

Imaging rectal cancer and its value for the assessment of response



Regina Beets -Tan, MD, PhD
Abdominal & Oncological Radiologist
Maastricht University Medical & Oncology Center
The Netherlands

Learning objectives

- ✓ Evidence of imaging

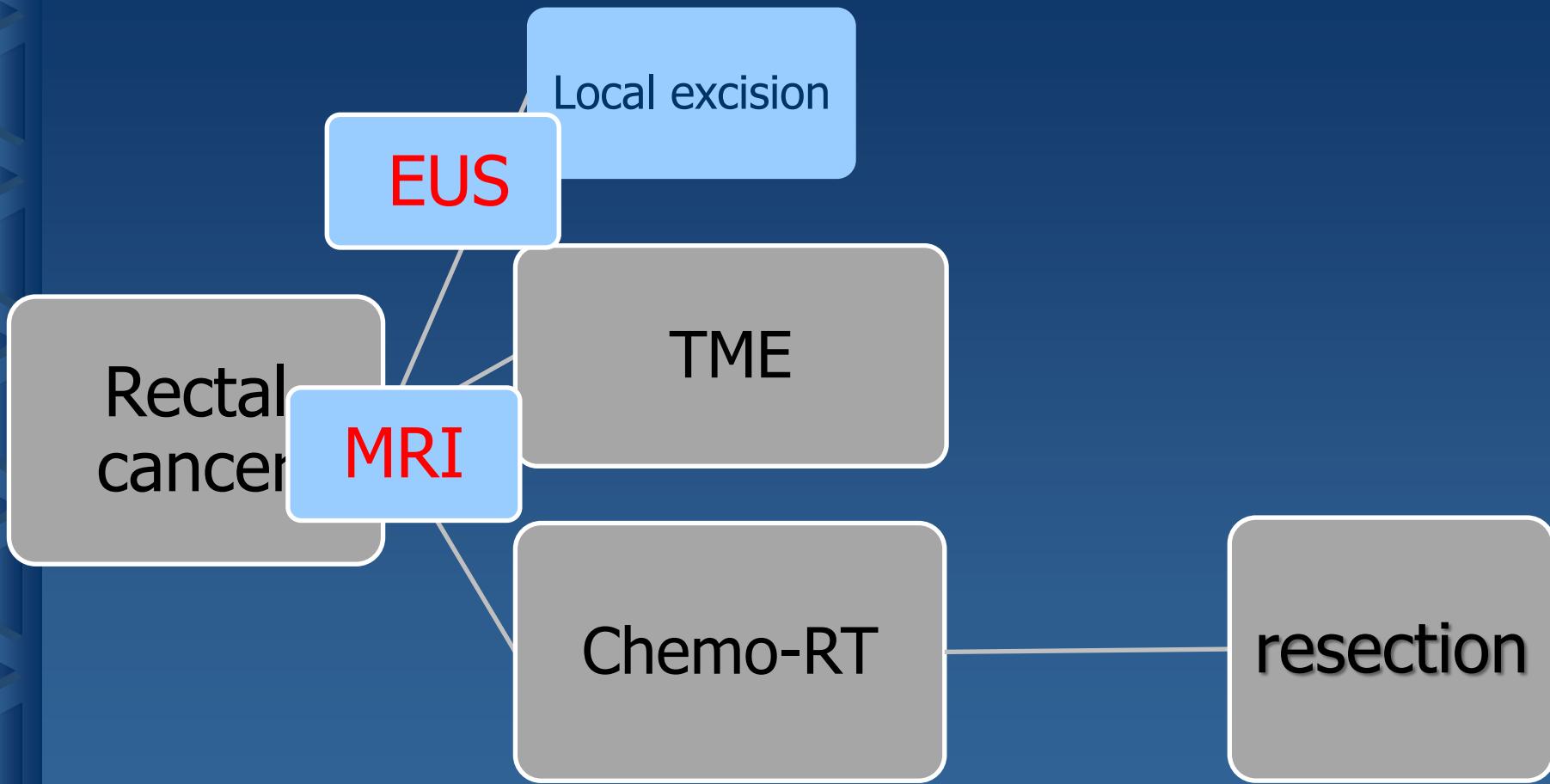
Learning objectives

- ✓ Evidence of imaging
- ✓ Assess and predict response to CRT

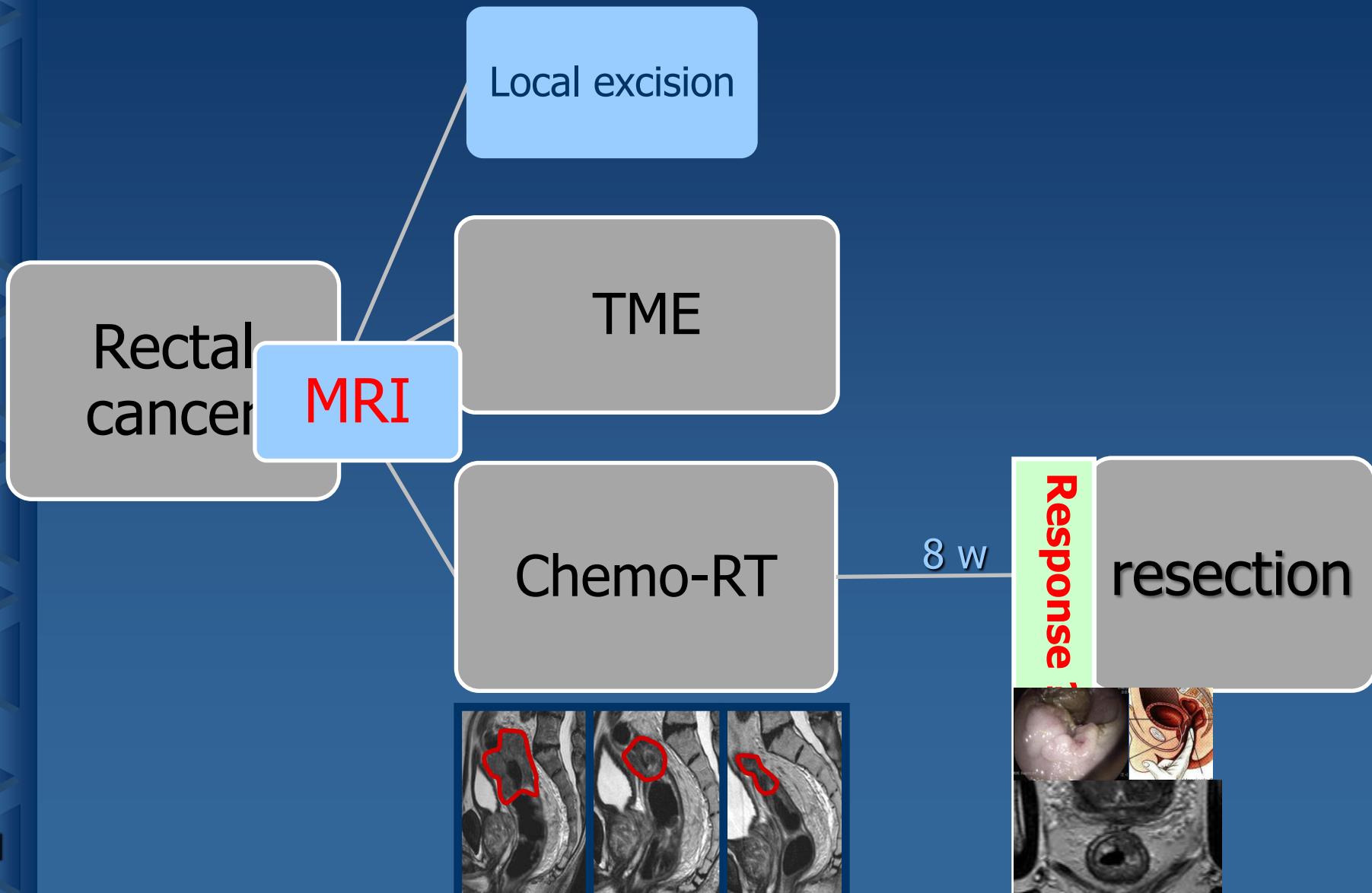
Learning objectives

- ✓ Evidence of imaging
- ✓ Assess and predict response to CRT
- ✓ Future Imaging

ESMO guidelines. Annals Oncology 2012
EURECCA-CRC consensus guidelines EJC 2014
ESGAR consensus guidelines. Eur Radiol 2013



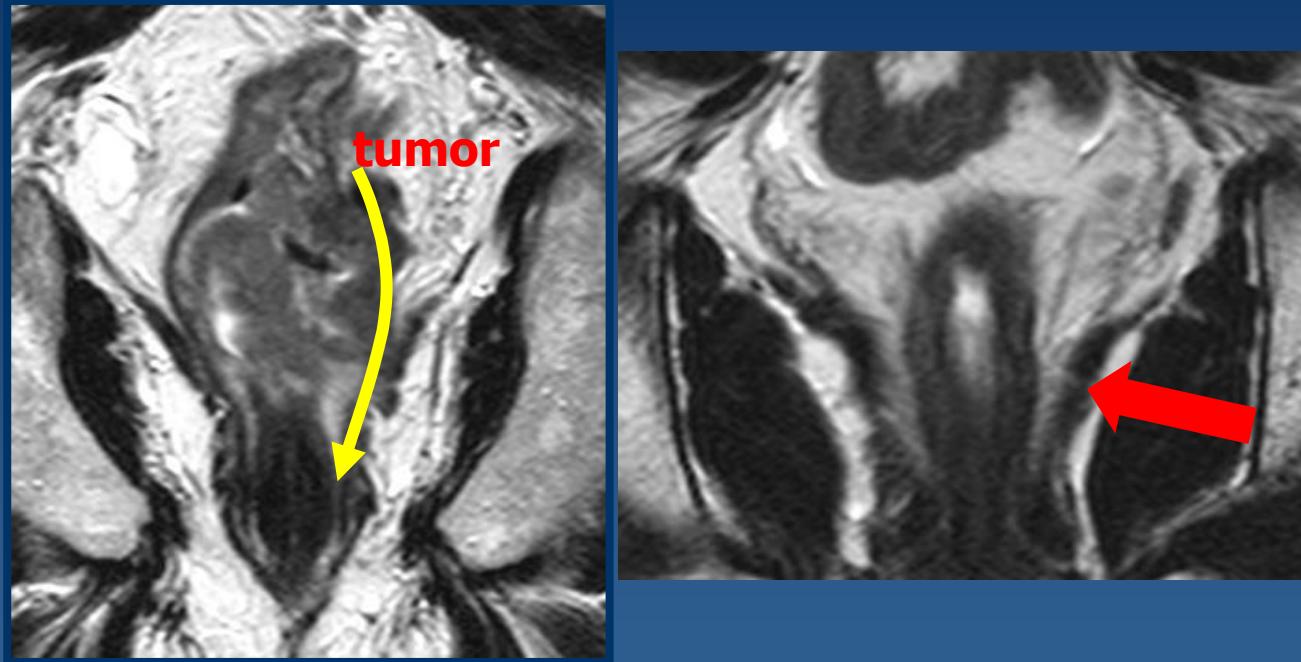
ESMO guidelines. Annals Oncology 2012
EURECCA-CRC consensus guidelines EJC 2014
ESGAR consensus guidelines. Eur Radiol 2013



Assessment of response

- ✓ alter surgical approach

Restaging MRI



90% predictive of tumor regression

Assessment of response

- ✓ alter surgical approach
- ✓ organ preservation

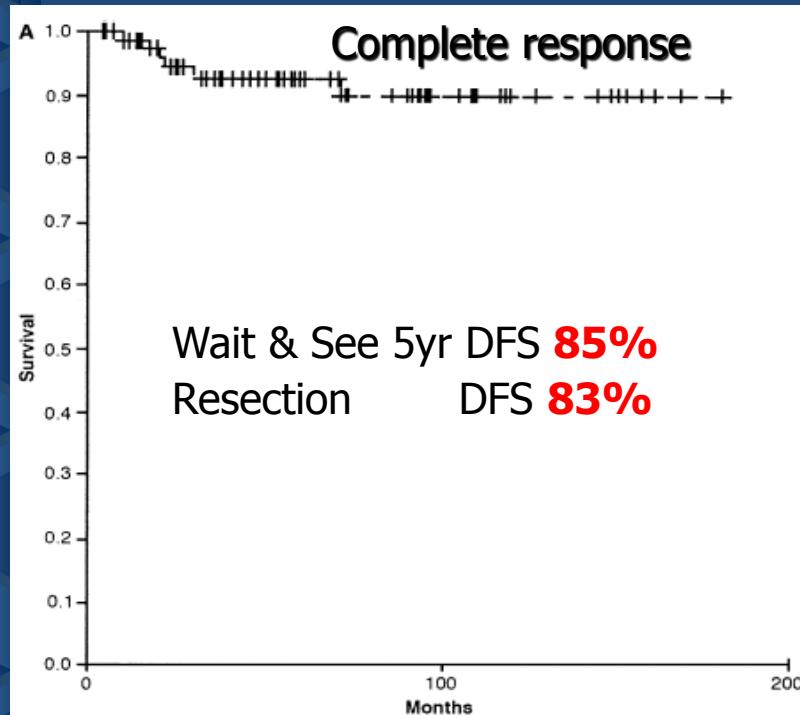
Non operative management after CRT

Operative Versus Nonoperative Treatment for Stage 0 Distal Rectal Cancer Following Chemoradiation Therapy

Long-term Results

Angelita Habr-Gama, MD,* Rodrigo Oliva Perez, MD,* Wladimir Nadalin, MD,† Jorge Sabbaga, MD,† Ulysses Ribeiro Jr, MD,‡ Afonso Henrique Silva e Sousa Jr, MD,* Fábio Guilherme Campos, MD,* Desidério Roberto Kiss, MD,* and Joaquim Gama-Rodrigues, MD‡

Ann Surg 2004



VOLUME 29 • NUMBER 36 • DECEMBER 10 2011

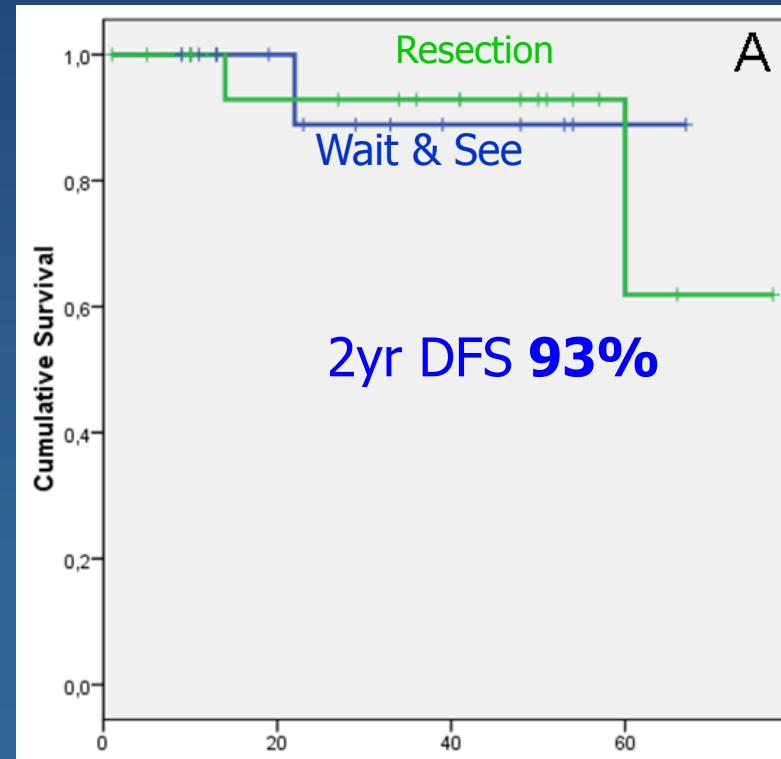
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Wait-and-See Policy for Clinical Complete Responders After Chemoradiation for Rectal Cancer

Monique Maas, Regina G.H. Beets-Tan, Doenja M.J. Lambregts, Guido Lammering, Patty J. Nelemans, Sanne M.E. Engelen, Ronald M. van Dam, Rob L.H. Jansen, Meindert Sosef, Jeroen W.A. Leijtens, Karel W.E. Hulsewé, Jeroen Buijsen, and Geerard L. Beets

JCO 2011



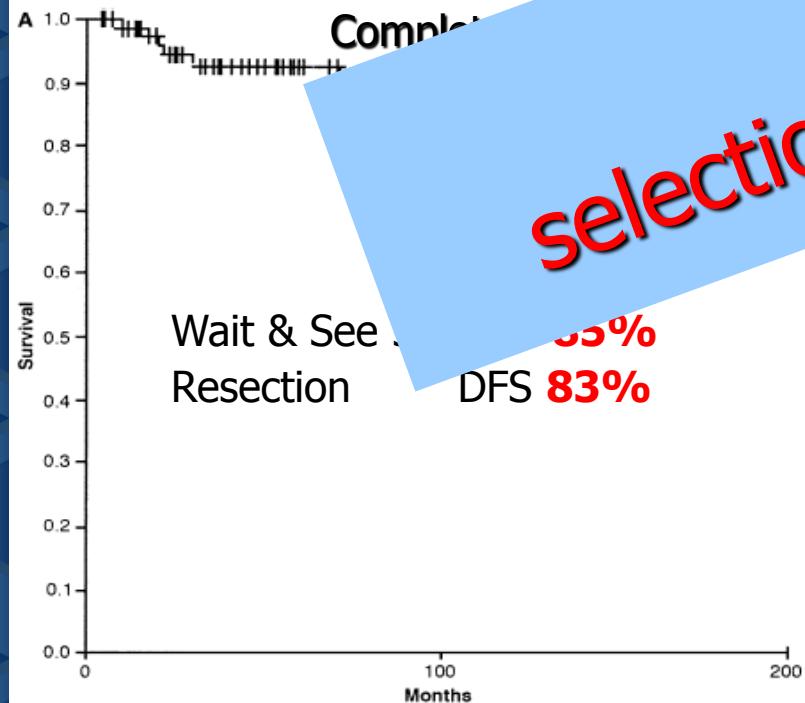
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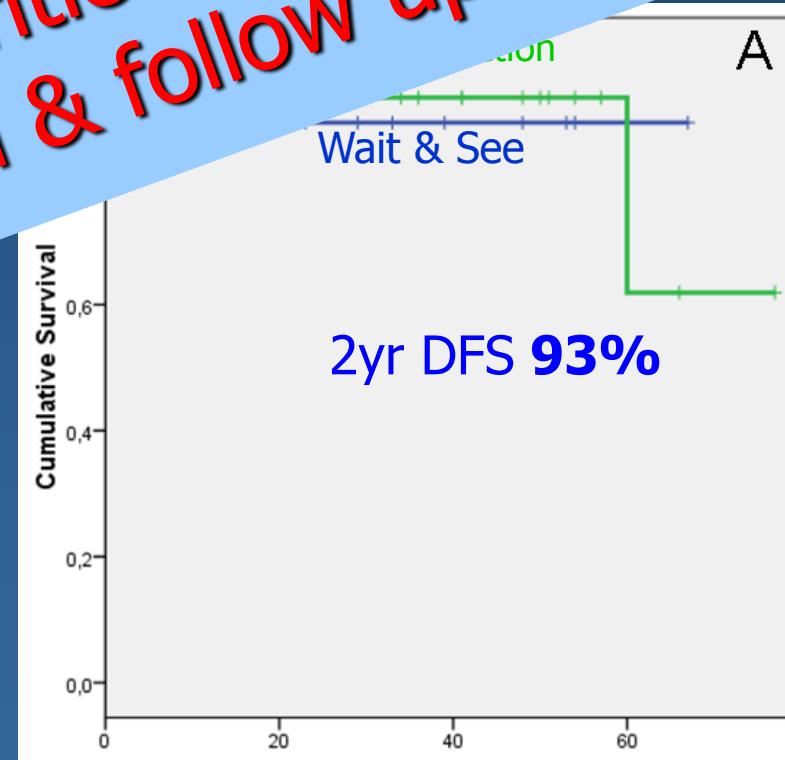
ORIGINAL REPORT

Wait-and-See Pol...
Chemoradiation

Complete Responders After

Mertens, P.J., Nelemans, G.J., Leijtens, W.A.

critical
selection & follow up !





► Tumor remnant in bowel wall?



- Tumor remnant in bowel wall?
- Nodes sterilized?

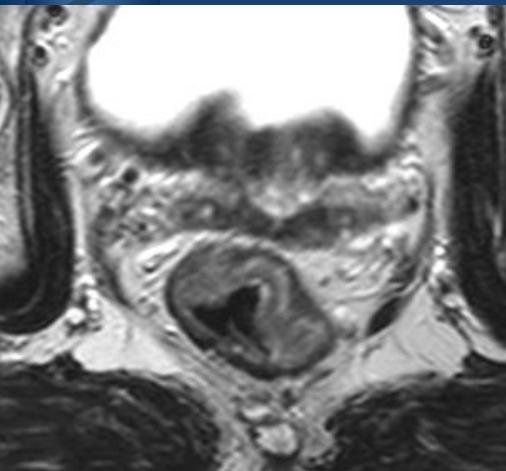
U
M



- Tumor remnant in bowel wall?
- Nodes sterilized?
- Early detection tumor regrowth?

U
M

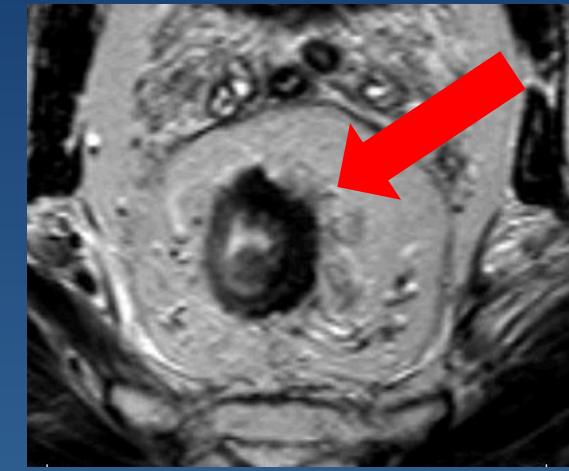
Fibrosis !



