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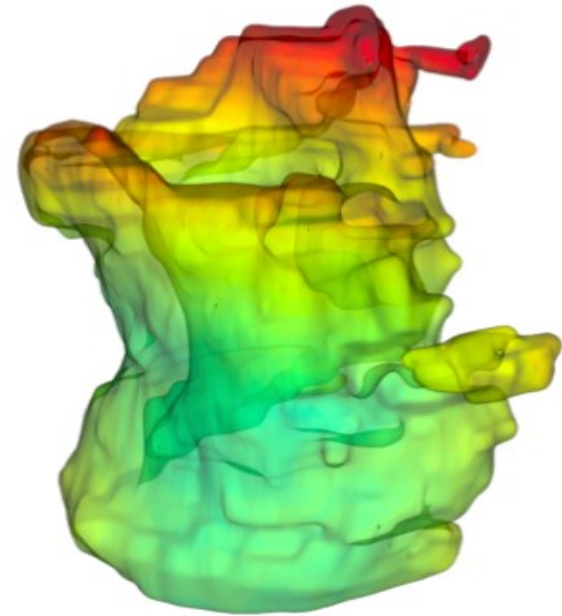
Gemelli



Fondazione Policlinico Universitario Agostino Gemelli IRCCS  
Università Cattolica del Sacro Cuore

*Dr. Angela Romano, MD*

## Theragnostic Utilities for Neoplastic DisEases of the Rectum by MRI guided radiotherapy. The THUNDER-2 study



# Working Group

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**Neoadjuvant radiochemotherapy** followed by **total mesorectal excision (TME)** is the standard treatment modality in locally advanced rectal cancer

