivalent. Increasing the radiation dose will improve local control but normal tissue toxicity is also increased, depending on the volume irradiated [7]. Single agent chemotherapy either 5FU or oral capecitabine given concurrently will improve local control to 10-15% [8]. Addition of second drugs either oxaliplatin or irinotecan will improve pCR rates to 20-25%, but this increases toxicity and surgical complications [9, 10]. Increasing the radiation dose with contact radiotherapy boost improves local control and the chance of sphincter preservation as the high dose is confined to the area of residual tumour [11]. The results from international single institutional experiences are shown in table [1].
Table 1

<table>
<thead>
<tr>
<th>No</th>
<th>Author</th>
<th>City (Country)</th>
<th>Year</th>
<th>Patients</th>
<th>Dose</th>
<th>Local failure</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Papillon</td>
<td>Lyon (Fr)</td>
<td>1951-1987</td>
<td>312(contact)</td>
<td>80-130/ 4-7</td>
<td>9%</td>
<td>75% (OS 5)</td>
</tr>
<tr>
<td>2</td>
<td>Horiot</td>
<td>Dijon (Fr)</td>
<td>1970-1996</td>
<td>151</td>
<td>90-150/3-5</td>
<td>15%</td>
<td>60% (OS 5)</td>
</tr>
<tr>
<td>3</td>
<td>Gerard</td>
<td>Lyon/Nice (Fr)</td>
<td>1980-1998</td>
<td>116(contact)</td>
<td>80-110/4</td>
<td>12%</td>
<td>83% (OS 5)</td>
</tr>
<tr>
<td>4</td>
<td>Bey</td>
<td>Nancy/Paris(Fr)</td>
<td>1981-1989</td>
<td>97</td>
<td>100/4</td>
<td>10%</td>
<td>64% (OS 5)</td>
</tr>
<tr>
<td>5</td>
<td>Sischy</td>
<td>Rochester(USA)</td>
<td>1973-1990</td>
<td>244</td>
<td>110/4</td>
<td>9%</td>
<td>96% (CSS5)</td>
</tr>
<tr>
<td>6</td>
<td>Myerson</td>
<td>St Louis (USA)</td>
<td>1980-1995</td>
<td>199</td>
<td>120/4</td>
<td>1.8%(pT1)</td>
<td>94%(DFS3)</td>
</tr>
<tr>
<td>7</td>
<td>Hull</td>
<td>Hamilton(Can)</td>
<td>1973-1992</td>
<td>126</td>
<td></td>
<td>21%</td>
<td>91% (DFS5)</td>
</tr>
<tr>
<td>8</td>
<td>Madoff</td>
<td>Mayo (USA)</td>
<td>1986-1993</td>
<td>37</td>
<td></td>
<td>16%</td>
<td>77%(DFS3)</td>
</tr>
<tr>
<td>9</td>
<td>Schild</td>
<td>Montreal(Can)</td>
<td>1986-1994</td>
<td>20</td>
<td>155/3-4</td>
<td>10%</td>
<td>70% (OS 5)</td>
</tr>
<tr>
<td>10</td>
<td>Sun Myint</td>
<td>Liverpool (UK)</td>
<td>1993-2007</td>
<td>220(124(contact))</td>
<td>90-110/ 3-4</td>
<td>10%</td>
<td>7%</td>
</tr>
</tbody>
</table>

Discussion and conclusions

Local treatment of early rectal cancer is a controversial and a complex issue that needs to be addressed and discussed. The clinician in charge has the responsibility of explaining all the treatment options that are available to the patient without personal bias. The advantages and disadvantages of each treatment options available should be clearly explained so that patients and their relatives can consider these options carefully and decide on which treatment option they wish to pursue. All discussions need to be carefully documented as the patients may be prepared to accept the higher risk of local recurrence with radiation in order to avoid a stoma. Complex and difficult cases should be referred to specialist centres with experience and expertise so that all available treatment options can be considered.
We need to have a robust treatment plan of management so that appropriate treatment could be offered to patients without compromising their chance of cure while at the same time respecting the patients’ wishes and their choice of the treatment option.

It is important to balance the benefits of radical surgery in terms of lower local recurrence (1-2%) against the increased mortality (5-10%) and morbidity (30-40%) from such procedures against slightly higher local recurrence (5-10%) and much lower mortality (<1%) and morbidity (5-10%) from conservative local treatments such as TEM and contact radiotherapy[12]. At present, it is difficult to organize a randomized trial due to relatively small number (5-10%) of patients treated for early rectal cancer at each cancer centres.

The Papillon treatment facility using Phillips 50 kV machine is now obsolete, as the aging machines are not being replaced. There is an urgent need for replacement machines as; currently there are only few centres in the world able to treat patients using the Papillon technique. This is the main reason why contact radiotherapy is not widely practice. Since 2005, Professor Gerard from Nice and the team from Clatterbridge together with engineers and physicist have been actively involved in designing a new Papillon 50 machine. The European Union (Ariane) company, which is based in the UK, has finally produced two prototype machines, one to be based at Clatterbridge and the other to be shared between Lyon and Nice. Hopefully, full production will start this year and several centres around the world including the ones in the UK have expressed intention to obtain them to treat patients with early rectal cancer. An international interest group called ICONE has been set up and observational trial (CONTEM) is planned. The
results of this trial will take some time to mature. Until such time, the controversy for local treatment in the UK is likely to continue.

References