CRT

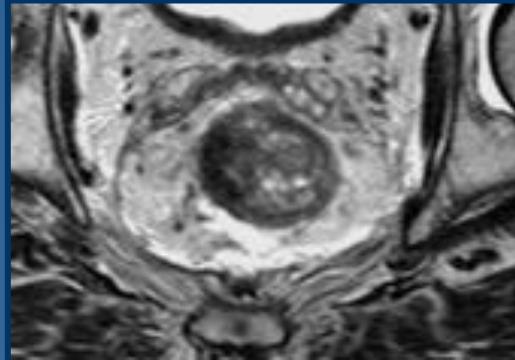
6-8 w

Assess



Meta analysis restaging MRI

	sens	spec
ypT0-2	55	90
ypCR	19	95



MRI for ypCR

	sens	spec	PPV	NPV
Suppiah Col Dis 2009	0.20	0.98	0.50	0.91
Kim Radiology 2009	0.55	0.76	0.46	0.81
Maastricht Multicenter	0.40	0.92	0.56	0.85

assessment ypCR

EUS	PPV	NPV
Vanagunas Am J Gastr 03	0.19	0.79
Lirsch Chir 03	1.00	0.85
Maretto Red J 09	0.36	0.74

assessment ypCR

EUS	PPV	NPV	PET/CT	PPV	NPV
Vanagunas Am J Gastr 03	0.19	0.79	Janssen Int J Rad Biol Onc Phys 09	0.17	0.88
Lirsch Chir 03	1.00	0.85	Kristiansen DCR 08	0.33	0.83
Maretto Red J 09	0.36	0.74	Capirci An Surg Onc 07	0.43	0.80

Neither FDG-PET Nor CT Is Able to Distinguish Between a Pathological Complete Response and an Incomplete Response After Neoadjuvant Chemoradiation in Locally Advanced Rectal Cancer

A Prospective Study

José G. Guillem, MD,* Jeannine A. Ruby, MD,* Tobias Leibold, MD,* Timothy J. Akhurst, MD,†

Henry W. Yeung, MD,† Marc J. Gollub, MD,† Michelle S. Ginsberg, MD,† Jinru Shia, MD,‡

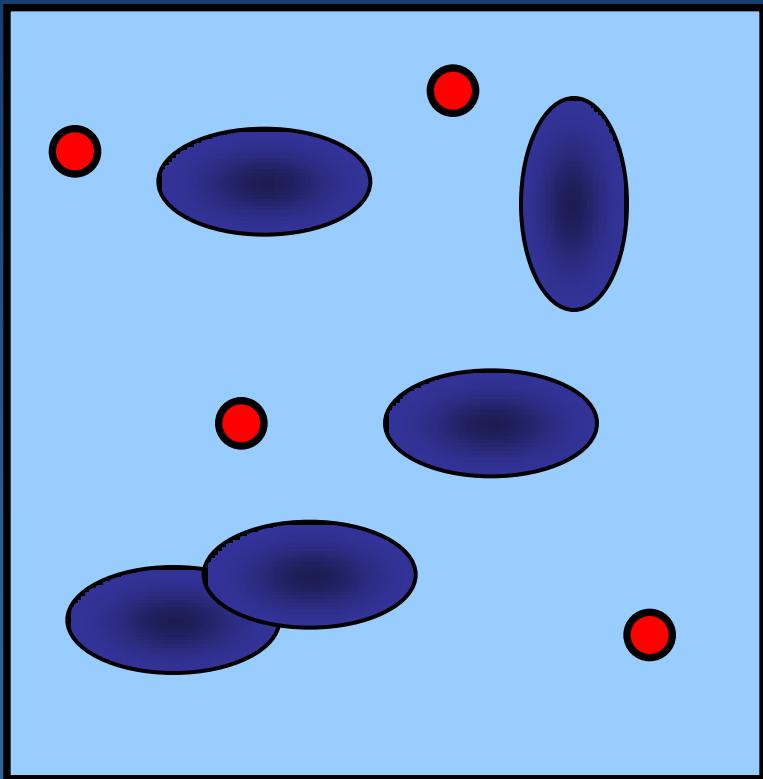
Arief A. Suriawinata, MD,‡ Elyn R. Riedel, MA,§ Madhu Mazumdar, PhD,§ Leonard B. Saltz, MD,||

Bruce D. Minsky, MD,¶ Garrett M. Nash, MD,* Philip B. Paty, MD,* Larissa K. Temple, MD,*

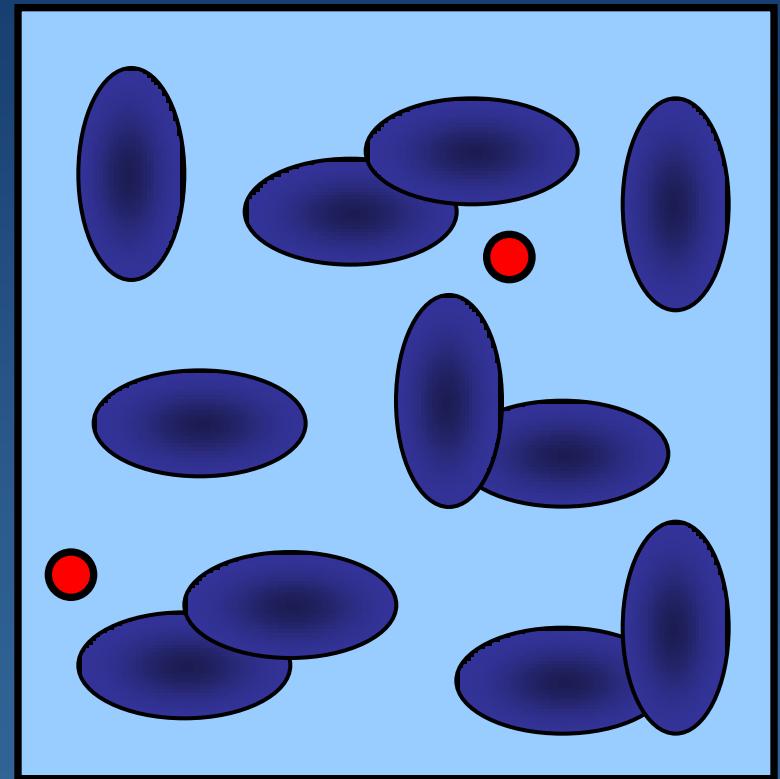
Martin R. Weiser, MD,* and Steven M. Larson, MD†

		Post CRT
FDG PET	AUC 0.64	
CT	AUC 0.64	

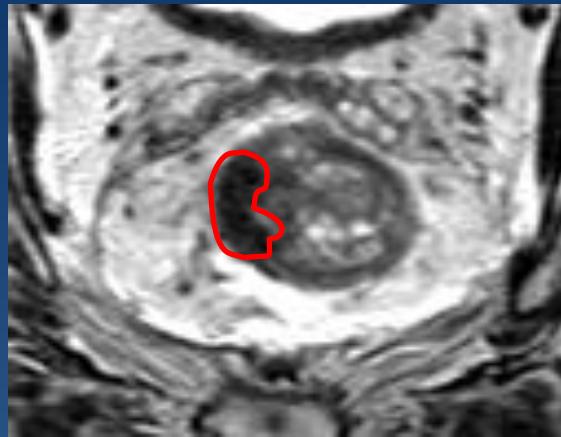
Diffusion MRI



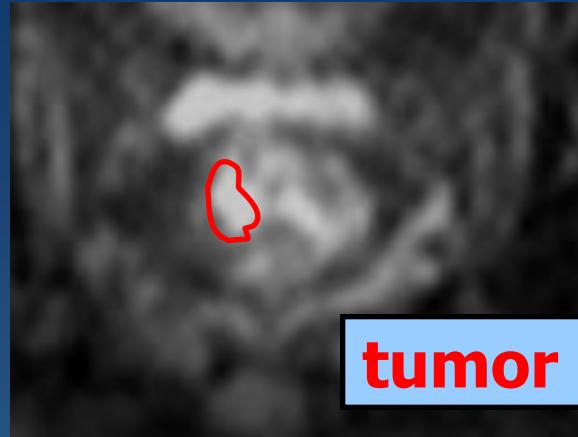
Normal diffusion



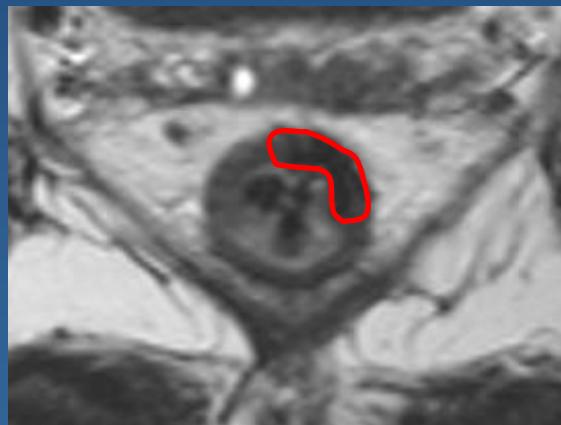
Restricted diffusion



STANDARD MRI



tumor



DIFFUSION MRI

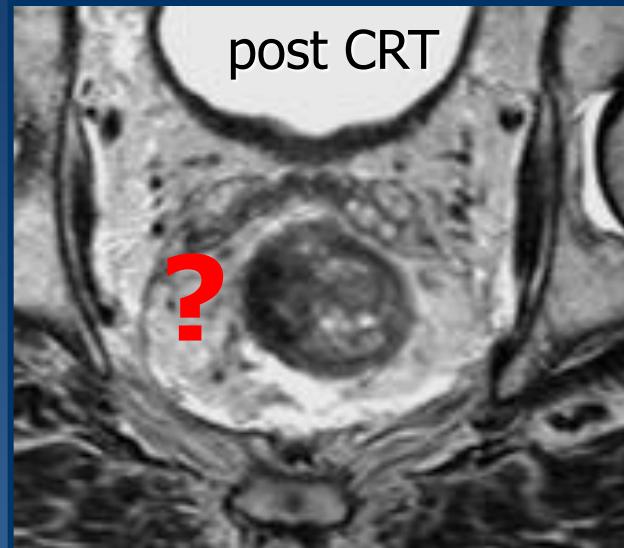
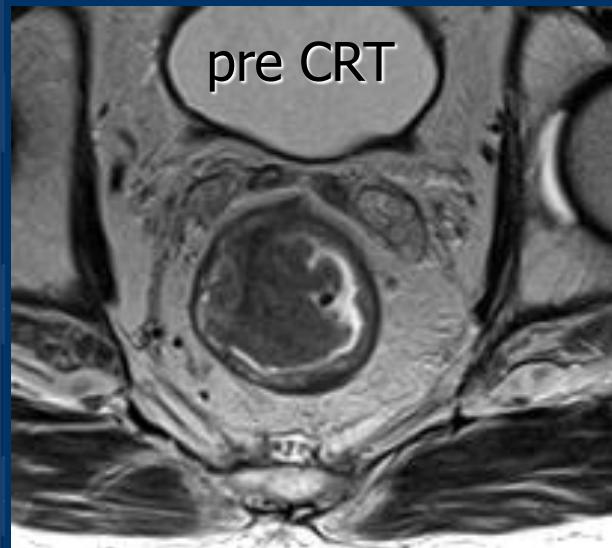
Complete response

Meta analysis DWI studies

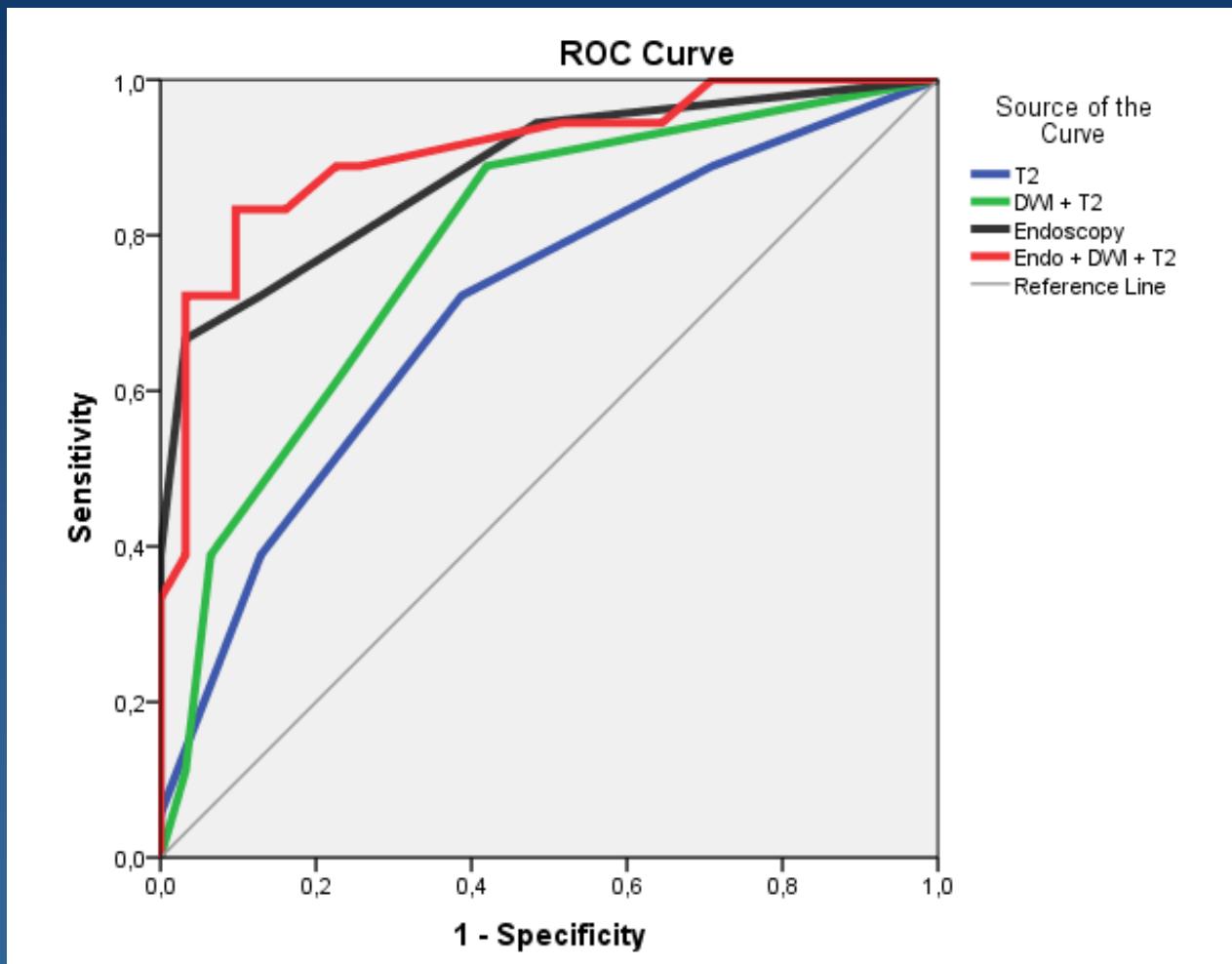
ypCR	MRI	MRI+DWI
Sensitivity	50  84	
Specificity	91	85
LR+	5.8	5.5
LR-	0.5	0.2

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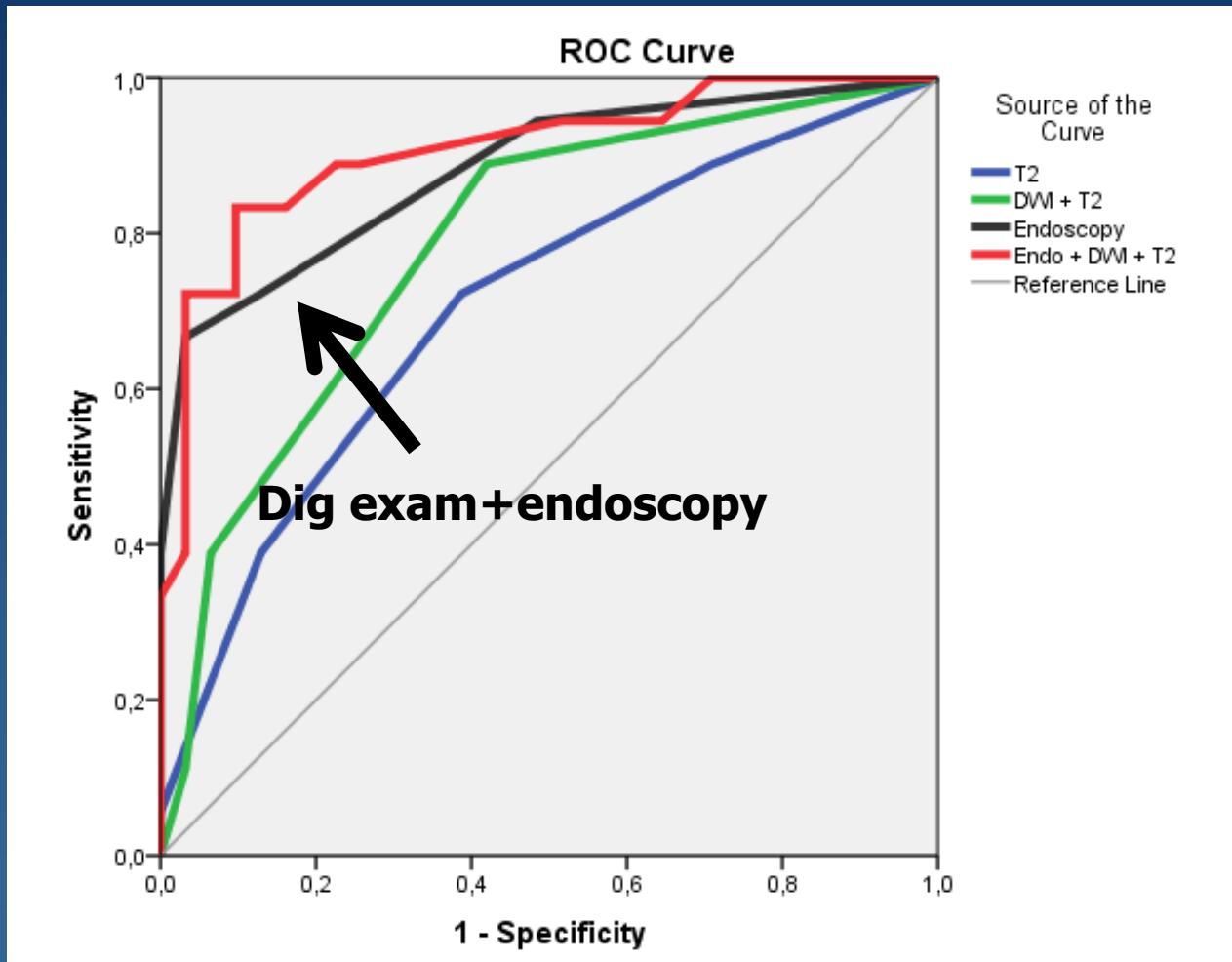
Tumor remnant



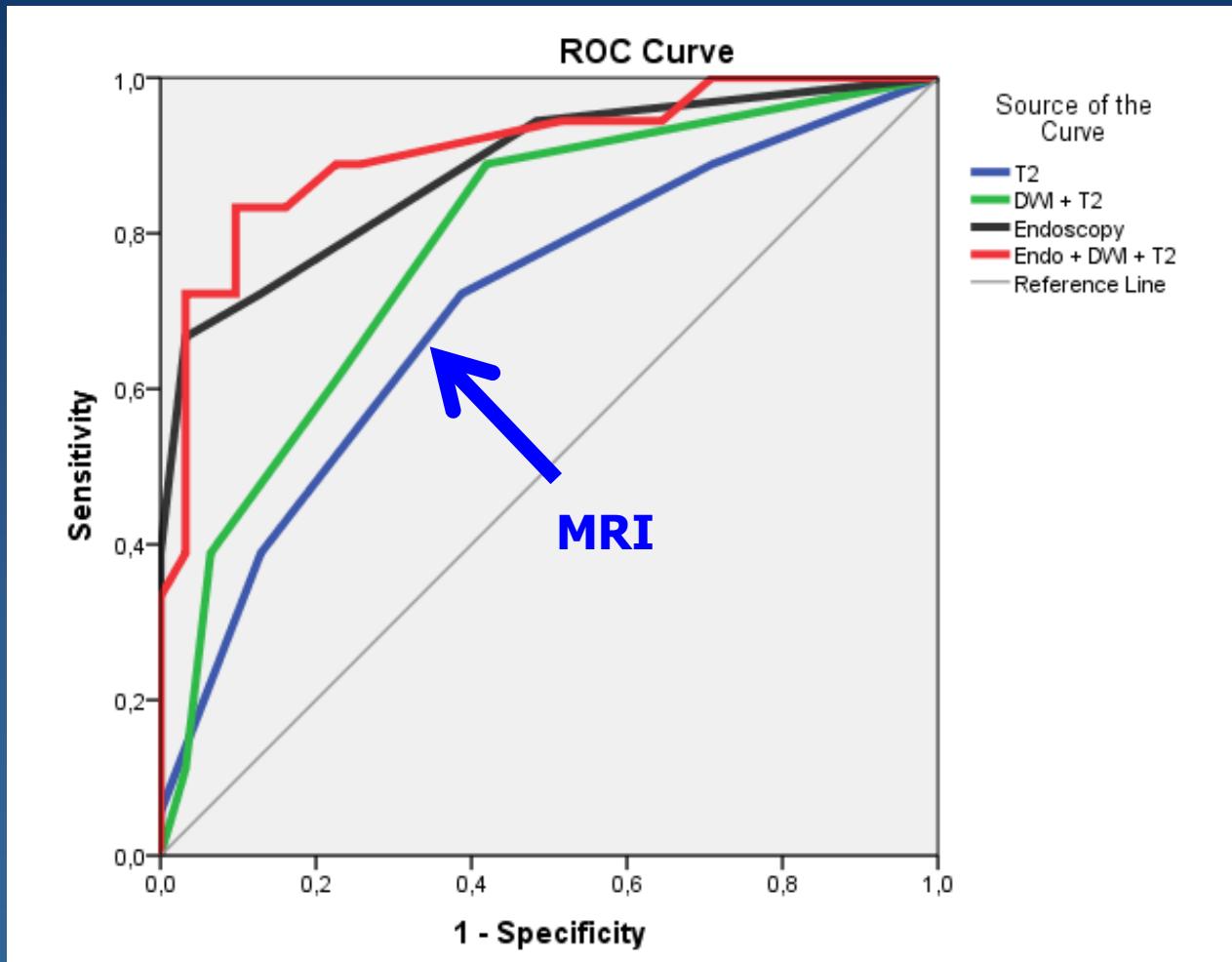
Endoscopy or DWI for selection ?



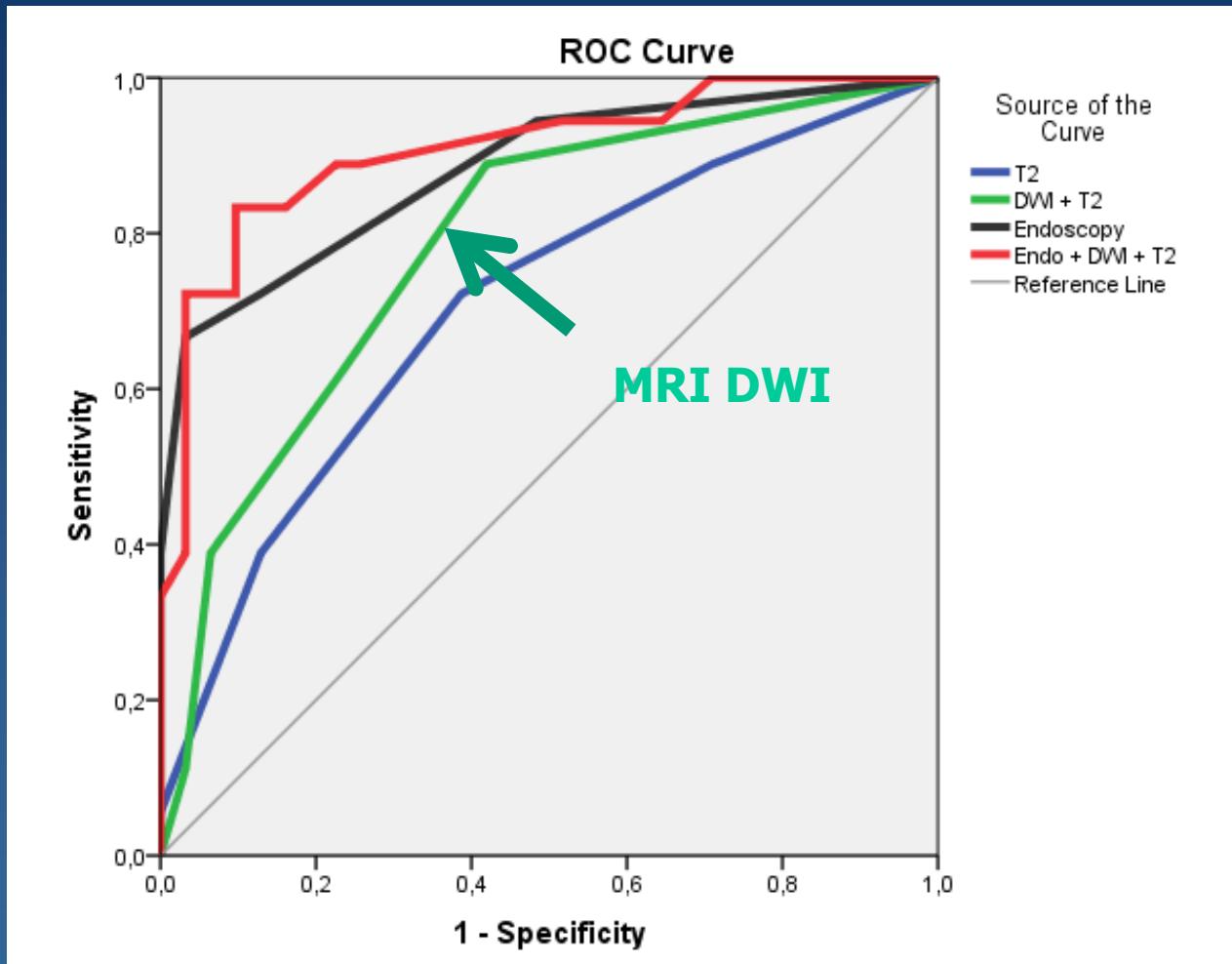
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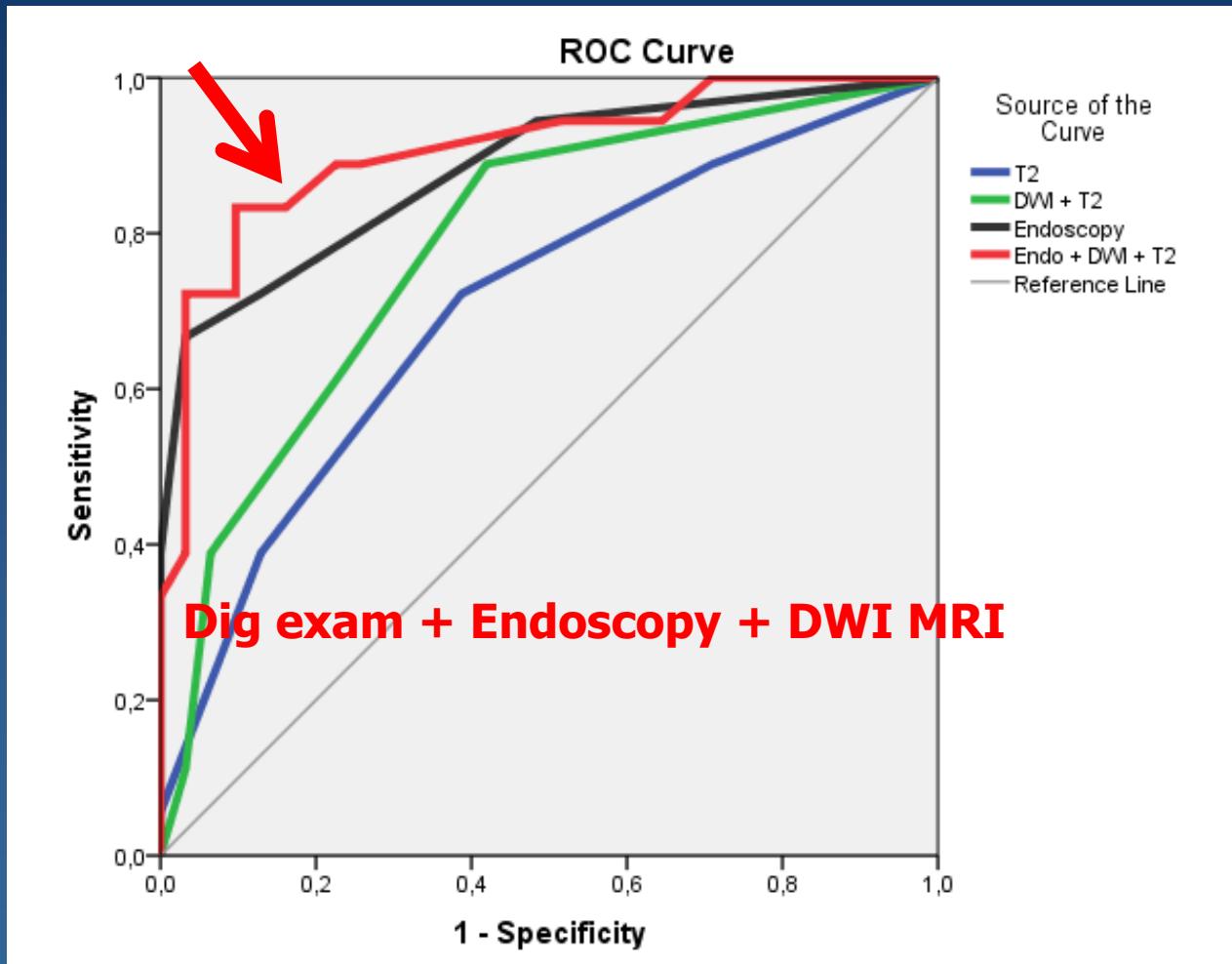
Endoscopy or DWI for selection ?