**11-45% pCR**

**pCR → better survival outcomes**

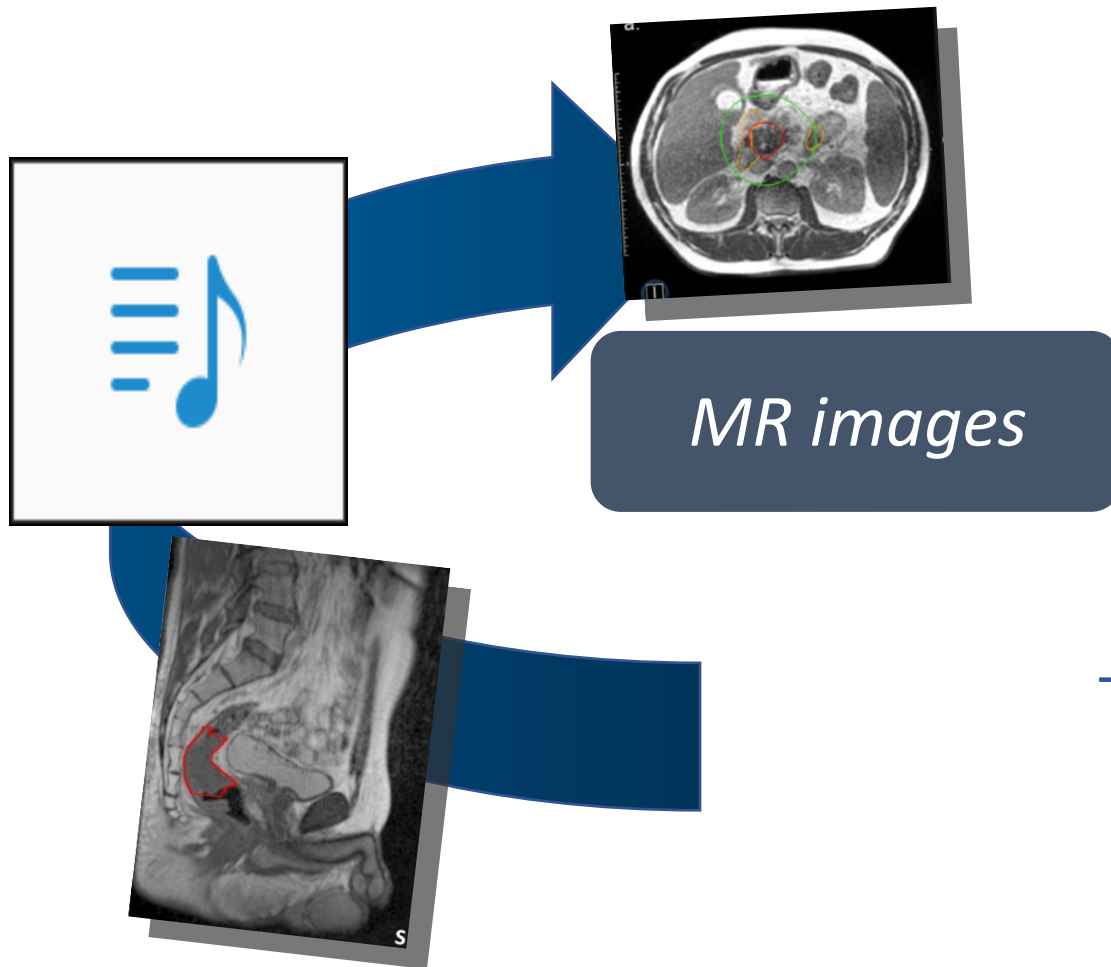


## Background



Magnetic resonance-guided radiotherapy (**MRIGRT**) is an **innovative technology** that the Fondazione Policlinico Gemelli was the first centre in Italy to adopt in 2017.

## Background



### Why MR images?

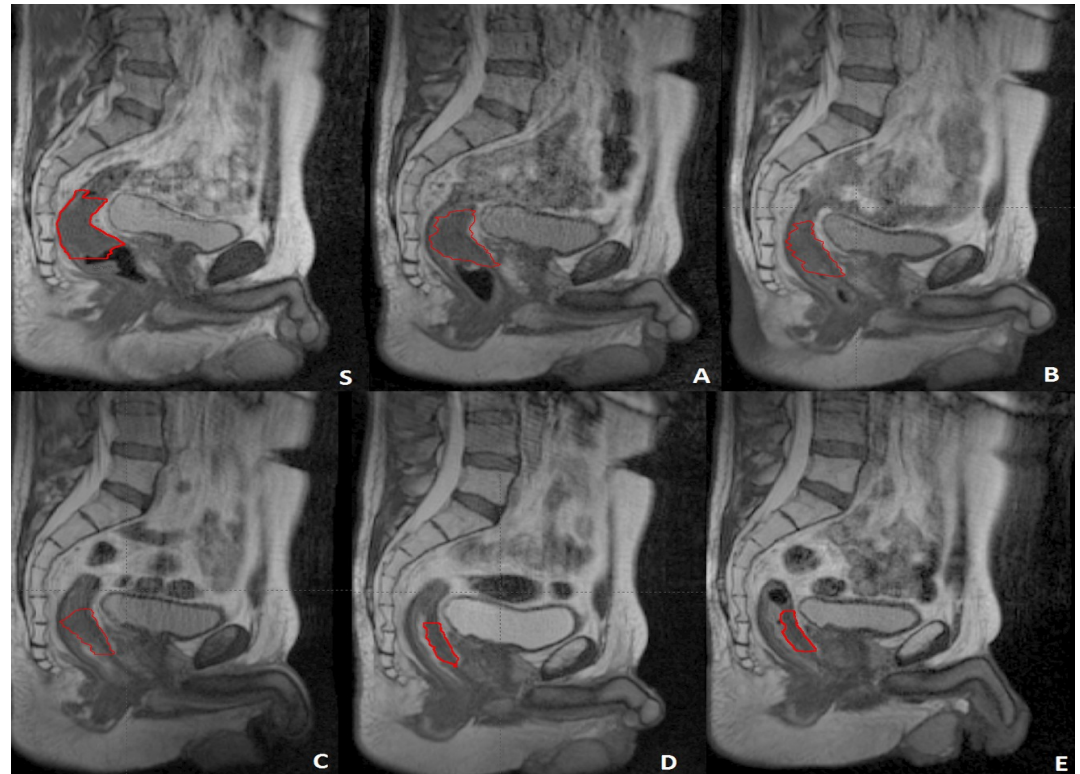
- To see better
- To gate better
- To adapt better



