

The Royal Marsden
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**Pan London
Early Rectal Cancer Meeting**

Royal Society of Medicine
1st November 2018

Dr Diana Tait
Consultant Clinical Oncologist



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Pan London Early Rectal Cancer Meeting
1st November 2018

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





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 – *Dr Diana Tait*
– *Consultant Clinical Oncologist*

Adjuvant Therapy - Selective post excision

- What is the role of Adjuvant Therapy?
- Which patients should be offered Adjuvant Therapy?
- Is there evidence that it's effective?
- What is optimal Adjuvant Therapy?



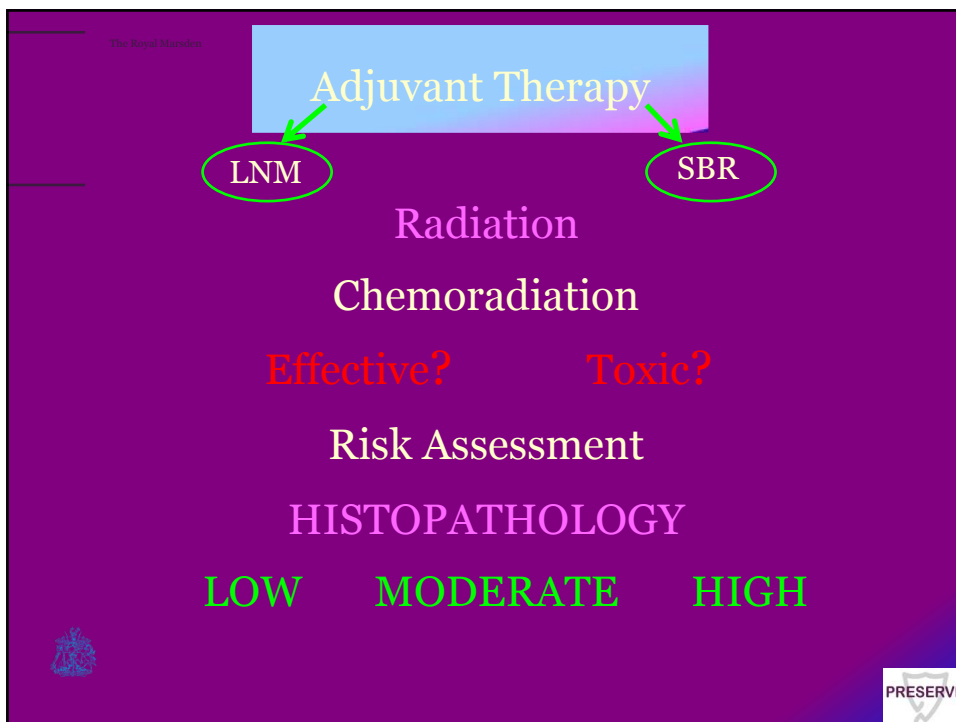
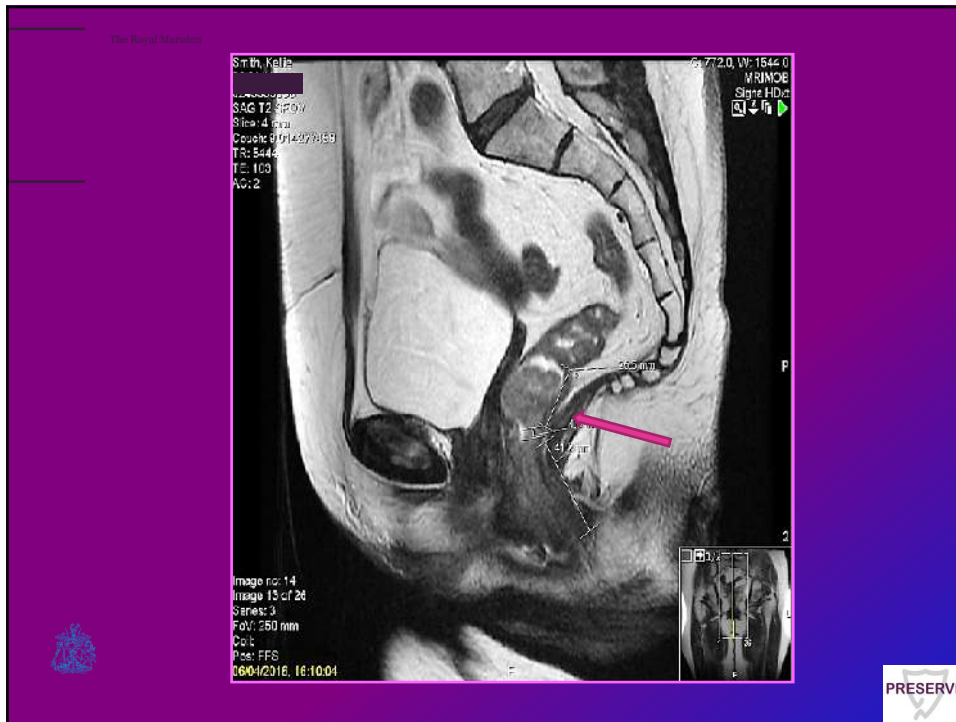
The Role of Adjuvant Therapy