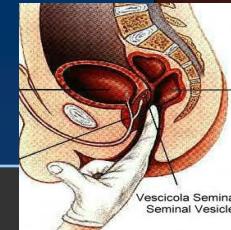
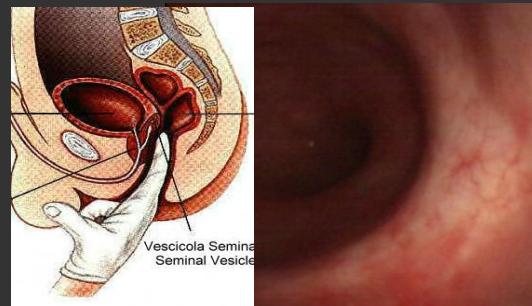
Endoscopy or DWI for selection ?



Endoscopy or DWI for selection ?



ypCR



LR+

16.13



56.2

LR-

0.52

0.19

Positive post-test probability

90%

98%

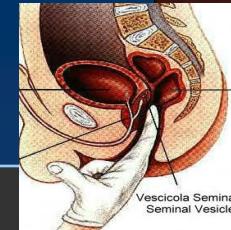
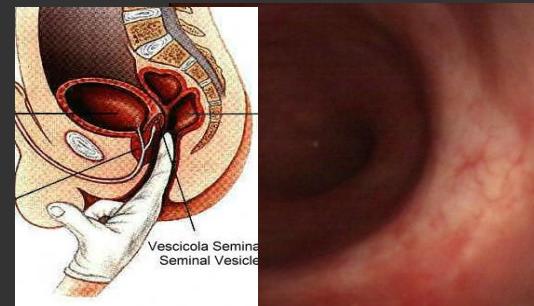
Negative post-test probability

22%

16%

Maastricht unpublished

ypCR



LR+

16.13



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0.19

Positive post-test probability

90%

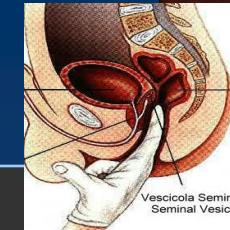
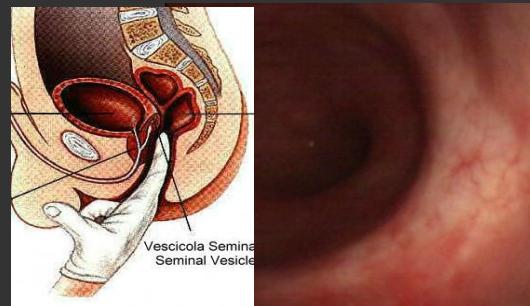
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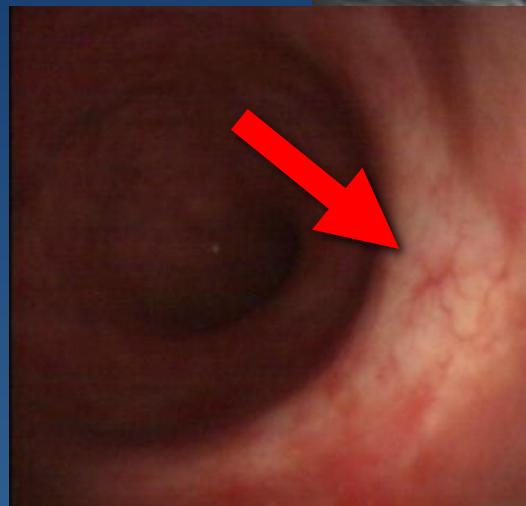
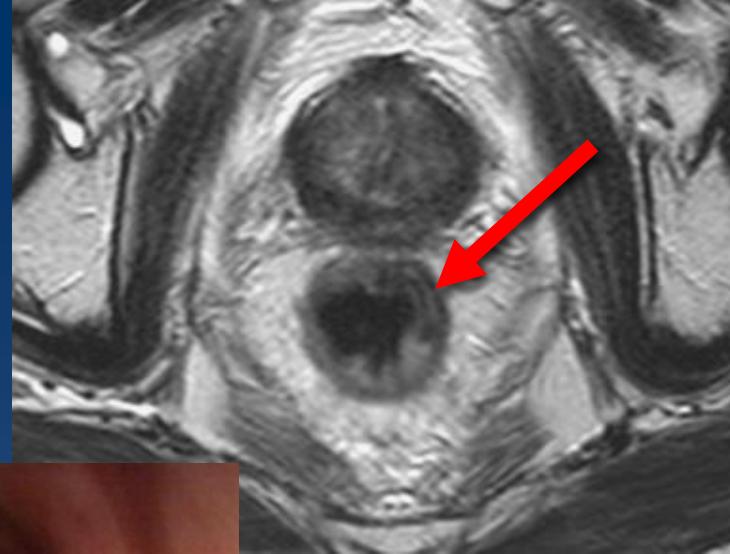
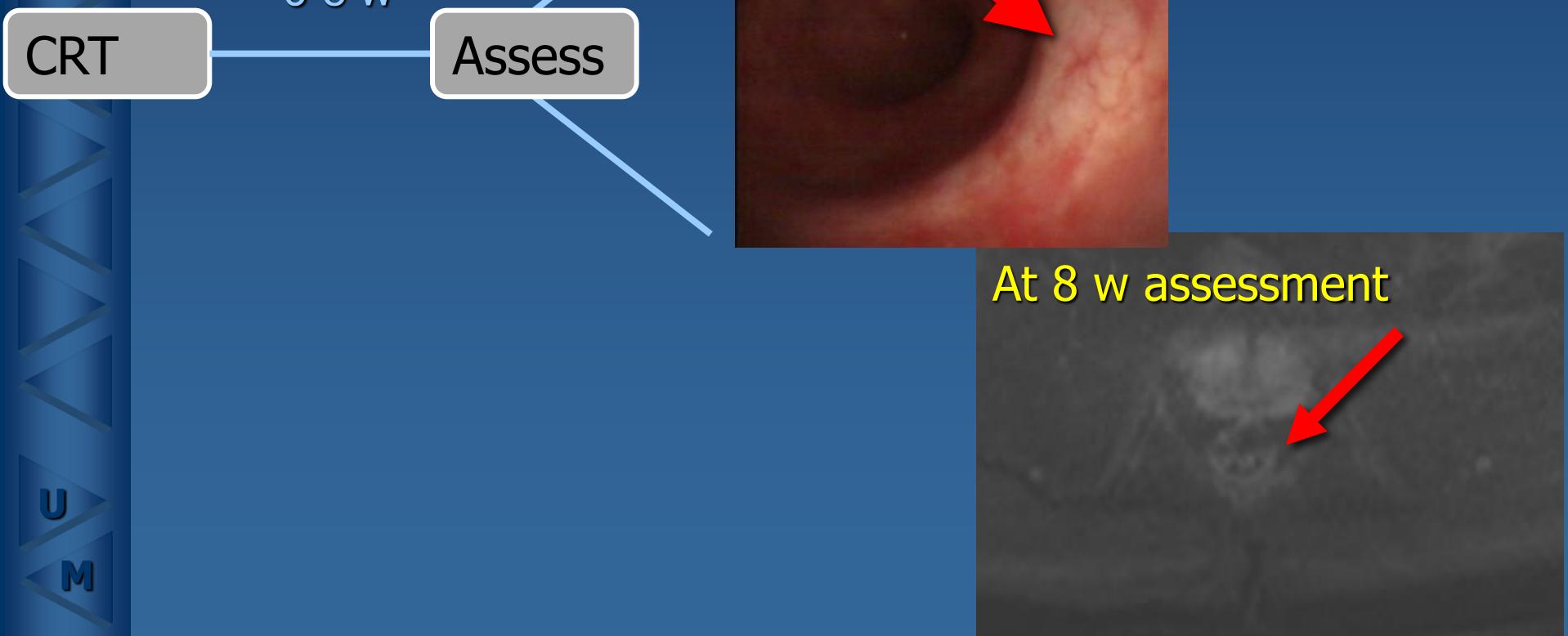
Negative post-test probability

22

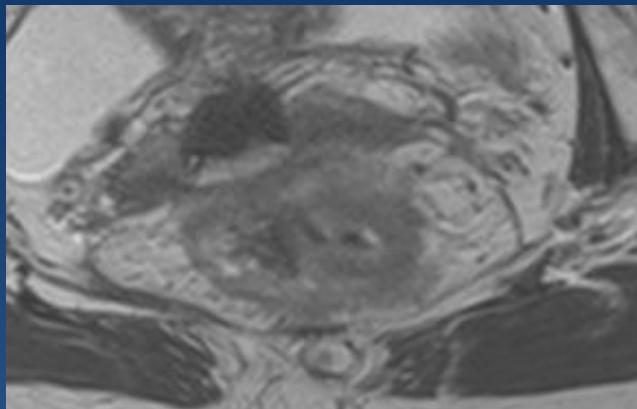
16%

Maastricht unpublished

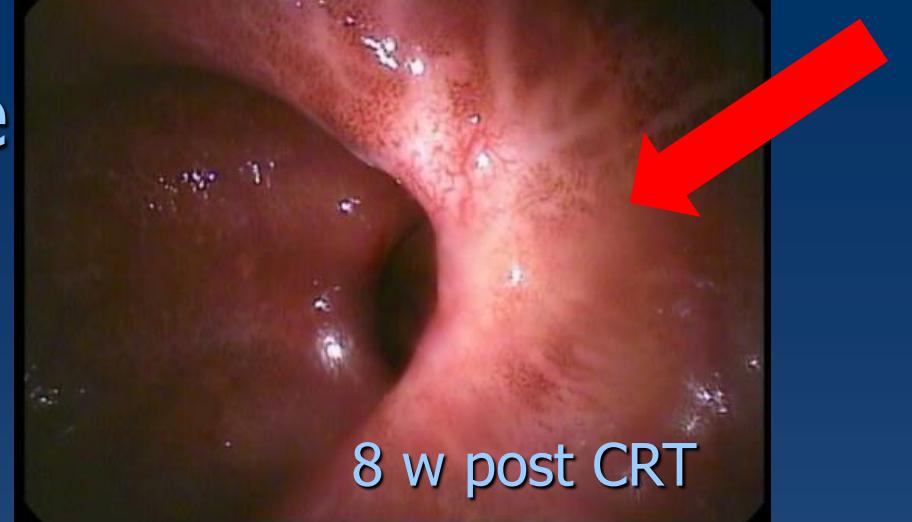
Typical pattern cCR



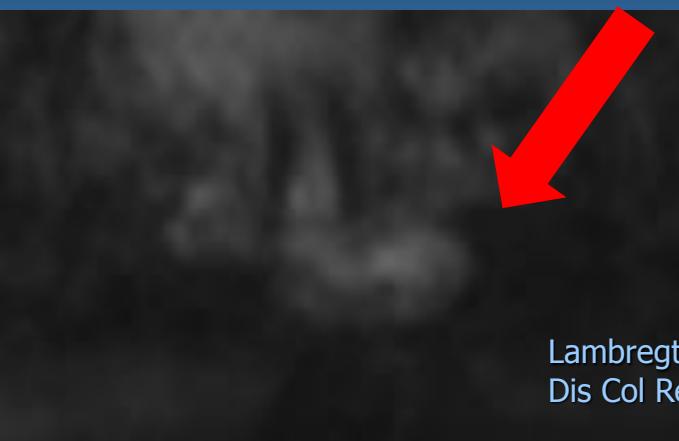
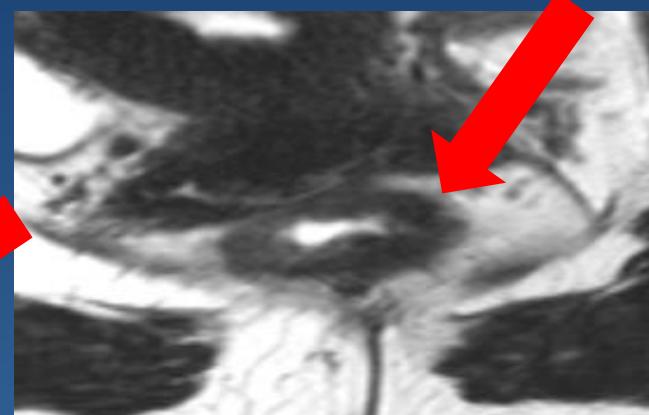
Clinical complete response

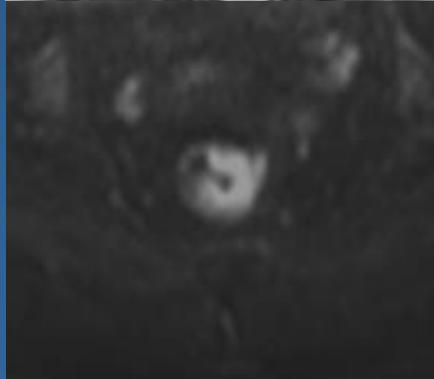
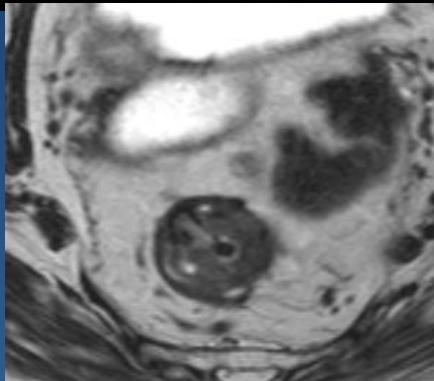
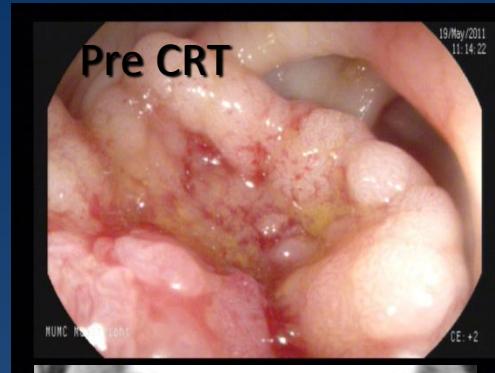


Pre CRT

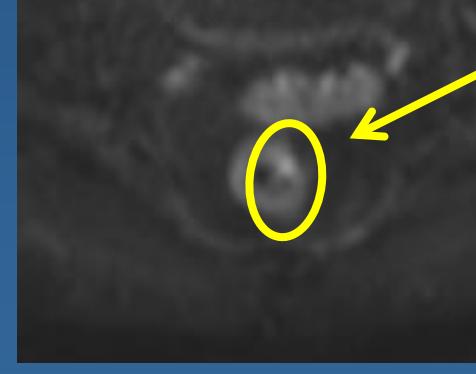
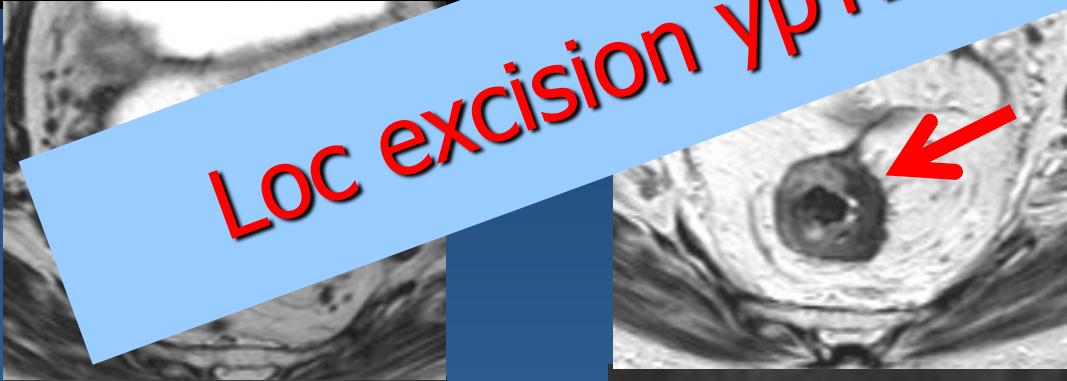
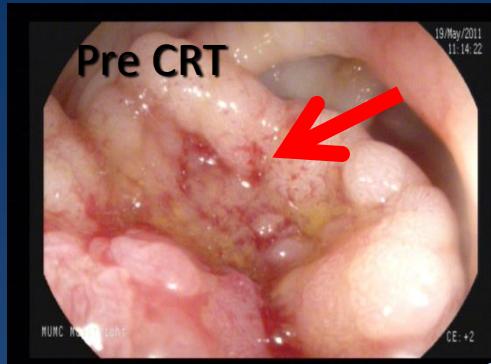


8 w post CRT



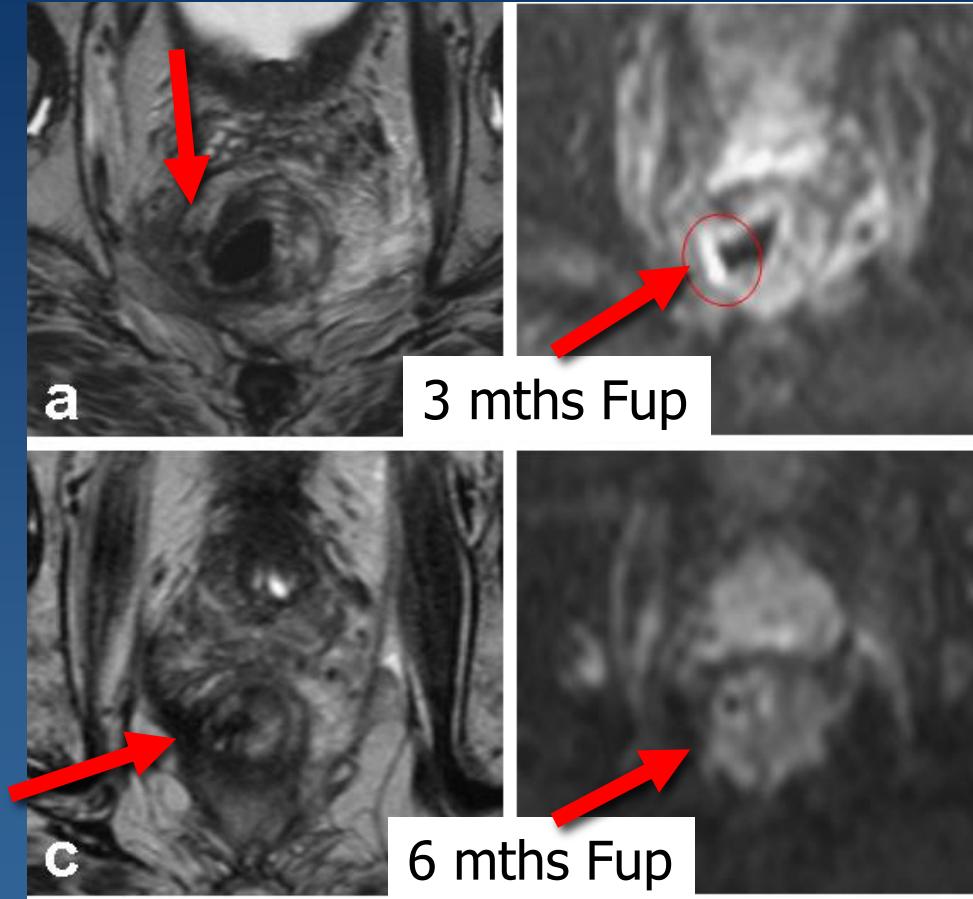


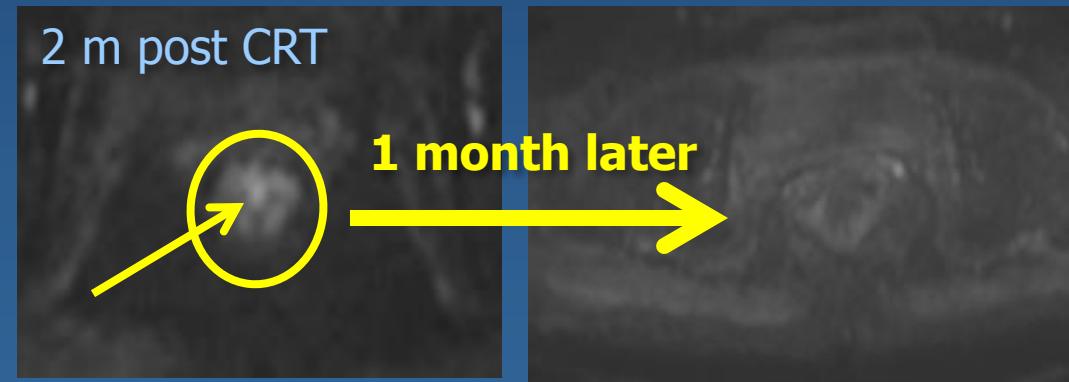
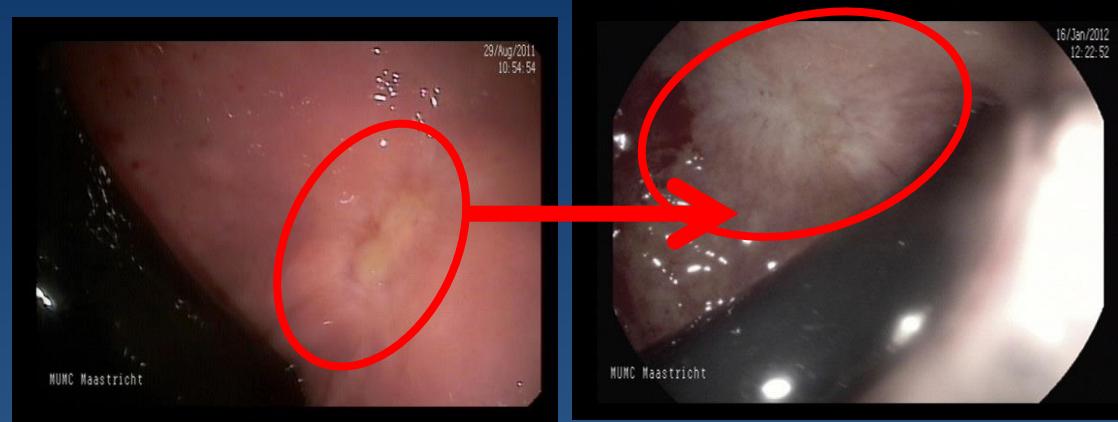
Tumor remnant