Treatment personalization

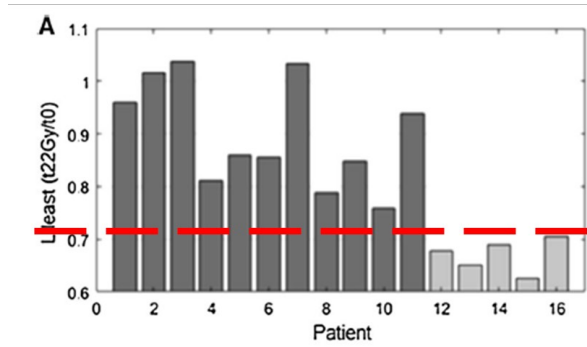
## MRgRT Delta Radiomics

- 16 patients, Long Course MRI-guided Radiochemotherapy
- 6 MRI per patient acquired @ 0.35T (T2\*/T1 weighted)
- Statistical, morphological and textural features
- Clinical Complete Response Prediction

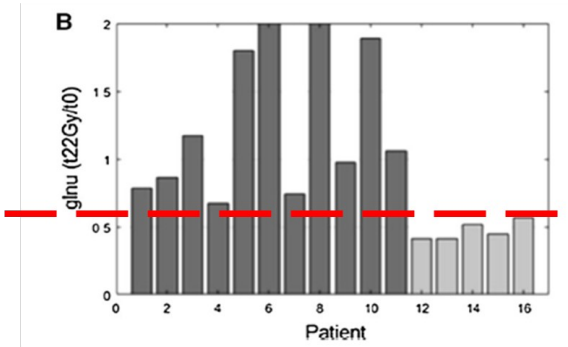




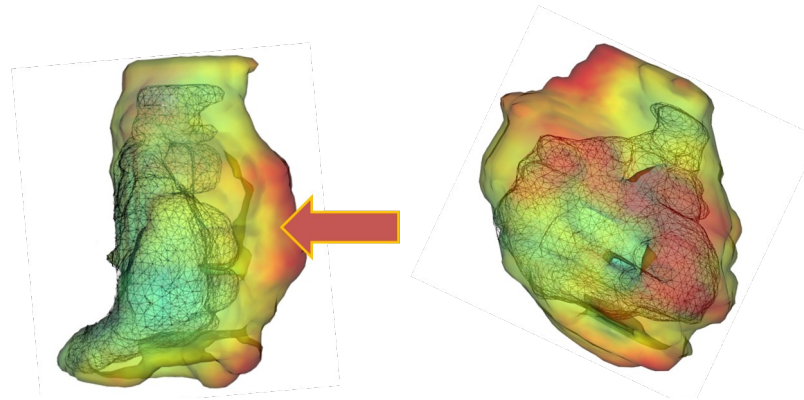
# MRgRT Delta Radiomics



**Δ Length least (W2)**



**Δ Gray level non uniformity (W2)**



**Responder**

**Not-responder**



ELSEVIER

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Radiotherapy and Oncology

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Original article

A TCP-based early regression index predicts the pathological response in neo-adjuvant radio-chemotherapy of rectal cancer

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$$\mathbf{ERI} = -\ln \left[ \mathbf{1} - \left( \frac{\mathbf{V}_{\text{mid}}}{\mathbf{V}_{\text{pre}}} \right)^{\mathbf{V}_{\text{pre}}} \right]$$

