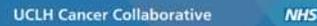


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Health Research

Pan London Early Rectal Cancer Meeting

1st November 2018

**Avoiding major surgery and improving quality of
life in patients with early rectal cancer**



Early Rectal Cancer Staging

Gina Brown

www.profginabrown.com

The Royal Marsden Hospital and Imperial
College, London



@profginabrown #preserve



New Philosophy

- Risk versus Reality
 - Risk assessment was a tool before detailed staging
 - Before detailed monitoring and surveillance of the mesorectum
 - Patient choice/flexibility



Staging of ERC used to be suboptimal

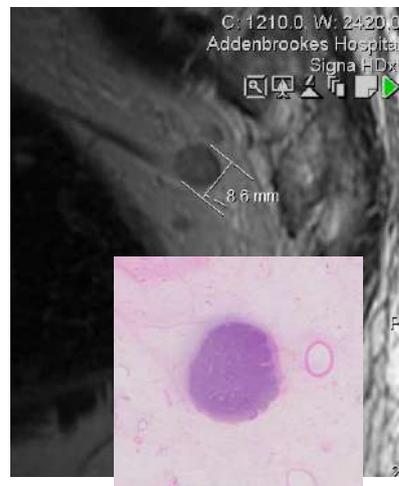
- Overstaging of lymph nodes
- Underestimation of tumour
- Underestimation of discontinuous EMVI
- “Free-style” TEM – destruction of TME plane/ intersphincteric plane
- Many missed pT1/earlyT2N0 undergoing radical surgery
- Many patients undergoing completion TME/proctectomy with pT0N0 in final specimen



Overstaging of nodes

pT	High-resolution MRI (morphological criteria)		High-resolution MRI (size criterion)		Low-resolution MRI (size criterion)		Total (73)
	N-	N+	N-	N+	N-	N+	
pT0N-	8	0	3	5	5	3	8
pT1N+	0	1	0	1	0	1	1
pT1N-	4	0	2	2	2	2	4
pT2N+	1	6	0	7	3	4	7
pT2N-	21	0	11	10	15	6	21
pT3a-bN+	3	4	2	5	2	5	7
pT3a-bN-	13	2	7	8	7	8	15
pT3c-T4N+	1	4	1	4	3	2	5
pT3c-T4N-	4	1	3	2	3	2	5
Rate of misdiagnosed	6%	3%	4%	37%	10%	29%	