False Positives

Inflammation mimics tumor on DWI

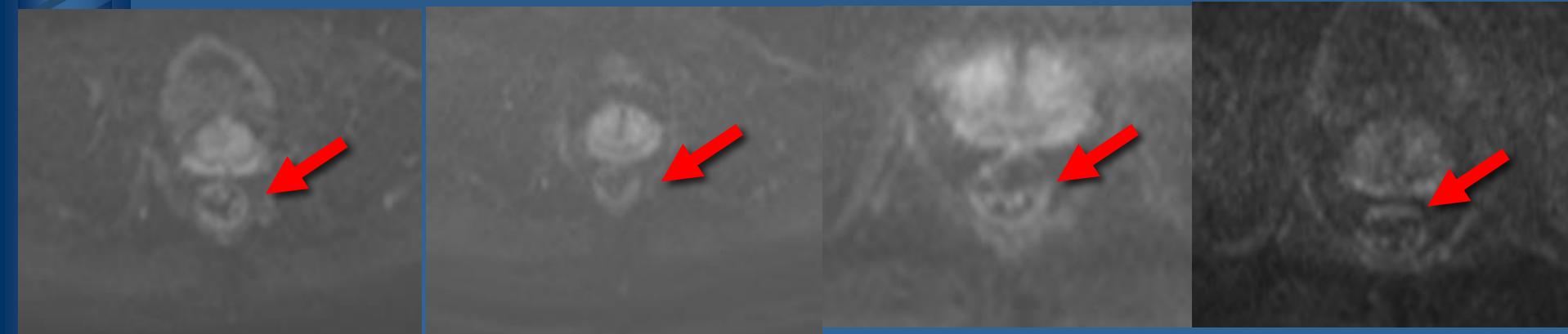
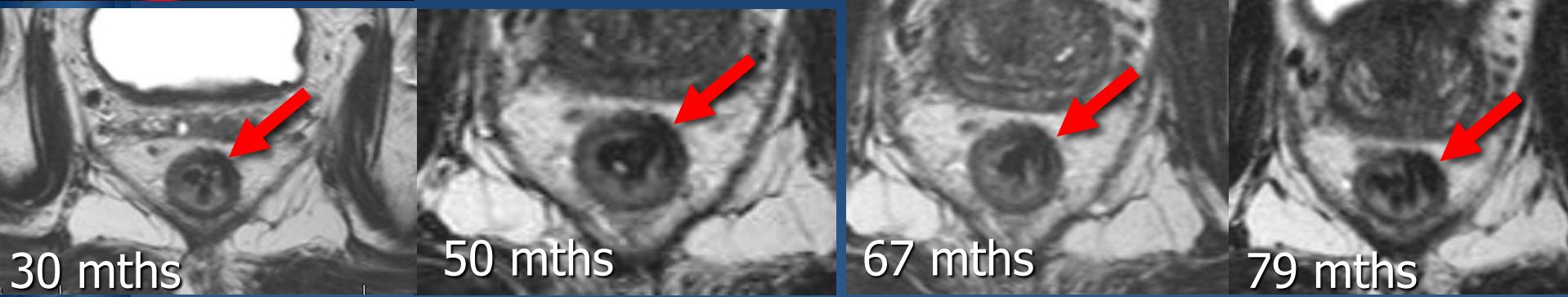
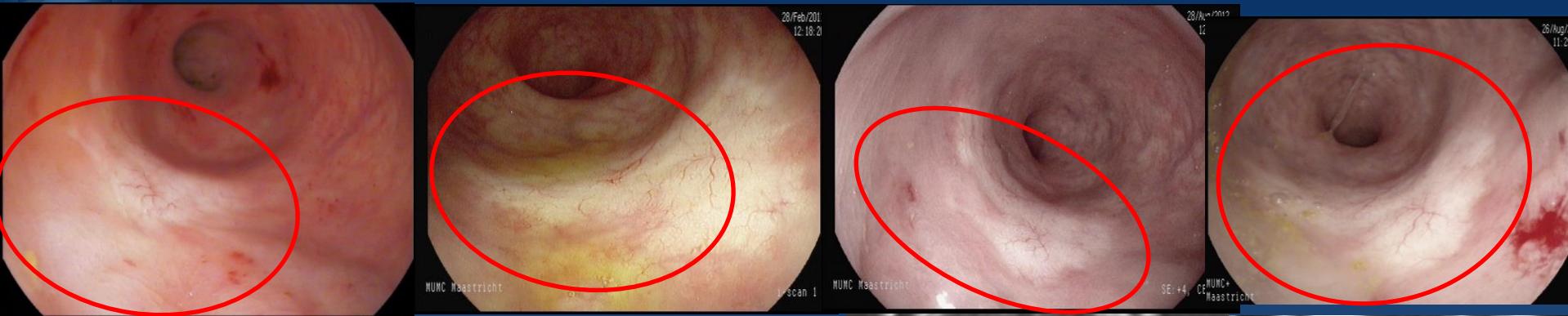




Follow up

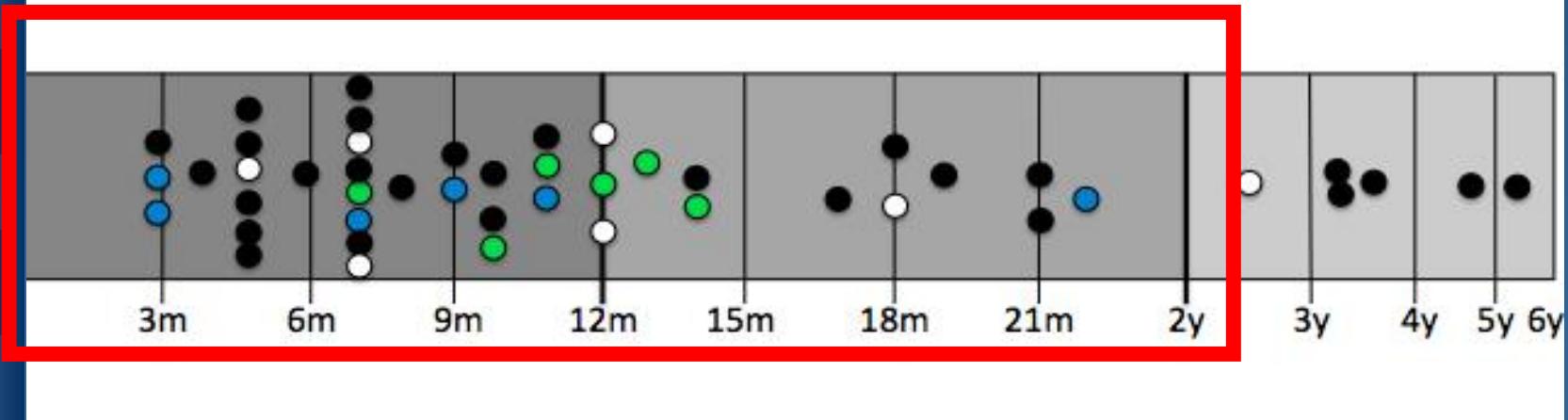


Jaar 1	Jaar 2	Jaar 3	Jaar 4	Jaar 5
4x CEA	4x CEA	4x CEA	2x CEA	2x CEA
2x CT	1x CT	1x CT	1x CT	1x CT
4x MRI	2x MRI	2x MRI	2x MRI	2x MRI
4x Endoscopie	2x Endoscopie	2x Endoscopie	2x Endoscopie	2x Endoscopie



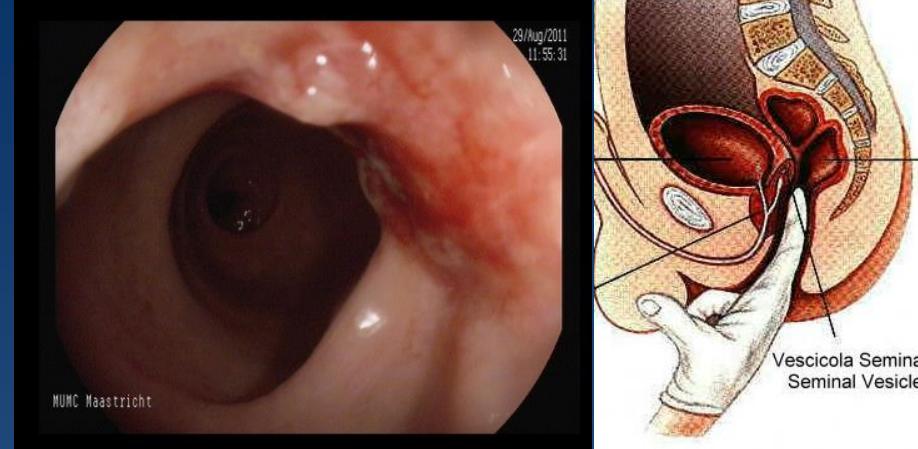
When do tumors regrow ?

	Post-CRT	FU Interval
Seshadri	4-6 weeks	Not specified
MUMC	6-10 weeks	From inclusion (6-10 weeks postCRT)
Habr-Gama	>8 weeks	From end CRT
MSKCC	4-10 weeks	Not specified



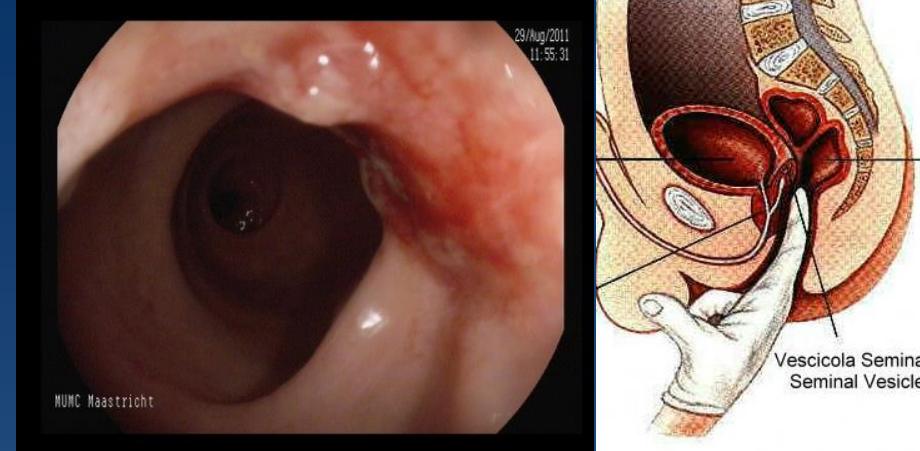
Where regrowth?

Luminal 80-90%

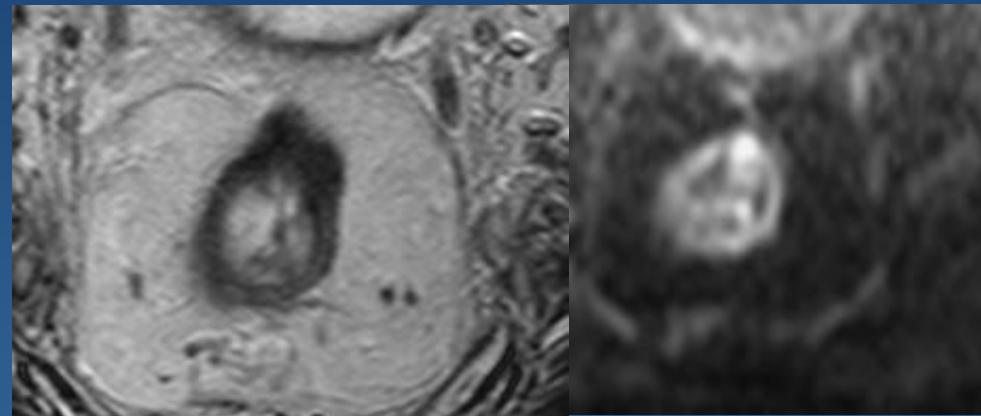


Where regrowth?

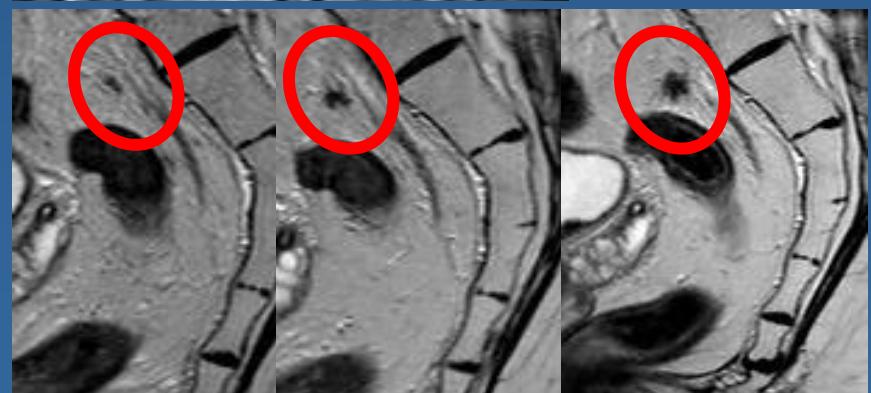
➤ Luminal 80-90%



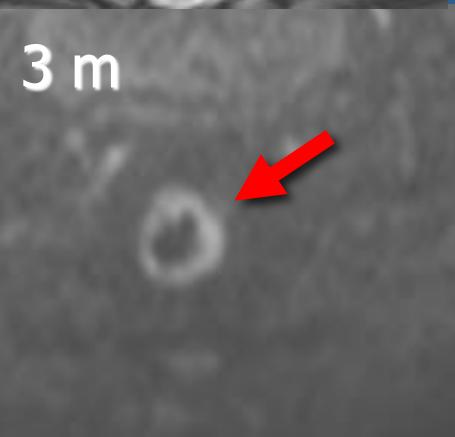
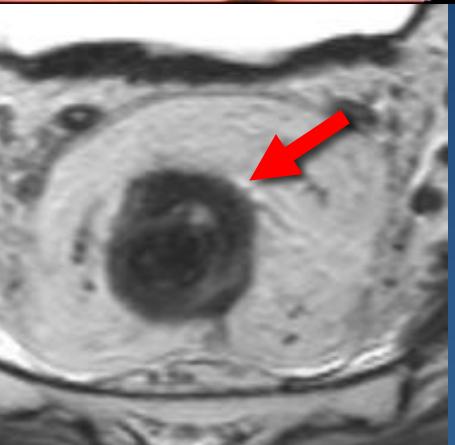
➤ Bowel wall 5-10%



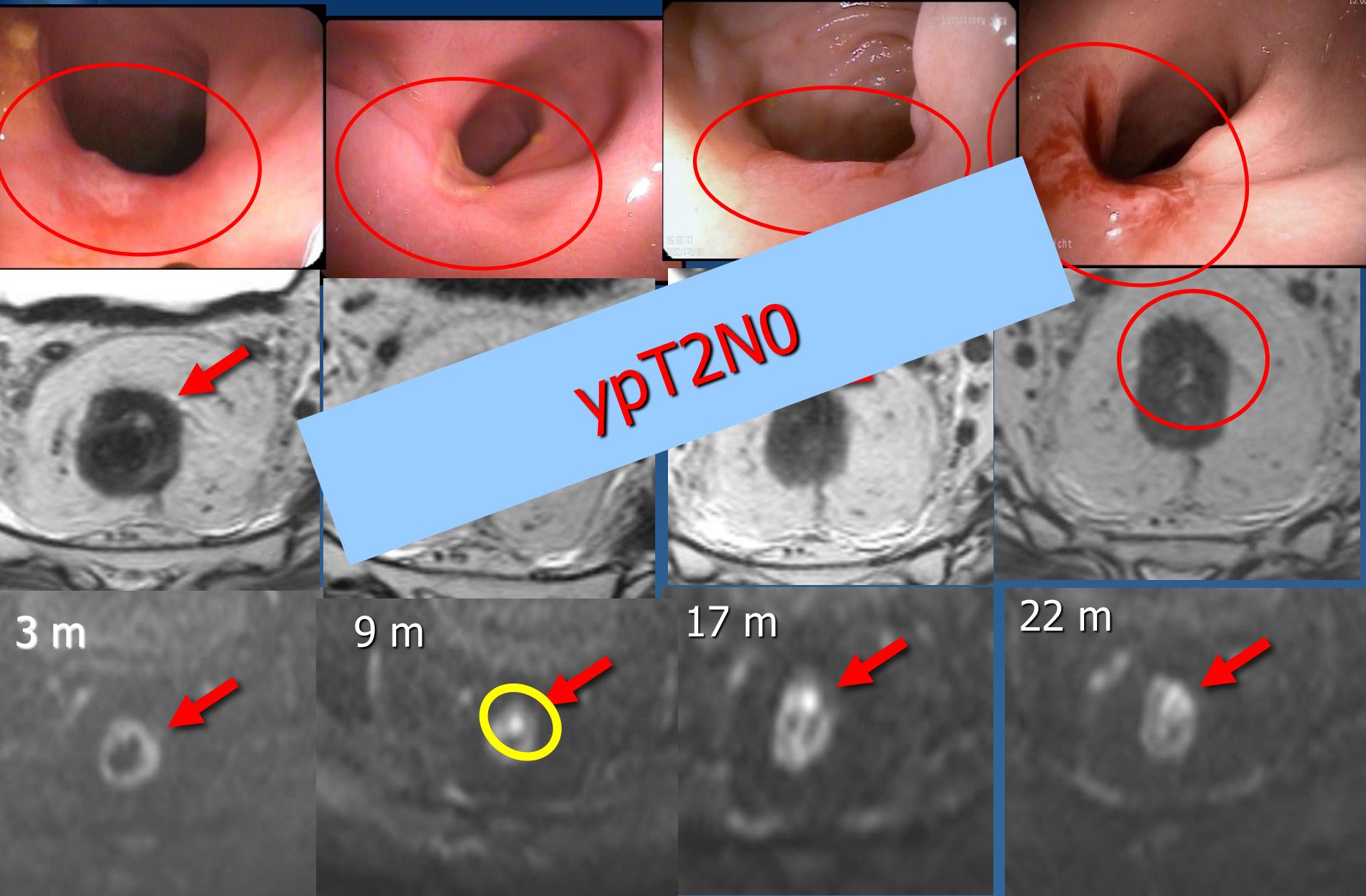
➤ Nodal 5-10%



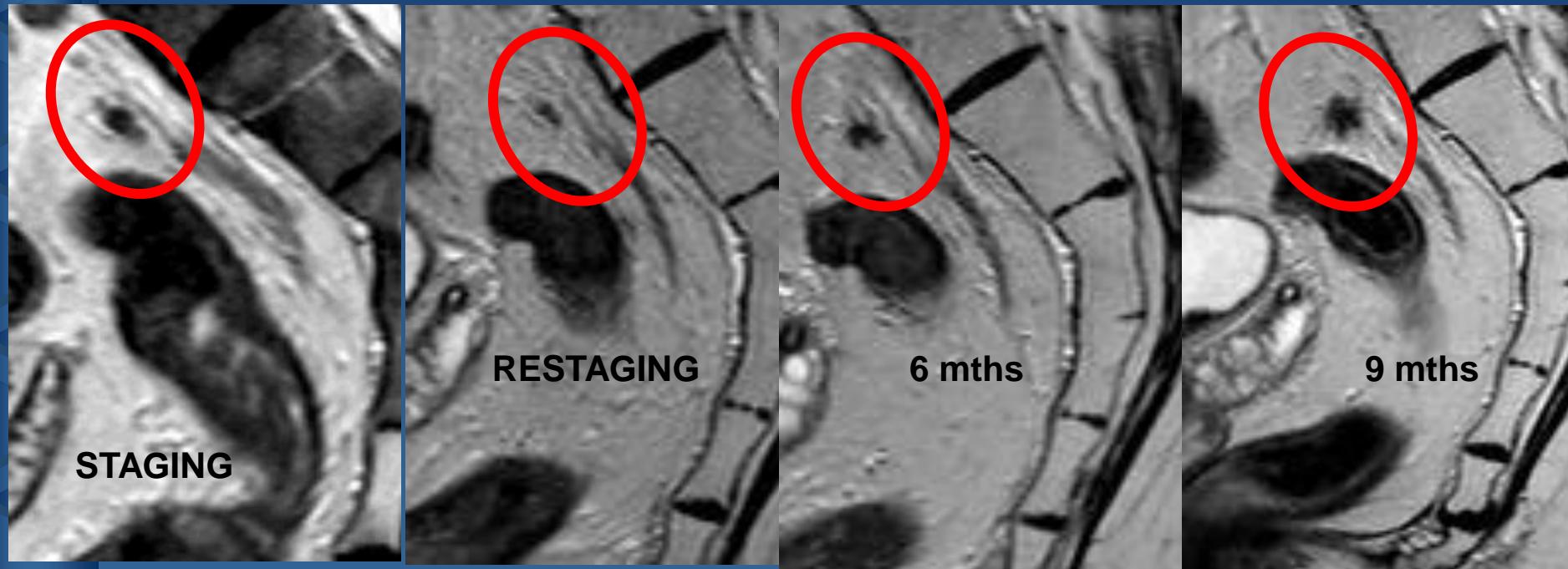
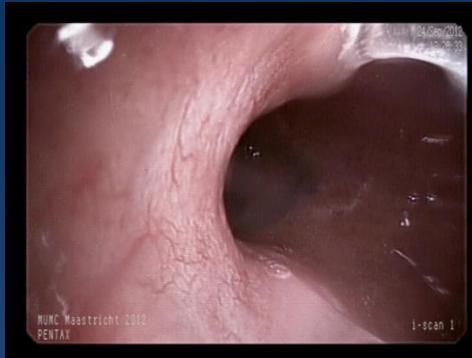
Tumor Regrowth



