Avoiding major surgery and improving quality of life in patients with early rectal cancer
The Role of Adjuvant Therapy

- Early Rectal Cancer
- Low/middle rectum
  - Oncological failure

Local nodal metastases (LNM)  Surgical bed regrowth (SBR)
Adjuvant Therapy

Radiation
Chemoradiation

Effective?  Toxic?

Risk Assessment

HISTOPATHOLOGY

LOW  MODERATE  HIGH
Which patients should be offered adjuvant therapy?

### Risk Assessment

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Risk Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Margin clear - &gt;0mm from the diathermy margin</td>
<td>0</td>
</tr>
<tr>
<td>Margin positive - 0mm to the diathermy margin</td>
<td>1</td>
</tr>
<tr>
<td>Margin positive - 0mm to the tumour margin</td>
<td>3</td>
</tr>
<tr>
<td>Sm1 / a</td>
<td>0</td>
</tr>
<tr>
<td>Sm2</td>
<td>1</td>
</tr>
<tr>
<td>Poorly differentiated / mucinous</td>
<td>1</td>
</tr>
<tr>
<td>Tumour budding</td>
<td>1</td>
</tr>
<tr>
<td>LVI</td>
<td>1</td>
</tr>
<tr>
<td>T2</td>
<td>3</td>
</tr>
<tr>
<td>Size of tumour &gt;4cm</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total Score</th>
<th>Grade of Risk</th>
<th>Recommended Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Low</td>
<td>Surveillance only</td>
</tr>
<tr>
<td>1 – 2</td>
<td>Moderate</td>
<td>Randomisation between surveillance or radiotherapy</td>
</tr>
<tr>
<td>≥3</td>
<td>High</td>
<td>Randomisation between radiotherapy or radical surgery</td>
</tr>
</tbody>
</table>

Criteria are based on histological description of locally removed rectal lesions, weighted for prognostic significance of each risk factor. Where more than one risk factor is present, the degree of risk is added together to give a total risk score.
Predicting lymph node metastases in ERC Swedish Rectal Cancer data

- Swedish Rectal Cancer Registry (T1, T2) 2007 - 2010
- Surgical Resection
  - No neoadjuvant therapy

Saraste D et al Eur Cancer 2013

Swedish Rectal Cancer data

Distribution of T-stage and lymph node metastases

<table>
<thead>
<tr>
<th>T-stage</th>
<th>Distribution of T-stage (%)</th>
<th>Proportion with node metastases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1, n = 205</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>T2, n = 472</td>
<td>29</td>
<td>22</td>
</tr>
<tr>
<td>T3, n = 830</td>
<td>51</td>
<td>46</td>
</tr>
<tr>
<td>T4, n = 105</td>
<td>7</td>
<td>65</td>
</tr>
</tbody>
</table>
The Royal Marsden

Swedish Rectal Cancer data

a-poor differentiation  b-vascular invasion.
The variables chosen for inclusion into the risk index are the variables with statistical significance in the multivariate analysis.
Italian meta-analysis data

Italian meta-analysis (2012)  
T<sub>1</sub>  
T<sub>2</sub>  
2010  

8 Studies  
1560 patients  
Surgical resection (TME)  
No neoadjuvant therapy

Carrara et al Int J Surg Oncol 2012

Risk of lymph node metastasis in GI versus G2/G3

Risk of lymph node metastasis in Vascular Invasion

Risk of lymph node metastasis in lymphatic invasion
Do all LNM have same impact on outcome?

Size?
- T1 Med size 0.3mm
- T2 Med size 4.1mm

Position?
- 63% level of Primary
- 17% 2cm proximity
- 98% 5cm proximity
- 0% distal


What’s the evidence for adjuvant RT?

- Small non-randomised series (<100)
- Time span large 2000 (18 years)
- Heterogeneous populations
  - Tumour stage
  - Histopath prognosis features
  - Surgical approach
  - Allocation to RT (RT)
  - RT (CRT) approach
  - Outcomes measures
The Royal Marsden

Nothing New — p T2 Poor outcomes

Local Recurrence data

<table>
<thead>
<tr>
<th>T1</th>
<th>T2</th>
<th>Radical Surgery</th>
<th>Local excision</th>
</tr>
</thead>
<tbody>
<tr>
<td>13%</td>
<td>3%</td>
<td>Nash (2009)</td>
<td>13%</td>
</tr>
<tr>
<td>37%</td>
<td></td>
<td>Garcia-Aguilar (2000)</td>
<td>37%</td>
</tr>
</tbody>
</table>

Disease-free survival according to pathologic T-stage

Impact Radiotherapy on Local Recurrence

<table>
<thead>
<tr>
<th></th>
<th>T1</th>
<th>T1</th>
<th>T1</th>
<th>T2</th>
</tr>
</thead>
<tbody>
<tr>
<td>RT+</td>
<td>24%</td>
<td>16%</td>
<td>16%</td>
<td>36%</td>
</tr>
<tr>
<td>RT-</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>9%</td>
</tr>
</tbody>
</table>
Cancer Specific survival
\[ T_1 \]

Fig. 2. Cancer specific survival of pT1 tumor according to adjuvant treatment. Those who received radiation therapy had a 5-year CSR of 100% and those that did not had a 5-year CSR of 76.0% (p=0.038).

Functional Outcome after post local excision adjuvant RT?

Even less data!

RMH series – LARS assessment underway
What is Optimal Adjuvant Therapy?
Radiotherapy

Target Volumes

- LNM
- SBR

Dose

- 45 Gy 25# equivalent
- +/- Bit more!

- No Data
- Extrapolate other oncological data
  e.g. breast

Adjuvant RT to reduce LNM

Mesorectal nodes

Inguinal nodes
Pelvic sidewall nodes
Superior nodes
Adjuvant RT to reduce SBR

Pre-excision MREndoscopic description
Histopathological assessment
Baseline post-op MR

CTV_{SB}  CTV_e

PTV_{Boost}  CTV_{all}  PTV_{45}
Pan London Early Rectal Cancer Meeting

Royal Society of Medicine
1st November 2018

Dr Diana Tait
Consultant Clinical Oncologist