

Diffusion-weighted MR (DW-MRI) imaging as an early predictor of pathologic tumor response to preoperative chemo-radiotherapy in patients with locally advanced rectal cancer: a study proposal

E.Pelle¹, F. Arcadipane¹, M.Levis¹, A. Ruggieri¹, N.Rondi¹,
F.Munoz¹, U.Ricardi¹

¹SCDU di Radioterapia, Università degli Studi di Torino,
ASO San Giovanni Battista - Molinette di Torino



II° CONGRESSO
Gruppo Interregionale
AIRO Piemonte-Liguria
Valle d'Aosta

“Aspetti clinici e tecnici
della radioterapia nei
tumori del colon-retto”

8 ottobre 2011

Castello di Grinzane Cavour

Con il patrocinio



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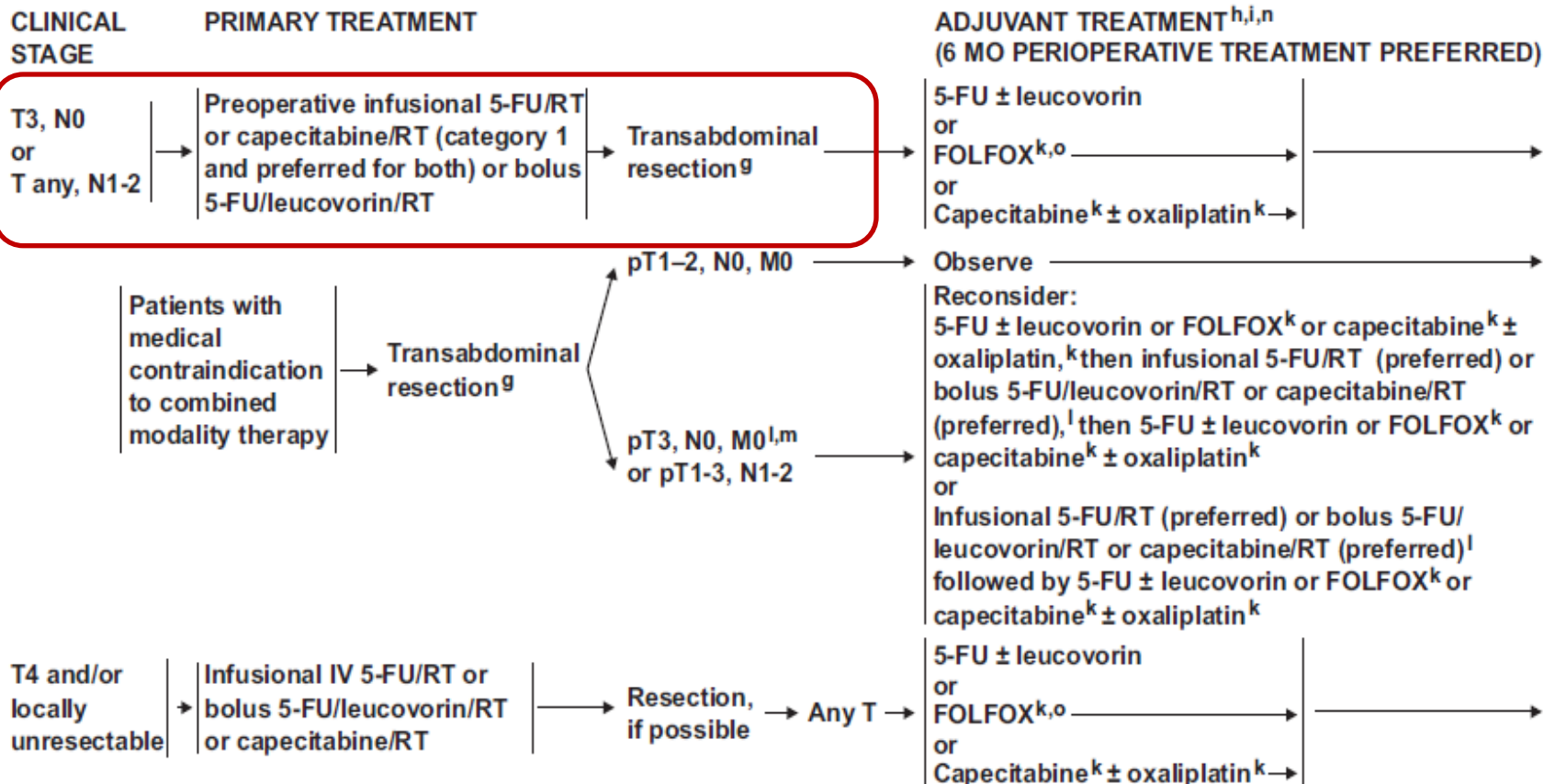


