

# APPROPRIATEZZA DELL'IMAGING NELLA DIAGNOSTICA E RADIOTERAPIA DEI TUMORI GASTROINTESTINALI

23 e 24 febbraio 2017

**Predizione della risposta  
patologica completa nei pazienti  
con cancro del retto: un  
approccio multidimensionale**

**B. Barbaro**

Università Cattolica del Sacro Cuore



**Staging**

**Terapie**

**Neoadiuvanti**

**RESPONDERS**

**NONRESPONDERS**

# RESPONDERS

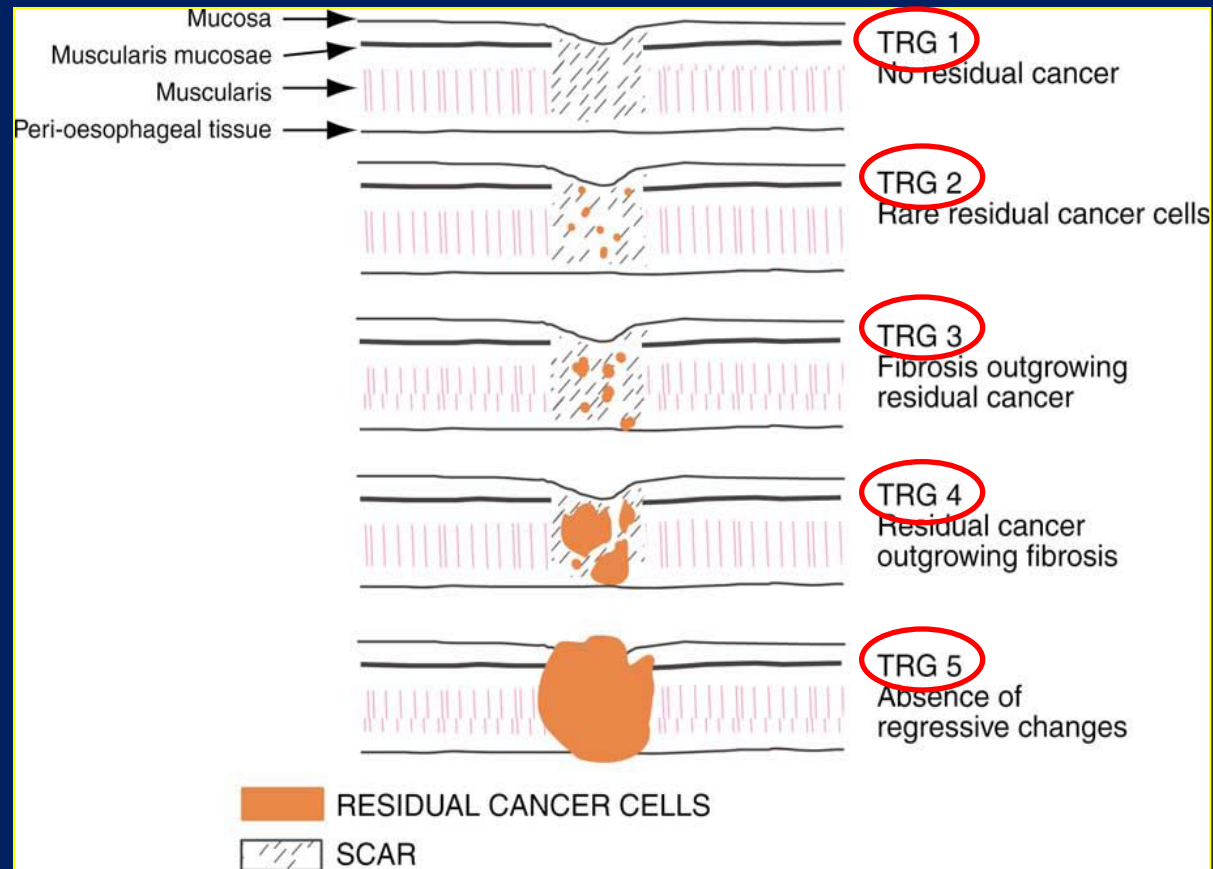


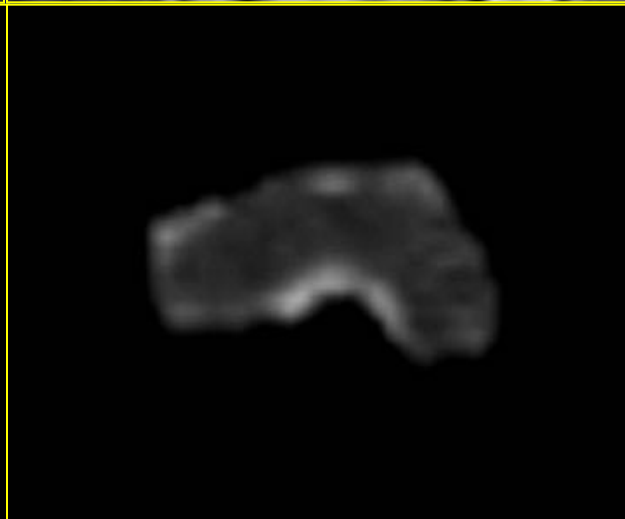
*T-downsizing*



*T-downstaging*

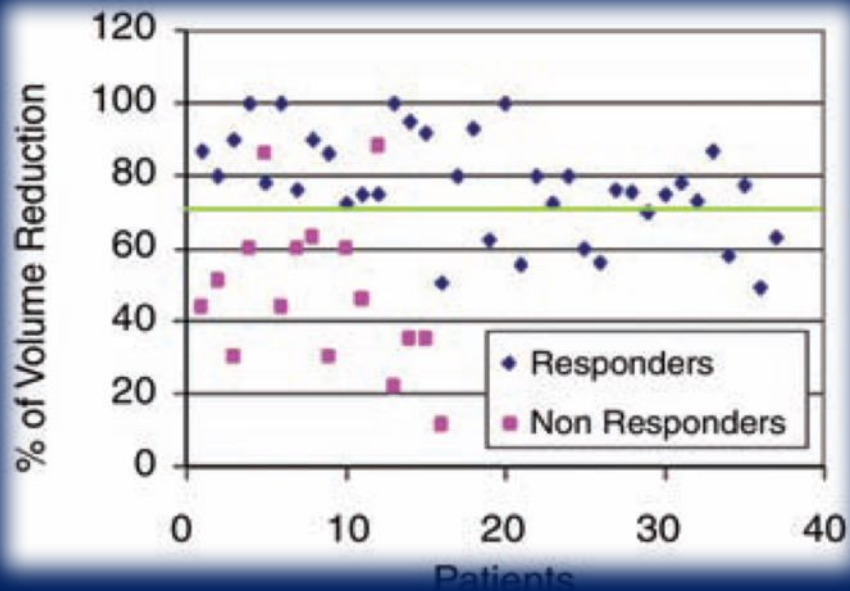
# Tumor Regression Grade





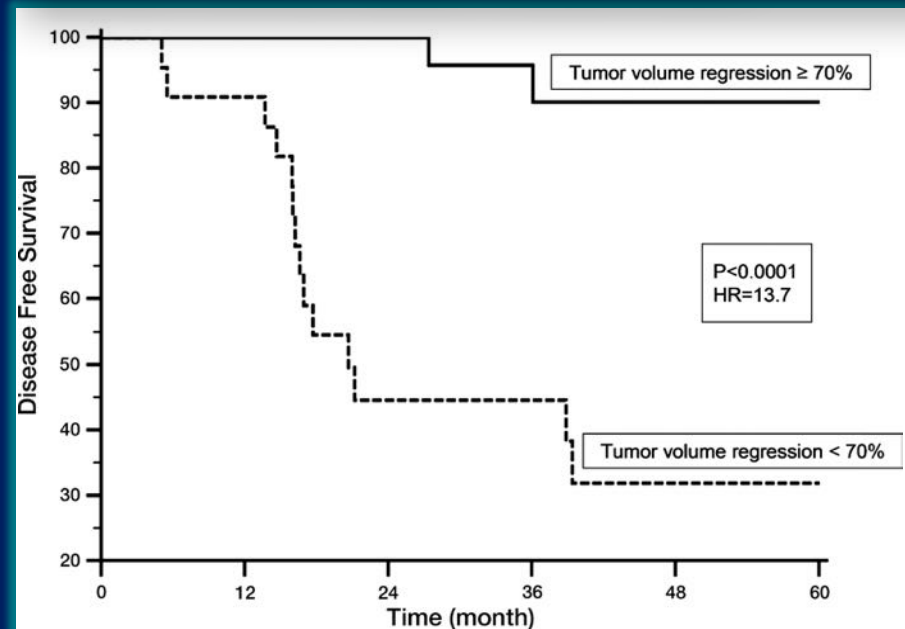


The cut-off 70%  
Positive predictive  
value > 90%



Barbaro B. *et al.*, Radiology 2009

The cut-off of 70% is an easy  
parameter to use as a surrogate  
for clinical response to predict  
both TRG and outcome



Nougaret S. *et al.*, Radiology 2012

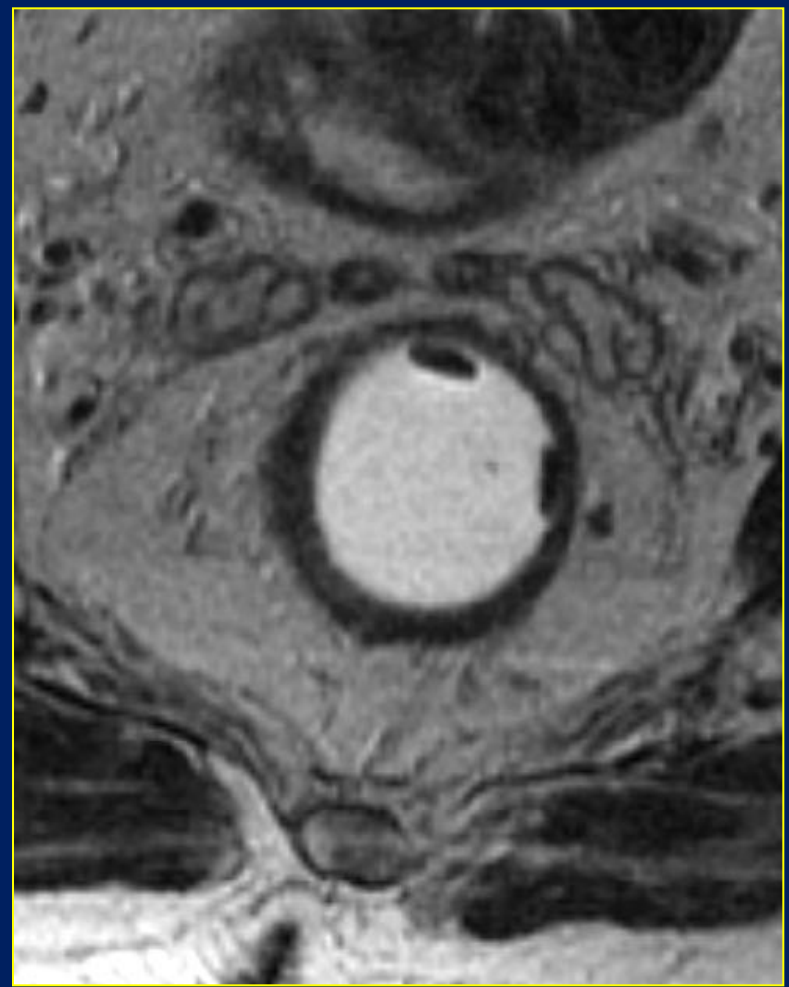
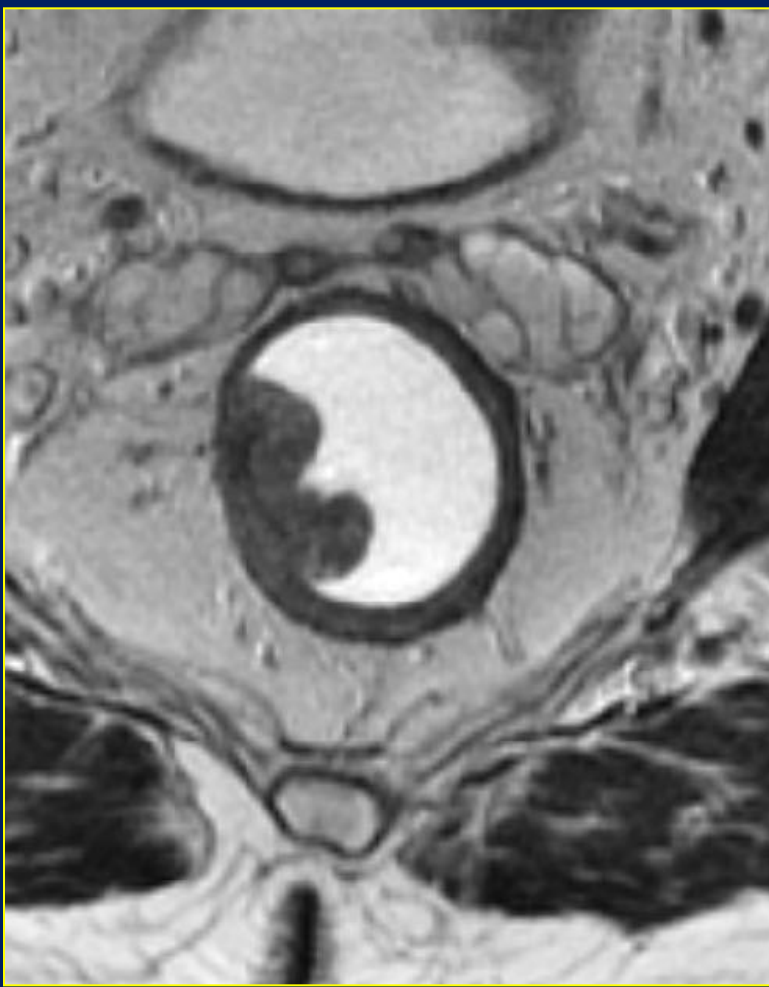
# Criteria to assume ypT0-2 on MR images