Tumor Regrowth



Nodal regrowth



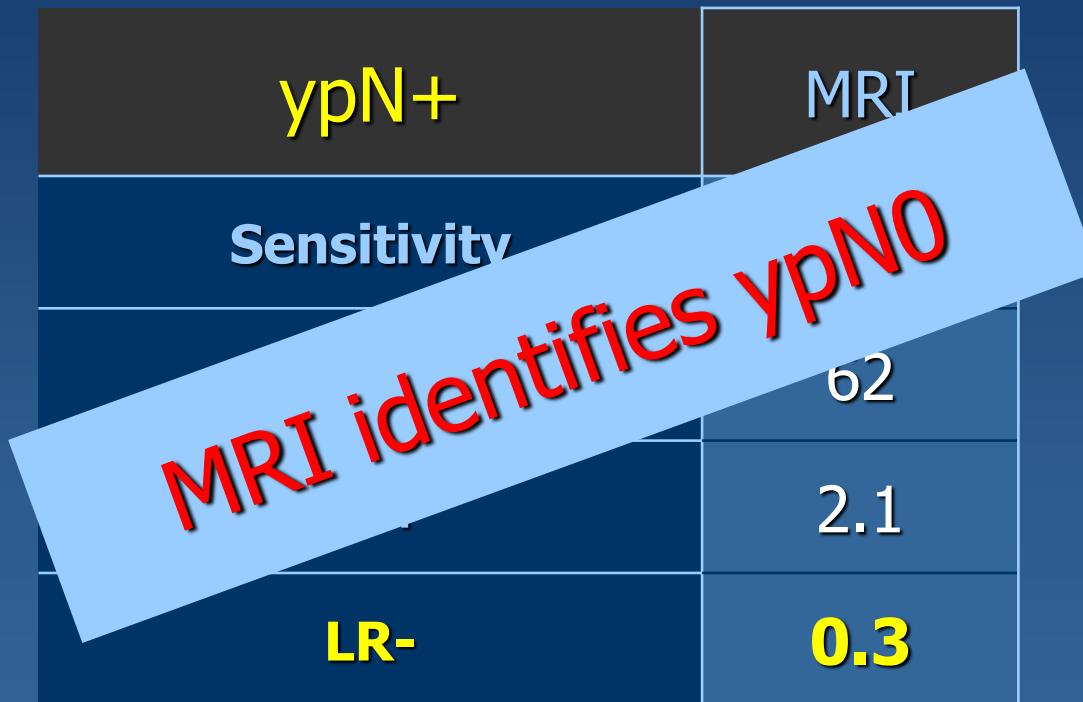
MR Restaging meta analysis

ypN+	MRI
Sensitivity	80
Specificity	62
LR+	2.1
LR-	0.3

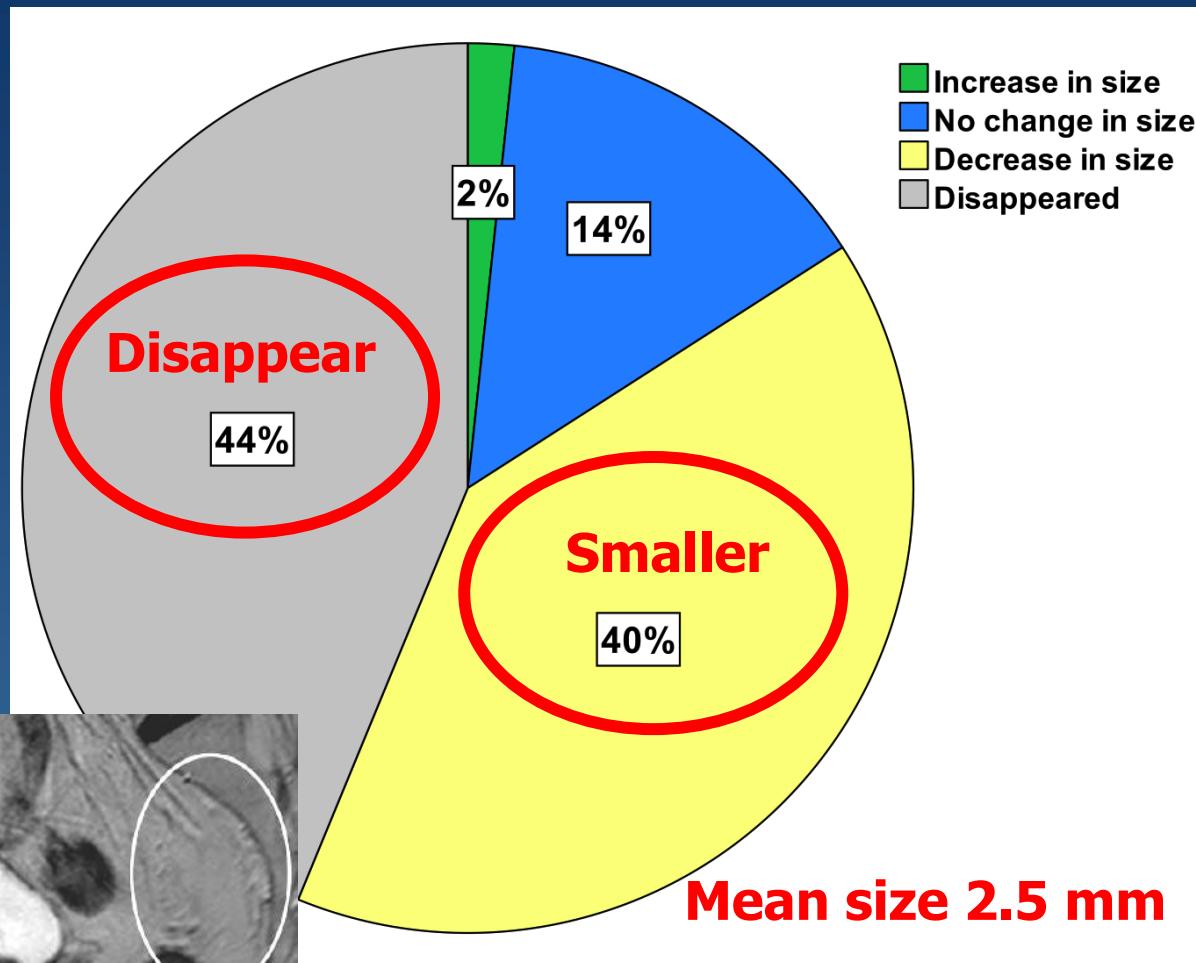
MR Restaging meta analysis

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MR Restaging meta analysis



How do nodes behave after CRT ?



Maastricht , unpublished data

ypN+	$\geq 5 \text{ mm}$ nodes
Maastricht data $n=512$	40% (18/45)
Perez at al DCR 09 $n=201$	40% (6/14)

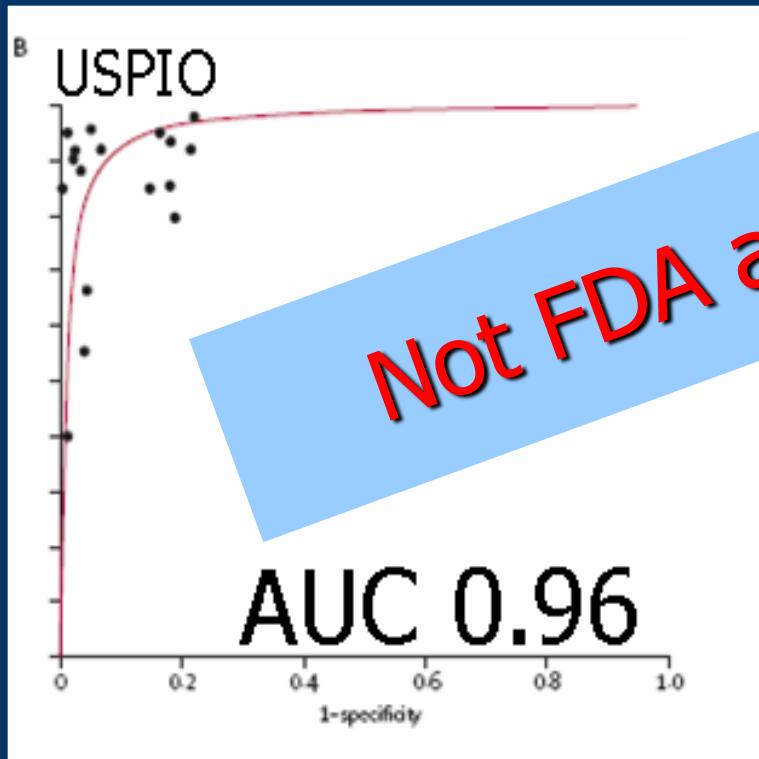


ypN+	$\geq 5 \text{ mm nodes}$	<5 mm nodes
Maastricht data n=512	40% (18/45)	6% (26/467)
Perez at al DCR 09 n=201	40% (6/14)	3% (6/187)

ypN+	$\geq 5 \text{ mm}$ nodes	<5 mm nodes
Maastricht data n=512	40% (18/45)	57%
Perez DCR n=201	40% (6/14)	3% (6/187)

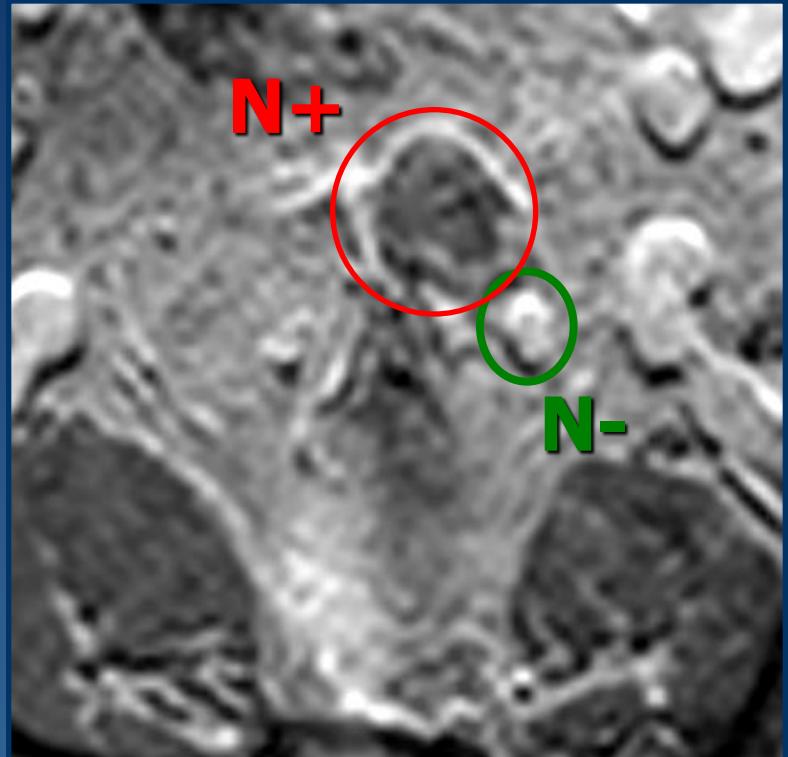
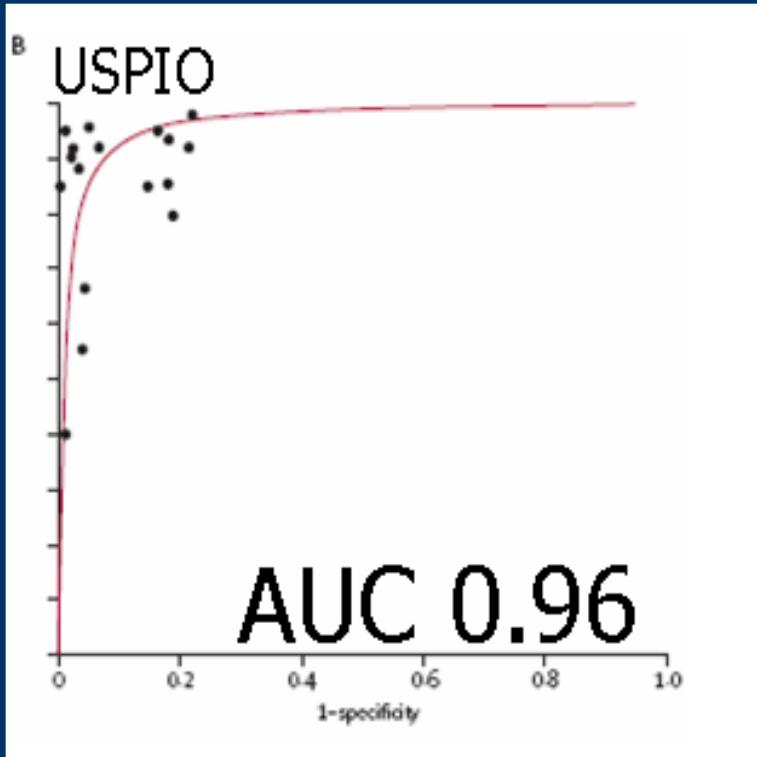
Sens 42% !

MR Lymph node contrast



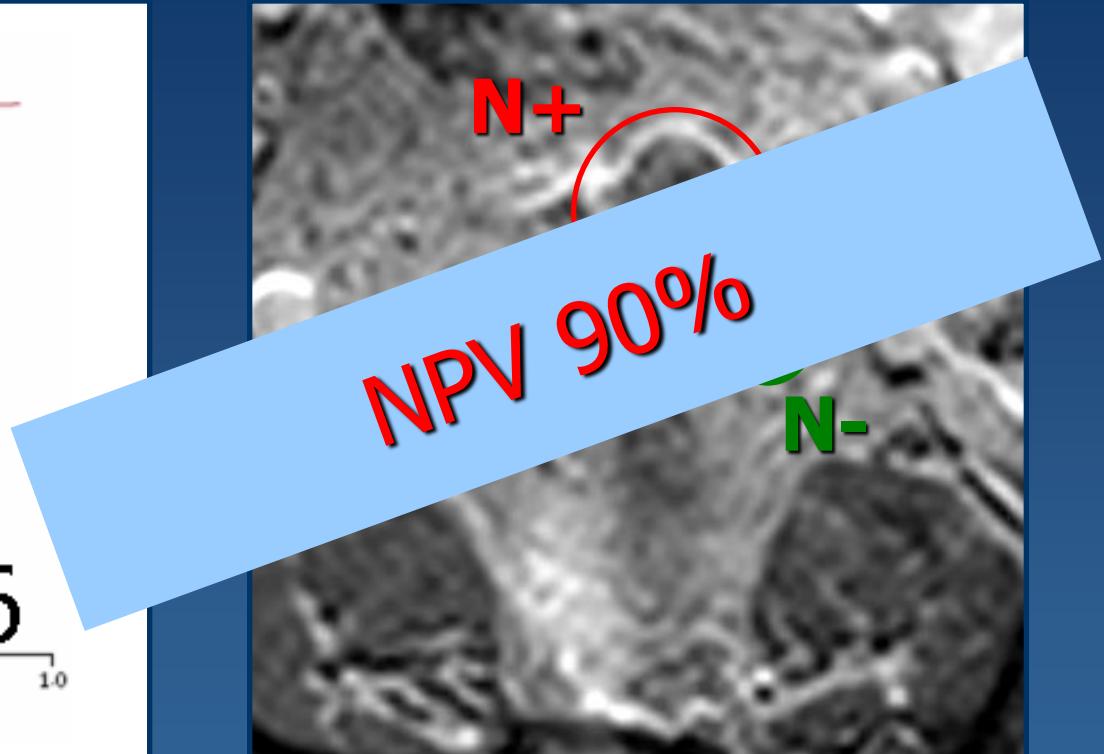
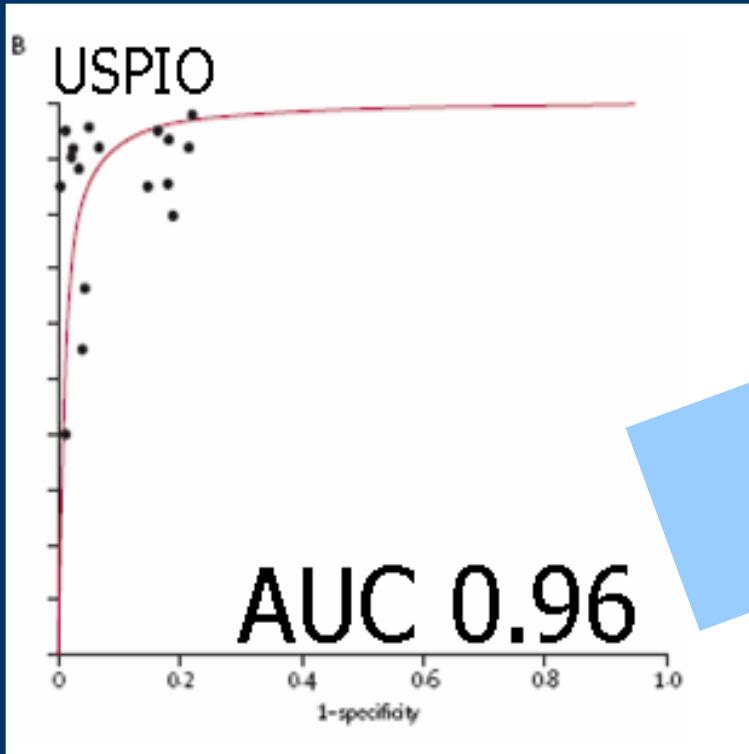
Lahaye et al. Rad 2008

New MR Lymph node contrast



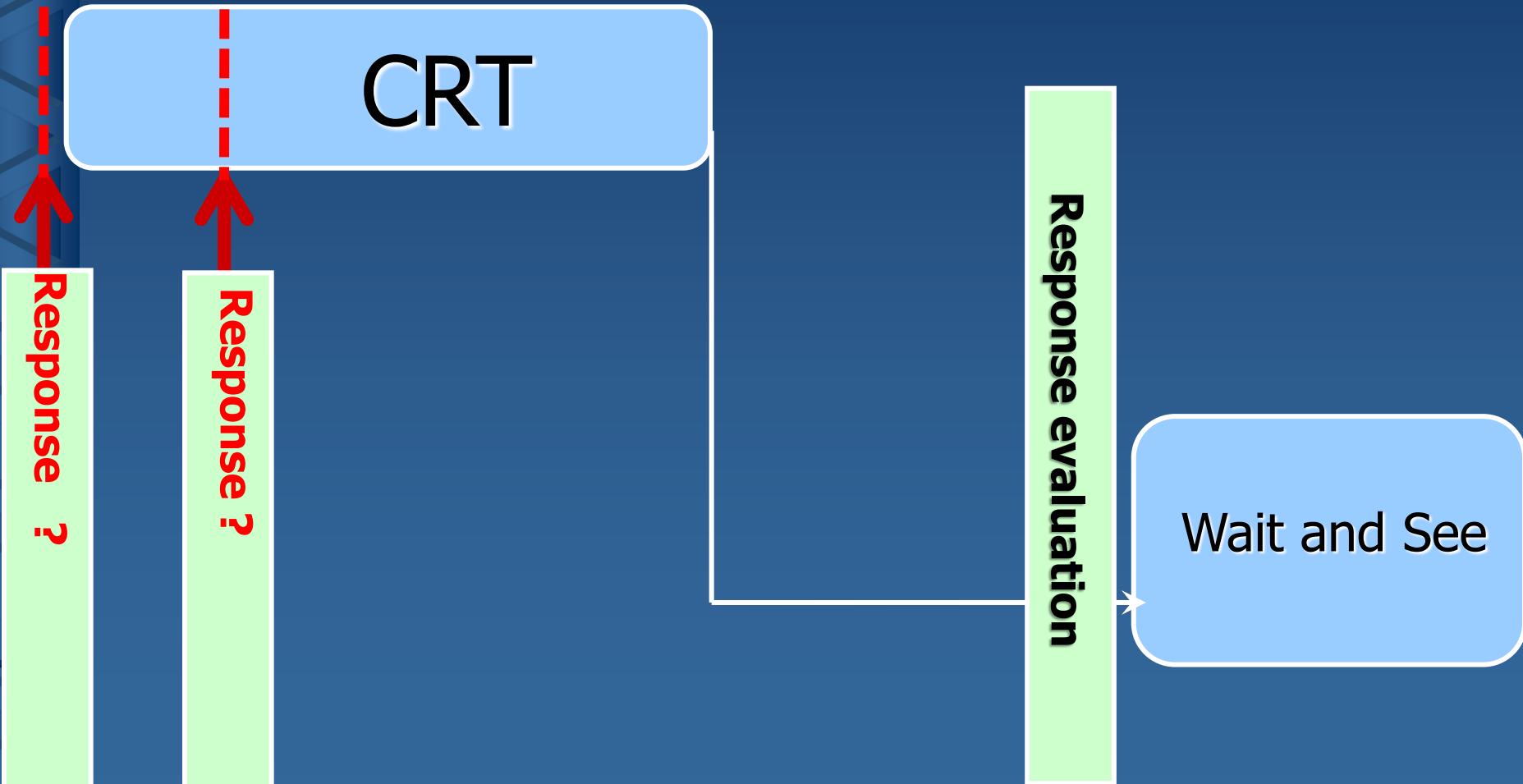
Gadofosveset MRI
Maastricht multicenter trial

New MR Lymph node contrast



Gadofosveset MRI
Maastricht multicenter trial

Prediction of response



Prediction of response

- ▶ Visualizing tumor heterogeneity

Prediction of response

- ▶ Visualizing tumor heterogeneity
- ▶ Morphology insufficient

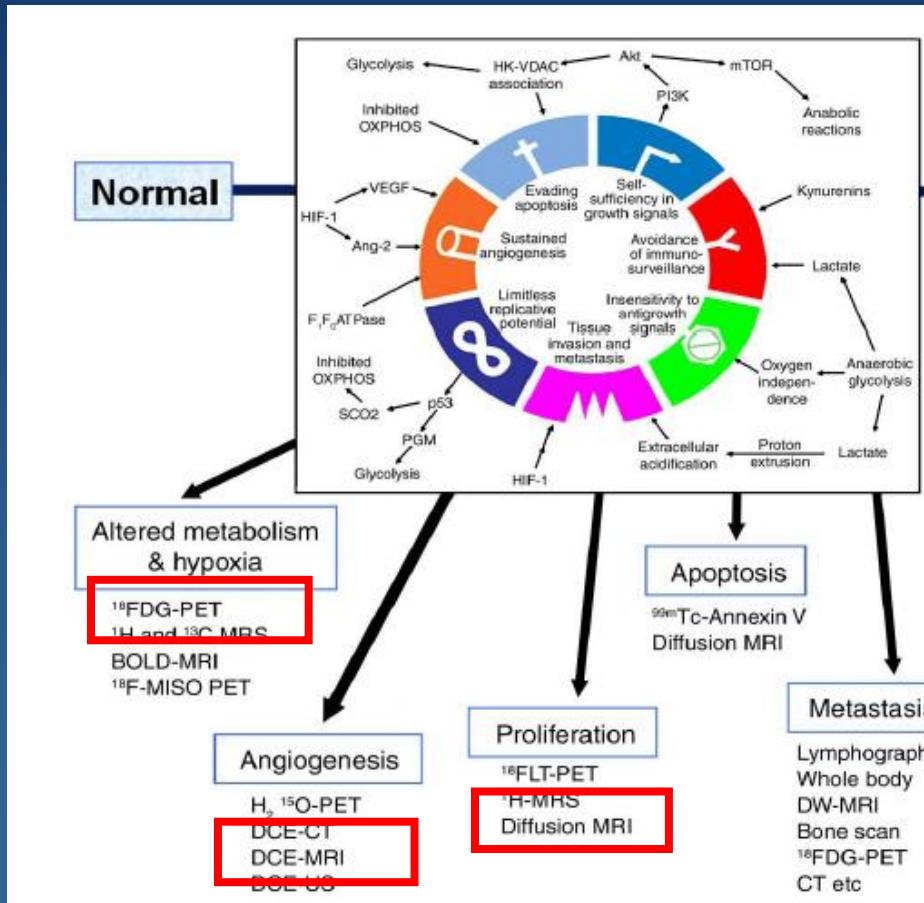
Prediction of response

- ▶ Visualizing tumor heterogeneity
- ▶ Morphology insufficient
- ▶ Increase objectivity

Prediction of response

- ▶ Visualizing tumor heterogeneity
- ▶ Morphology insufficient
- ▶ Increase objectivity
- ▶ Imaging tissue characteristics