LILT
LEGA ITALIANA PER LA
LUTTA CONTRO I TUMORI
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**CLINICAL
PRESENTATION^a**

WORKUP

CLINICAL STAGE

Rectal cancer
appropriate
for resection

- Biopsy
- Pathology review
- Colonoscopy
- Rigid proctoscopy
- Chest/abdominal/pelvic CT
- CEA
- Endorectal ultrasound or pelvic MRI
- Enterostomal therapist as indicated for preoperative marking of site, teaching
- PET-CT scan is not routinely indicated

T1-2, N0

[See Primary Treatment \(REC-3\)](#)

T3, N0
or
T any, N1-2

[See Primary Treatment \(REC-4\)](#)

T4 and/or locally
unresectable

[See Primary Treatment \(REC-4\)](#)

T any, N any, M1
Resectable
metastases

[See Primary Treatment \(REC-5\)](#)

T any, N any, M1
Unresectable
metastases or
medically inoperable

[See Primary Treatment \(REC-6\)](#)



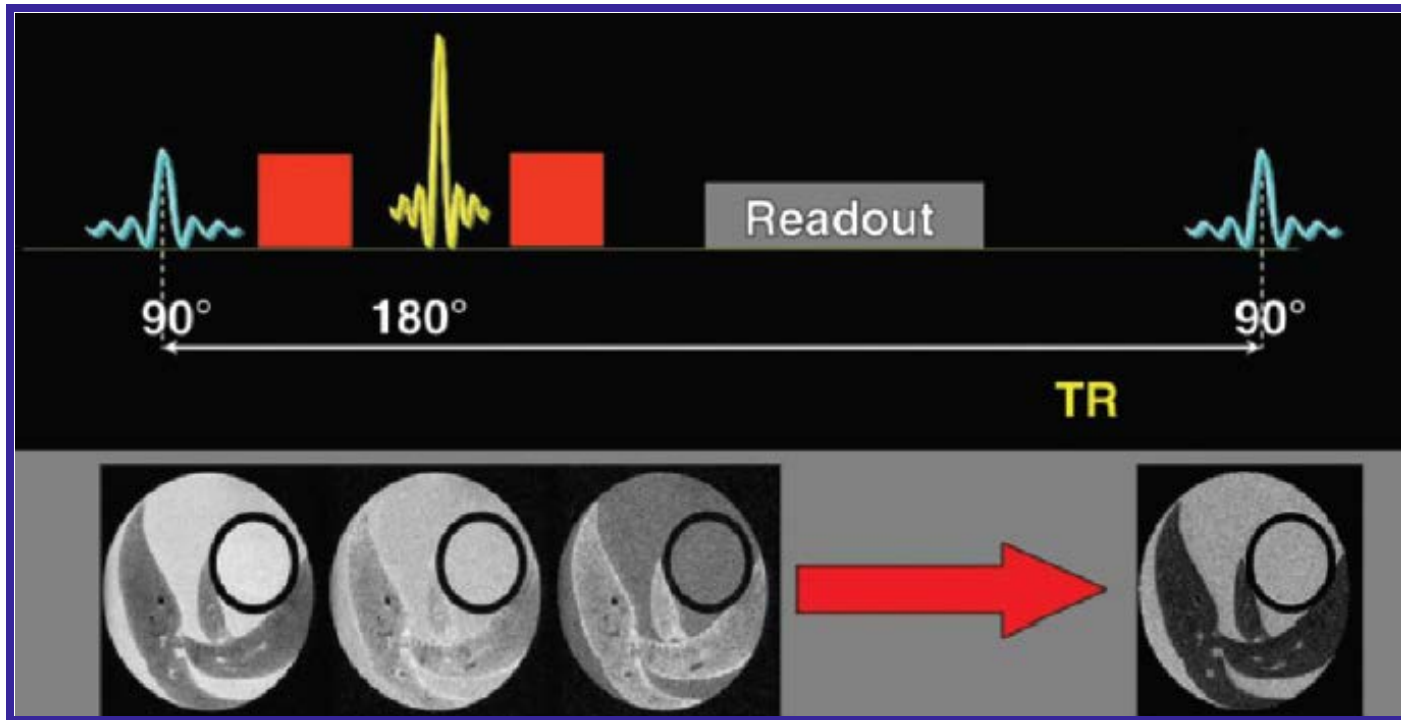
The use of FDG-PET/CT and diffusion-weighted magnetic resonance imaging for response prediction before, during and after preoperative chemoradiotherapy for rectal cancer