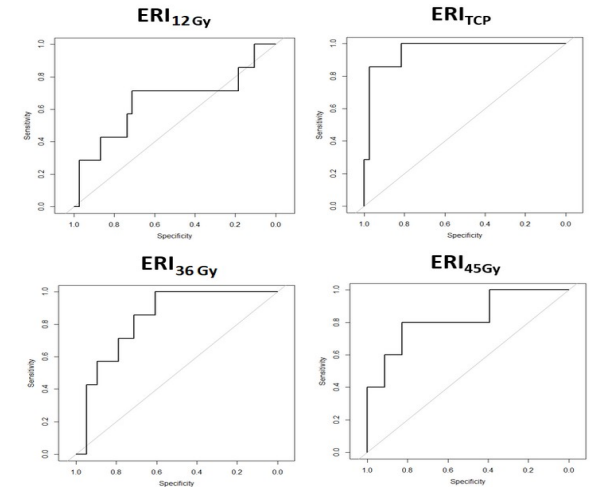
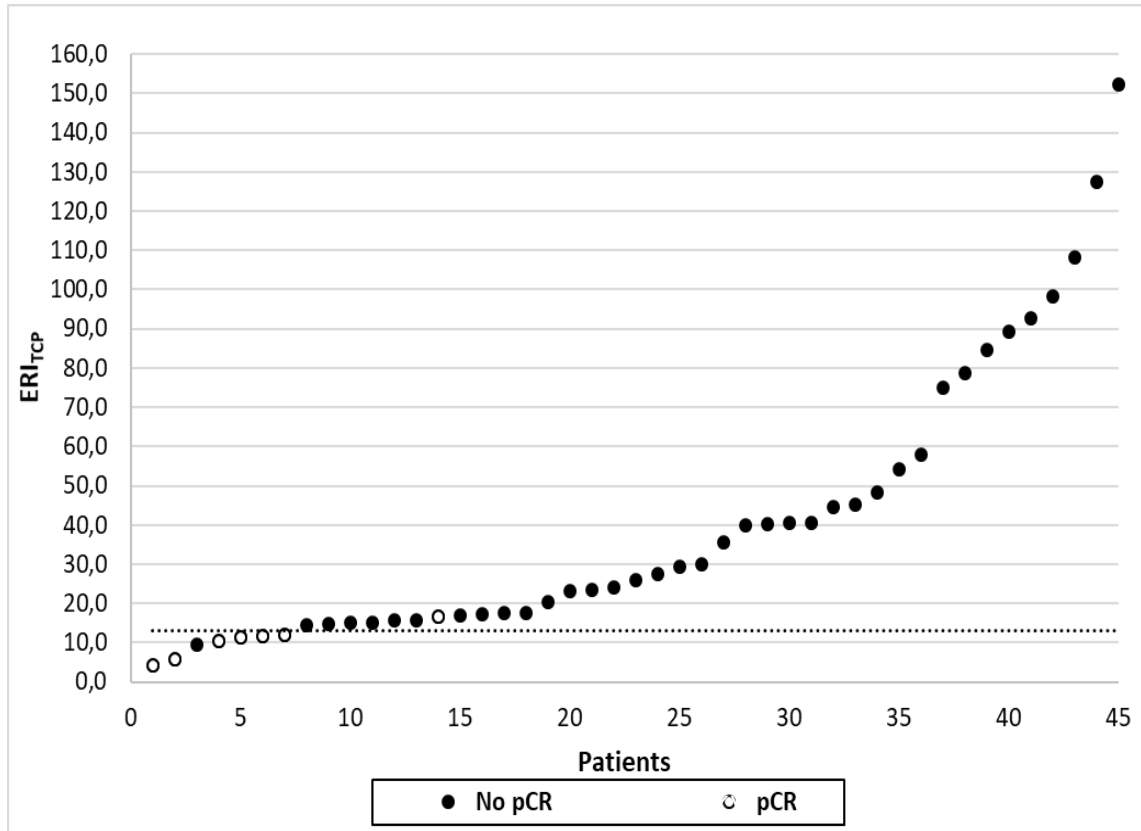
$V_{\text{pre}}$  GTV volume during simulation  
 $V_{\text{mid}}$  GTV volume at the mid of therapy