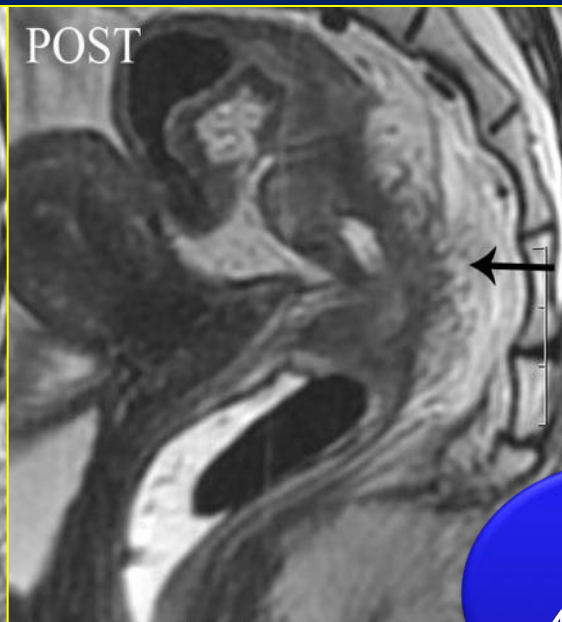
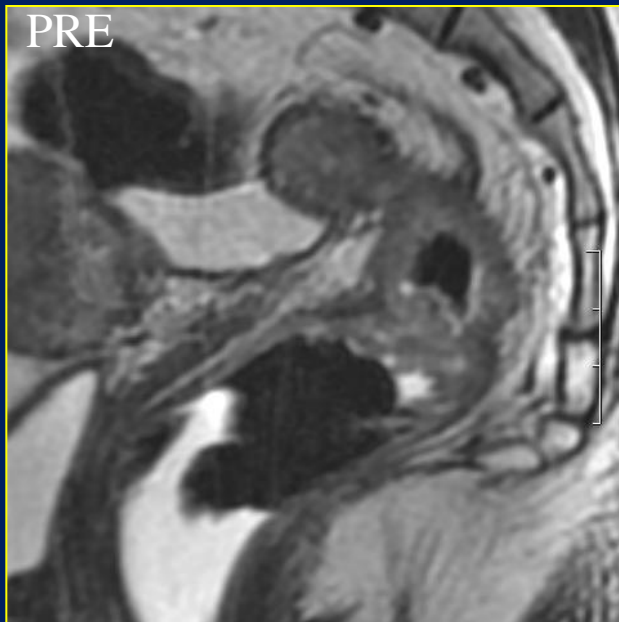
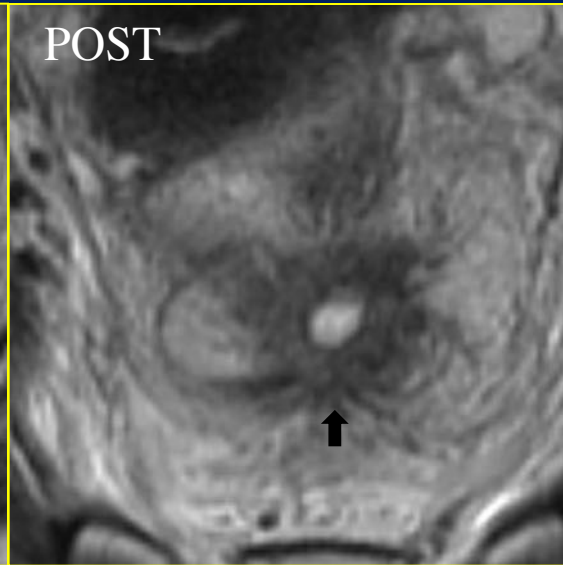
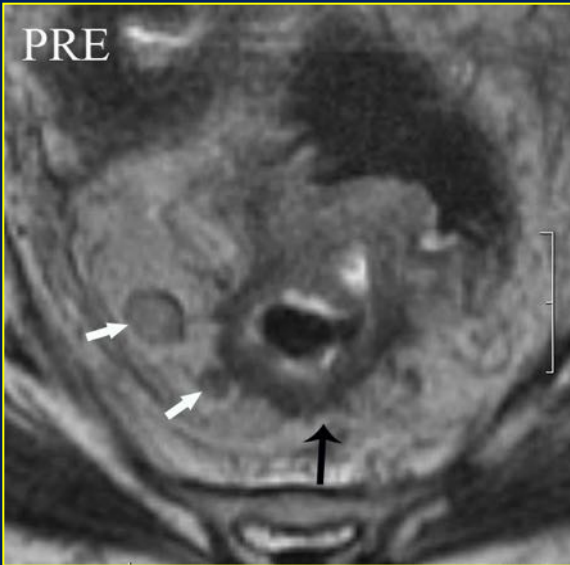
ypT

TpY

Barbaro B. *et al.*, Radiology 2009  
Dresen RC, *et al.* Radiology 2009

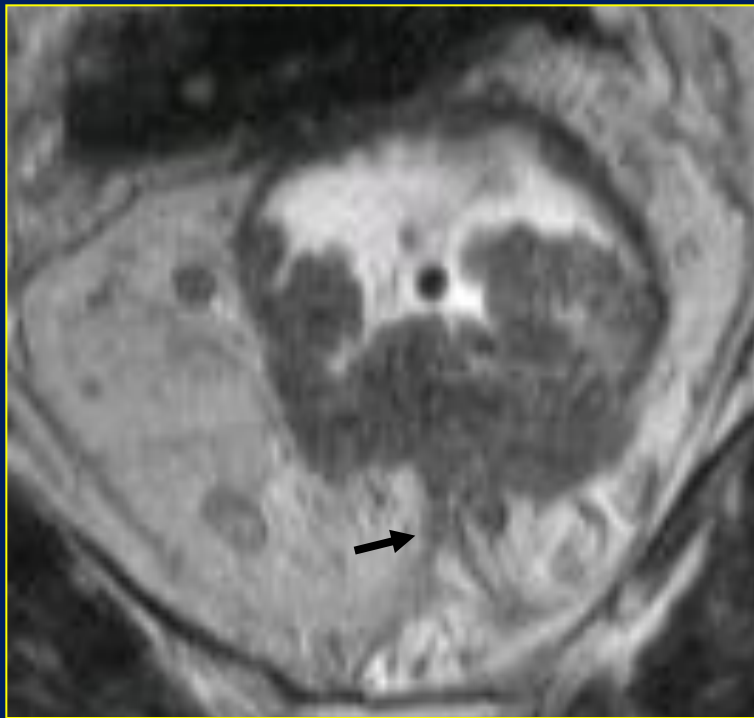




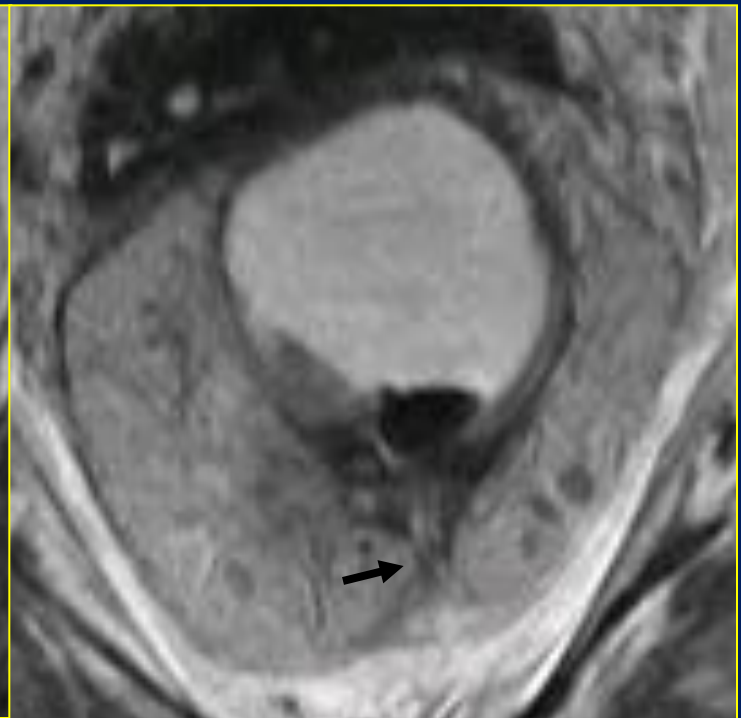


**PPV  
42.8%**

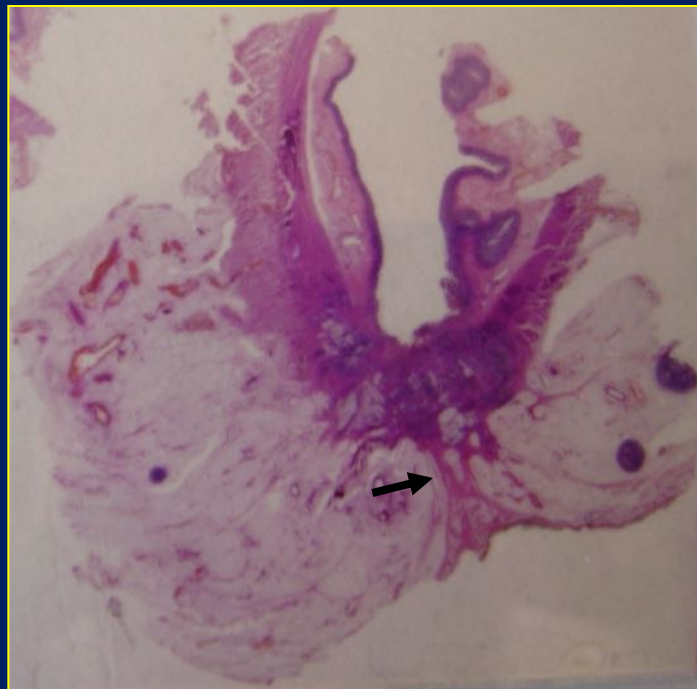
Barbaro et al. Radiology 2009 PPV 42,8%



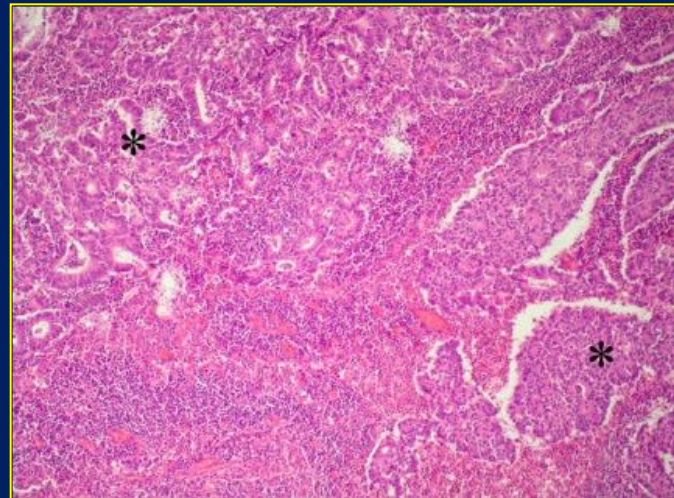
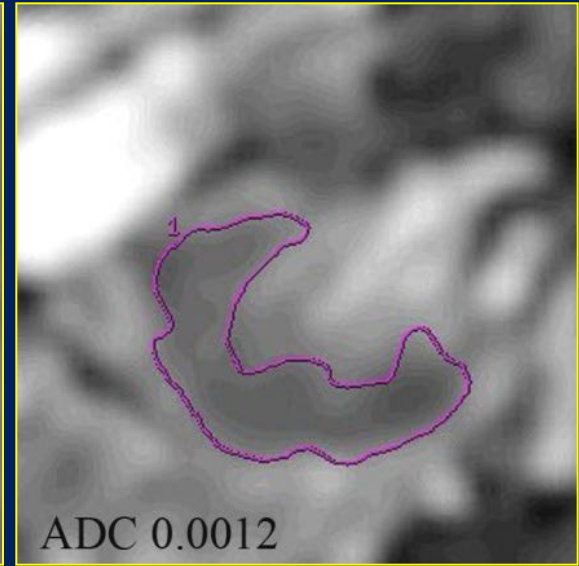
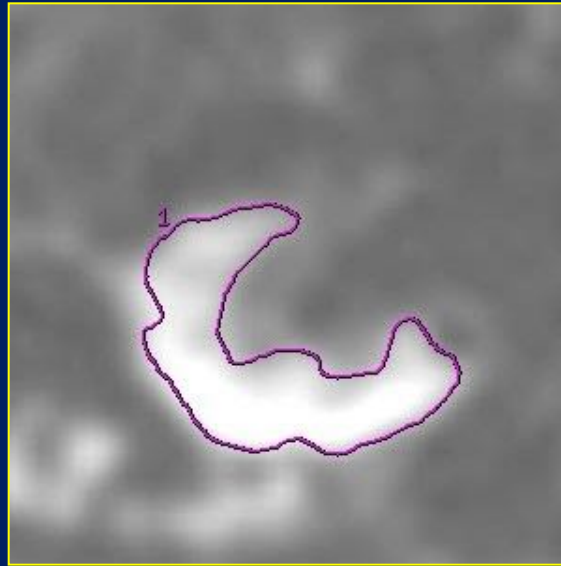
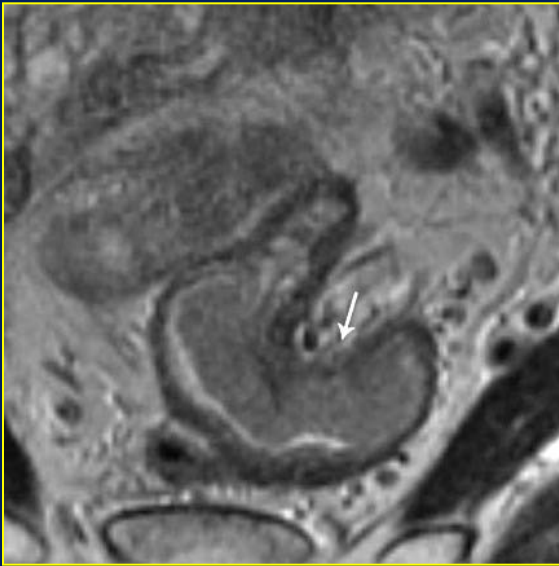
PRE



POST



# RM: diffusion weighted imaging (DWI)





# Restaging Locally Advanced Rectal Cancer with MR Imaging after Chemoradiation Therapy<sup>1</sup>

*Brunella Barbaro, MD • Renata Vitale, MD • Lucia Leccisotti, MD  
Fabio M. Vecchio, MD • Luisa Santoro, MD • Vincenzo Valentini, MD  
Claudio Coco, MD • Fabio Pacelli, MD • Antonio Crucitti, MD  
Roberto Persiani, MD • Lorenzo Bonomo, MD*

A new question is now being posed by the multidisciplinary team:  
How and when should rectal cancer be restaged after CRT?