MAARTEN LAMBRECHT¹, CHRISTOPHE DEROOSE², SARAH ROELS¹,
VINCENT VANDECAVEYE³, FREDDY PENNINCKX⁴, XAVIER SAGAERT⁵,
ERIC VAN CUTSEM⁶, FREDERIK DE KEYZER³ & KARIN HAUSTERMANS¹

In rectal cancer two imaging techniques show great promise for response prediction during and after preoperative treatment as **18F-FDG PET-CT** and **Diffusion-Weighted MRI (DW-MRI)**

The ability of DW-MRI to differentiate with high specificity persistent tumor after therapy from radio-induced inflammation or necrosis makes it potentially useful

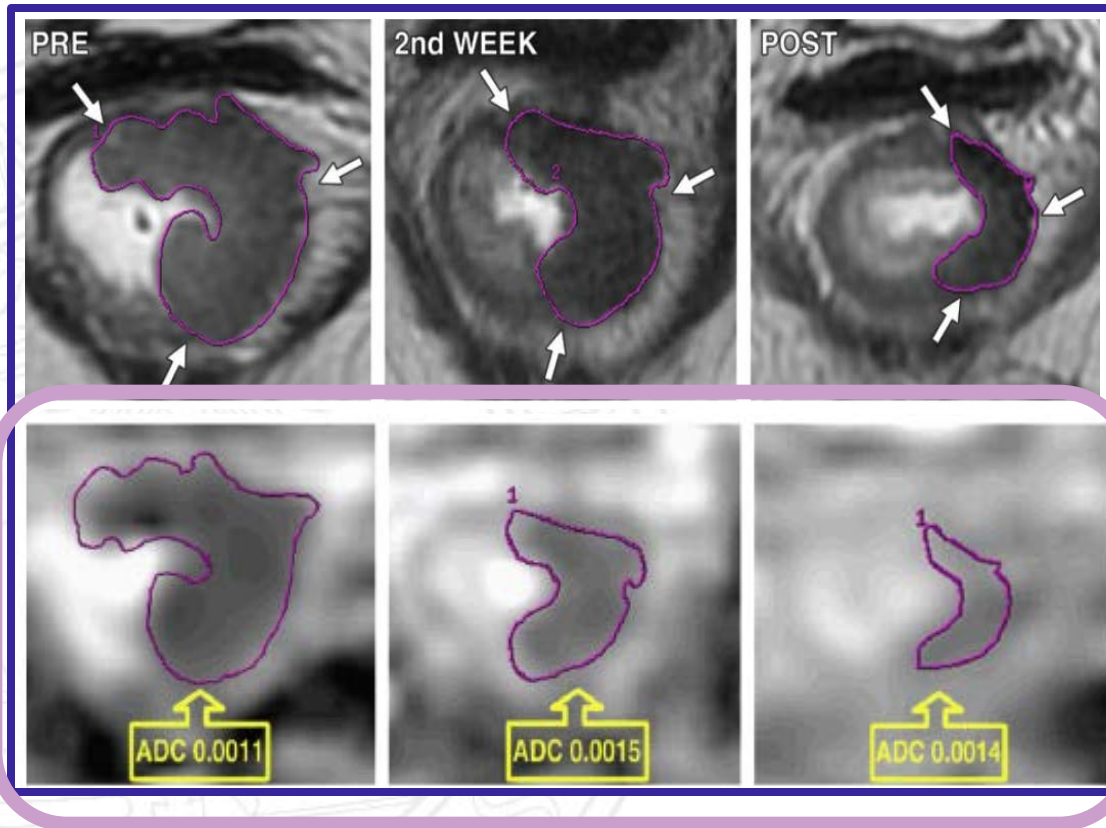