Imaging Biomarkers



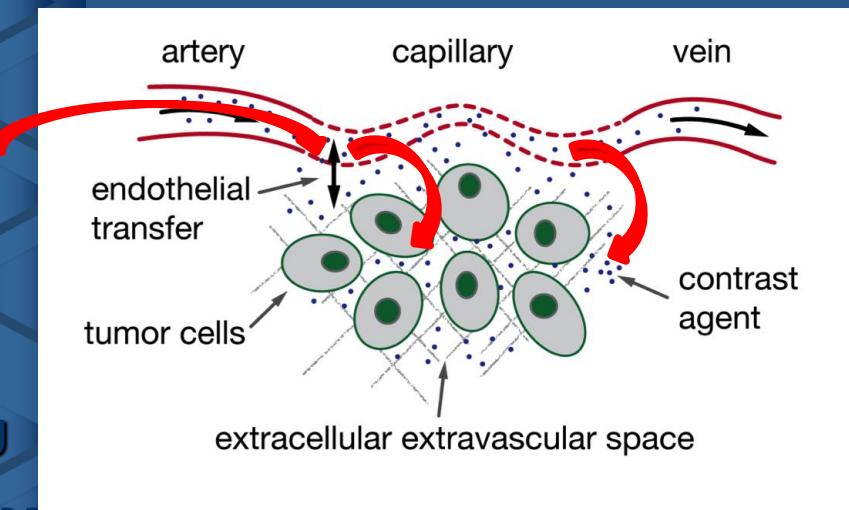
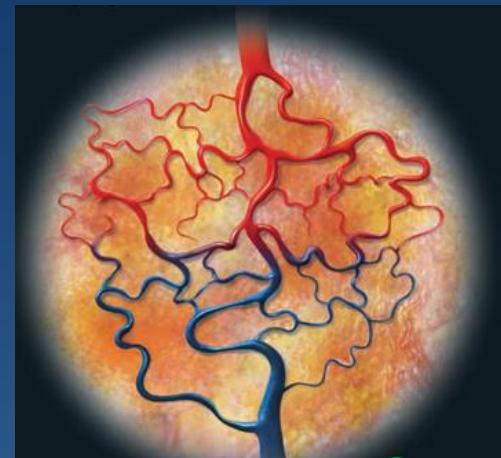
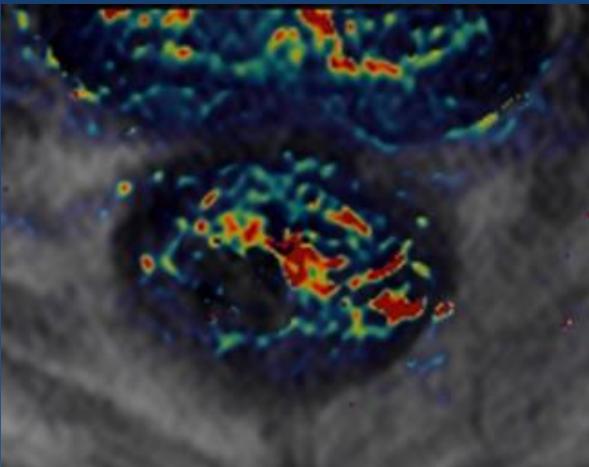
Beets-Tan, Beets, Nature reviews Gastro Hep
Padhani et al, Radiology 2010

Meta analysis FDG PET

2002-11

Good response	sens	spec	AUC
-Δ SUV 40-50% wk 2 CRT	86	80	0.95

Perfusion MRI Quantitative



K_{trans}
wash in rate

K trans

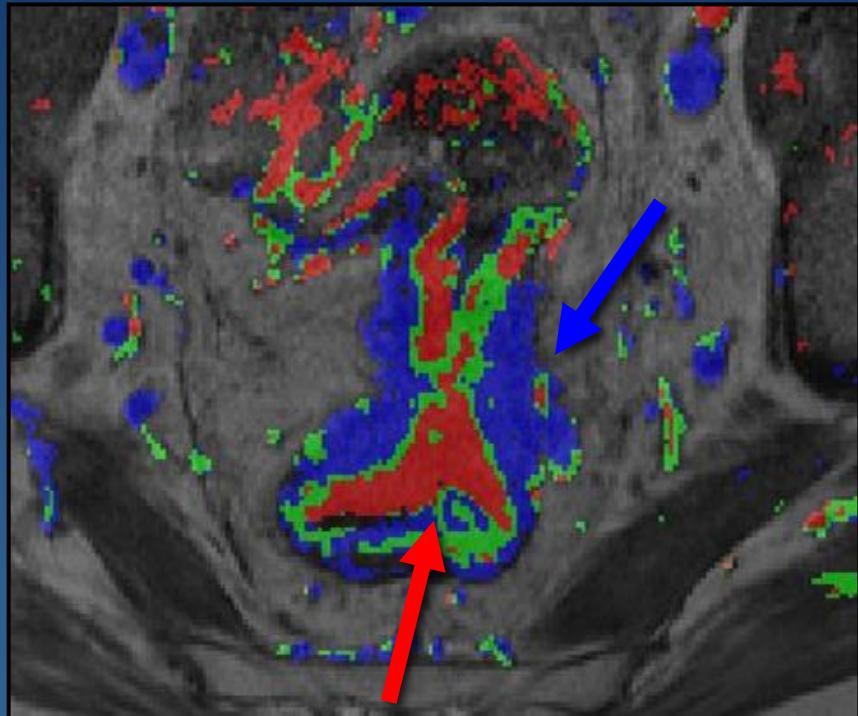
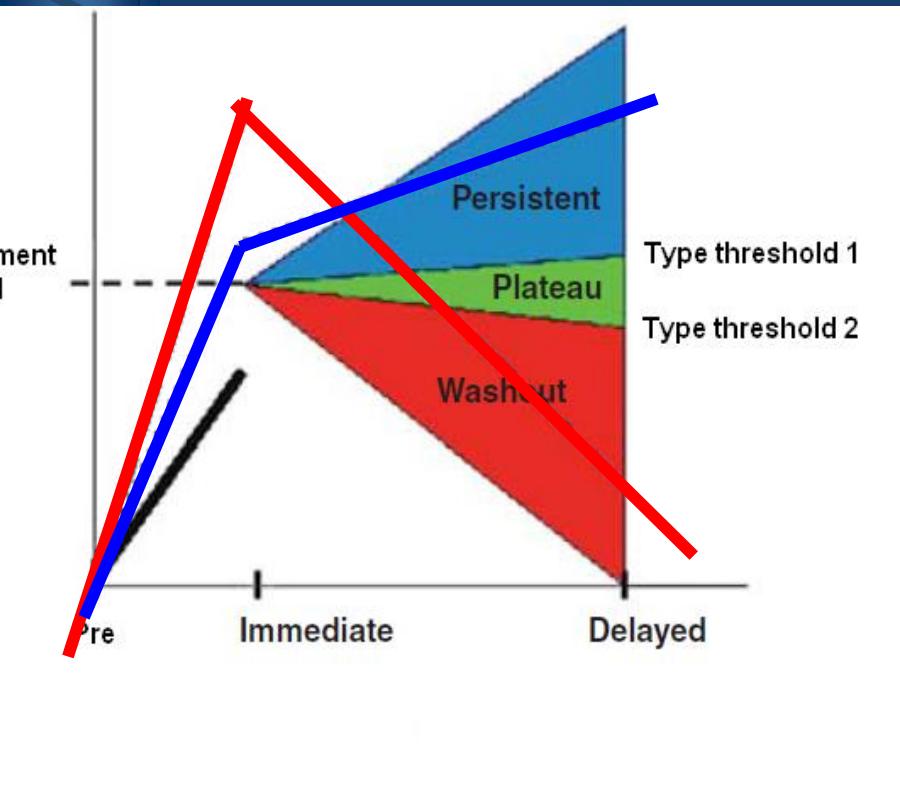
Good response	Pre CRT	Post CRT
Gollub et al Eur Rad 2011 n=23	X pCR	✓
Lim et al Eur Rad 12	✓	✓
George et al BJS 01 n=31	✓	
Oberholzer et al JMRI 2013 n=95	✓	
De Lussanet et al Radiol 2009	✓	

K trans

Good response	Pre CRT	Post CRT
Gollub et al Eur Rad 2011 n=23	X pCR	
Lim et al Eur Rad 12		✓
Berholzer et al JMRI 2013 n=95	✓	✓
De Lussanet et al Radiol 2009	✓	

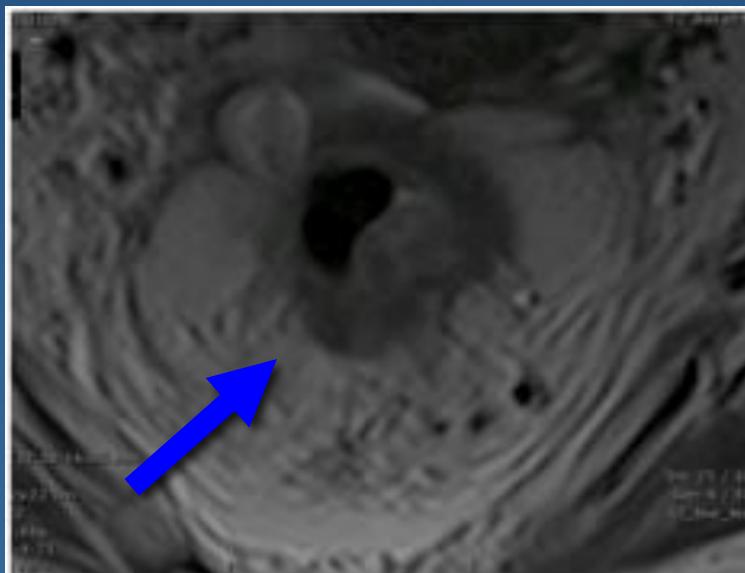
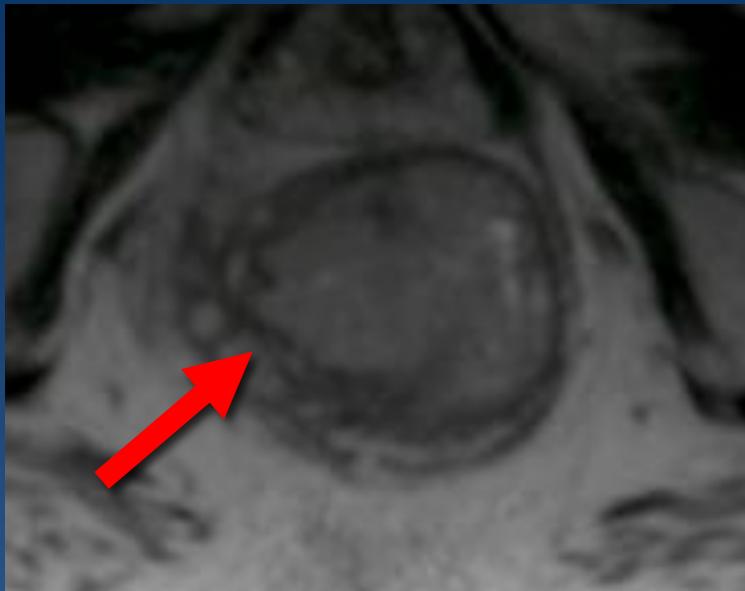
K trans → complex processing method

Perfusion MRI Semi quantitative

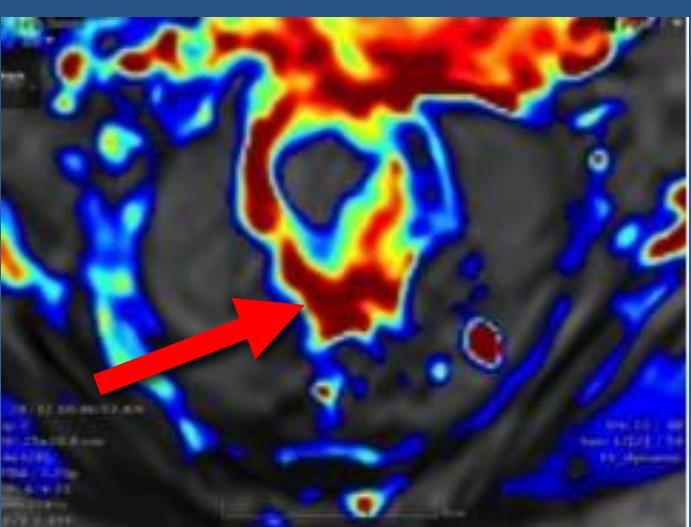
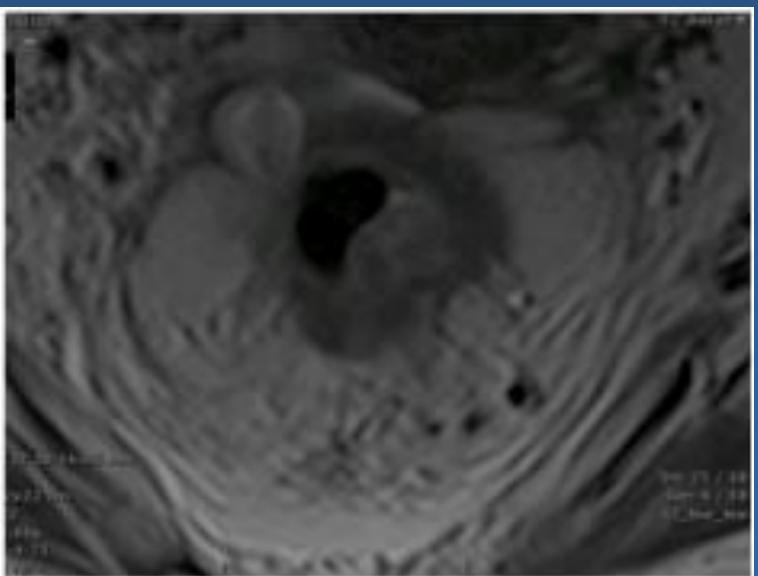
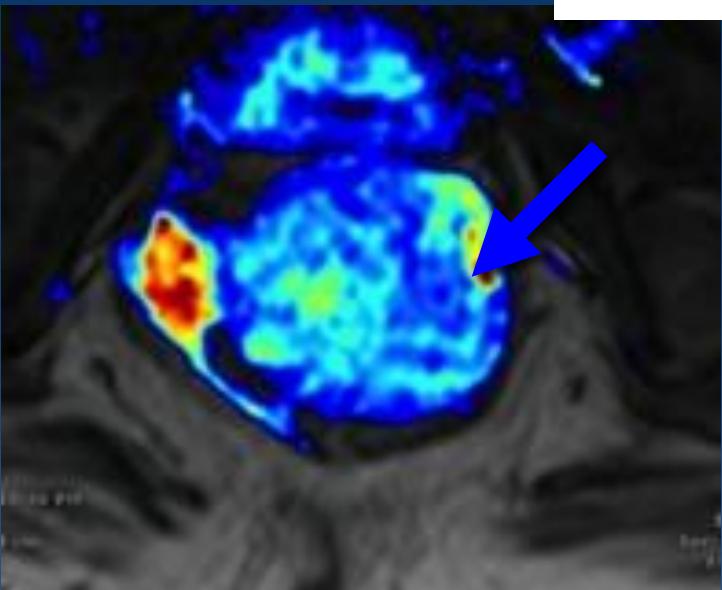
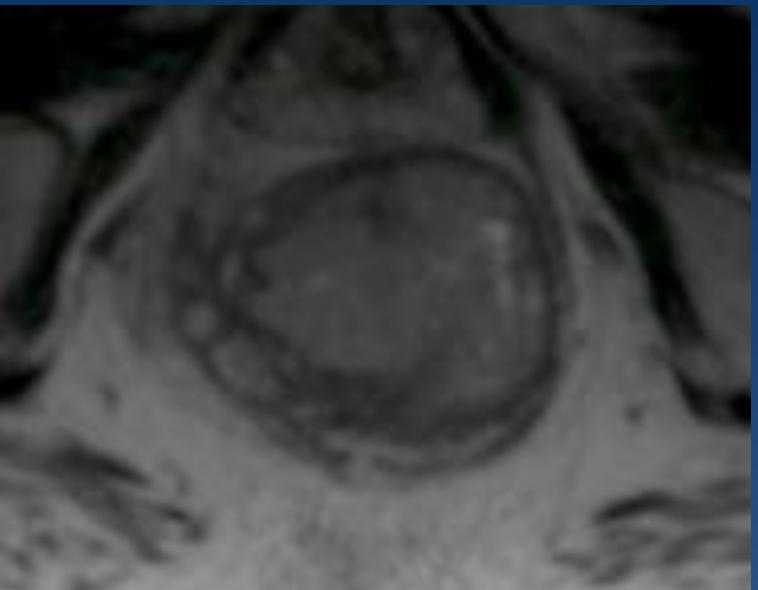
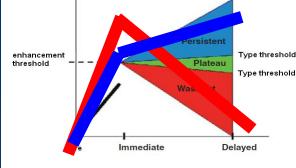


Semiquantitative MR perfusion parameters

Good response	Pre CRT	during CRT
Bellomi et al Radiology 07	✓	
Sahani et al Radiology 05	✓	
Kremser et al Radiology 09	✓	
Dinter et al Onkologie 01		✓
De Vries et al Radiology 01	✓	
Maastricht, unpublished	✓	

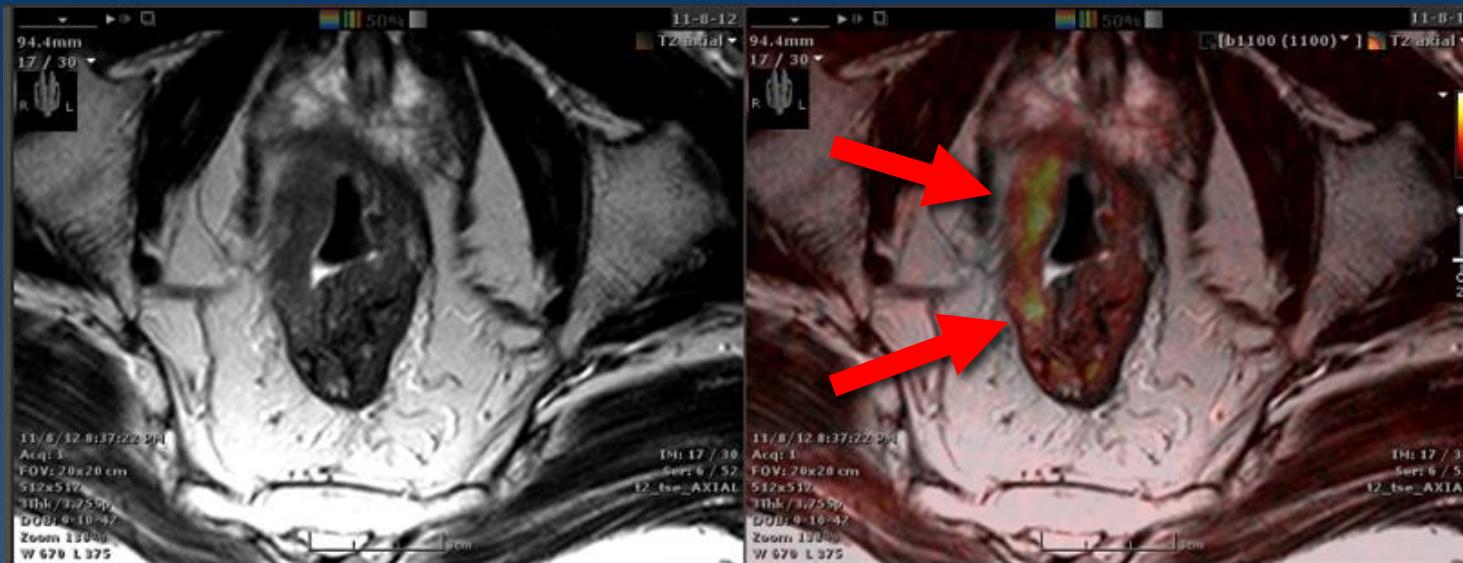


Courtesy N. Papanikolaou

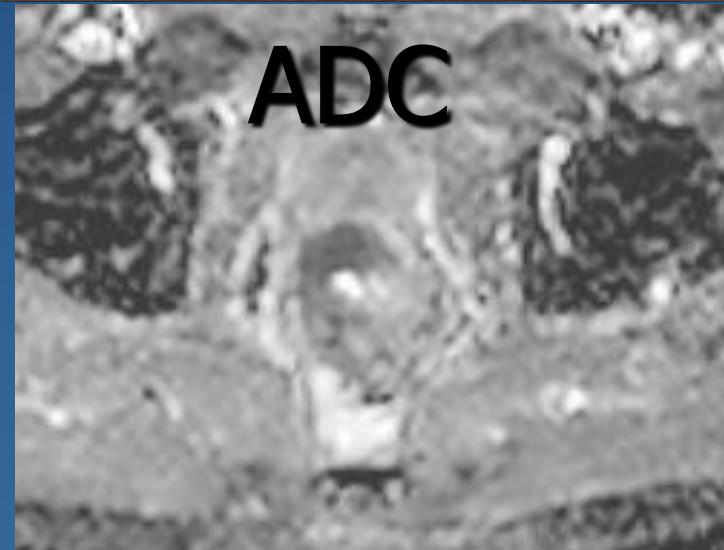


Courtesy N. Papanikolaou

Diffusion MRI



ADC



Courtesy N. Papanikolaou

Pretreatment ADC

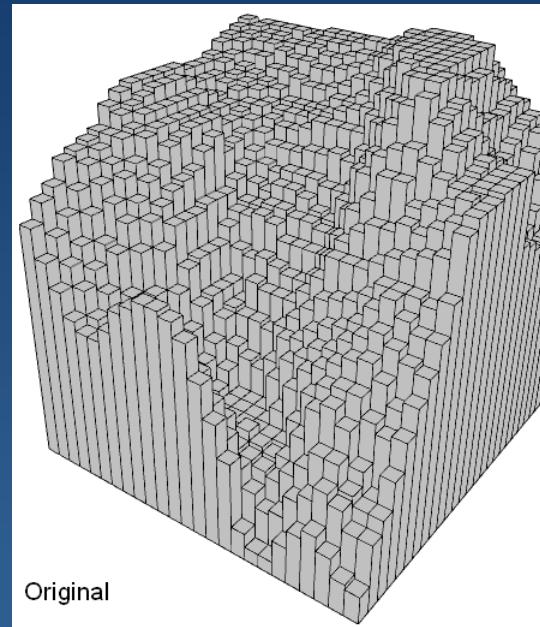
	N=	good vs poor response	ADC responders	ADC non responders	p =
Pre-CRT ADC					
deVries (Red Journ 2003)	34	ypT0-2 vs ypT3	0.65	0.66	0.8
Sun (Radiology 2009)	37	cT > ypT	1.07	1.19	0.013
Kim (JMRI 2012)	34	cT > ypT	0.87	0.91	0.61
Jung (JMRI 2011)	35	cT > ypT	0.93	1.03	0.034
Lambrecht (Red J 2012)	20	ypT0-2 vs ypT3-4	1.06	1.19	0.27
Barbaro (Red Journ 2012)	53	TRG 1-2 vs TRG 3-4	1.5	1.2	0.007
Ippolito (Abd Ima 2012)	30	TRG 1-2 vs TRG 3-4	0.88	0.78	0.331
Intven-StrahltherOncol 13	59	TRG1-2 vs TRG 3-4	0.95	1.12	0.001
Monguzzi (Eur J Rad 2013)	31	TRG1-2 vs TRG3-5	0.83	0.82	0.2726

2D → pixel



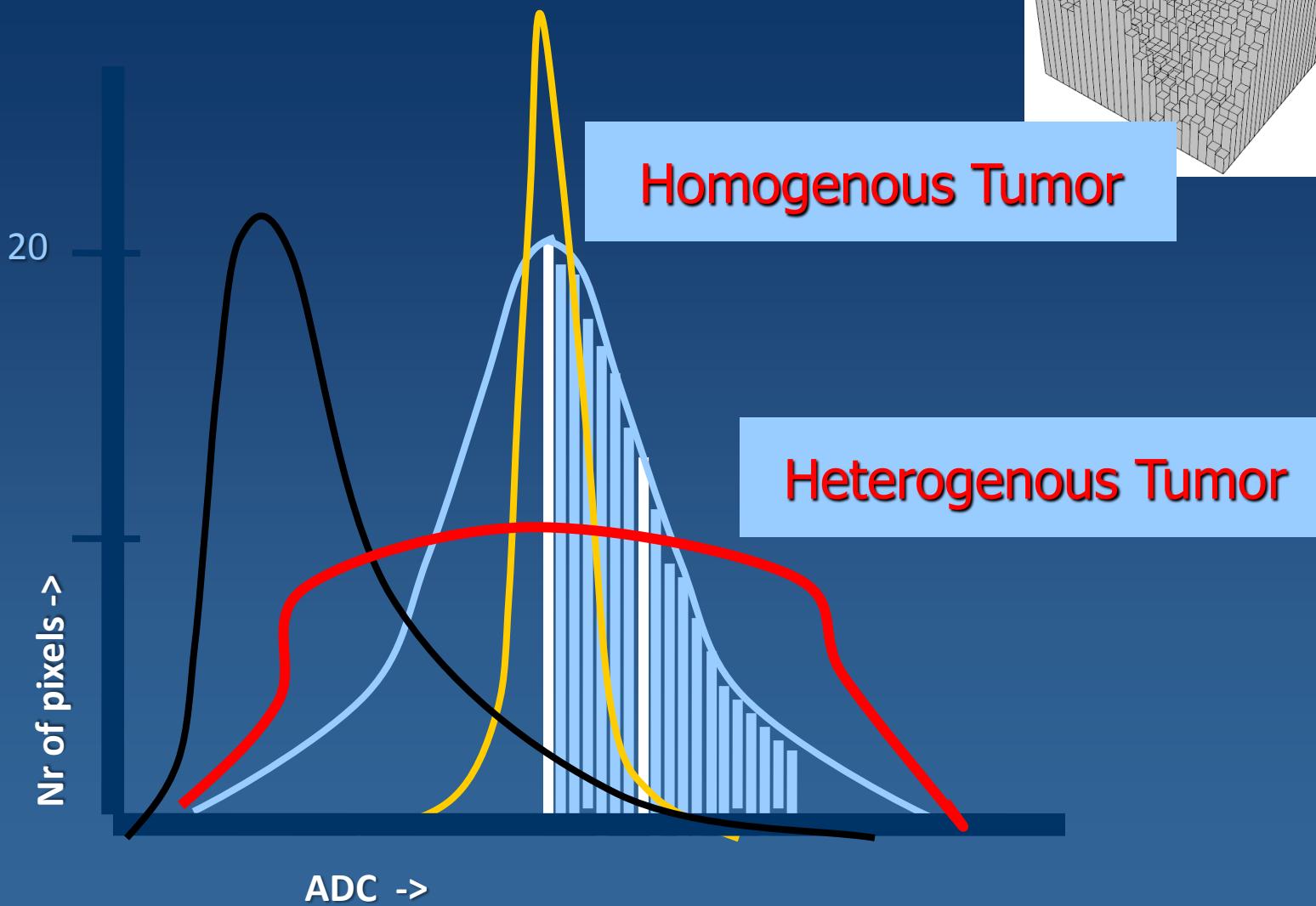
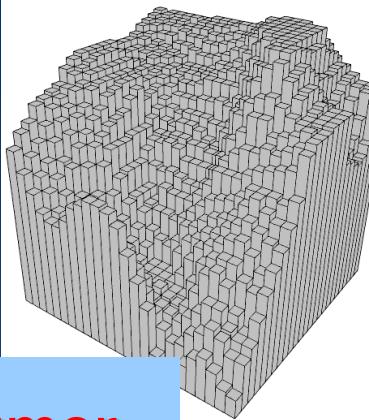
Mean ADC