# Restaging Locally Advanced Rectal Cancer with MR Imaging after Chemoradiation Therapy<sup>1</sup>

*Brunella Barbaro, MD • Renata Vitale, MD • Lucia Leccisotti, MD  
Fabio M. Vecchio, MD • Luisa Santoro, MD • Vincenzo Valentini, MD  
Claudio Coco, MD • Fabio Pacelli, MD • Antonio Crucitti, MD  
Roberto Persiani, MD • Lorenzo Bonomo, MD*

Restaging with imaging could be relevant for surgeons.

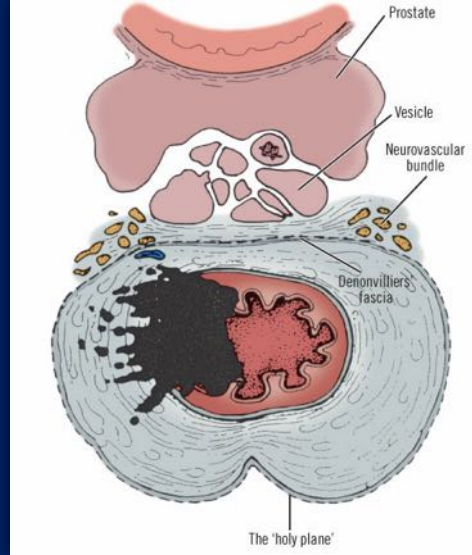
The first question to be answered is, Can MR imaging help determine whether the tumor has regressed from other organs or the mesorectal fascia before standard total mesorectal excision is performed?

The second question is whether MR imaging can be used prior to treatment to identify stage T3 tumors that will convert to T2 or lower-stage tumors after CRT, thereby allowing more conservative resection (26)



# Ristadiazione

**Goal**



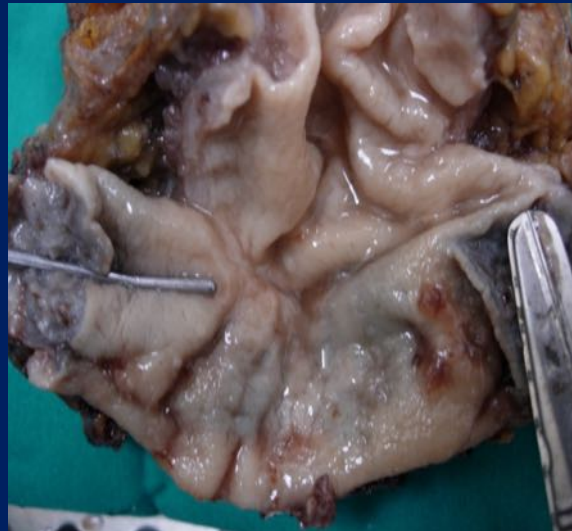
**IORT**

# *Looking for the best choice...*

Local transanal  
full-thickness  
excision TEM



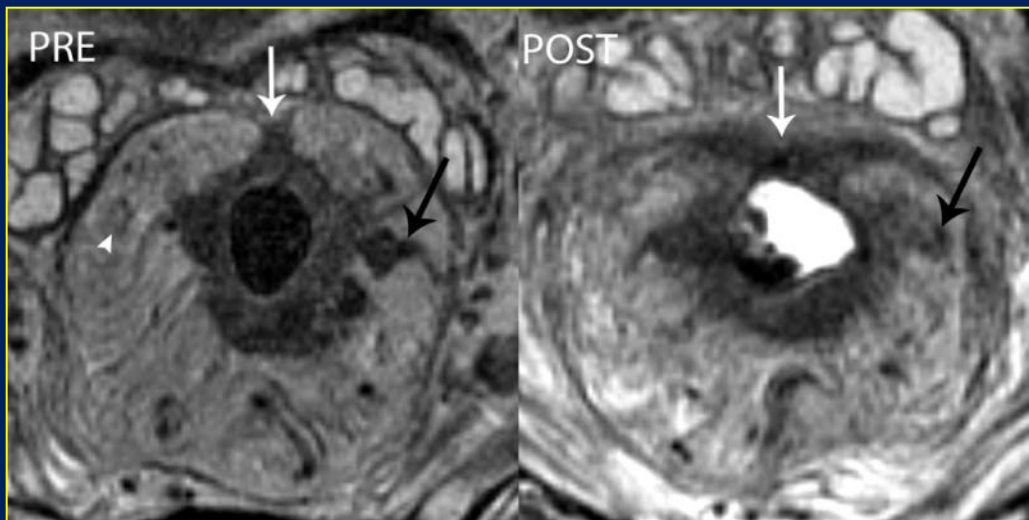
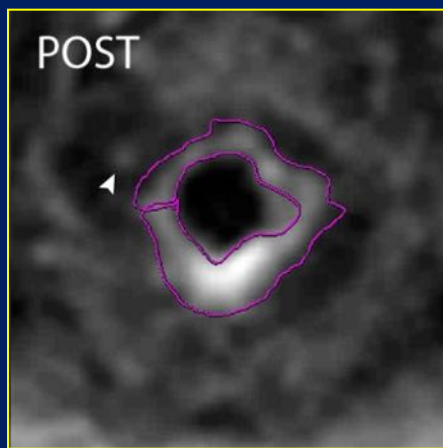
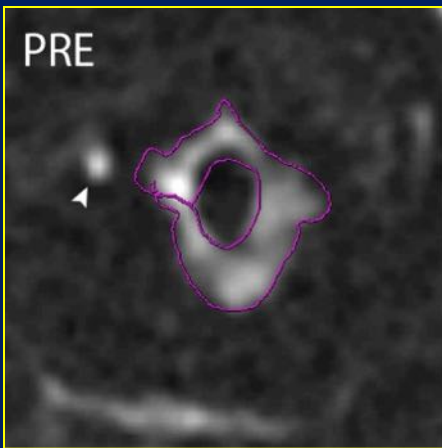
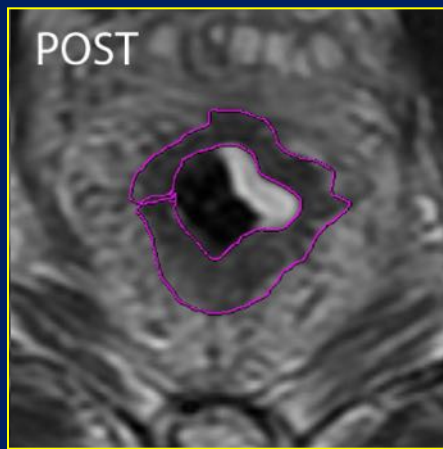
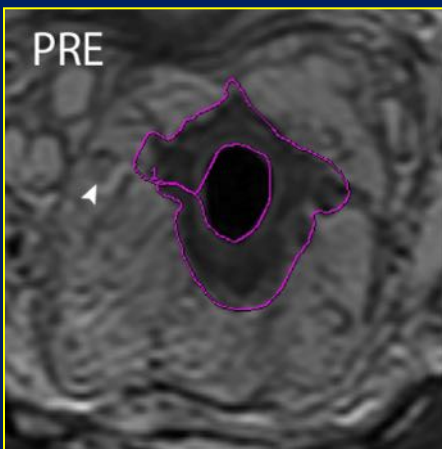
Non-operative  
treatment?  
Wait and See



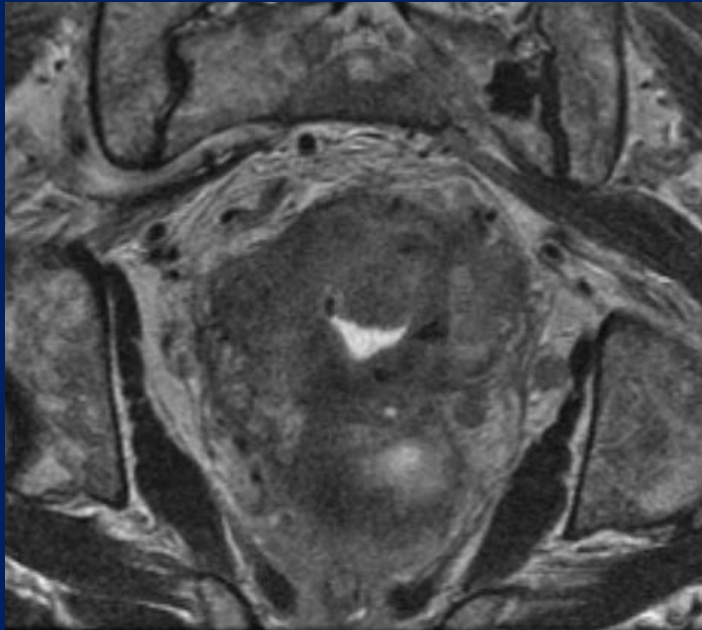
Total Mesorectal  
Excision  
TME





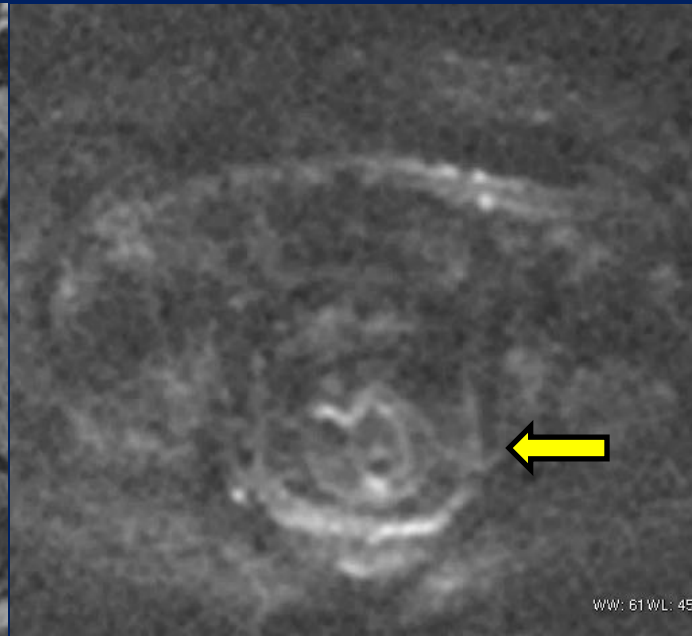
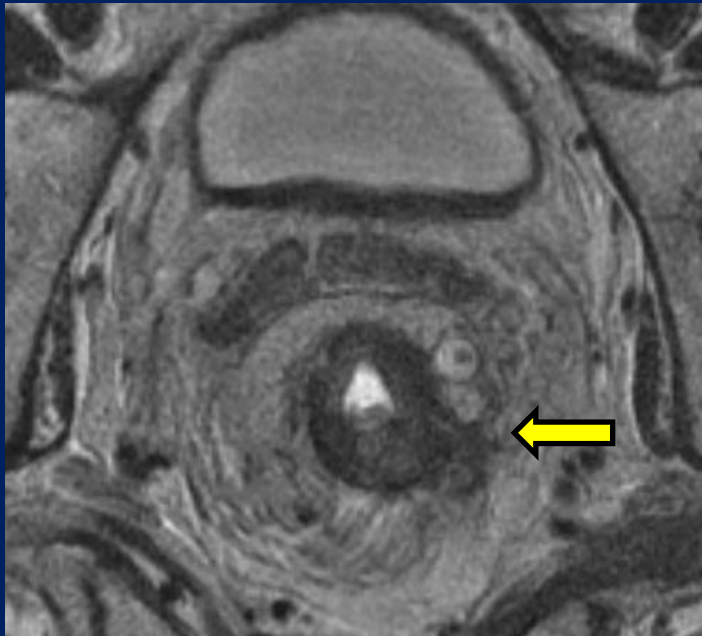
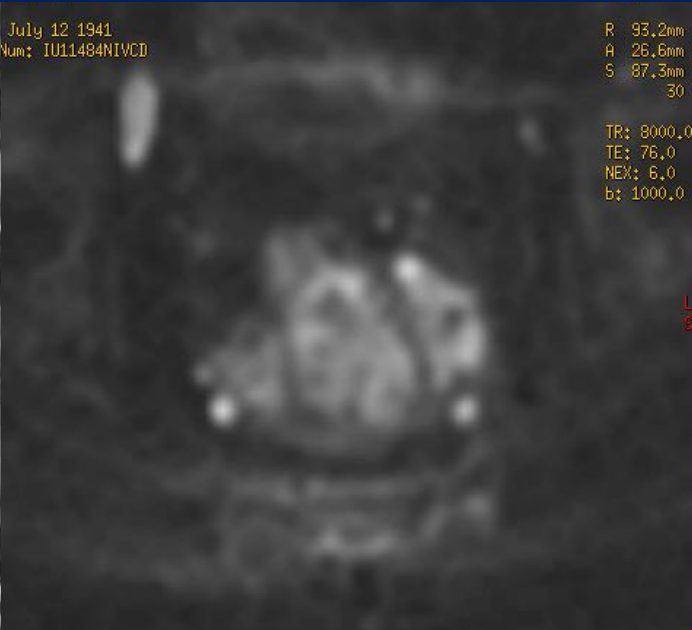


yCRM+N1

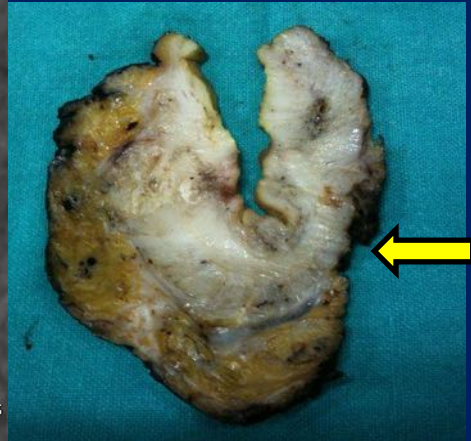


July 12 1941  
Num: IU11484NIVCD

R: 93.2mm  
A: 26.6mm  
S: 87.3mm  
30  
TR: 8000.0  
TE: 76.0  
NEX: 6.0  
b: 1000.0