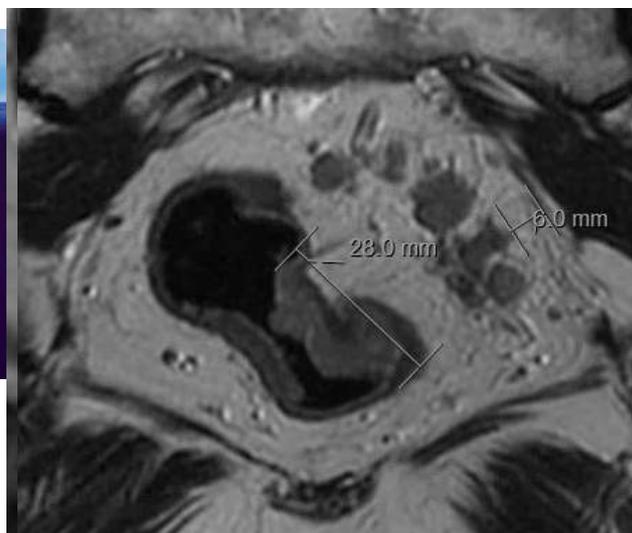
Understaged
 Overstaged

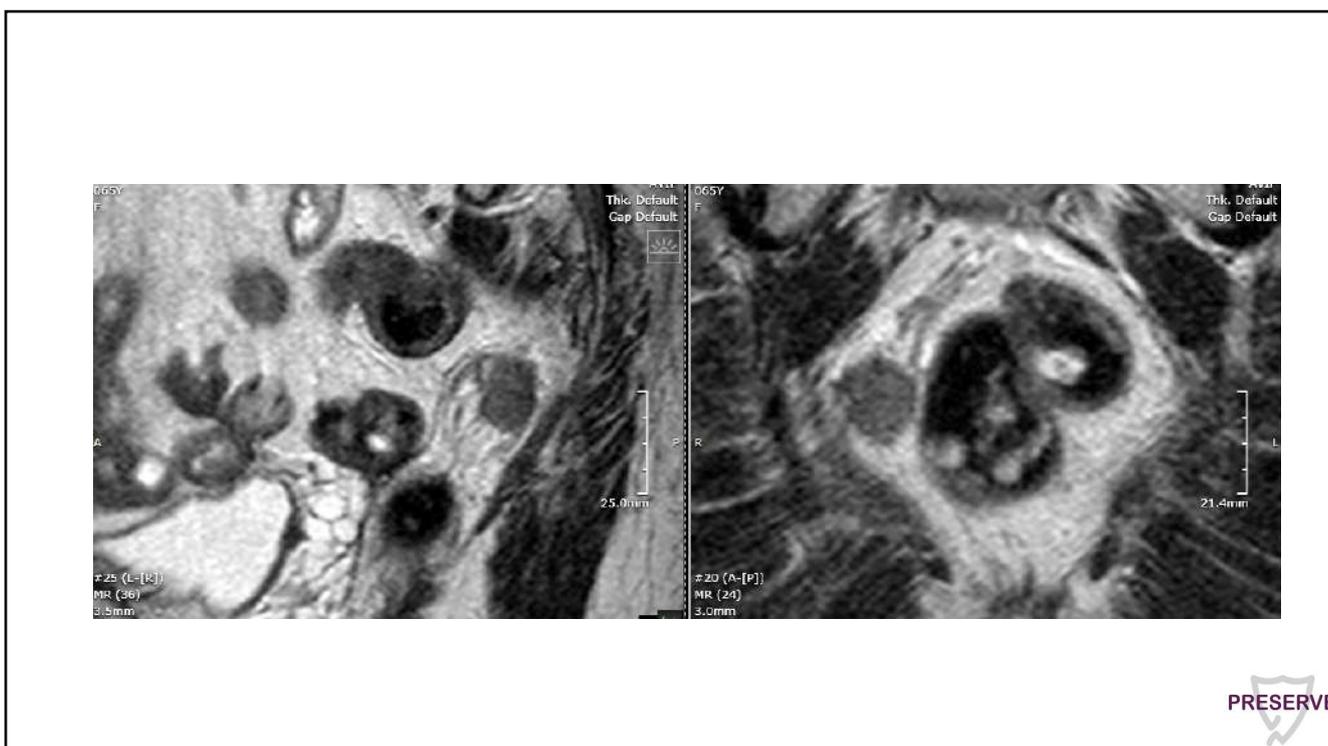
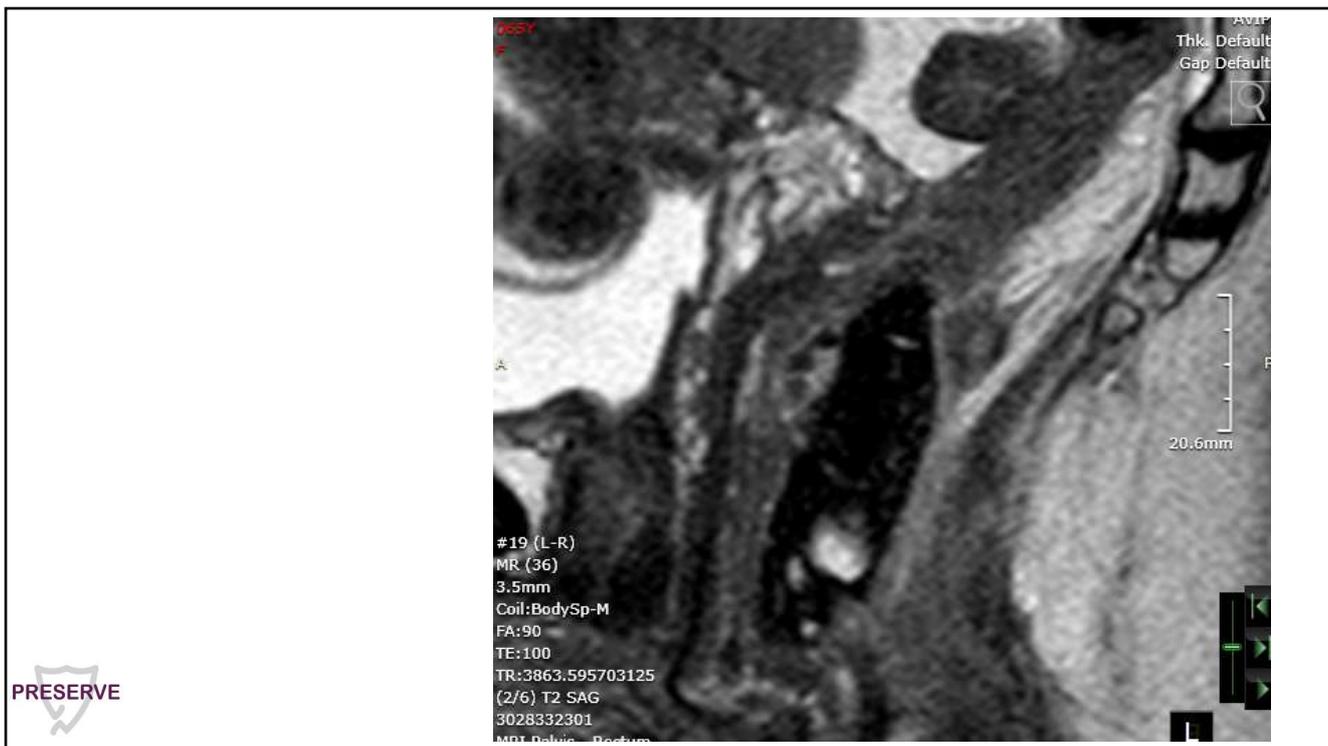