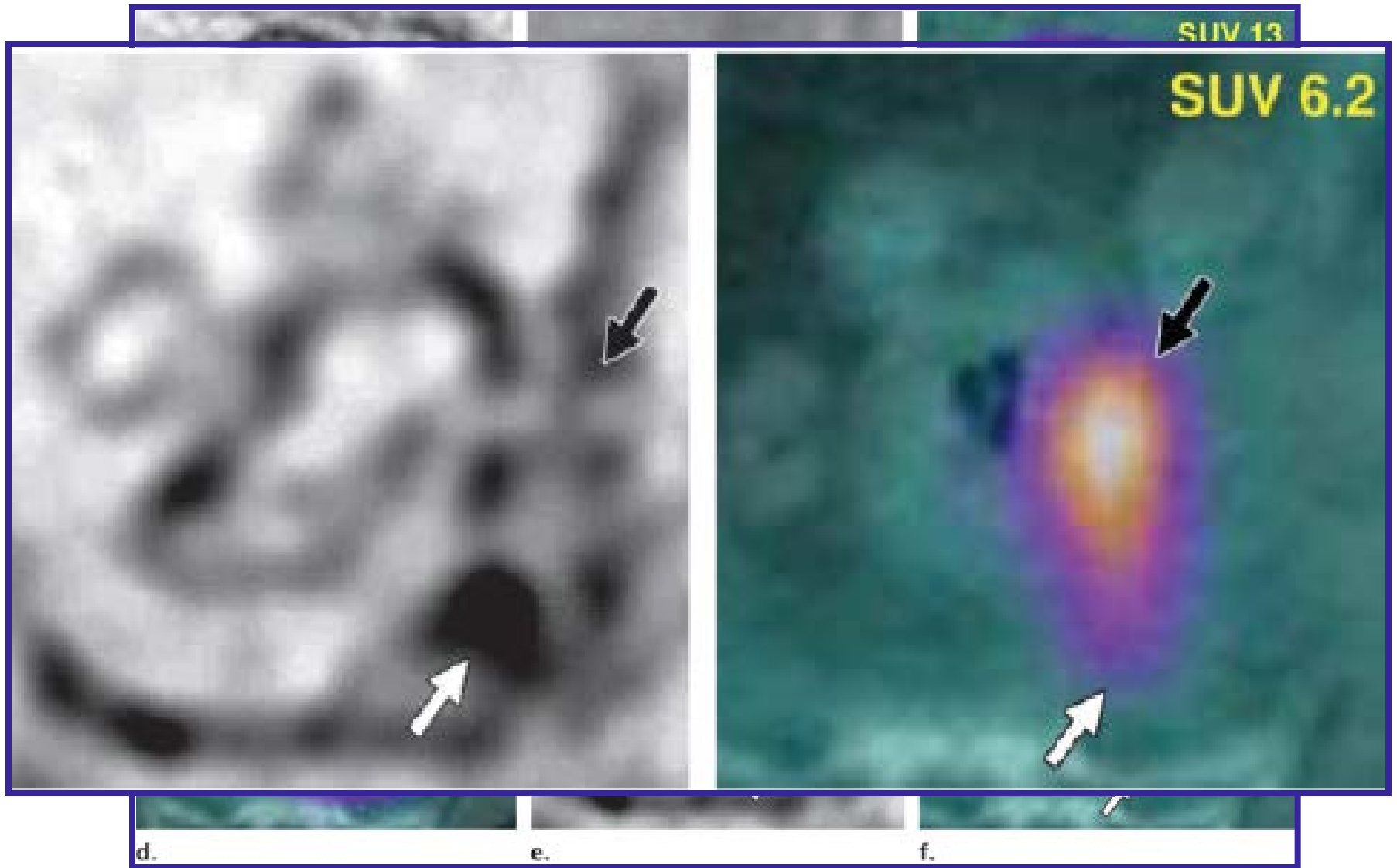
DW-MRI derives its image contrast from differences in the motion of water molecules in various tissues
 The grade of restriction to water diffusion in biologic tissue is inversely correlated with cellular density. With this technique a grayscale map based on a value called **apparent diffusion coefficient (ADC)** is generated

The pretreatment ADC-value correlates with the degree of tumor response after CRT

Patients who respond to treatment show a lower ADC at presentation compared to non-responders, with an higher change in ADC during and after-CRT