WW: 61 WL: 45





Locally Advanced Rectal Cancer: Added Value of Diffusion-weighted MR Imaging for Predicting Tumor Clearance of the Mesorectal Fascia after Neoadjuvant Chemotherapy and Radiation Therapy

Radiology

Park MJ  
Kim SH  
Lee SJ  
Jang  
KM  
Rhim F

Adding DW imaging to T2-weighted imaging can improve the prediction of tumor clearance in the MRF after neoadjuvant CRT (accuracy 89-93% vs 40-69% )

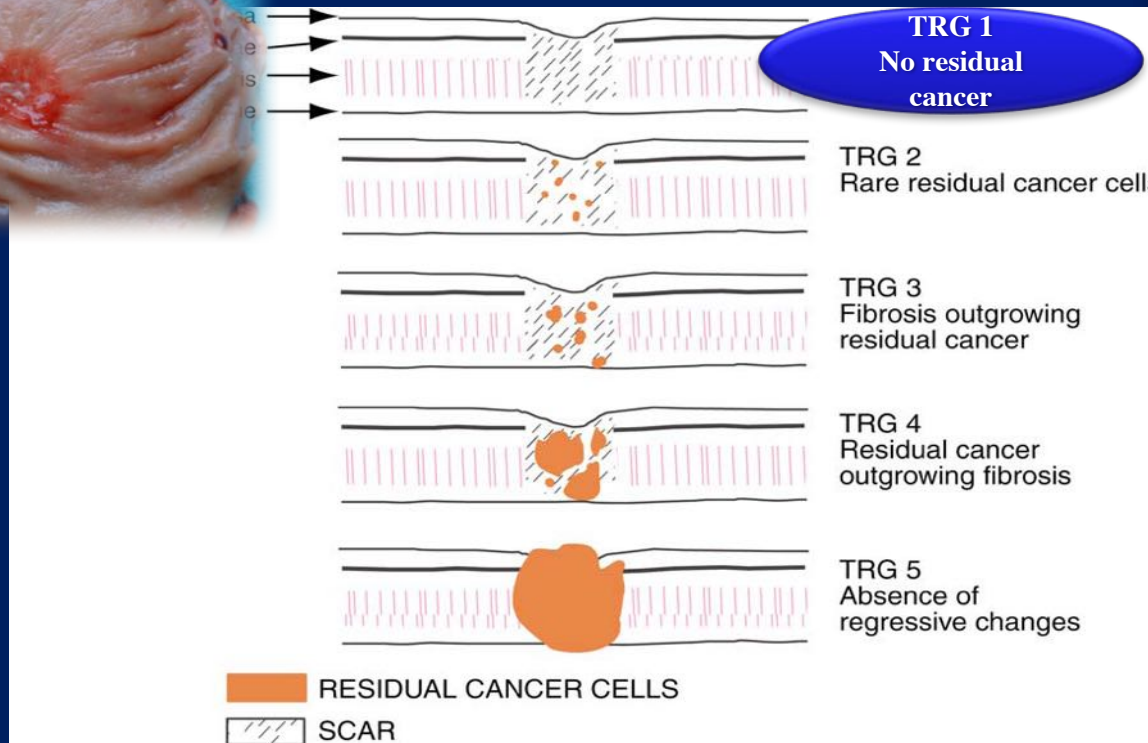
However, when DW images are used in combination with T2-weighted images, the T2-weighted images serve as a reference for the tumor location, which in turn leads to more accurate assessment of the distance between viable tumor and the MRF, despite the comparatively low spatial resolution of DW imaging alone.

# Ristadiazione

Goal



*Pathological complete response 10-30%*



pCR

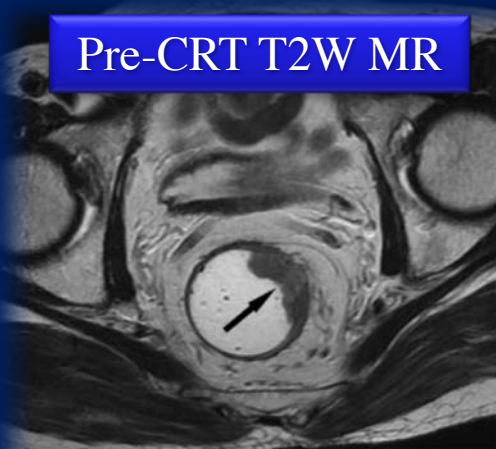
BC

**Locally Advanced Rectal Cancer:**  
Added Value of Diffusion-weighted MR  
Imaging in the Evaluation of Tumor  
Response to Neoadjuvant Chemo-  
and Radiation Therapy<sup>1</sup>

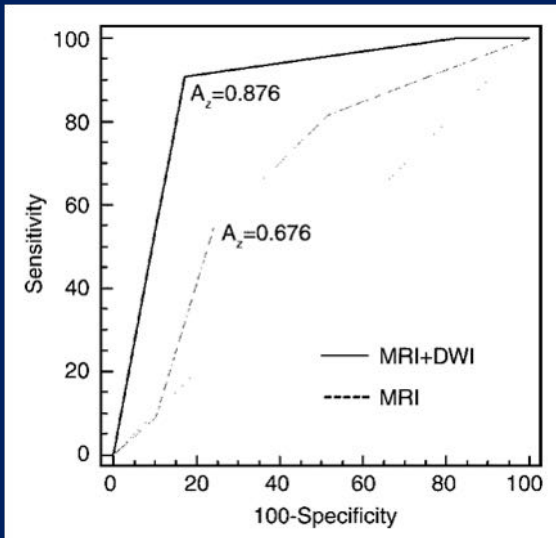
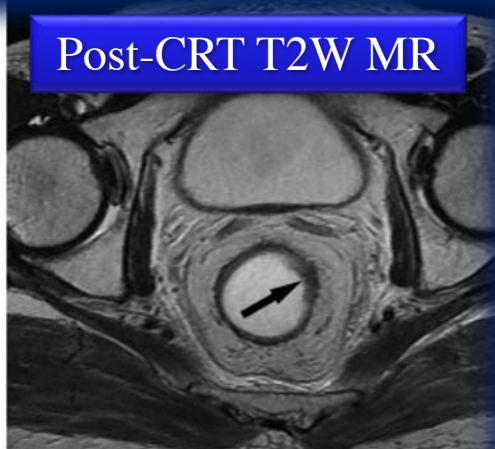
Radiology

# Diffusion – weighted ( DW ) MRI

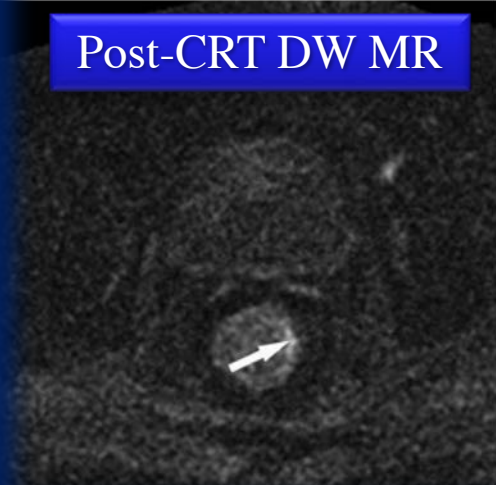
Pre-CRT T2W MR



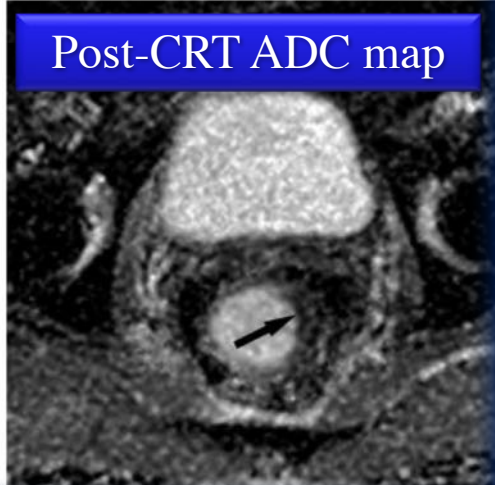
Post-CRT T2W MR



Post-CRT DW MR



Post-CRT ADC map



Adding DWI to conventional MRI  
can be **useful** in determination of  
the **complete response** AA

## Diffusion-Weighted MRI for Selection of Complete Responders After Chemoradiation for Locally Advanced Rectal Cancer: A Multicenter Study

Doenja M. J. Lambregts, MD<sup>1,2</sup>, Vincent Vandecaveye, MD<sup>3</sup>, Brunella Barbaro, MD<sup>4</sup>, Frans C. H. Bakers, MD<sup>1</sup>, Maarten Lambrecht, MD<sup>5</sup>, Monique Maas, MD<sup>1,2</sup>, Karin Haustermans, MD<sup>5</sup>, Vincenzo Valentini, MD<sup>6</sup>, Geerard L. Beets, MD<sup>2</sup>, and Regina G. H. Beets-Tan, MD<sup>1</sup>

<sup>1</sup>Department of Radiology, Maastricht University Medical Center, Maastricht, The Netherlands; <sup>2</sup>Department of Surgery, Maastricht University Medical Center, Maastricht, The Netherlands; <sup>3</sup>Department of Radiology, University Hospitals Leuven, Leuven, Belgium; <sup>4</sup>Department of Radiology, Università Cattolica del Sacro Cuore, Rome, Italy; <sup>5</sup>Department of Radiation Oncology, University Hospitals Leuven, Leuven, Belgium; <sup>6</sup>Department of Radiation Oncology, Università Cattolica del Sacro Cuore, Rome, Italy

**Conclusions.** Addition of DWI to standard rectal MRI improves the selection of complete responders after chemoradiation.

..... it resulted in a substantial reduction in the number of equivocal scores and an improved interobserver agreement.

ORIGINAL ARTICLE – COLORECTAL CANCER

**Diffusion-Weighted MRI for Selection of Complete Responders  
After Chemoradiation for Locally Advanced Rectal Cancer:**

**A Multicenter Study**

Doenja M. J. Lambregts, MD<sup>1</sup>, Frans C. H. Bakers, MD<sup>1</sup>,  
Maarten Lambrecht, MD<sup>5</sup>, Monia Valentini, MD<sup>6</sup>,  
Geeraard L. Beets, MD<sup>2</sup>, and Regine G. H. J. van Erven, MD<sup>3</sup>

<sup>1</sup>Department of Radiation Oncology, Maastricht University Medical Center, Maastricht University Hospitals, Leuven, Leuven, Belgium; <sup>2</sup>Department of Radiation Oncology, Universita Cattolica del Sacro Cuore, Rome, Italy; <sup>3</sup>Department of Surgery, Maastricht University Hospitals, Maastricht, The Netherlands; <sup>4</sup>Department of Radiation Oncology, Universita Cattolica del Sacro Cuore, Rome, Italy; <sup>5</sup>Department of Radiation Oncology, Universita Cattolica del Sacro Cuore, Rome, Italy; <sup>6</sup>Department of Radiation Oncology, Universita Cattolica del Sacro Cuore, Rome, Italy

Performs better to  
confirm than to  
exclude residual  
tumor

... were still observed with DWI resulting in a suboptimal sensitivity of 52–64%.

Specificity for MRI and DWI is >90%, indicating that the residual tumors are accurately detected and the risk for undertreatment will be <10%.



