Rectal Cancer using MRI to improve treatment strategy

1st SAMO workshop on Multidisciplinary Approaches to GI tumors
Lucerne

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TME surgery -
• Dissection plane behind mesorectal fascia
• Rectosacral fascia division
• Lateral dissection separates the mesorectum from neurovascular bundles
• Dissection continues in front of Denonvilliers' fascia in the male
Non TME surgery

- Blunt intramesorectal dissection
- Rectosacral fascia traction
- Disruption of neurovascular bundles
- Dissection on to front of rectum
Conventional surgery

TME Surgery

Heald et al, Lancet 1986
Local Recurrence

"Eur J Surg Oncol 1999;25:368-374"

**Standardized TME surgery should be standard of care in rectal cancer**
Anatomical definition is key to good staging
Standardised Technique

- 1.5T Flexible surface multichannel phased array coil, no endorectal coils
- In plane resolution 0.6mm x 0.6mm 3mm slice thickness
- 16cm-18cm Field of view
- 4-6 signal acquisitions (longer scan duration)
- 256x256 matrix
- T2 weighting: TR >3,000, TE 80-100, ETL 16

Layers of the bowel wall: MRI
T staging MRI
pT3<5mm, N any

• T2 and T3 tumours <5mm have 85-90% 5 year cancer specific survival

T3 tumours >5mm spread 54%
5 year cancer specific survival

Merkel et al 2001
295/311 (95 %) patients who underwent primary surgery. The mean difference between MRI and histopathology assessment of tumor EMD was -0.046 mm, SD = 3.85 mm, the 95 % CI was -0.487 to 0.395 mm. MRI and histopathology assessment of tumor spread are considered equivalent to within 0.5 mm (θR).
Conclusions from MERCURY

- reproducible in multiple centres and established the technique as a robust standard for preoperative staging.
- Workshop training for standardisation of technique and reporting - essential
- allows individualized treatment planning by a multidisciplinary team.
- Measurements of tumour depth show direct equivalence with histopathology.
Afferent lymphatic
Efferent lymphatics and vessels
Medullary sinus
Follicle
Capsule
Criteria for predicting malignancy = mixed signal intensity and/or irregular border
Size of nodes not a useful predictor (Radiology 2003)
Accuracy = 85%, sensitivity 83%, specificity 86% (BJS 2003)
Nodal involvement of the CRM remote from the tumour
Importance of predicting the CRM

Cancer specific survival on potentially curative cases n=488 cases (Quirke et al Lancet 1994)

Logrank p < 0.0001

CRM -ve 70%
CRM +ve 36%
MERCURY Centres

Ashford St Peters Hospital, England
Epsom General Hospital, England
Frimley Park Hospital, England
Mayday University Hospital, England
Karolinska Institute, Sweden
Krankenhaus Friedrichshain, Germany
Leeds General Infirmary, England
Llandough Hospital, Wales
North Hampshire Hospital, England
National Radium Hospital, Norway
Royal Marsden Hospital, England
St James’ University Hospital, England

(Adopted by NCRI in 2002,
Principal Investigators: G Brown, IR Daniels)
**Standardised MRI technique and reporting criteria**

<table>
<thead>
<tr>
<th>Radiologist:</th>
<th>Patient Name:</th>
<th>Date:</th>
<th>Date of Birth:</th>
<th>Hosp. No.</th>
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- **Exam performed elsewhere:** Yes | No  
  If yes, where ____________________________
- **Exam technically satisfactory (3mm):** Yes | No  
  Date: ___________
- **Image quality:** Optimal | Sub-Optimal
- **Pathology identified:** Yes | No  
  Date: ___________
- **Has the patient received Radiotherapy:** Yes | No  
  Date: ___________
- **Has the patient had a previous rectal MRI:** Yes | No  
  Date: ___________
- **If yes, date of previous examination:** ___________

### Gross Morphology

- **Polypoidal:** □  
  **Annular ulcerating:** □  
  **Annular non ulcerating:** □

### Infiltrating margin of extramural spread

- **Eroding:** □  
  **Pushing:** □  
  **Infiltrating:** □  
  **No Extramural spread:** □

### Mucinous Tumour

- **Nodes demonstrated not suspicious:** Yes | No  
  Date: ___________
- **Nodes demonstrated suspicious:** Yes | No  
  Date: ___________
- **Extramural venous invasion:** Yes | No  
  Date: ___________
- **Tumour deposits / satellites present:** Yes | No  
  Date: ___________

### Local invasion

- **Submucosa (T1):** □  
  **Muscularis (T2):** □
- **Beyond Muscularis <1.00 mm (T3a):** □  
  **Beyond Muscularis 1.01-5.00 mm (T3b):** □
- **Beyond Muscularis >5.01-15.00 mm (T3c):** □  
  **Beyond muscularis >15.01 mm (T3d):** □
- **Into adjacent organs (T4a):** □  
  **Perforation of visceral peritoneum (T4b):** □

### Margins

- **Distance to mesorectal fascia <1.00 mm:** Me1 | □  
  **Distance to mesorectal fascia >1.01 mm:** Me2 | □
- **Low tumour (below levator) >T2:** MeLev | □

### Measurements

- **Maximum extramural spread of tumour:** ________mm
- **Min distance to mesorectal fascia/potential CRM from outer edge of tumour:** ________mm

Please state distance to CRM for:

- **Main tumour:** ________mm
- **Suspicious lymph node:** ________mm
- **Extramural venous invasion:** ________mm
- **Tumour satellite/deposit:** ________mm
- **Distance to sphincter (Low tumours only):** ________mm
MERCURY Results: CRM

327/349 predicted clear by MRI, 94% had clear margins (95% CI = 91-96%)

Diagnostic Accuracy of Preoperative MRI
MERCURY Study Group
British Medical Journal Sept 2006
Roll-out of technique

- National training development 2 day TME-MDT workshops – whole Multidisciplinary team successful in UK (189 centers)
  - Increase in MRI before and after
  - Change in use of radiotherapy
- Similar scheme now started in Denmark
MDT discussion of Preoperative MRI: impact on CRM

- 2% (4/182) CRM+ve rate in resected patients discussed at MDT
- 8% (16/194) CRM+ve rate in all discussed patients including irresectable disease
- 26% (16/62) CRM+ve rate in patients not discussed

CRM +ve rate in all cases discussed by MDT was significantly lower than in cases not discussed (p<0.001)

Burton et al 2006 Br J Cancer 94(3): 351-7
EMVI detection by MRI

EMVI is Present in 26% of rectal cancer patients
MRI is accurate in the pre-operative detection of EMVI.

Upper rectal tumour (red arrow) + separate ‘nodule’ in superior rectal vein (green arrow)

Histology of ‘nodule’ shows some microscopic EMVI (black arrows) and tumour filling lumen of larger vessel
Treatment in colorectal cancer could potentially be refined by MRI-EMVI score-based prognostic stratification.
Histological EMVI status & Outcome

n = 135. Median follow-up = 3.12 (0.9-5.7) years.

Histological EMVI-
Histological EMVI+

p < 0.00001

73% 28%
MRI-EMVI score & Outcome

n = 135. Median follow-up = 3.12 (0.9-5.7) years.

MRI-EMVI score = 0-2
MRI-EMVI score = 3-4

p = 0.0015

71% 32%

Time since operation (Years)
Localised rectal cancer assessed by MRI

Good risk
T1-T3a-b <5mm
N0/N1, tumour in mid/upper third of rectum
5yr Survival 85-90%

Locally advanced
T3>5mm or N2
Or extramural venous spread
Risk of systemic failure high
Margin safe (>1mm to fascia)
Low risk of local recurrence
High risk of distant failure 50-60%

Poor risk
Potential margin positive disease
Risk of local recurrence +/- distant failure

Neoadjuvant therapy

TME
T staging EUS

85-90% accuracy

Tendency to overstage

German RT trial: EUS overstaged pT1/pT2 as T3/T4 in 18%
Lymph node staging EUS

N staging accuracy ranges from 63-82%, nodes within immediate vicinity
EUS or MRI?

- Both techniques offer T and N staging.
- MRI gives extra information:
  - Predicts CRM (Circular Resection Margin)
  - EMVI (Endometrial Vein Invasion)
  - Depth of spread
  - Anatomic detail

Peritoneal reflection

EMVI

Distance to rectal mucosa

L node
## Costs of DRE vs EUS vs MRI

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<tr>
<th></th>
<th>DRE</th>
<th>EUS</th>
<th>MRI</th>
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<tr>
<td>Procedure costs</td>
<td>£0</td>
<td>£7,644</td>
<td>£13,524</td>
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<tr>
<td>Costs of incorrect staging*</td>
<td>£99,696</td>
<td>£117,132</td>
<td>£19,008</td>
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<tr>
<td><strong>TOTAL COSTS</strong></td>
<td>£99,696</td>
<td>£124,776</td>
<td>£32,532</td>
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<tr>
<td>Total cost per staged patient</td>
<td>£1,017</td>
<td>£1,273</td>
<td>£332</td>
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Trial schema

**CAPECITABINE** 2000mg/m²/day for 14 days every 21 days

RT 45Gy in 25# phase 1
5.4-9Gy phase 2
Capecitabine 1650mg/m²/day continuously

Post operatively
**CAPECITABINE** 2500mg/m²/day for 14 days every 21 days

4-6 weeks rest for recovery of acute RT toxicity.
Repeat MRI then TME SURGERY

MRI and CT scans at 12 weeks and after radiotherapy to reassess tumour response.
Results

- 3 patients remained inoperable
- 27 patients had anterior resection and 21 patients had AP resection
- R0 resections were achieved in all but one patient (98%)
- 13 pathological complete responses (27%) were observed
- In a further 19 patients (40%), only microscopic tumour foci were found on the surgical specimens
EXPERT Trial findings

- First implementation of a pre-operative treatment strategy based on MRI assessment of poor risk factors
- Capecitabine and oxaliplatin prior to synchronous CRT and TME produces almost universal tumour regression, rapid symptomatic response and allows R0 resection to be achieved
- EXPERT-C trial – multicentre phase II randomisation comparing EXPERT vs EXPERT+cetuximab
MR lymphography can identify partially replaced malignant nodes that are not enlarged and appear normal at conventional imaging.

Pre USPIO T2* (630/25.8)

Post USPIO T2* (630/25.8)
Multimodality imaging

T2-weighted

DWI

PET

PET-CT
Clinical problems

- Low rectal tumours – when to give preoperative therapy?
- Apparent radiological and clinical complete response in patient with low rectal tumour
- Nodes lying within 1mm of the margin
- Locally advanced tumours above peritoneal reflection
- Synchronous metastatic disease
- Post chemoradiotherapy fibrosis