Size cannot be used to diagnose malignant nodes



Underestimation of tumour





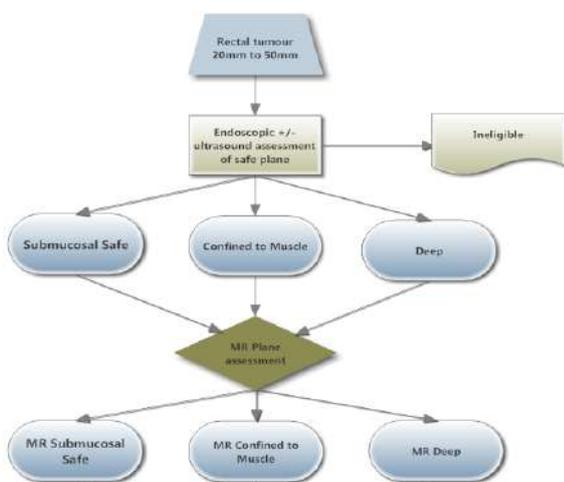
Current problem

- Almost 1/3 of screen detected rectal cancers are limited to the bowel wall without nodal spread but 90% undergo major anterior resection or abdominoperineal surgery with a high associated rate of co-morbidity and economic cost.
- This is because previous attempts at offering less radical surgery have failed due to poor identification of patients suitable for the procedure.



PELICAN
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www.minstrelstudy.co.uk



- Radiologists at recruiting sites are trained and hold delegated responsibility
- Eligible patients are identified on colonoscopy if they are found to have a 20mm to 50mm rectal tumour within 150mm of the anal verge (consent and completion of endoscopy CRF)
- All patients who enter the trial will be sent for an MRI. The MRI will be reported using the novel staging proforma (radiology CRF)
- The patients will proceed to excision or resection of the tumour as per clinician / MDT discussion. (MDT CRF)
- The appropriateness of preoperative stage will be compared against histopathology gold standard (Pathology CRF)



Target Recruitment reached



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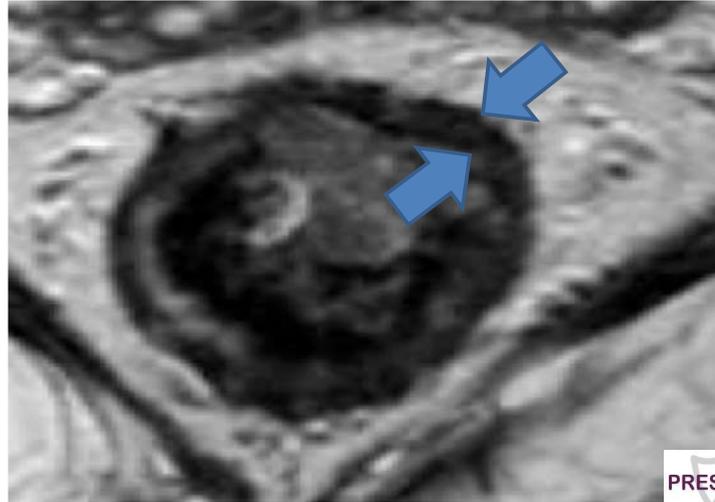