# Patients Who Undergo Preoperative Chemoradiotherapy for Locally Advanced Rectal Cancer Restaged by Using Diagnostic MR Imaging: A Systematic Review and Meta-Analysis

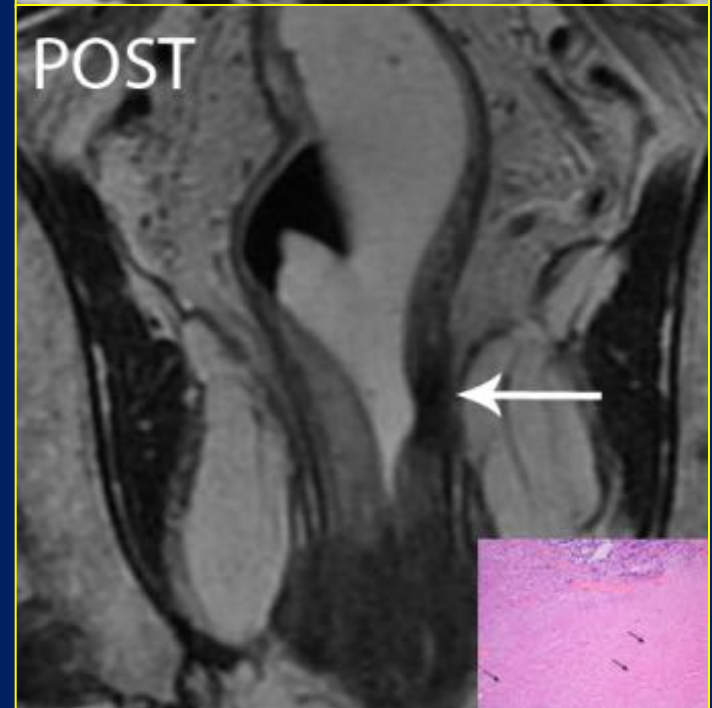
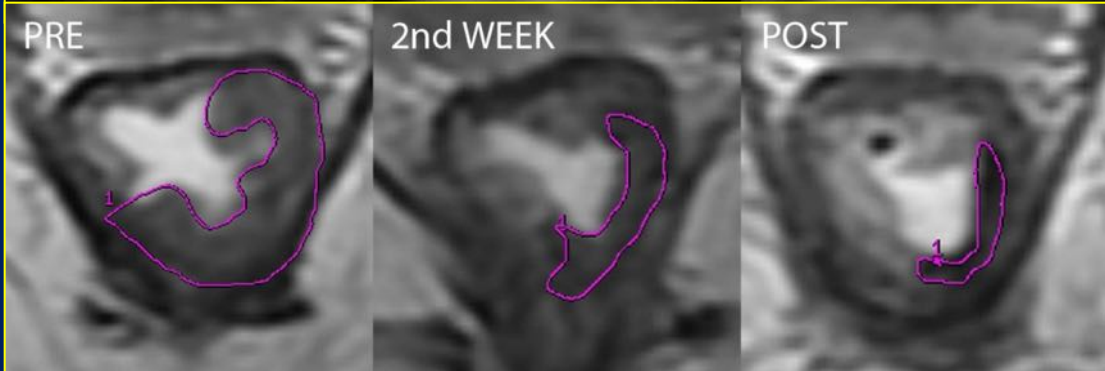
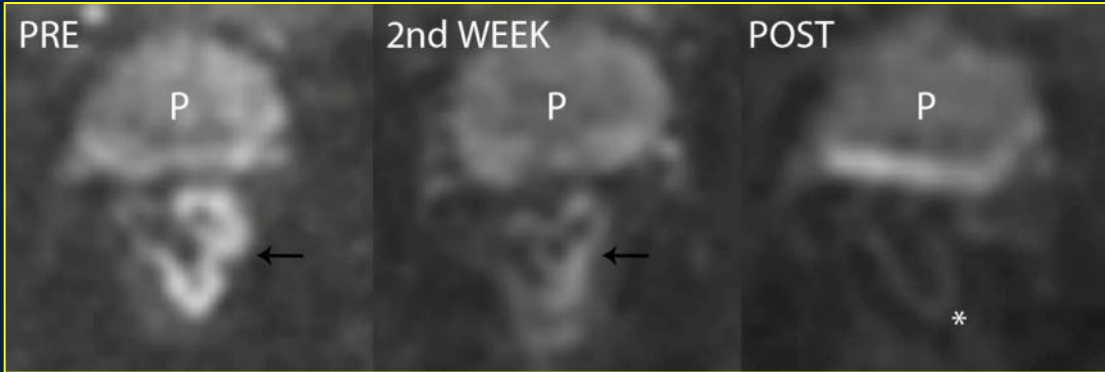
*Radiology: October 2013*

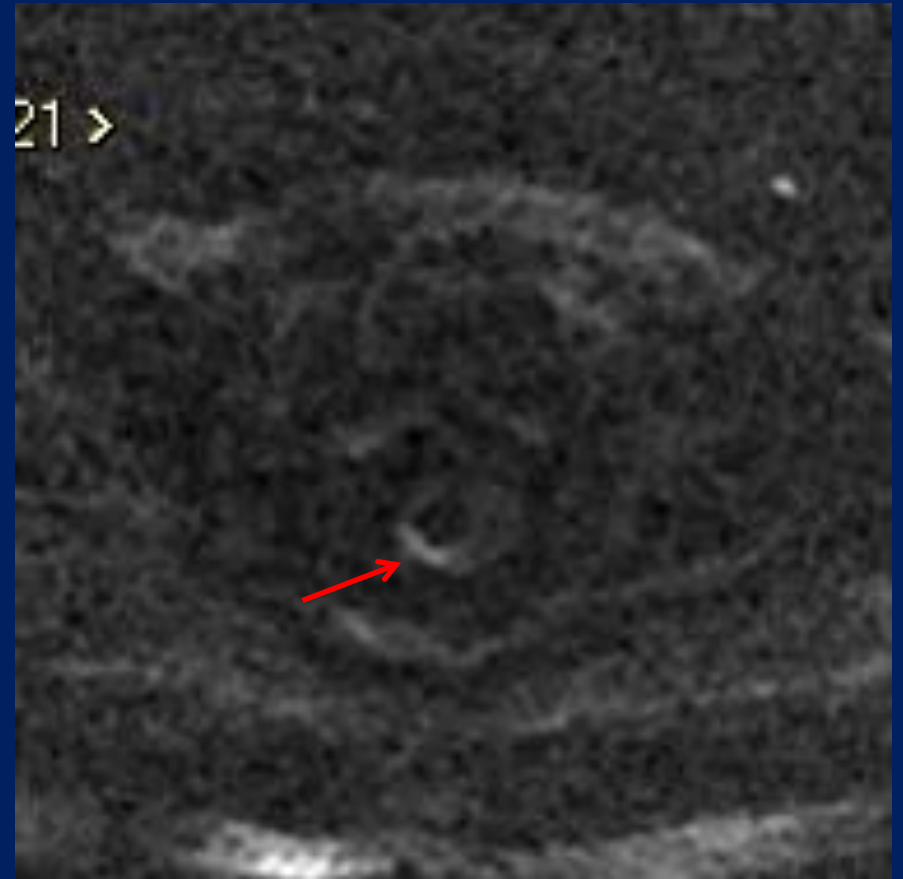
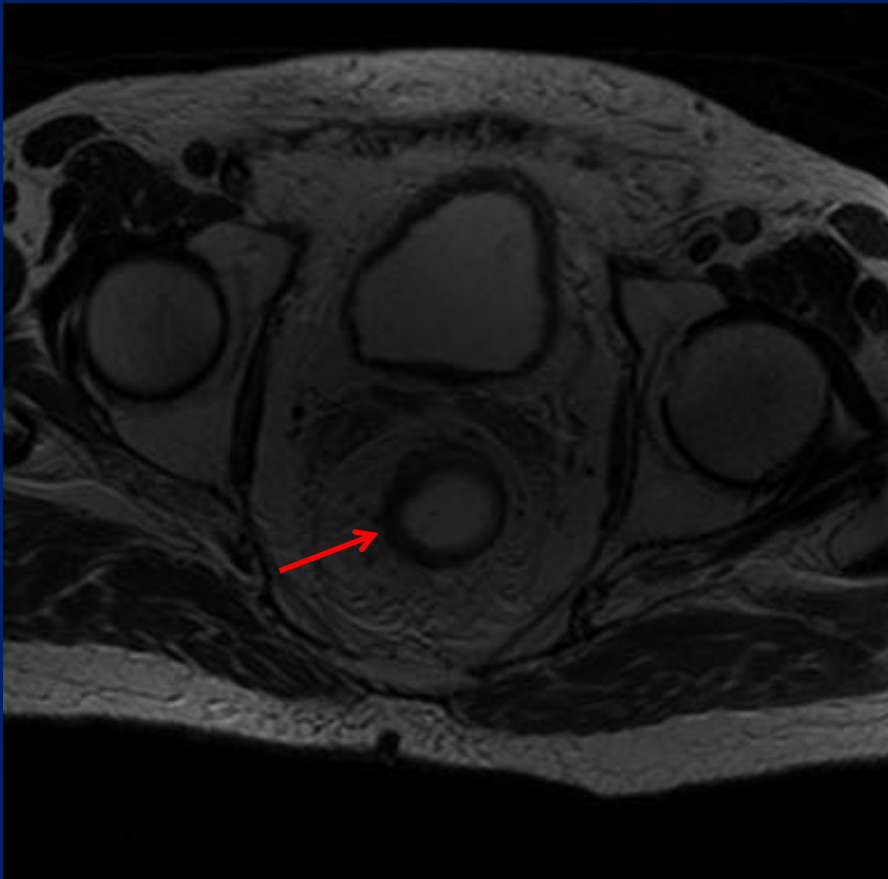
- 33 studies evaluated **1556** patients

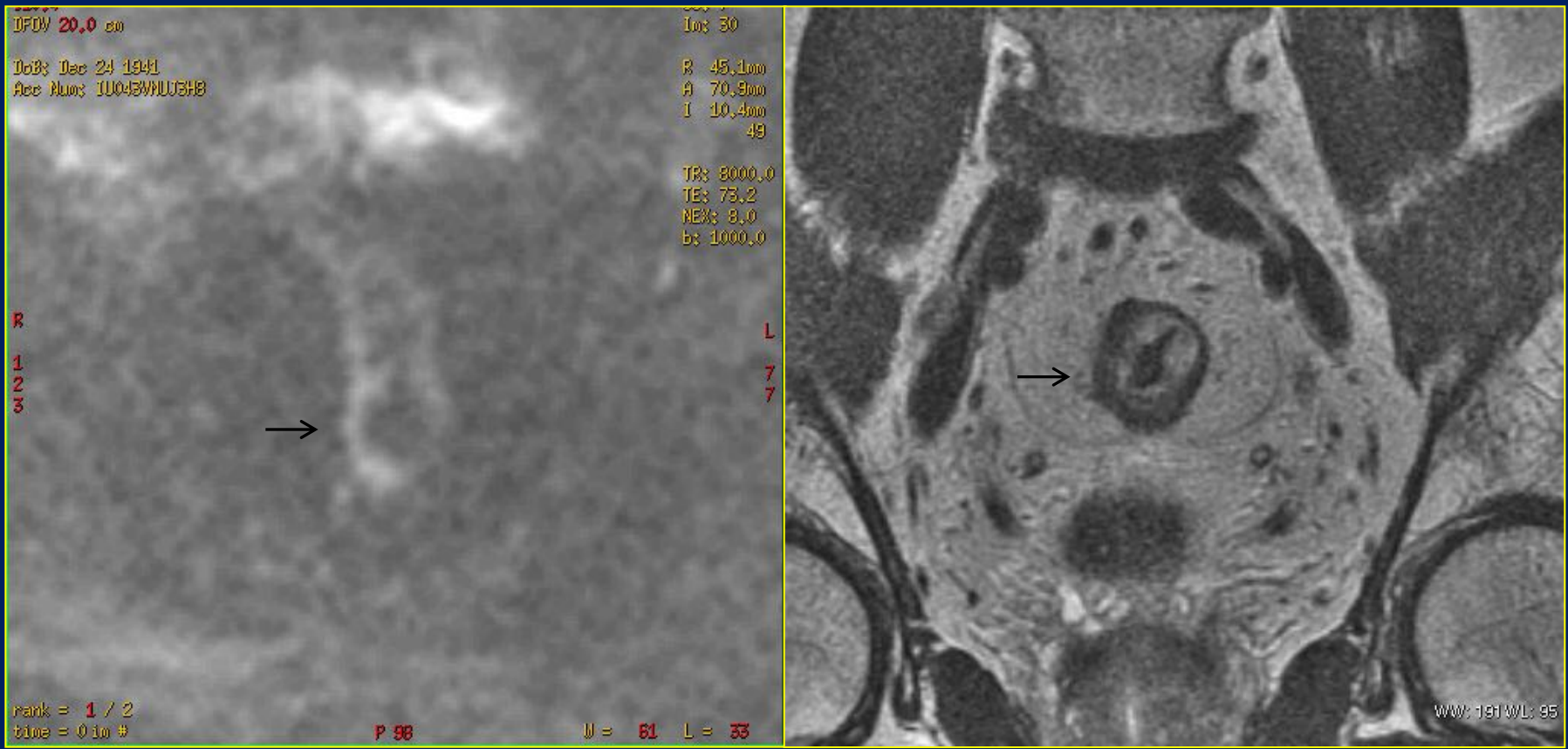
## Implications for Patient Care:

- **MR imaging** for restaging of patients with locally advanced rectal cancer who are undergoing preoperative chemoradiotherapy is difficult to interpret; however, **DW imaging and experienced readers** seem helpful for improvement of tumor stage evaluation.
- For evaluation of **CRM** staging MR imaging can also be used, but MR imaging is still a challenge for **nodal staging**.