As a tumor responds to treatment, the ADC value increases at first, but reequilibrium with ingrowth of fibrosis may occur, leading to a decrease in ADC at the end of treatment



Restaging Locally Advanced Rectal Cancer with MR Imaging after Chemoradiation Therapy
Barbaro B. *RadioGraphics* 2010; 30:699–721



Restaging Locally Advanced Rectal Cancer with MR Imaging after Chemoradiation Therapy¹

TEACHING POINTS

See last page

*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*

MR imaging is the most promising imaging modality for assessing **T stage** and **CRM**. An accurate prediction of pCR can help in the selection of patients for more optimized treatment sphincter-preserving surgery, less extensive resection, more intense RT or even delayed surgery with wait and see policy

Tumor staging is crucial for prognosis and treatment planning



Magnetic Resonance Imaging–Detected Tumor Response for Locally Advanced Rectal Cancer Predicts Survival Outcomes: MERCURY Experience

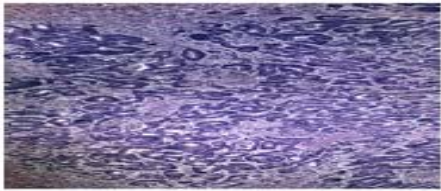
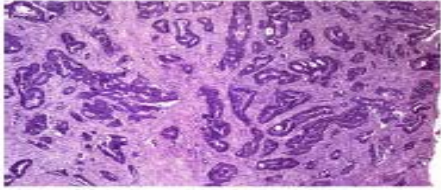
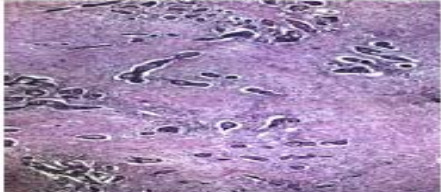
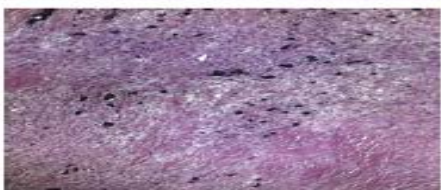
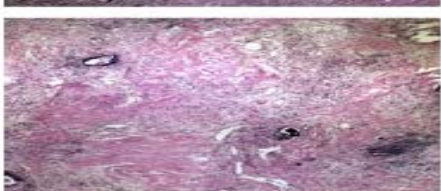
Uday B. Patel, Fiona Taylor, Lennart Blomqvist, Christopher George, Hywel Evans, Paris Tekkis, Philip Quirke, David Sebag-Montefiore, Brendan Moran, Richard Heald, Ashley Guthrie, Nicola Bees, Ian Swift, Kjell Pennert, and Gina Brown

Methods

In a prospective cohort study, 111 patients who had rectal cancer treated by neoadjuvant therapy were assessed for response by MRI and pathology staging by T, N and CRM status. Tumor regression grade (TRG) was also assessed by MRI. Overall survival (OS) was estimated by using the Kaplan-Meier product-limit method, and Cox proportional hazards models were used to determine associations between staging of good and poor responders on MRI or pathology and survival outcomes after controlling for patient characteristics