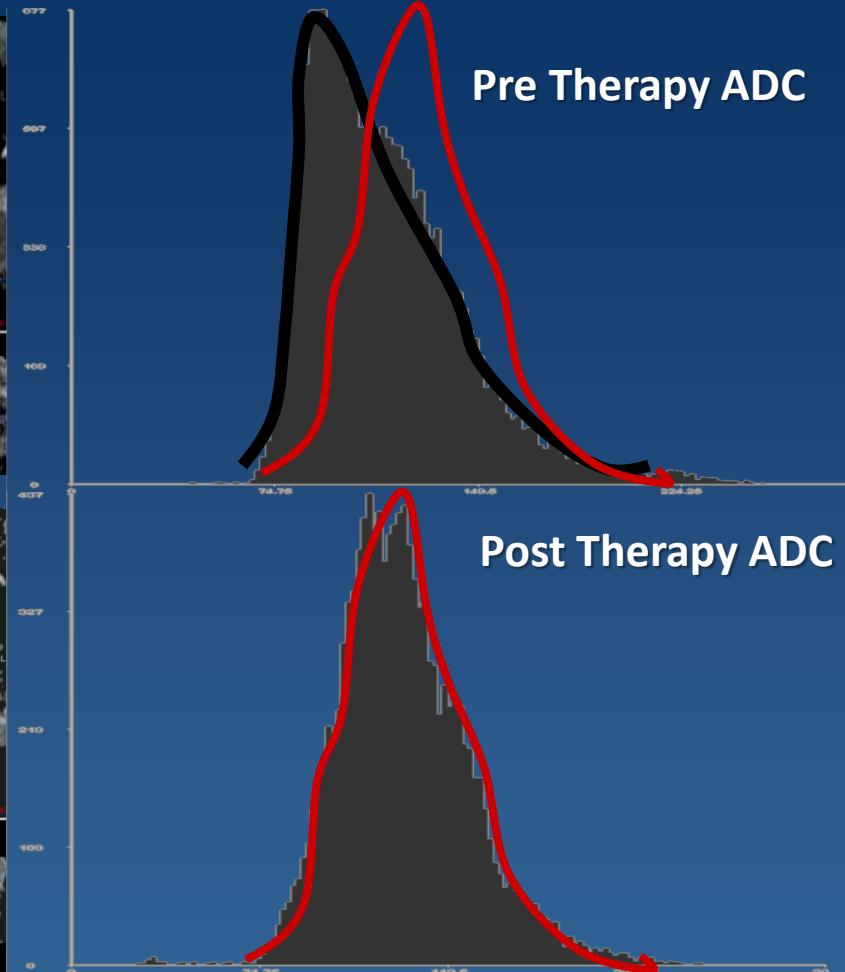
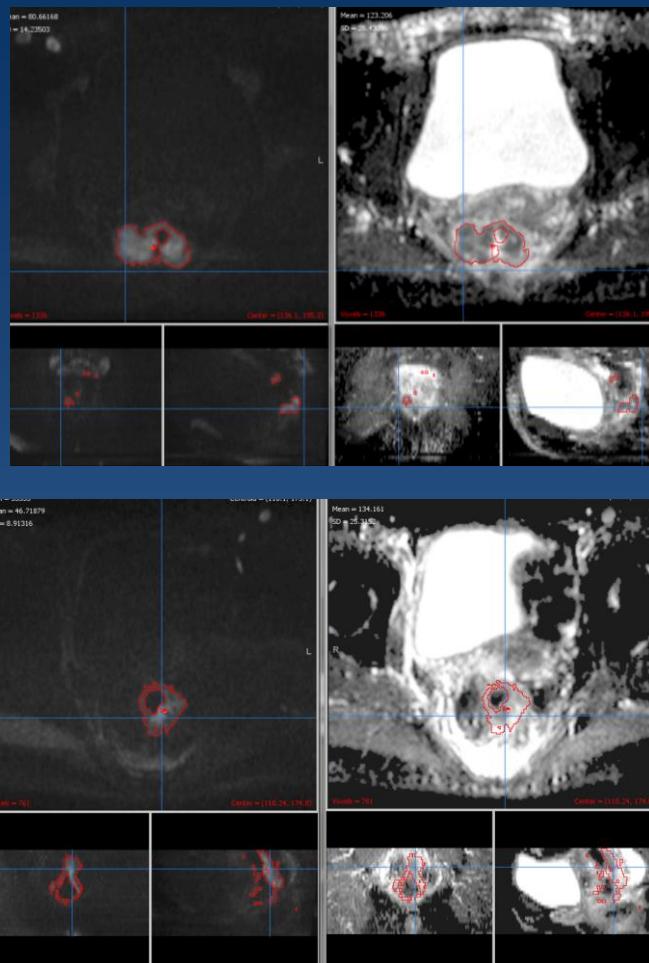
3D → voxel



Distribution of ADC
→ tumor heterogeneity

Histogram

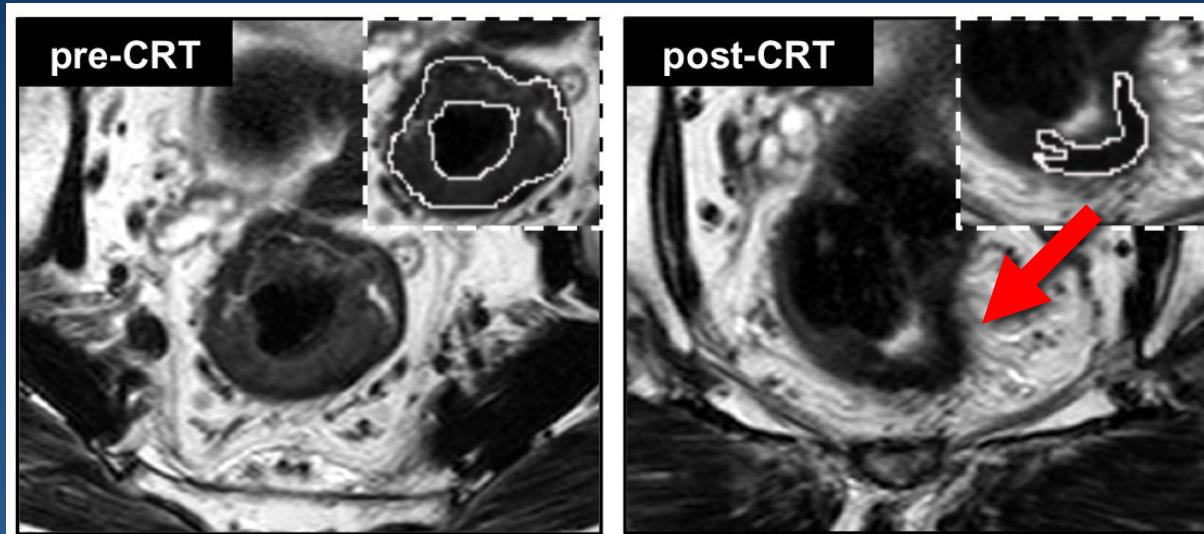




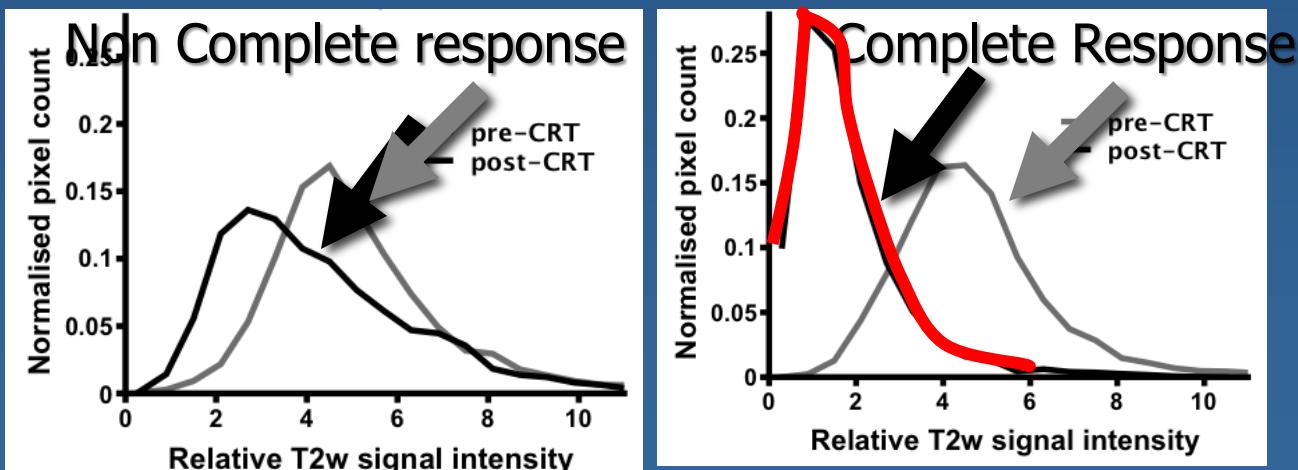
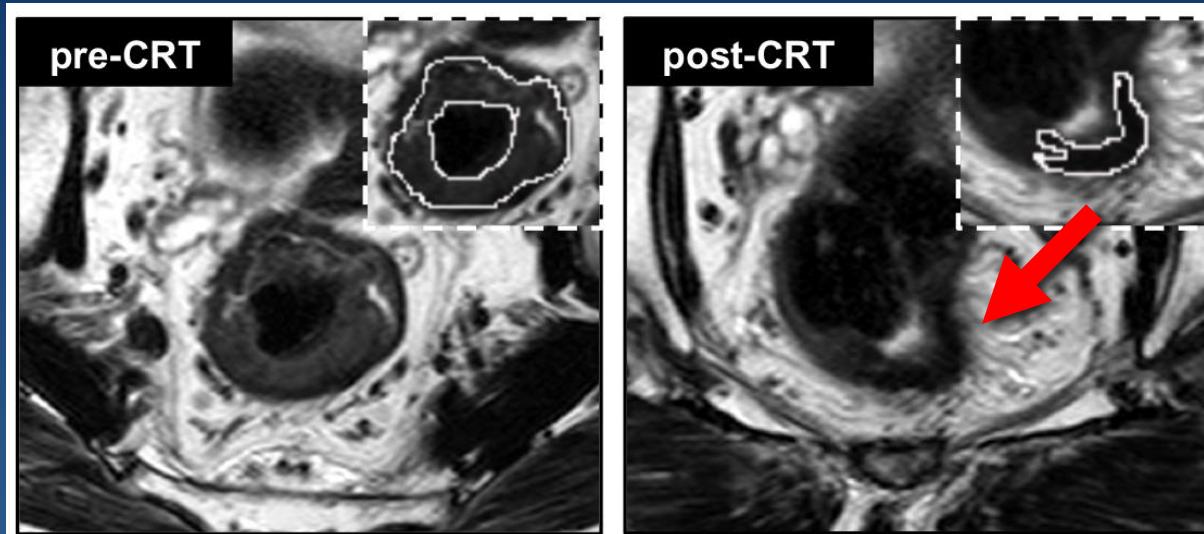
	Mean	Std	Skewness	Kurtosis	Mode	5 percentile	95 percentile
Post therapy	1,31	0,25	0,5803	4,0295	1,17	0,95	1,77
Pre therapy	1,14	0,27	1,1623	4,8527	0,91	0,81	1,67

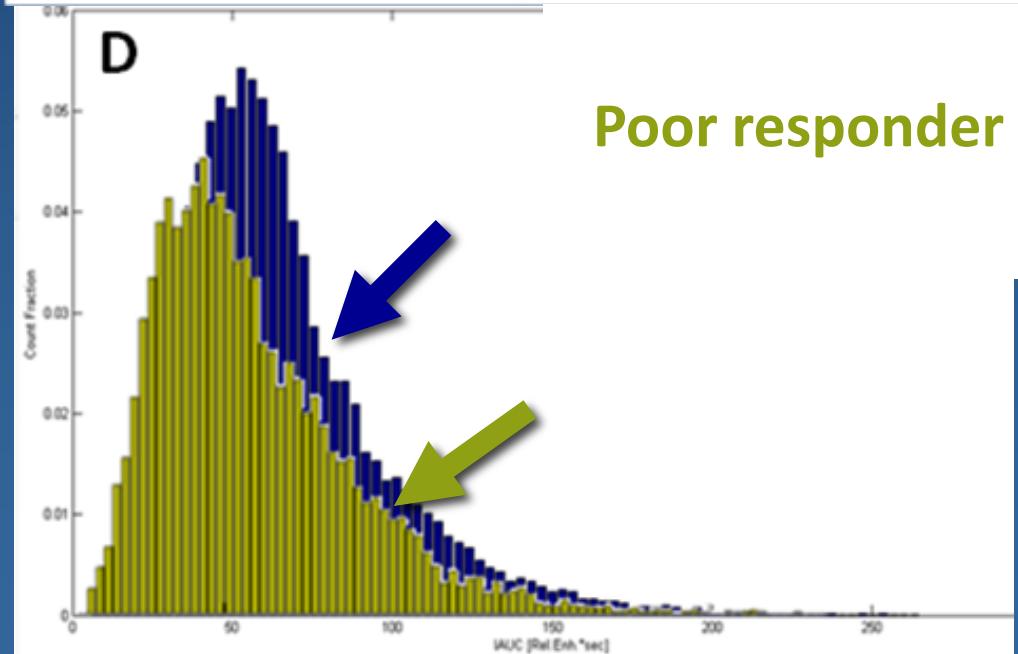
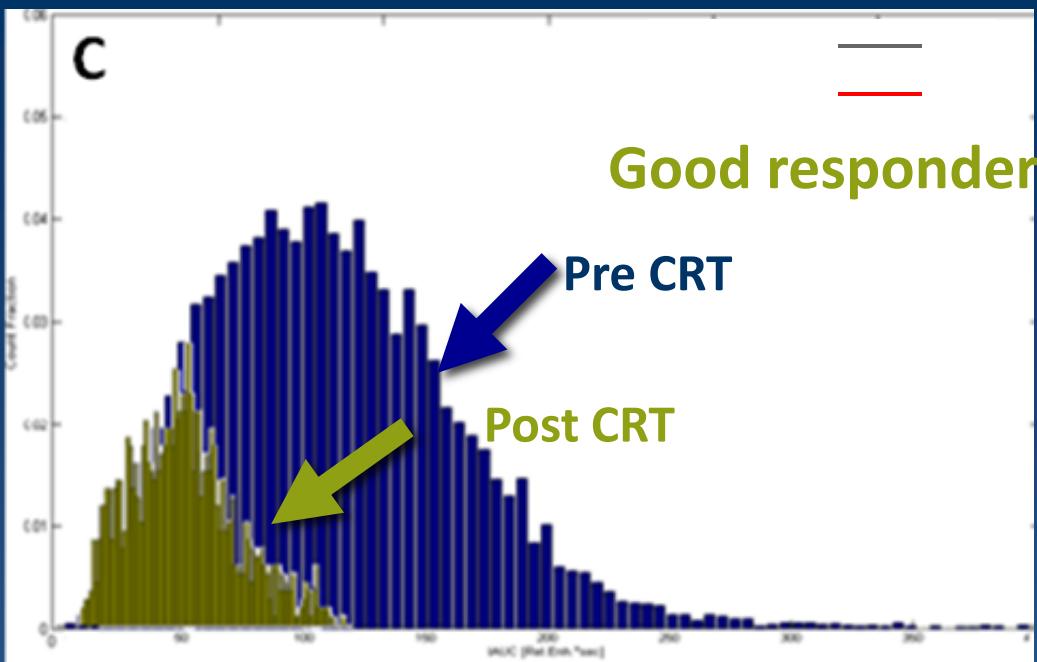
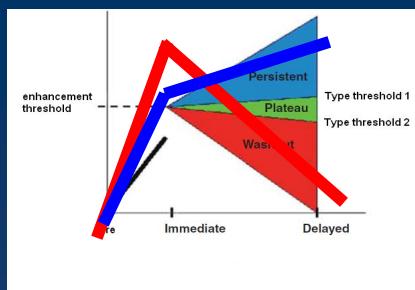
Maatricht work in progress

T2W Signal intensity

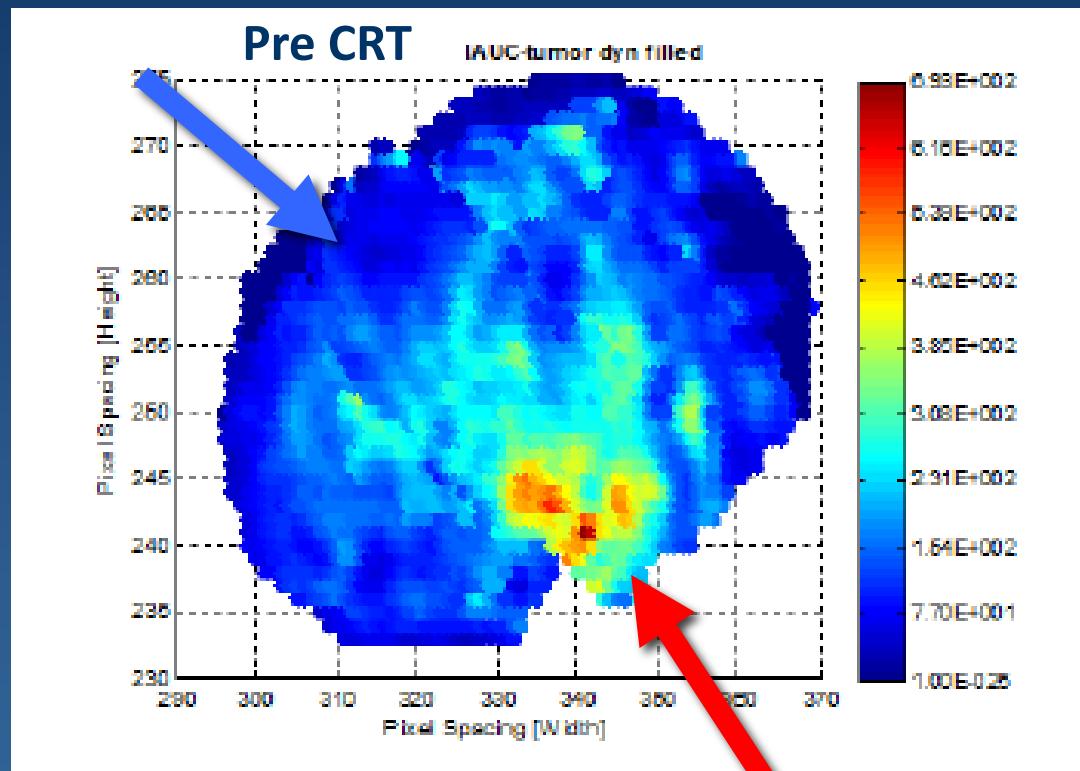


T2W Signal intensity





Pretreatment Parametric MR perfusion map



Future

- ▷ Image segmentation

Future

- ▶ Image segmentation
- ▶ Parametric MR imaging

Parametric MR Imaging not yet ready!

- ✓ Natural variation or treatment effect ?

Parametric MR Imaging not yet ready!

- ✓ Natural variation or treatment effect ?
- ✓ Standardization

	1.5T	
ADC	Center 1	Center 2
Measurement 1 (lymph node)	0.98	0.92
Measurement 2 (nerve)	1.47	1.19
Measurement 3 (bone)	0.55	0.40
Measurement 4 (phantom)	2.16	2.06
.... Etc
TOTAL	1.40	1.10
	P = 0.001	

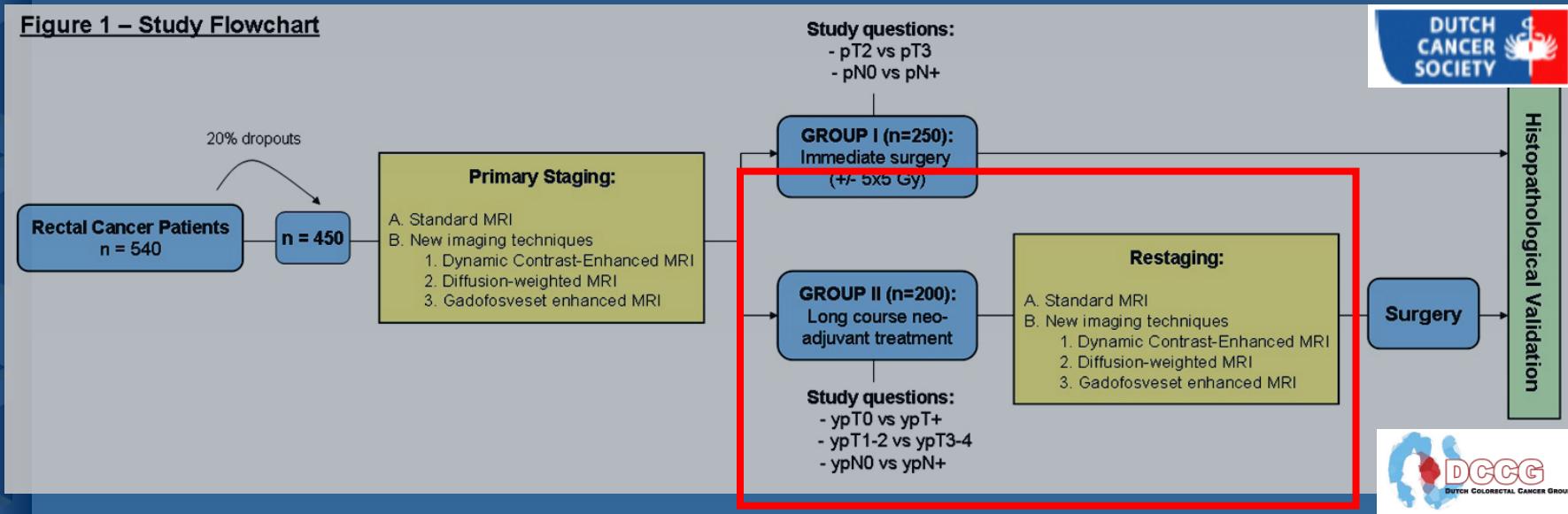
Parametric MR Imaging not yet ready!

- ✓ Natural variation or treatment effect ?
- ✓ Standardization
- ✓ Image processing

Parametric MR Imaging not yet ready!