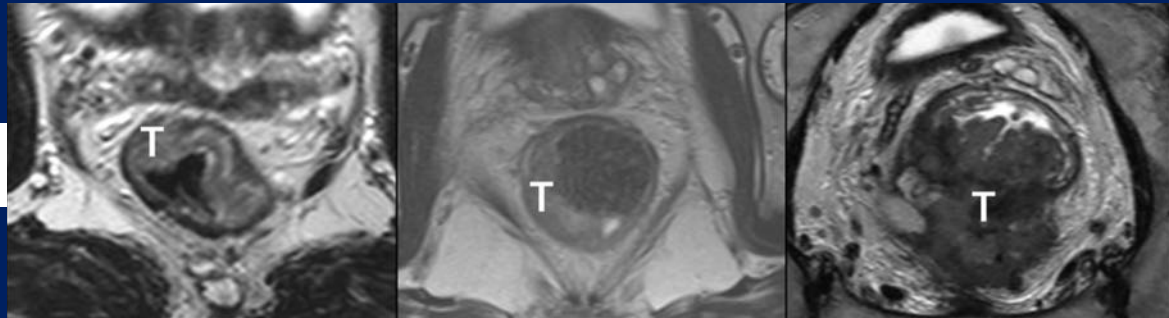
**TRG ?**



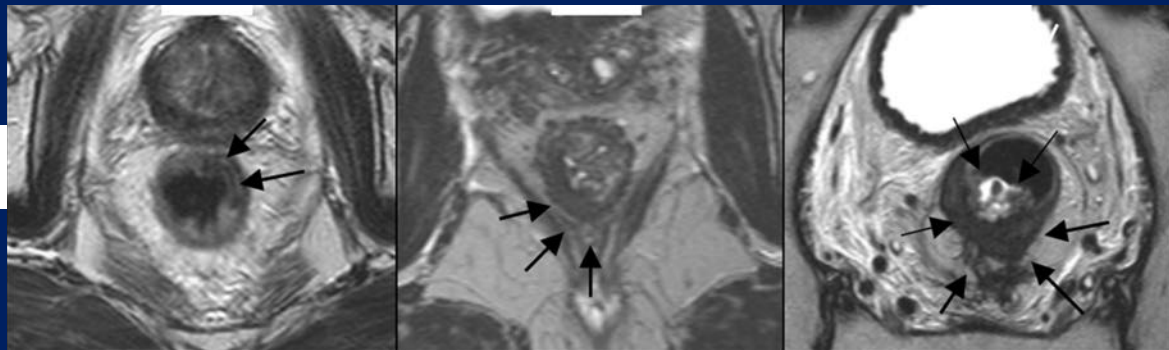
# Assessment of Clinical Complete Response After Chemoradiation for Rectal Cancer with Digital Rectal Examination, Endoscopy, and MRI: Selection for Organ-Saving Treatment

Monique Maas et al *Ann Surg Oncol* (2015) 22:3873–3880

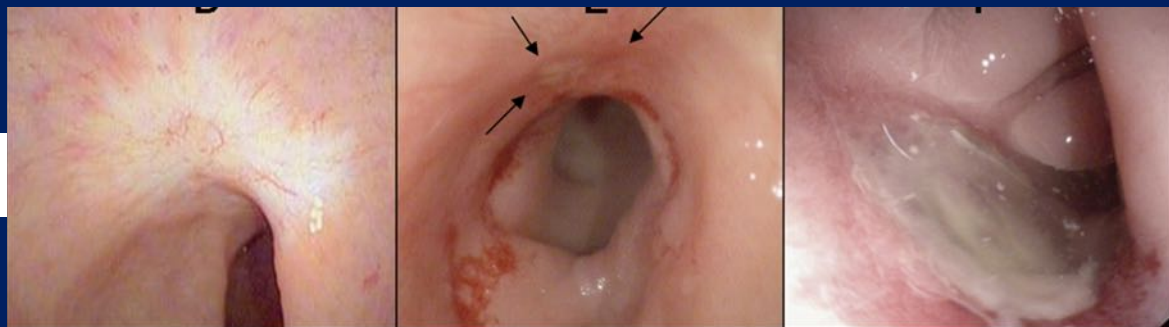
Pre-CRT



Post-CRT

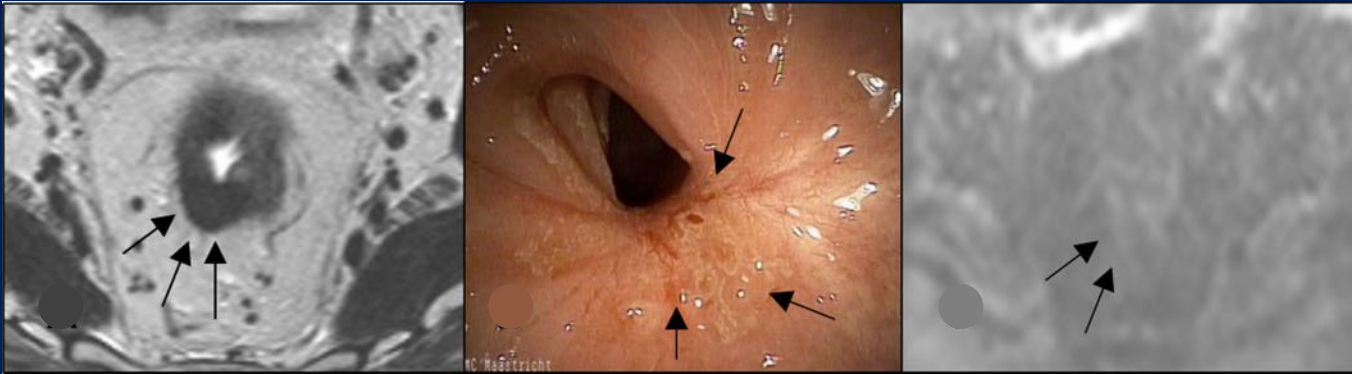


Endoscopy



# Assessment of Clinical Complete Response After Chemoradiation for Rectal Cancer with Digital Rectal Examination, Endoscopy, and MRI: Selection for Organ-Saving Treatment

Monique Maas et al Ann Surg Oncol (2015) 22:3873–3880

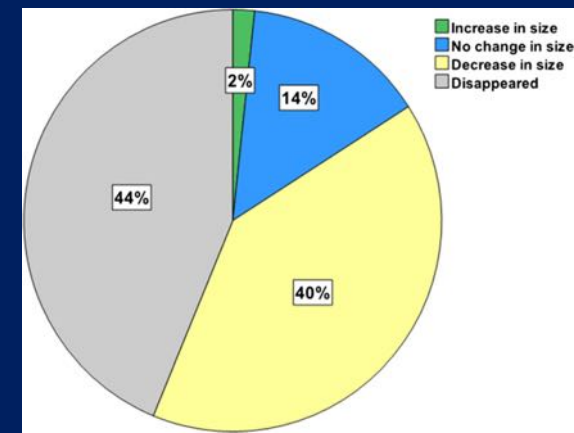


- When all three modalities were combined, the post-test probability for a CR was 98 %, indicating that when all three modalities predict a CR, this is correct in **98%** of the cases, with only a **2%** risk of missing residual tumor.
- When all three modalities indicate residual tumor, there still is a **15%** chance for a CR.
- The combination of the two (clinical assessment and MRI) can be recommended as a strategy for a safe and accurate selection of CR after CRT.

## Nodal staging in rectal cancer: why is restaging after chemoradiation more accurate than primary nodal staging?

Luc A. Heijnen Int J Colorectal Dis (2016) 31:1157–1162

- After CRT a **decrease in size** of at least 70% indicates ypN0 status in 100 % of the cases
- Accuracy, and mainly sensitivity, increases in the restaging setting compared to primary staging with the highest accuracy obtained at a **size cutoff of 2.5 mm** (sensitivity of 75% and a specificity of 64%).



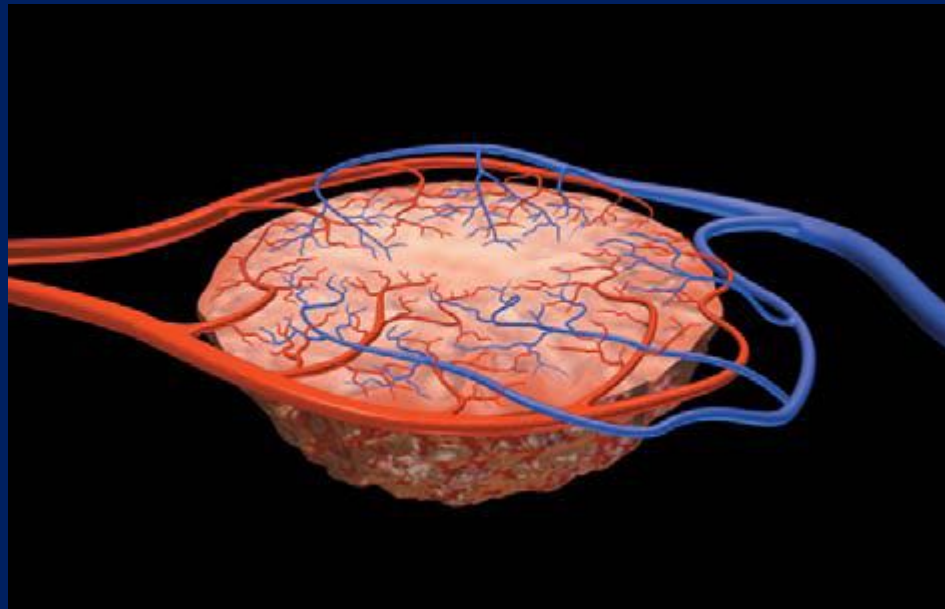


# Magnetic Resonance Imaging and Other Imaging Modalities in Diagnostic and Tumor Response Evaluation.

Doenja M.J.Lambregts,MD,PhD,\* Monique Maas,MD,PhD et al - Semin RadiatOncol26:193-198 C 2016 \*

- **Functional imaging is emerging** as a valuable contributor to the clinical management of patients with rectal cancer. Techniques such as **diffusion-weighted magnetic resonance imaging, perfusion imaging**, and positron emission tomography can offer meaningful insights into tissue architecture, vascularity, and metabolism.
- Moreover, **new techniques targeting** other aspects of tumor biology are now being developed and studied.

→  
Arterial inlet



→  
Venous outlet

Tumor angiogenesis is associated with chaotic vessel formation and incompetent arteriovenous shunts.....

Dynamic contrast-enhanced MR imaging is a noninvasive technique that helps characterize the microvasculature, thereby providing markers specific to perfusion, permeability of blood vessels, and the volume of extracellular space.

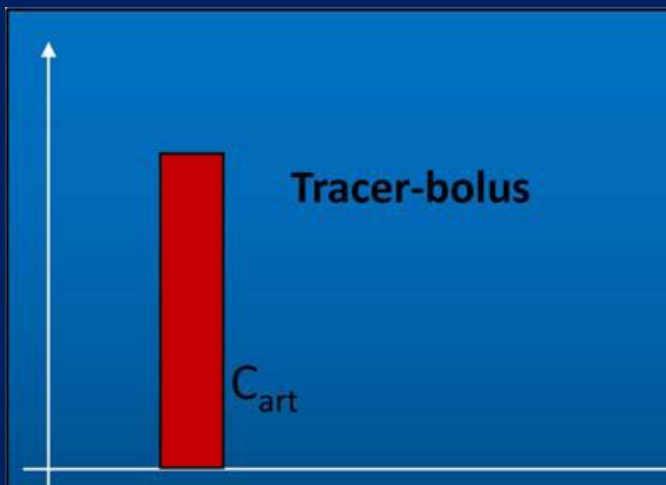
Review Article

Perfusion Imaging

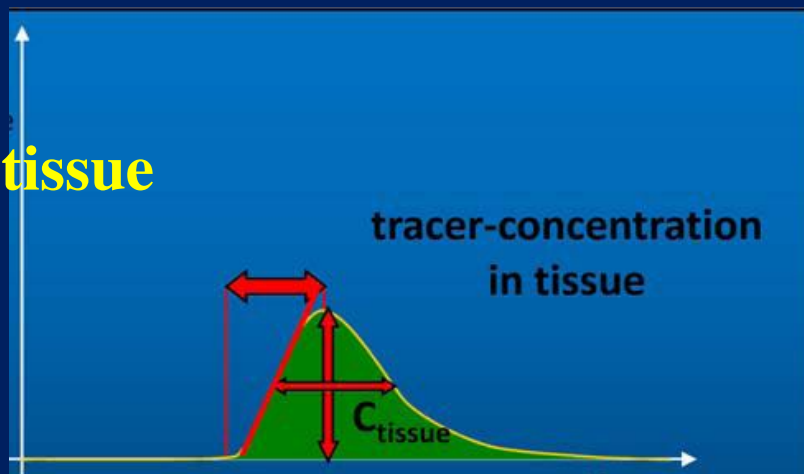
Matthias Günther PhD<sup>1,2,3,\*</sup>

Journal of Magnetic  
Resonance Imaging

Volume 40, Issue 2, pages  
269–279, August 2014



$C_{tissue}$



time t

$$\frac{C_{tissue}}{C_{art}} = \text{blood volume}$$

amplitude  $\sim$  perfusion

width = mean transit time (MTT)

Central volume theorem:

MTT = blood volume / perfusion

Time to peak (TTP) after deconvolution

slope

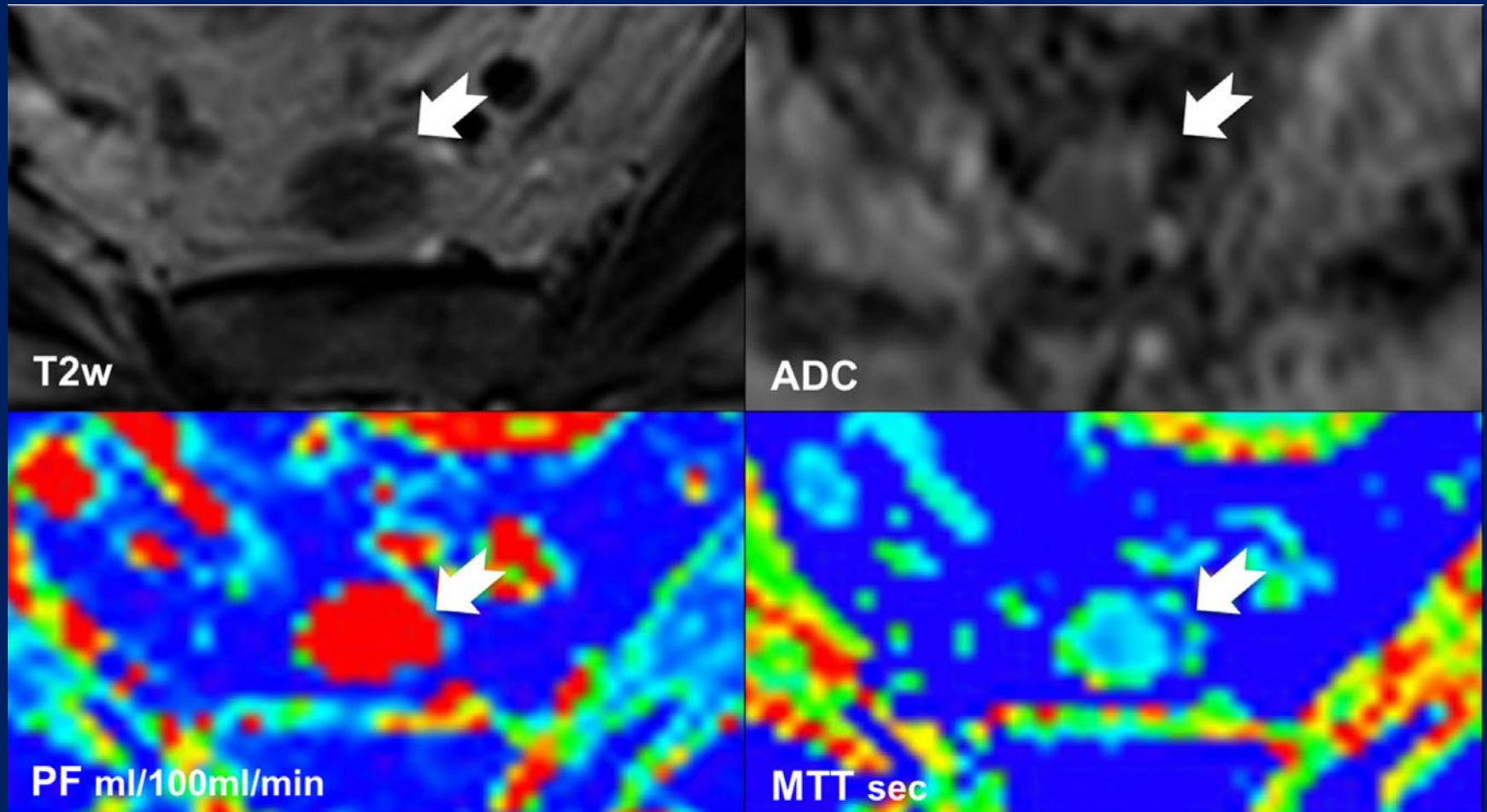
after deconvolution

Original Research

Dynamic contrast-enhanced MRI to evaluate the therapeutic response to neoadjuvant chemoradiation therapy in locally advanced rectal cancer

Seung Ho Kim MD<sup>1</sup>, Jeong Min Lee MD<sup>2,\*</sup>,  
Sandeep N. Gupta PhD<sup>3</sup>, Joon Koo Han  
MD<sup>2</sup> and Byung Ihn Choi MD<sup>2</sup>

Volume 40, Issue 3, pages 730–737, September 2014





Review Article

## Perfusion Imaging

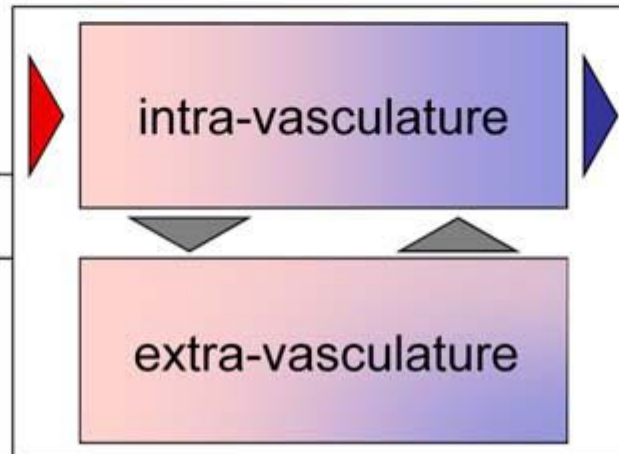
Matthias Günther PhD<sup>1,2,3,\*</sup>

Journal of Magnetic  
Resonance Imaging

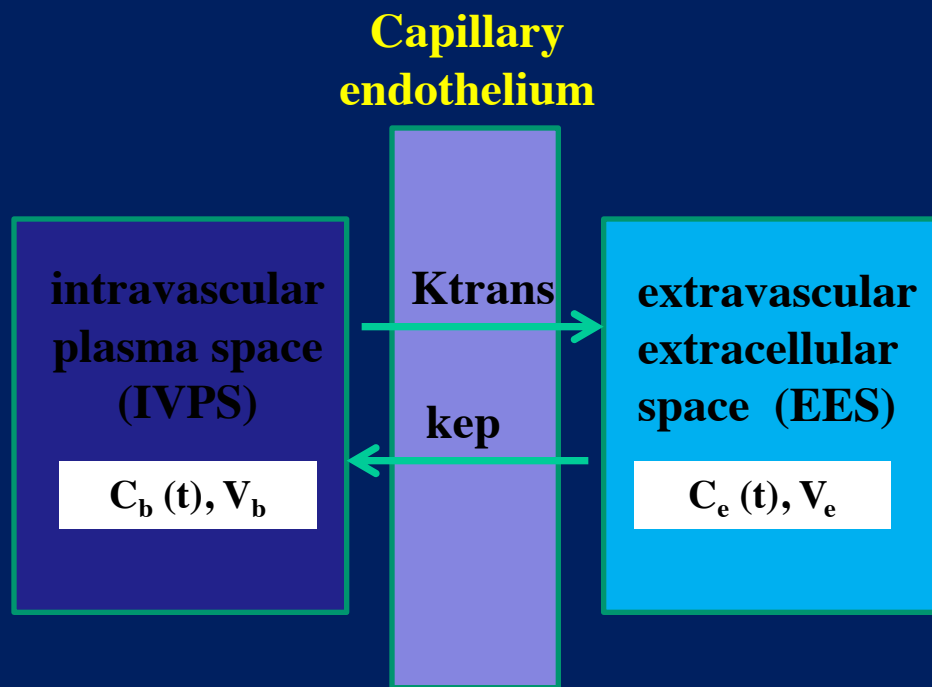
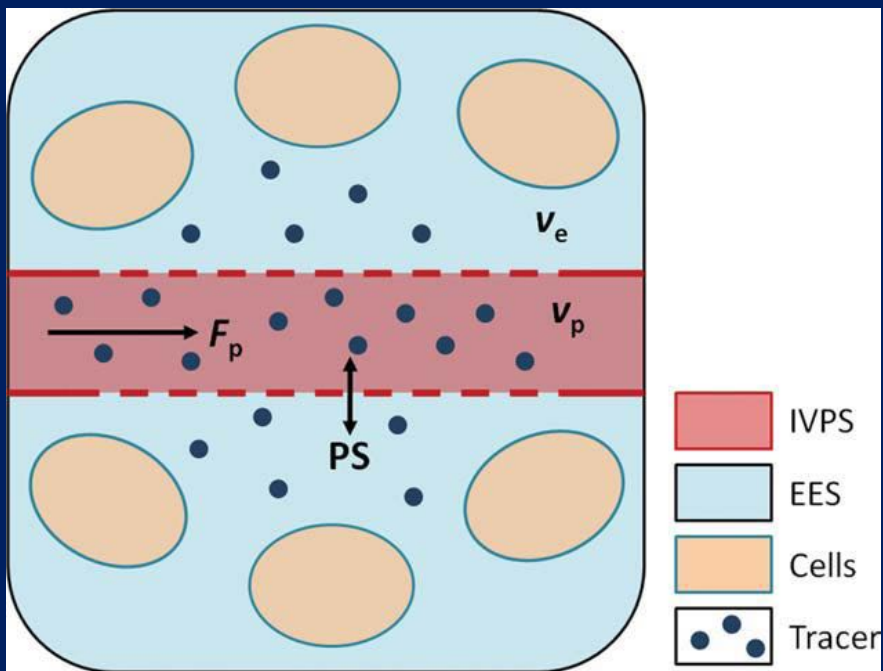
Volume 40, Issue 2, pages  
269–279, August 2014

### two-compartment model

arterial inflow  $f$



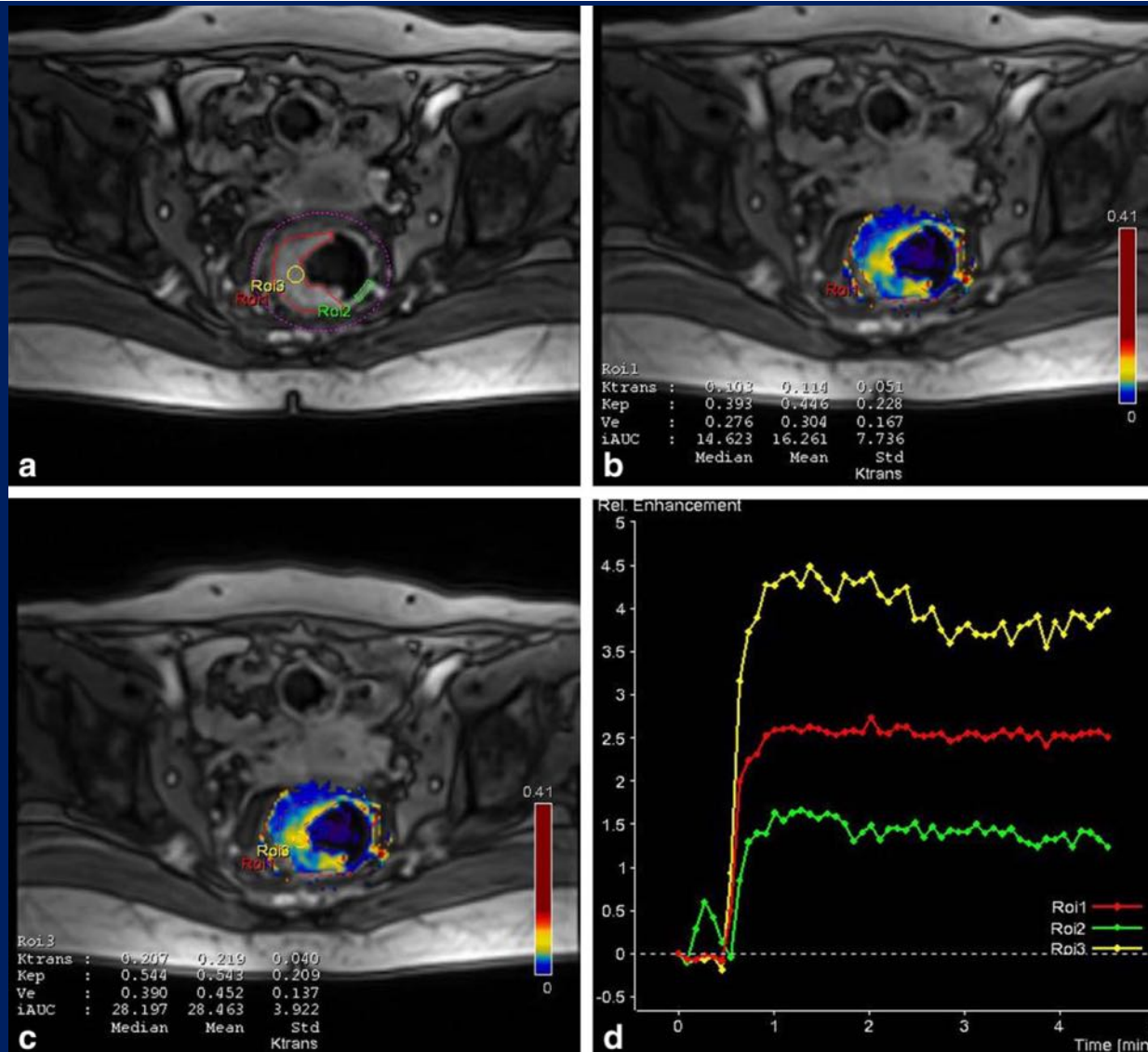
venous outflow  $f/\lambda$



Original Research

## Correlation of dynamic contrast-enhanced MRI perfusion parameters with angiogenesis and biologic aggressiveness of rectal cancer: Preliminary results

Dong-Myung Yeo MD<sup>1</sup>, Soon Nam Oh MD<sup>1,2</sup>, Chan-Kwon Jung MD<sup>2</sup>, Myung Ah Lee MD<sup>3</sup>, Seong Taek Oh MD<sup>4</sup>, Sung Eun Rha MD<sup>1</sup>, Seung Eun Jung MD<sup>1</sup>, Jae Young Byun MD<sup>1</sup>, Peter Gall PhD<sup>5</sup> and Yohan Son PhD<sup>6</sup>





Can perfusion MRI predict response to preoperative treatment in rectal cancer?

Martens MH, Subhani S, Heijnen LA, et al. - Radiother Oncol 2015;114(2):218e223

GASTROINTESTINAL

**Dynamic contrast enhanced-MRI for the detection of pathological complete response to neoadjuvant chemotherapy for locally advanced rectal cancer**

Gollub MJ, Gultekin DH, Akin O, et al.. Eur Radiol 2012;22(4):821e831.