Hypotheses

- Precision MRI staging of ERC significantly reduces the need for radical surgery compared with current national rates by instead offering a local endoluminal excision.
- The study further aims to show that through improved rates of rectal preservation there is a significant improvement in quality of life in patients diagnosed with early rectal cancer.

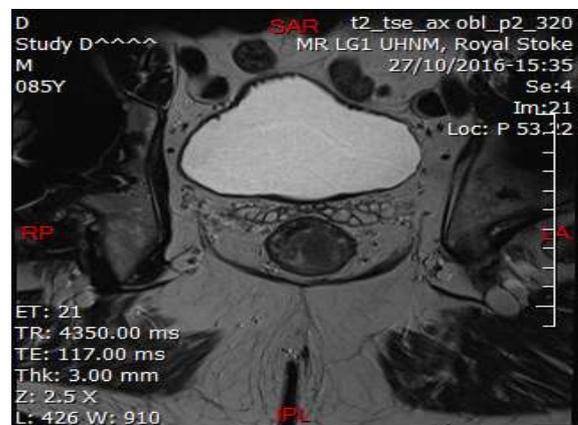


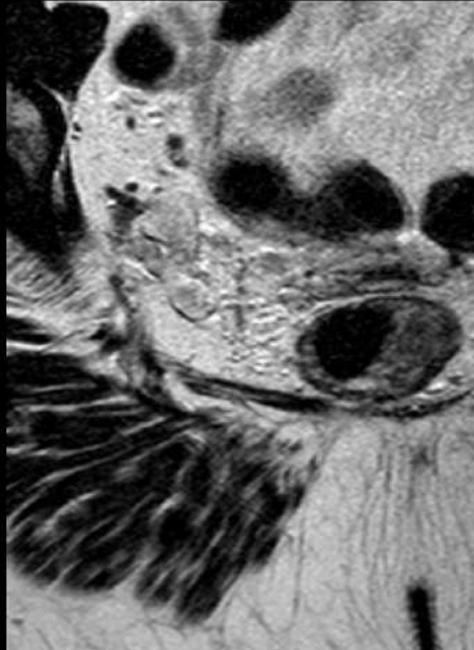
Just look for the black stripe



Recommended reporting structure for staging early rectal cancer using MRI

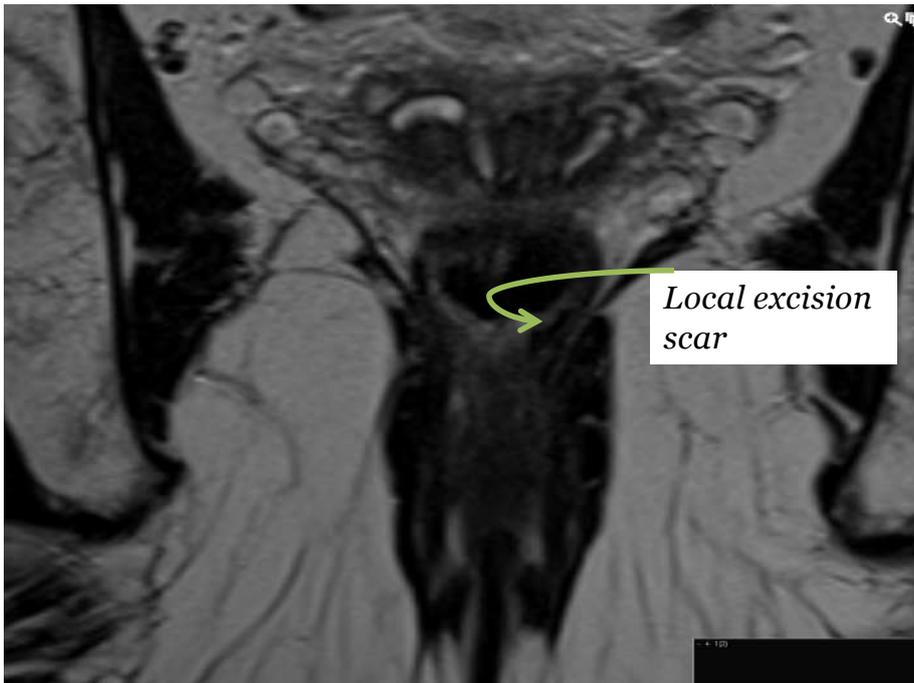
- State morphology – flat, polypoidal, mucin containing
- Measure diameter and thickness of lesion
- If polypoidal –state site and diameter of fibromuscular stalk
- If flat – quadrant or clockface location of central depression versus raised rolled edges
- Measure extent/diameter of invasive border
- Assess degree of preservation of the mucosa, submucosa, muscularis propria layers at the stalk
- Assess lymph nodes for malignant characteristics based on nodal capsule breach or heterogeneity of signal
- Assess height of lesion in relation to anal verge and puborectalis sling
- Evaluate extramural veins for discontinuous spread