**ERI values < 13.1 predicts pCR with an AUC of ROC curve = 0.81**



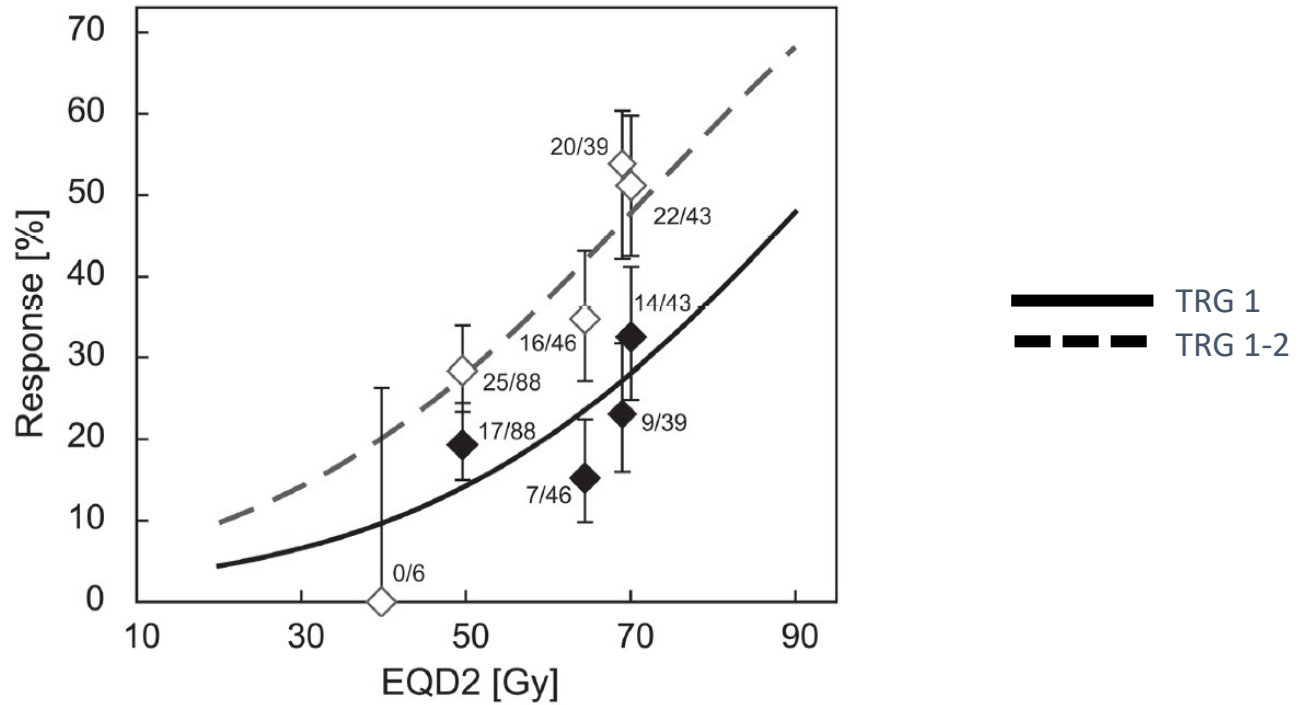
# Implementing multidimensional models

43 LARC patients were retrospectively enrolled (7 pCR, 16.2%)



**AUC = 0.95**  
**Sensitivity = 0.86**  
**Specificity = 0.97**  
**Accuracy = 0.95**

## Response and RT dose





MRIgRT makes it possible to safely increase the dose of radiotherapy for locally advanced rectal cancer, thanks to the '**online' adaptive radiotherapy** approach, which is not possible with conventional radiotherapy equipment.



It also enables the implementation **of predictive models** based on **radiomic analysis** of images obtained during treatment **to predict which patients will not respond to therapy.**

STUDY PROTOCOL

Open Access



# THUNDER 2: THERAGNOSTIC UTILITIES FOR NEOPLASTIC DISEASES OF THE RECTUM BY MRI GUIDED RADIOTHERAPY

Giuditta Chiloiro, Davide Cusumano, Luca Boldrini, Angela Romano<sup>\*</sup>, Lorenzo Placidi, Matteo Nardini, Elisa Meldolesi, Brunella Barbaro, Claudio Coco, Antonio Crucitti, Roberto Persiani, Lucio Petruzzello, Riccardo Ricci, Lisa Salvatore, Luigi Sofo, Sergio Alfieri, Riccardo Manfredi, Vincenzo Valentini and Maria Antonietta Gambacorta

**THUNDER-2 (NCT04815694) combines MRIGRT and radiomics for the first time .**

The study will enrol patients with **locally advanced rectal cancer** undergoing neoadjuvant radiochemotherapy and will be treated with MR-Linac 0.35 T.



Increasing of **10%** of **CR** rate in “*not responder*” rectal cancer patients treated with MRI-LINAC hybrid machine