European  
Radiology

JMRI

Journal of Magnetic Resonance Imaging

**Dynamic contrast-enhanced MRI: Use in predicting pathological complete response to neoadjuvant chemoradiation in locally advanced rectal cancer**

Tong T, Sun Y, GollubMJ, et al - J Magn Reson Imaging 42:376-680, 2015

JMRI

Journal of Magnetic Resonance Imaging

**Dynamic contrast enhanced MR imaging for rectal cancer response assessment after neoadjuvant chemoradiation**

Intven M, Reerink O, Philippens ME - J Magn Reson Imaging 41:1646-1653, 2015



# Rectal Cancer Magnetic Resonance Imaging: Imaging Beyond Morphology

D. Prezzi \*y, V. Goh - Clinical Oncology 28 (2016)



- Introduces the concept of an integrated, multi-modality and **multi-sequence quantitative imaging approach (multiparametric)**, made practicable in rectal cancer by recent technological advances



## Magnetization transfer imaging to assess tumour response after chemoradiotherapy in rectal cancer

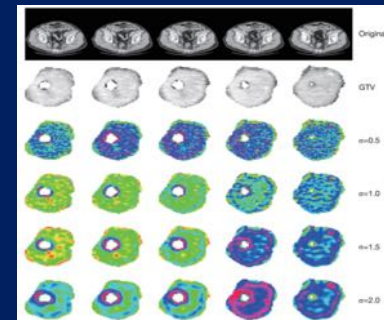
Milou H Martens<sup>1,2,3</sup> & Doenja M. J. Lambregts<sup>1</sup> & Nickolas Papanikolaou<sup>4</sup> & al - Eur Radiol (2016) 26:390–397

- Single-slice magnetization transfer (MT) imaging has shown promising results for evaluating post radiation fibrosis

## Radiomics for rectal cancer

Nicola Dinapoli<sup>1</sup>, Calogero Casà<sup>1</sup>, Brunella Barbaro<sup>2</sup>, Giuditta Valentina Chiloiro<sup>1</sup>, Andrea Damiani<sup>1</sup>, Marialuisa Di Matteo<sup>2</sup>, Alessandra Farchione<sup>2</sup>, Maria Antonietta Gambacorta<sup>1</sup>, Roberto Gatta<sup>1</sup>, Vito Lanzotti<sup>1</sup>, Carlotta Masciocchi<sup>1</sup>, Vincenzo Valentini<sup>1</sup>

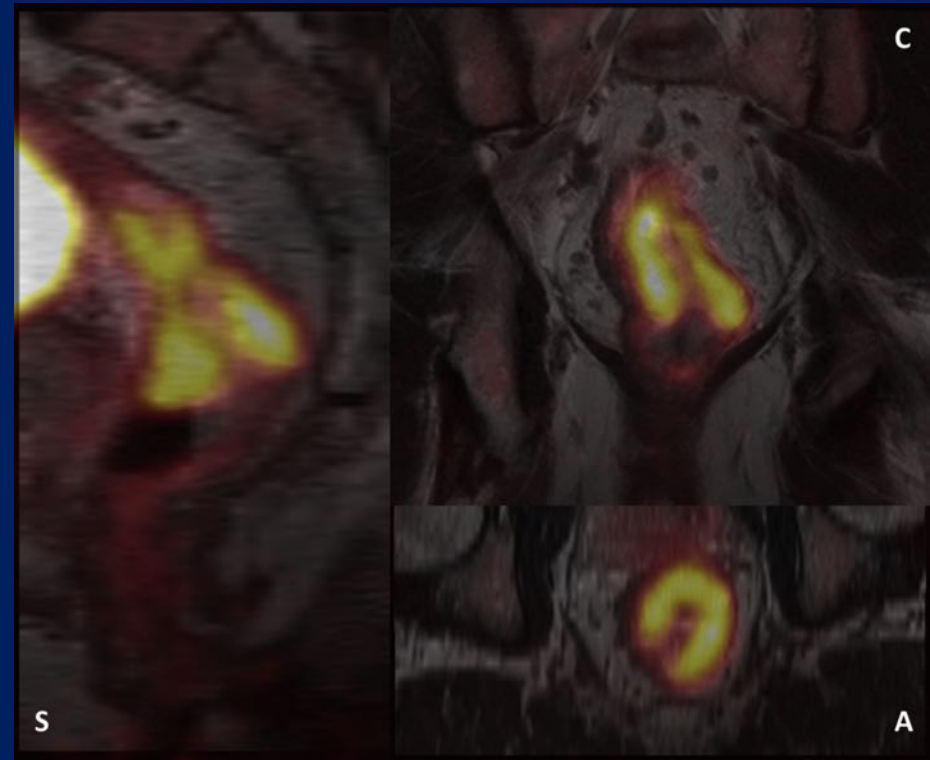
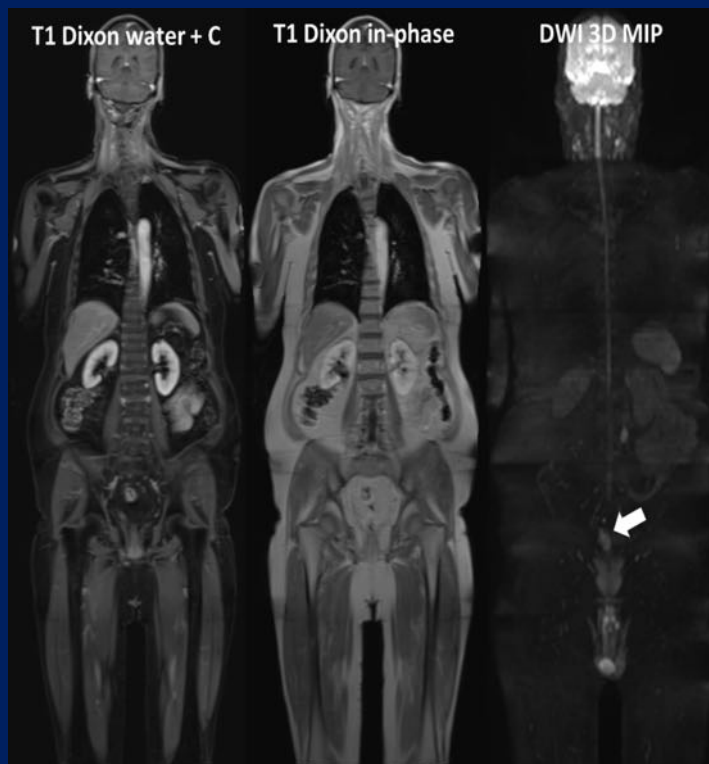
Translational Cancer Research, Vol 5, No 4 August 2016



# Multi-modality Assessment: the Next Step?

Comparison of hybrid FDG PET/MRI compared with PET/CT in colorectal cancer staging and restaging: a pilot study

Paspulati RM, Partovi S, Herrmann KA et al - *Abdom Imaging* 2015; 40(6):1415e1425.





# Future directions



As MR techniques continue to advance, quantification of acquired MR data enables us

**to combine**

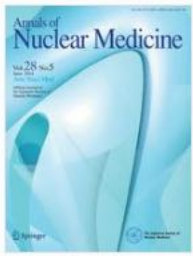
*the morphological information on the tumor*

*with functional information*

The challenge is whether these new MR techniques will be able

**to solve the problem**





## $^{18}\text{F}$ -FDG PET predicts pathological response to preoperative chemoradiotherapy in patients with primary rectal cancer: a meta-analysis

Li C, Lan X, Yuan H, et al: Ann Nucl Med 28:436-446, 2014 33.

IJC

International Journal of Cancer

## $^{18}\text{F}$ -FDG-PET evaluation of treatment response to neo-adjuvant therapy in patients with locally advanced rectal cancer: A meta-analysis

Zhang C, Tong J, Sun X, et al - Int J Cancer 131:2604-2611, 2012

- SUV after treatment and response index in differentiating between good and poor responding tumors after CRT with a pooled sensitivity ranging from 74%-78% and a pooled specificity between 64%-67%.
- In a subgroup analysis, the specificity was relatively low (59%-61%) for the specific identification of patients with a complete tumor response.
- PET offered better results in predicting response early during treatment (sensitivity 82%-86% and specificity 78%-80%)

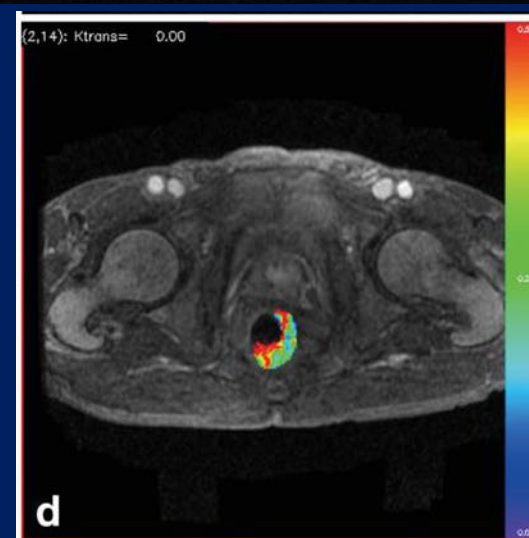
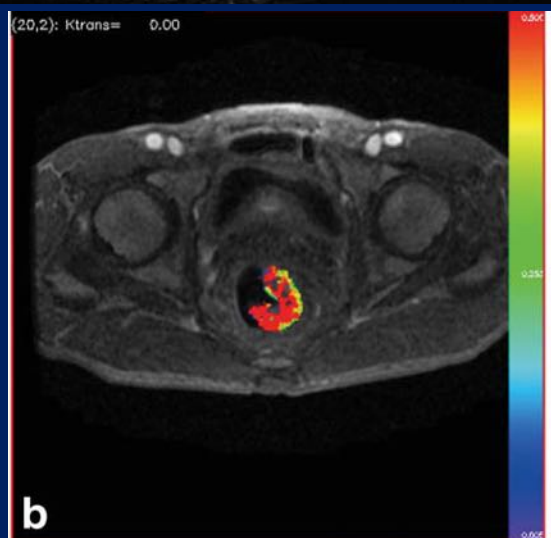
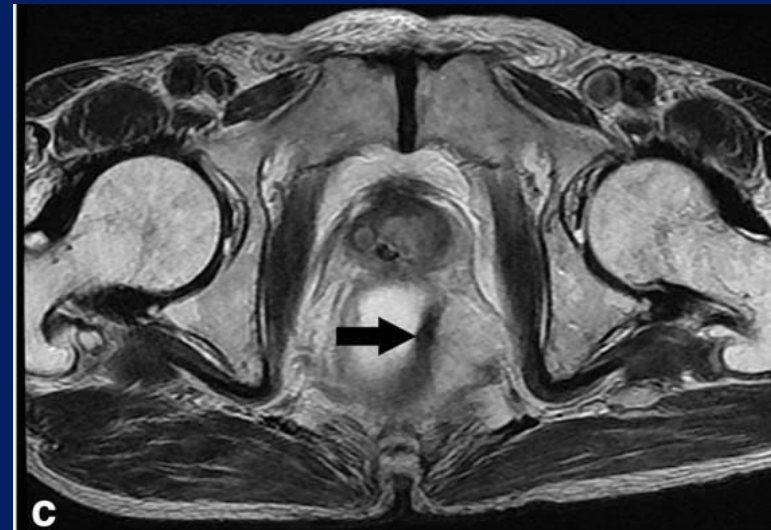
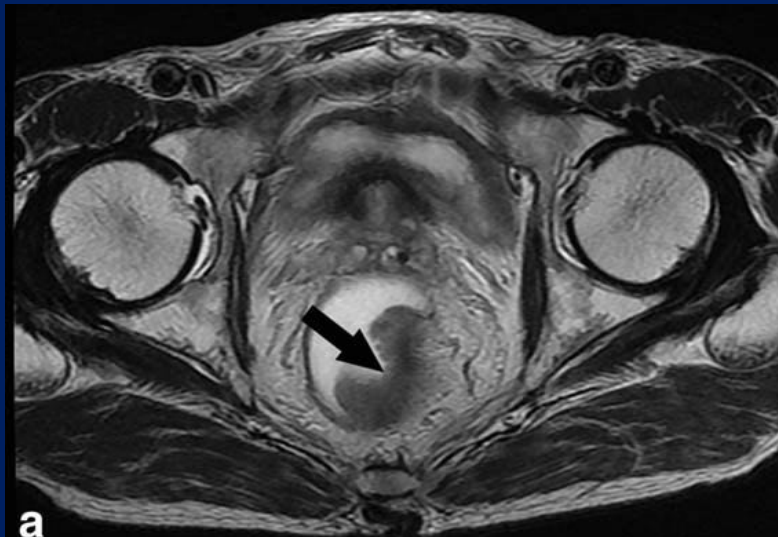


Original Research

Dynamic contrast-enhanced MRI to evaluate the therapeutic response to neoadjuvant chemoradiation therapy in locally advanced rectal cancer

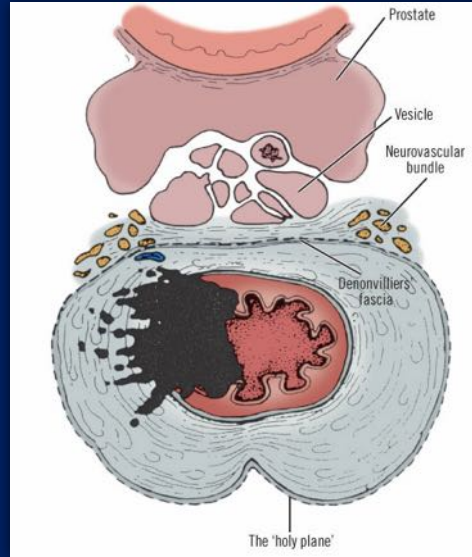
Seung Ho Kim MD<sup>1</sup>, Jeong Min Lee MD<sup>2,1</sup>,  
Sandeep N. Gupta PhD<sup>3</sup>, Joon Koo Han  
MD<sup>2</sup> and Byung Ihn Choi MD<sup>2</sup>

Volume 40, Issue 3, pages 730–737, September 2014



# Ristadiazione

**Goal**



**IORT**