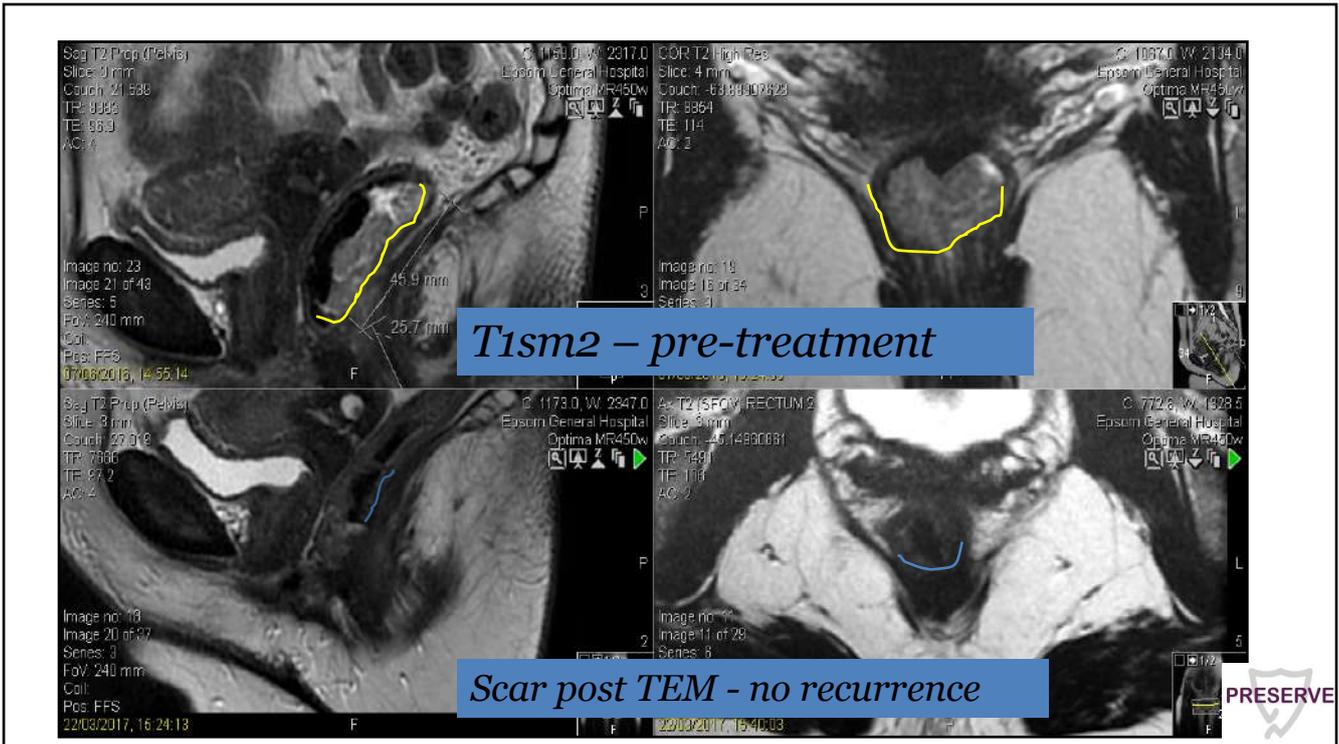
*Morphology – flat semi-annular
Diameter 16mm
Thickness of lesion : 7mm
Clockface location of central depression
=4 o'clock
Invasive edge = 5mm diameter
Muscularis fully preserved
Submucosa/muscle interface lost over
3mm distance on single slice at 4 o'clock
Lymph nodes show smooth nodal
capsule and no heterogeneity - benign
Assess height of 6.5 cm above anal ver
and 12mm above puborectalis sling
No extramural venous invasion
T1sm3/ with potential focal early T2
invasion on a single slice section*