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

Local nodal metastases
(LNM)

Surgical bed regrowth
(SBR)







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Which patients should be offered adjuvant therapy?

Risk Assessment



Criteria	Risk Score	
Margin clear - >0mm from the diathermy margin	0	
Margin positive - 0mm to the diathermy margin	1	
Margin positive - 0mm to the tumour margin	3	
Sm1 / 2	0	
Sm3	1	
Poorly differentiated / mucinous	1	
Tumour budding	1	
LVI	1	
T2	1	
Size of tumour >4cm	1	
Total Score	Grade of Risk	Recommended Treatment
0	Low	Surveillance only
1 – 2	Moderate	Randomisation between surveillance or radiotherapy
≥3	High	Randomisation between radiotherapy or radical surgery

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.

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Predicting LNM in ERC






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Predicting lymph node metastases in ERC

Swedish Rectal Cancer data



- ❖ Swedish Rectal Cancer Registry (2013)
 - T₁ 2007
 - T₂ 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

T-stage lymph	Distribution of T-stage (%)	Proportion with node metastases (%)
T₁, n = 205	13	12
T ₂ , n = 472	29	22
T₃, n = 830	51	46
T ₄ , n = 105	7	65

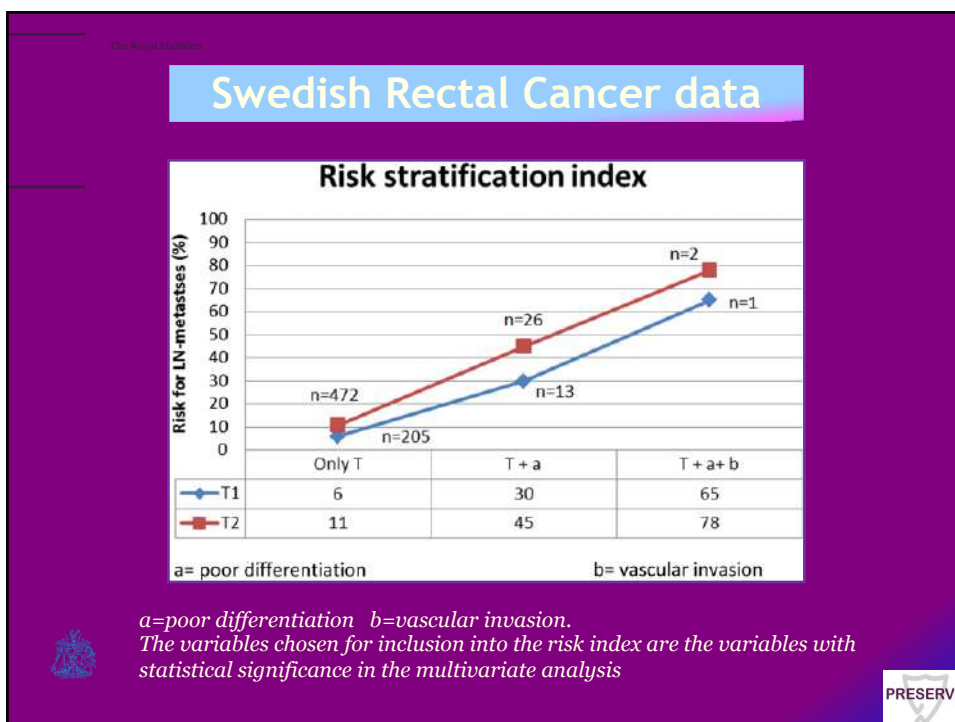
 

Swedish Rectal Cancer data

Uni- and multivariate analyses of risk factors for lymph node metastases.