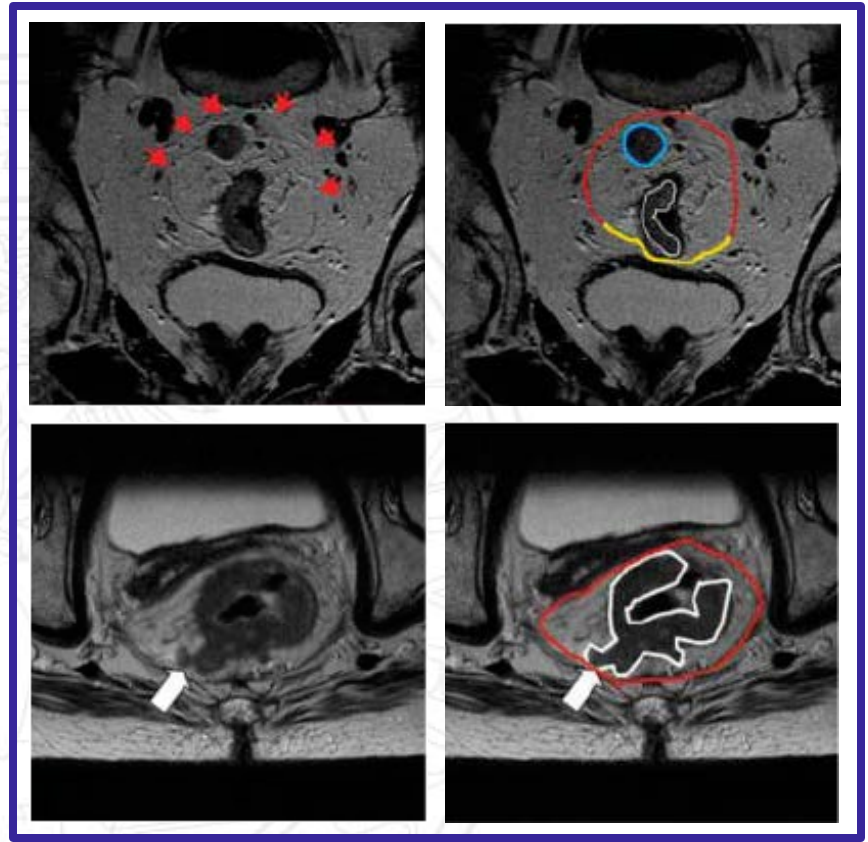


A pathologic response to CRT depends on amount of residual viable tumor versus amount of fibrous or fibroinflammatory tissue within the gross tumor (**Tumor Regression Grade – Dworak**)

	Grad 0 No Regression	No Regression
	Grad 1 Regression <25%	Predominantly tumor cells, amongst radiogenic transformed tissue
	Grad 2 Regression 25-50%	Predominantly fibrotic tissue, simply detectable tumor cell nests
	Grad 3 Regression >50%	Tumor cells isolated and microscopically hard to detect. Predominantly fibrotic tissue
	Grad 4 Complete Regression	No tumor cells, only fibrotic tissue



The MRI accuracy for predicting the circumferential resection margin status pre or post-CRT, before surgery, demonstrate to be equivalent to histopathologic assessment



Conclusion: MRI assessment of TRG and CRM predict survival outcomes for good and poor responders and offer additional treatment options before planning definitive surgery. Postoperative histopathology assessment of ypT and CRM but not post-treatment N status were important postsurgical predictors of outcome



AIM OF THE STUDY

To develop an accurate model to predict pathologic complete response in rectal cancer patients for more individualized treatment approaches in the future



METHODS

Inclusion Criteria

- ✓ Age 18-75 years with PS 0 or 1
- ✓ Biopsy-proven adenocarcinoma rectal cancer
- ✓ T3 N0 or any T N1-2, M0
- ✓ Patients undergoing preoperative CT-RT

Exclusion Criteria

- ✓ History of cancer
- ✓ Contraindications to MRI
- ✓ Primary surgery



METHODS

Extent of disease

- clinical examination
- colonoscopy + biopsy
- thorax abdomen and pelvis CT
- endorectal ultrasonography
- **DW-MRI**



METHODS

DW-MRI:

- ✓ **Pre-CRT**
- ✓ **Post-CRT after 4 weeks**

DW-MRI post-chemoradiotherapy assess TN stage,
Circumferential Resection Margin status, Tumor
regression grade and ADC maps



METHODS

Preoperative radiotherapy

Volumetric Modulated Arc Therapy

50 Gy/25 fr/2 Gy SIB with 45 Gy/25fr/1,8 Gy to pelvis lymph nodes

Preoperative chemotherapy

Capecitabine 1000 mg/m² administered orally twice daily at 1°,2°,4°,5° week of radiotherapy

Surgery

Standard TME plane surgery or **extended TME** with or without sphincter preservation 4-6 weeks after completing neoadjuvant CRT



STATISTICAL ANALYSIS

Study population characteristics

50 patients

Age

Sex

WHO performance status

Distance to anal verge

Tumor stage

Tumor differentiation

Type of surgery

Methods for assessing response following oncologic therapies include reduction of tumor size (**TRG**) and **ADC value trend**.





CONCLUSIONS

- The **TIMING of presurgical DW-MRI** is an important discussion point because tissues challenges can compromise the results.
- It would be interesting to perform **DW-RMI during CRT** in order to eventually modify radiotherapy treatment planning (*dose escalation for good responders*).
- Additional research needed to evaluate if **the combination of 18FDG-PET/CT and DW-MRI** can increase the specificity of the response assessment during and after CRT.



Thank you!