Full thickness TEM



*Local excision
scar*

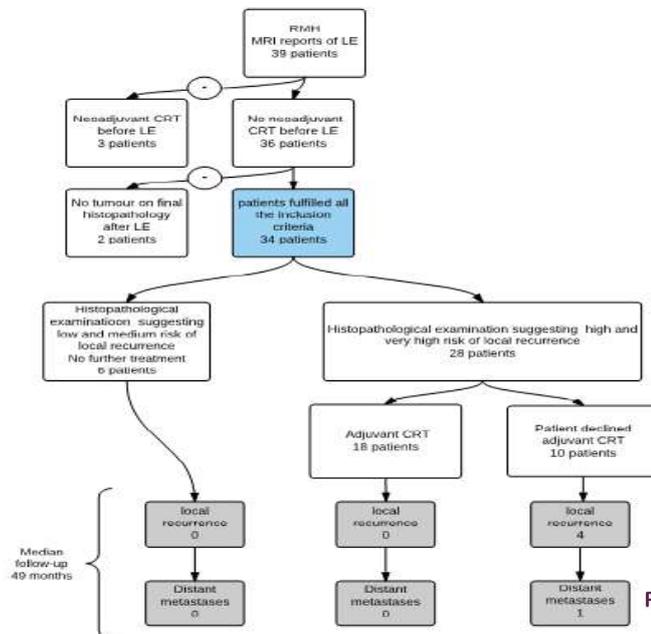


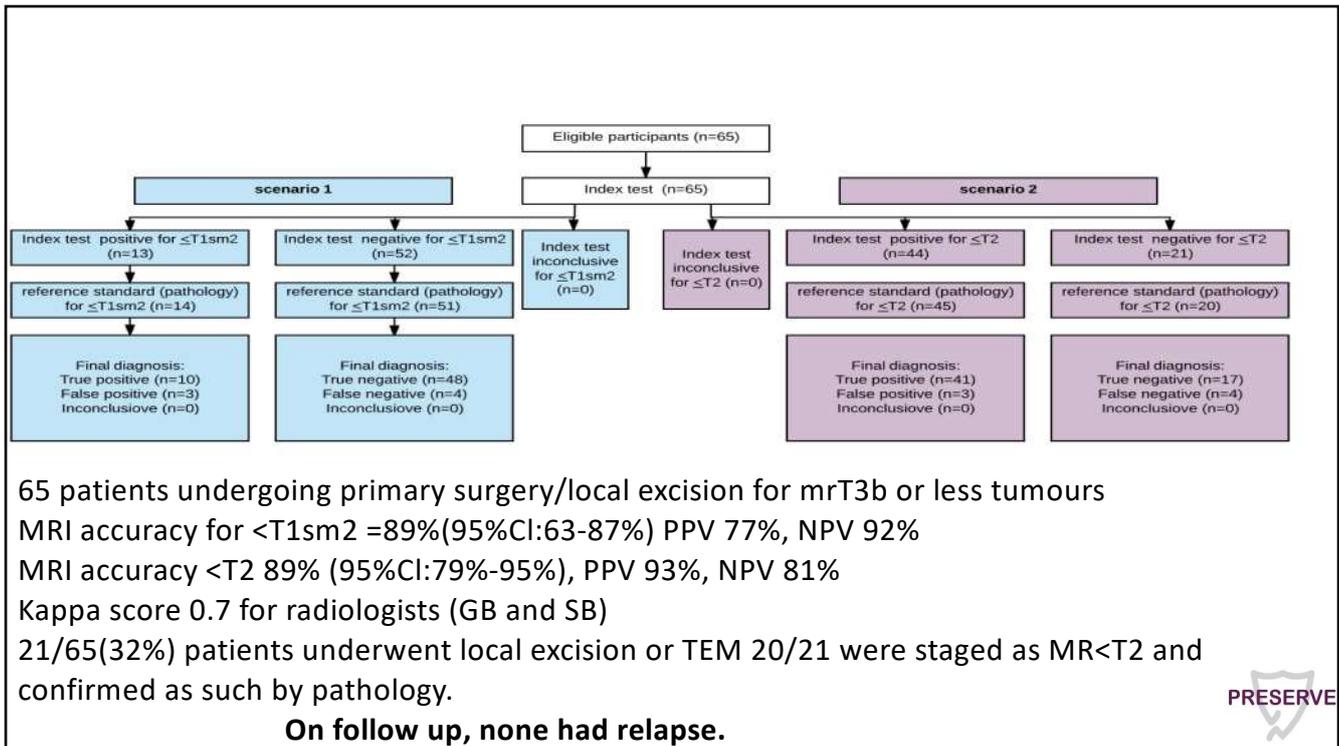


The results of local excision with or without postoperative adjuvant chemoradiotherapy for early rectal cancer among patients choosing to avoid radical surgery

Balyasnikova S, Read J, Tait D, Wotherspoon A, Swift I, Cunningham D, Tekkis P, Brown G. Colorectal disease. 2016.

22/24 patients with low tumours and high risk features which would have required APER have so far avoided radical surgery and remain disease free at a median follow up 3.2 years.





MRI staged patients $\leq T2$ undergoing radical surgery

- 22/44 were $\leq mrT2$. MRI accuracy in predicting lymph node status was 84%(95%CI:70%-92%), PPV 71% and NPV 90%
- If the decision had been made to offer local excision on MRI TN staging rather than clinical assessment a significant increase in organ preservation surgery from 32% to 60% would have been observed (difference 23%, 95%CI:9%-35%)

The PRESERVE trial

- Non randomised control trial comparing MRI pathway with matched controls: non recruiting sites using Public Health England registry data for pT1 and pT2 rectal cancer patients

Primary Endpoint:

- To compare proportion of patients with pT1/pT2 cancers avoiding radical surgery in control versus interventional arm

Secondary

- Measure the impact of this approach on patient reported quality of life outcome measures compared with matched patients undergoing primary surgery (using historic controls – MERCURY 2 trial)
- Compare survival outcomes at 3 and 5 years
- Measure the cost savings to the NHS compared to the current standard of major surgery for ERC (hospital stay, perioperative mortality, complications and permanent colostomy)

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Quality assurance within the trial