Univariate analysis	Number	OR	95% CI	Multivariate analysis	
				OR	95% CI
T-stage/sn-level					
Sn1	54	1	Ref		
Sn2	24	0.54	(0.06-5.12)		
Sn3	50	2.38	(0.67-8.46)		
Sn missing	77	2.08	(0.63-6.93)		
T2	472	3.45	(1.22-9.77)	1.97	(1.19-3.25)
Tumour differentiation					
High	114	1	Ref	1	Ref
Intermediate	498	1.98	(1.04-3.75)	1.72	(0.92-3.18)
Low	39	7.39	(3.06-17.4)	6.47	(2.71-15.4)
Differentiation missing	26	0.71	(0.15-3.36)		
Vascular infiltration					
Yes	61	4.81	(2.75-8.40)	4.34	(2.46-7.65)
No	492	1	Ref	1	Ref
Missing	124	0.96	(0.56-1.66)		
Perineural infiltration					
Yes	10	1.85	(0.46-7.31)		
No	458	1	Ref		
Missing	209	0.93	(0.61-1.42)		
Mucinous type					
Yes	52	1.87	(0.99-3.55)		
No	539	1	Ref		
Missing	86	0.97	(0.54-1.77)		
Tumour location (cm from anal verge)					
0-5 cm	118	1.03	(0.59-1.84)		
6-10 cm	259	1.23	(0.80-1.88)		
11-15 cm	300	1	Ref		
Gender					
Male	389	0.94	(0.63-1.39)		
Female	288	1	Ref		
Age*		0.99	(0.98-1.01)		

OR, odds ratio; CI, confidence interval.
 * Age was set as a continuous predictor. OR was not calculated for missing data n = 1.



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Italian meta-analysis data

Italian meta-analysis (2012) → T₁ T₂ 2010

8 Studies
1560 patients

Surgical resection (TME)
No neoadjuvant therapy

Carrara et al Int J Surg Oncol 2012

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Study	Diagnostic OR (95% CI)
Kobayashi 2007	0.42 (0.28-0.65)
Rashied 2008	0.35 (0.14-0.87)
Blumberg 1999	1.52 (0.31-7.48)
Brodsky 1992	0.16 (0.01-2.84)
Goldstein 1989	0.08 (0-1.38)
Pooled	0.4 (0.29-0.54)

Fixed effects model
Cochran-Q = 4.47; df = 4 (P = 0.3467)
Inconsistency (I-square) = 10.4%

χ^2 (Yates): 21.14 P value: 0.0000

Risk of lymph node metastasis in GI versus G2/G3

Study	Diagnostic OR (95% CI)
Kobayashi 2007	0.47 (0.3-0.71)
Rashied 2008	0.44 (0.22-0.9)
Blumberg 1999	0.4 (0.11-1.21)
Brodsky 1992	0.68 (0.22-1.99)
Sachlides 1994	0.34 (0.11-1.01)
Pooled	0.46 (0.35-0.6)

Fixed effects model
Cochran-Q = 0.87; df = 4 (P = 0.9283)
Inconsistency (I-square) = 0%

χ^2 (Yates): 27.78 P value: 0.0000

Study	Diagnostic OR (95% CI)
Kobayashi 2007	0.22 (0.12-0.39)
Blumberg 1999	0.43 (0.08-2.27)
Brodsky 1992	0.59 (0.2-1.76)
Pooled	0.26 (0.18-0.38)

Fixed effects model
Cochran-Q = 2.88; df = 2 (P = 0.2409)
Inconsistency (I-square) = 29.8%

χ^2 (Yates): 25.81 P value: 0.0000



Risk of lymph node metastasis in Vascular Invasion

Risk of lymph node metastasis in lymphatic invasion

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Do all LNM have same impact on outcome?