- ✓ Natural variation or treatment effect ?
- ✓ Standardization
- ✓ Image processing
- ✓ Multicenter validation

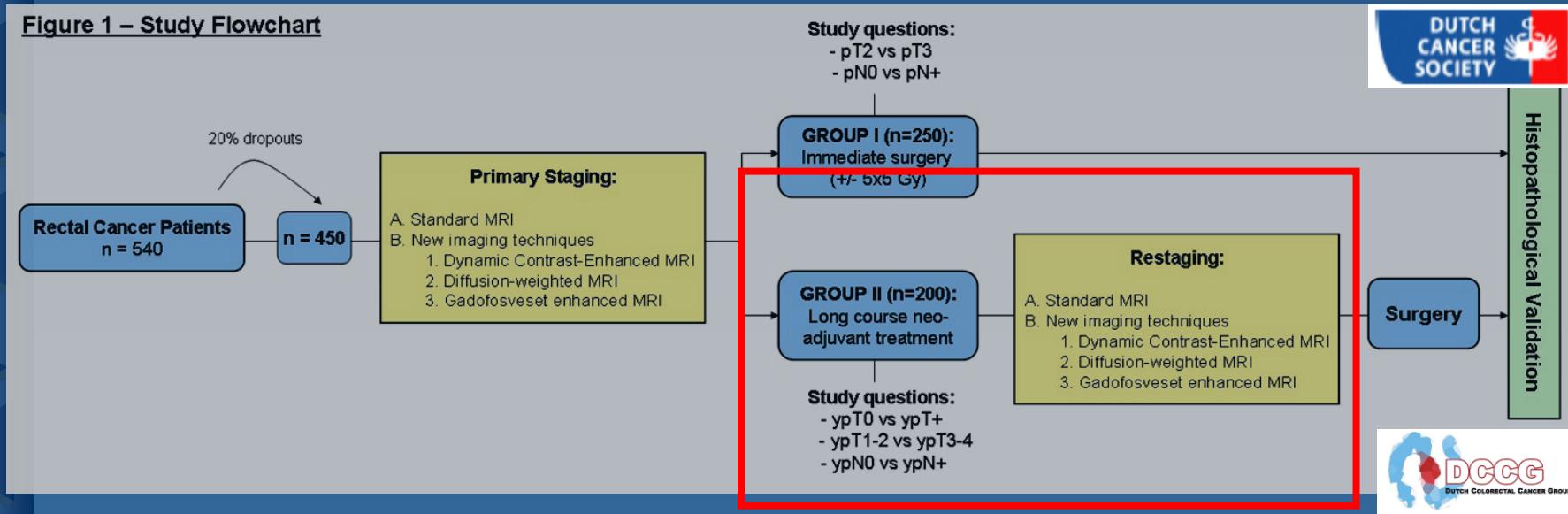
Figure 1 – Study Flowchart



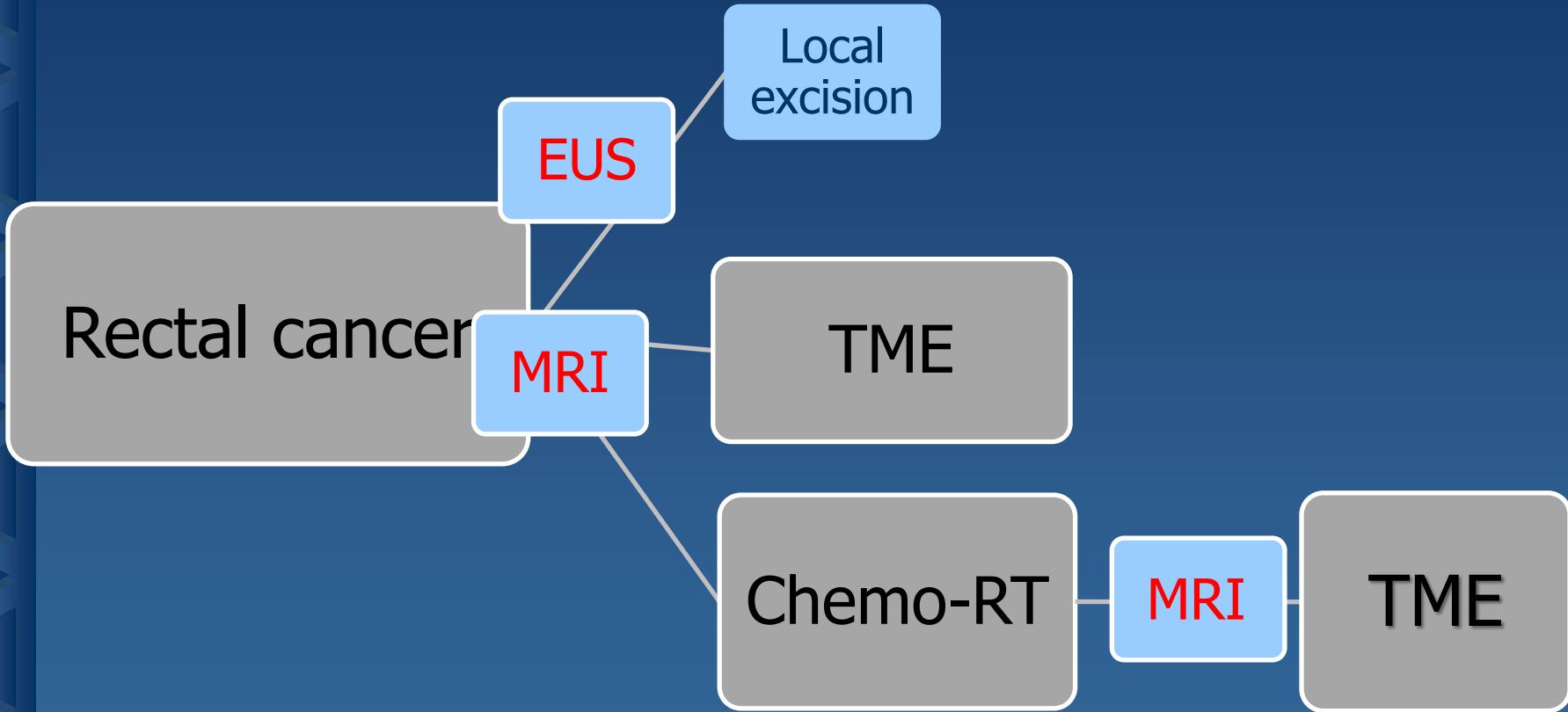
Parametric MR Imaging not yet ready!

- ✓ Natural variation or treatment effect ?
- ✓ Standardization
- ✓ Image processing
- ✓ Multicenter validation
- ✓ Incorporate biomarker in clinical trials

Figure 1 – Study Flowchart

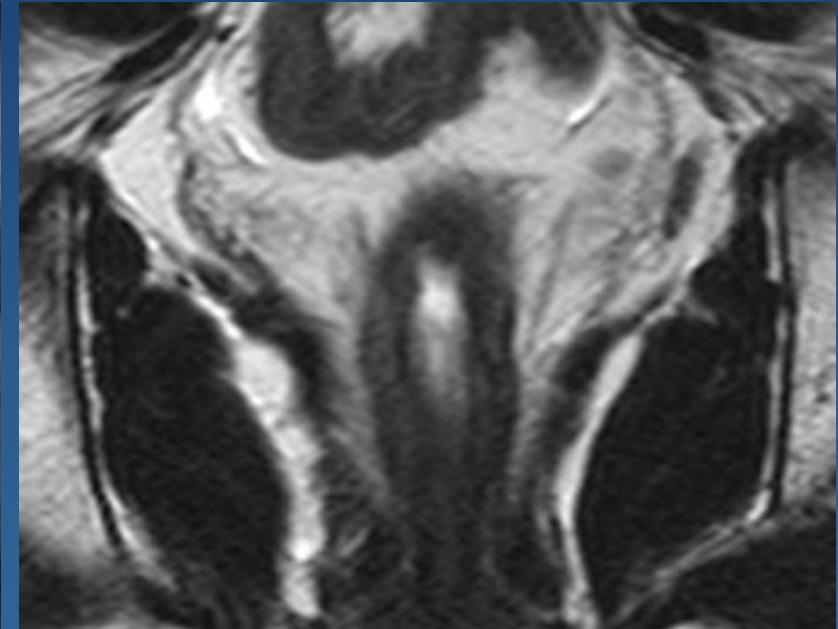
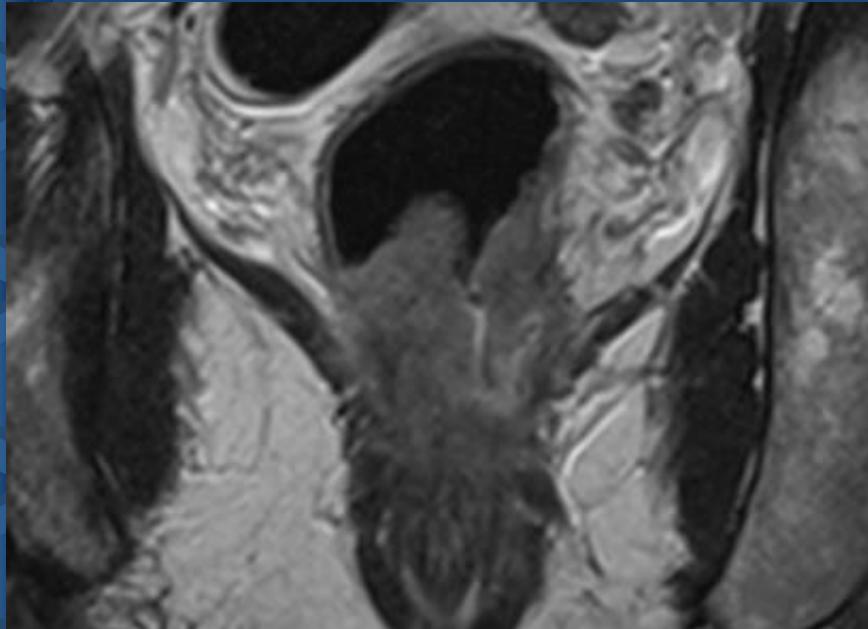


TAKE HOME MESSAGES

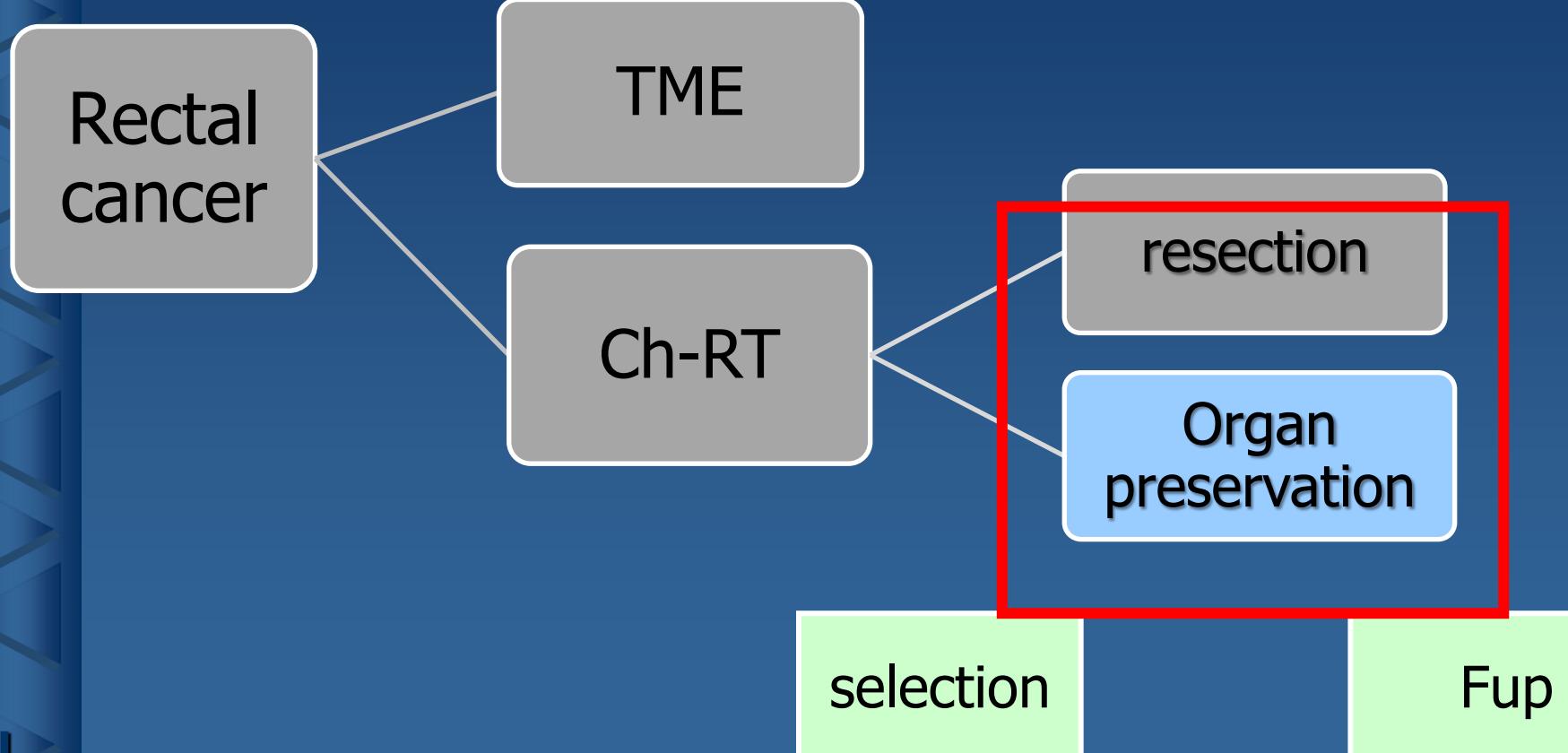


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Regression

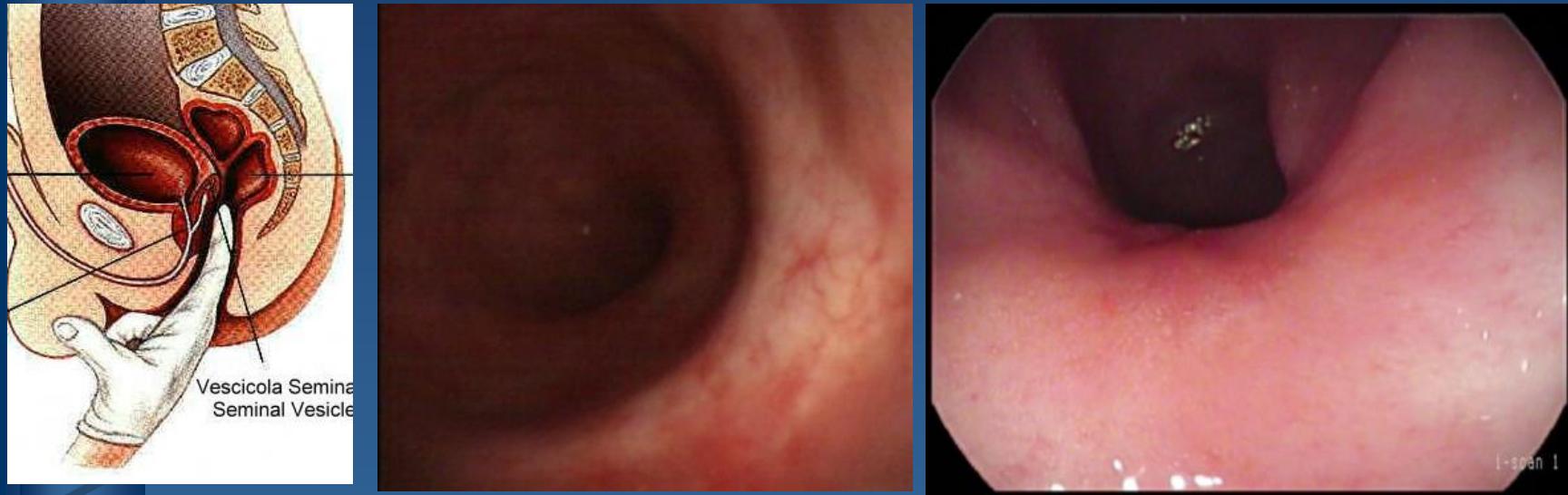


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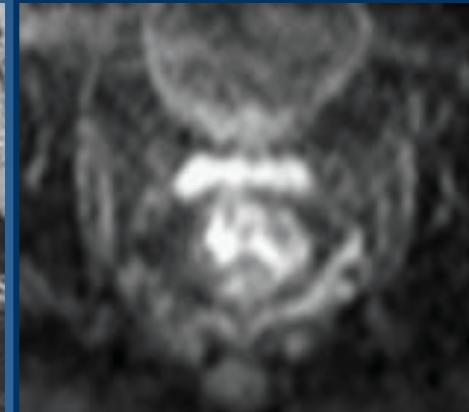
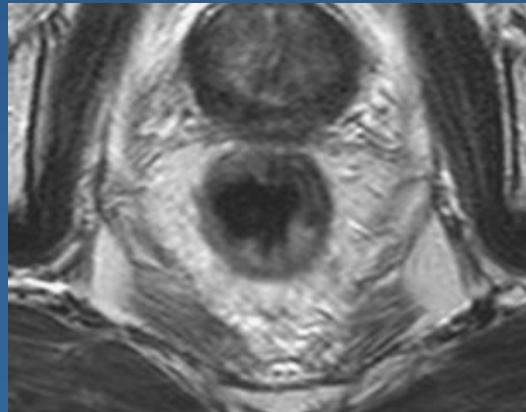
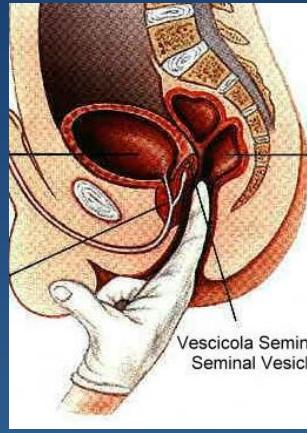
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Clinical Complete Response



TAKE HOME MESSAGES

Clinical Complete Response



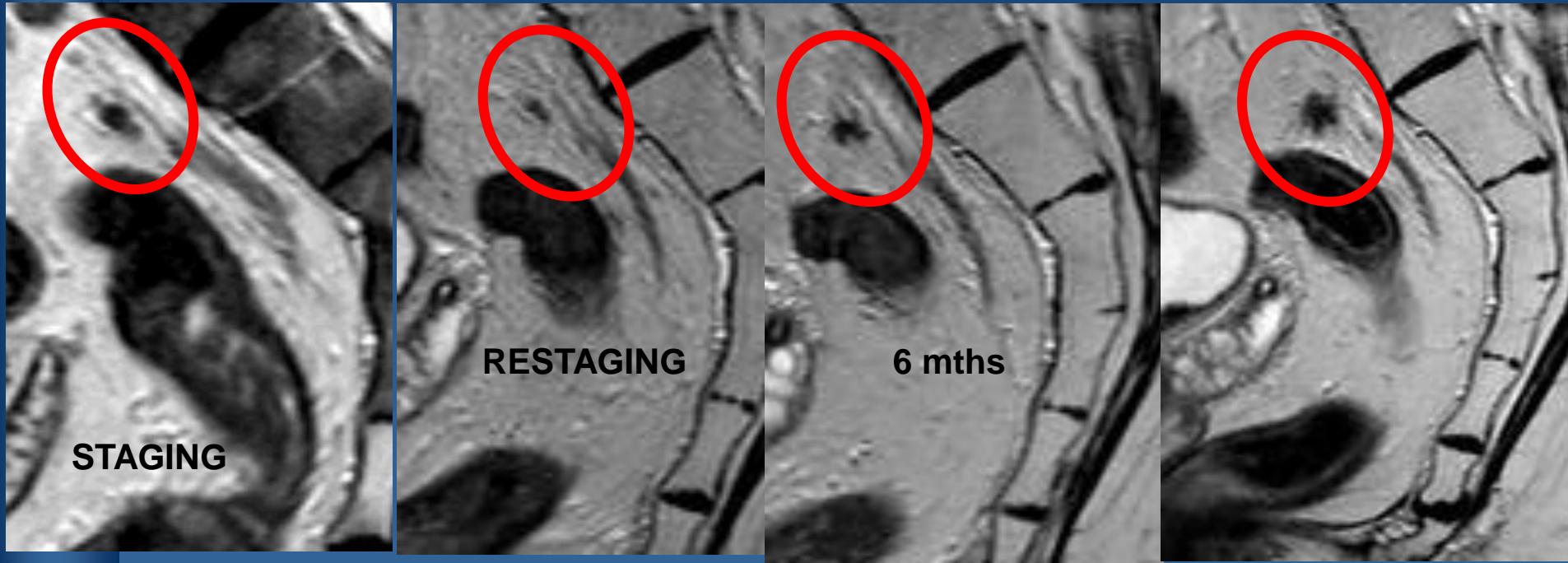
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identify ycN0



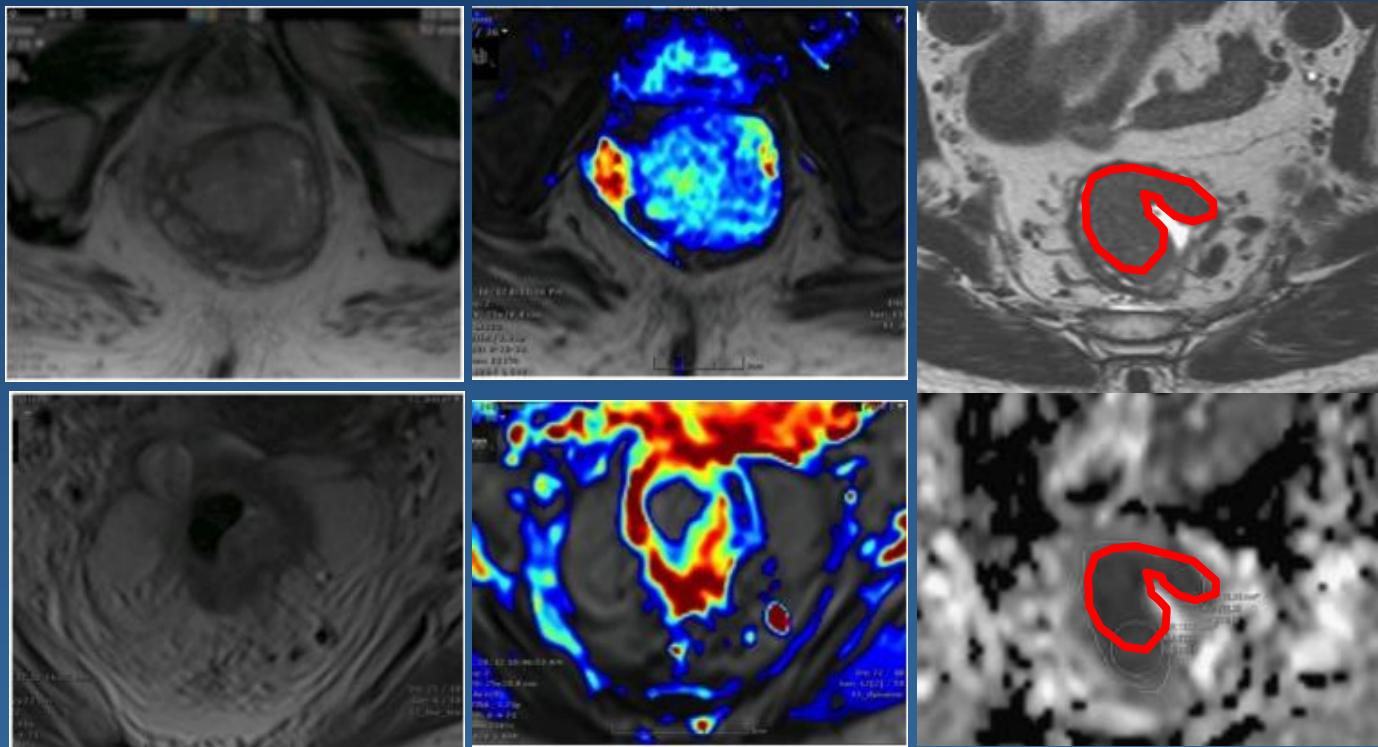
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follow nodes



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Multiparametric MR imaging



Not ready for clinical practice !



ASKLEPIOS Course on Multidisciplinary Approach to Cancer Imaging

November 6-8, 2014; Maastricht/Netherlands