1. MRI as a method of improving identification of patients suitable for LE
2. Detailed staging and roadmap to facilitate local excision and to guide surgical and endoscopic techniques
3. Quality assurance and training of gastroenterologists and surgeons to perform local excision by endoscopic and surgical techniques respectively
4. Implementation of modern surgical innovations and techniques to ensure optimal removal of early rectal cancers
5. Histopathological verification of complete excision and biomarker capture
6. Close monitoring and surveillance of patients following local excision to ensure successful resection for residual/recurrent disease
7. Impact of pathway on quality of life
8. Cost analysis of pathway

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Statistical plan

- In 2014, the NBOCA data showed that a total 4907 were T1/T2 colorectal cancers.
- Only 15% underwent organ preservation by TEM/local excision/TAMIS
- 2017 accrual rates from 9 centres of 4 patients per month.
- A further 5 new sites for PRESERVE.

Exact test for single proportion, 2-sided test	endpoint	endpoint	endpoint
	10%	20%	25%
	improvement	improvement	improvement
Test significance, alpha	0.05	0.05	0.05
Null hypothesis proportion, P0	0.15	0.15	0.15
Alternative proportion, P1	0.25	0.35	0.45
Power	0.85	0.9	0.9
Sample size	144	54	26

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Investigators

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 Mr Christopher Cunningham: Oxford
 Professor Robert Goldin : Imperial College
 Mr Muti Abulafi : Croydon Hospital
 Ms Karen Thomas : RMH
 John Amos: Patient representative
 Annabel Shaw : Research Fellow



What has changed for early rectal cancer?

- Better techniques and access
- Improved pathology
- Improved selection of patients with ERC
- Better surveillance after TEM

www.profginabrown.com



Prof Wendy Atkin 1947 -2018