Size?	Position?
<ul style="list-style-type: none"> T1 Med size 0.3mm T2 Med size 4.1mm 	<ul style="list-style-type: none"> 63% level of Primary 17% 2cm proximity 98% 5cm proximity 0% distal

 *Koh DM et al Int J Radiat Oncol. Biol. Phys. 2008* 

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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

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Nothing New — p T₂ Poor outcomes

Local Recurrence data

	Local excision	Radical Surgery	
T1	13%	3%	Nash (2009)
T2	37%		Garcia-Aguilar (2000)

Disease-free survival according to pathologic T-stage

No. of patients	68	68	65	65	64	64
pT1	15	13	12	11	11	11
pT2						

Jeong et al Radiat Oncol 2016

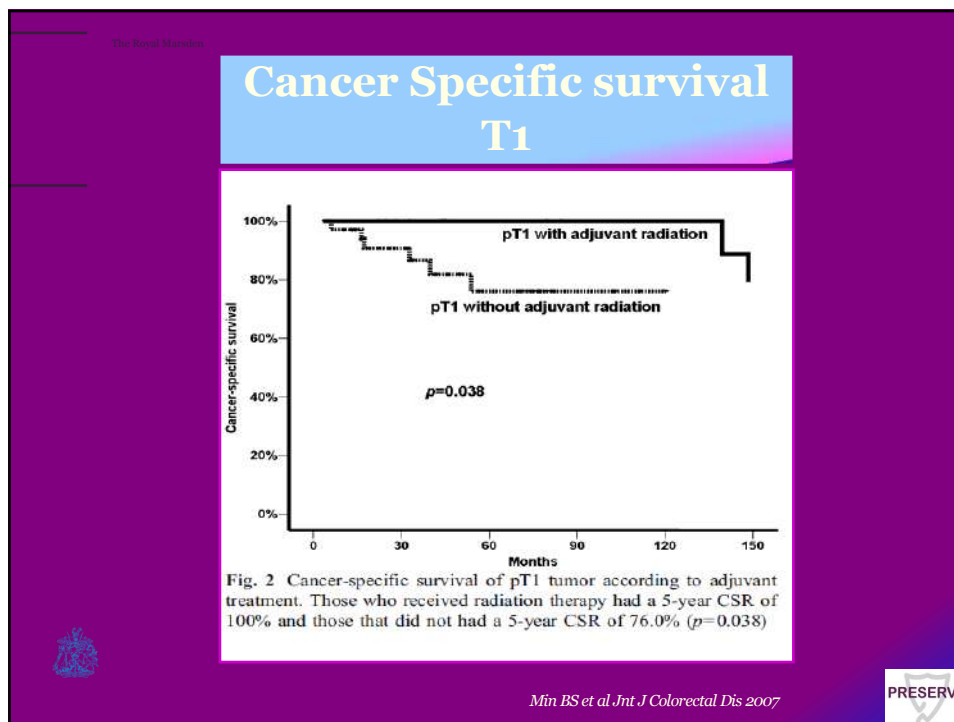
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Impact Radiotherapy on Local Recurrence

	T1	T1	T1	T2
RT ⁻	24%	16%	16%	36%
RT ⁺	0%	0%	0%	9%
	Lamont (200)	Gopaul (2004)	Min (2007)	Min (2007)

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Functional Outcome after post local excision adjuvant RT?

Even less data!

RMH series – LARS assessment
underway

Pucciarelli S et al BJS 2017

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What is Optimal Adjuvant Therapy? Radiotherapy

Target Volumes

LNM



SBR

Dose

45Gy 25# equivalent

+/- Bit more!

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



Adjuvant RT to reduce LNM

Mesorectal nodes

Inguinal nodes

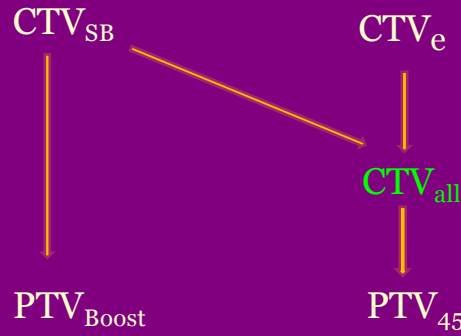
Pelvic sidewall nodes

Superior nodes

Adjuvant RT to reduce SBR

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



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