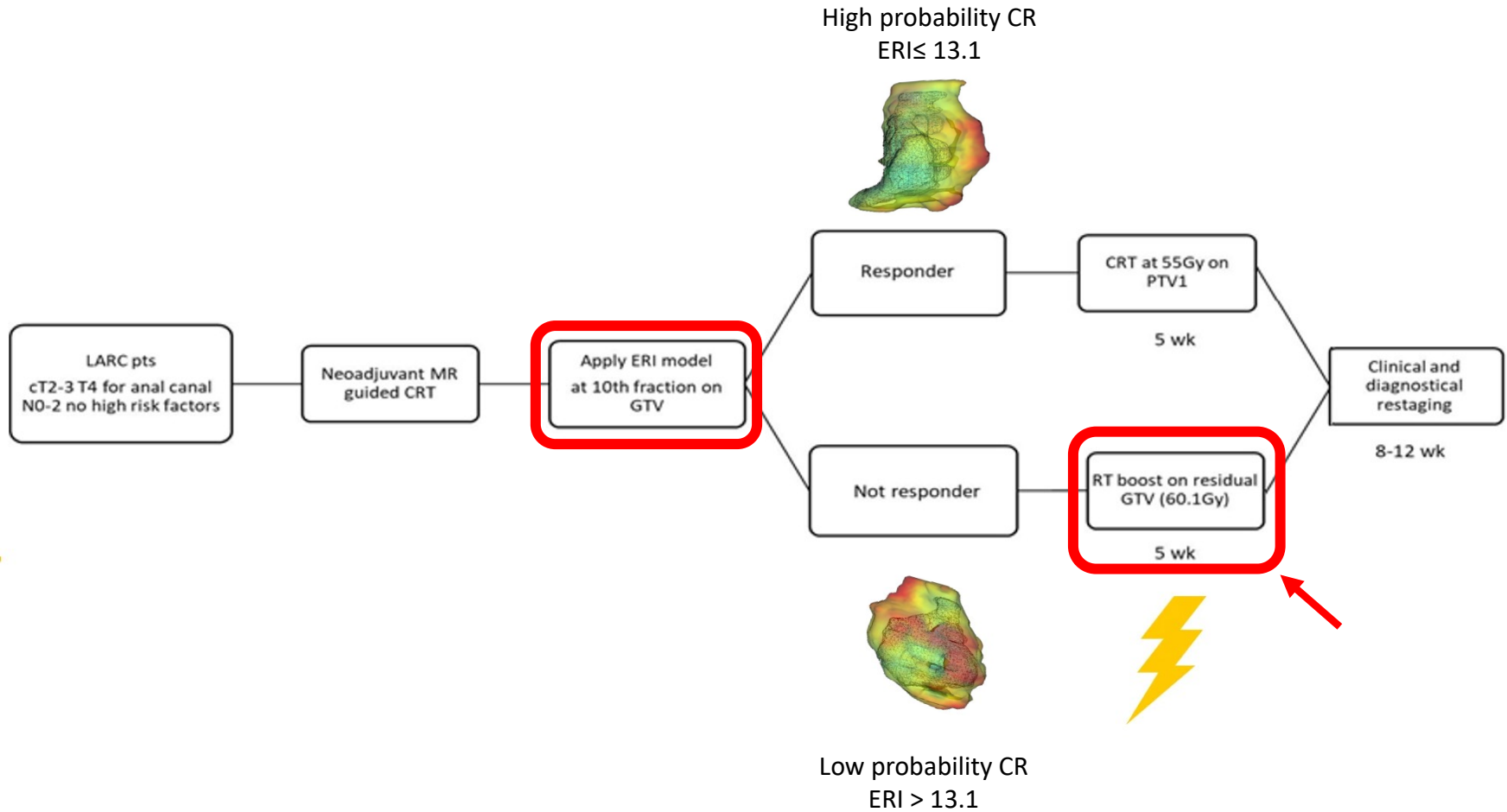
Evaluating the **feasibility** of delta radiomic-based predictive models in MRI-guided RT

## Inclusion criteria

- Histological proven adenocarcinoma of the rectum (0-15 cm above the anal verge) **cT2-3, N0-2 or cT4 for anal sphincter involvement N0-2a, M0**
- No prior radiotherapy in pelvic region;
- **Not mesorectal fascia involvement for tumor**
- **No extramesorectal nodes involvement**
- **No extramural venous invasion (EMVI)**
- **No rectal mucinous adenocarcinoma histology**
- No contra-indications for MRI
- ECOG 0-1 , Age >18 years
- Adequate hematological function:
- No other malignancies in the previous history;
- Absence of important comorbidities:
- Absence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule;
- Absence of pregnancy or lactating female patients;



# Trial design



## Response to treatment evaluation



Restaging at 8-10 weeks  
after the end of nCRT



In case of major or complete  
clinical response ***endoscopic***  
***examination should be***  
***performed***



In case of partial/stable or  
progression disease: **total**  
**(or partial) mesorectal**  
**excision\_**



In case of cCR: **W&W or LE**  
approach could be followed

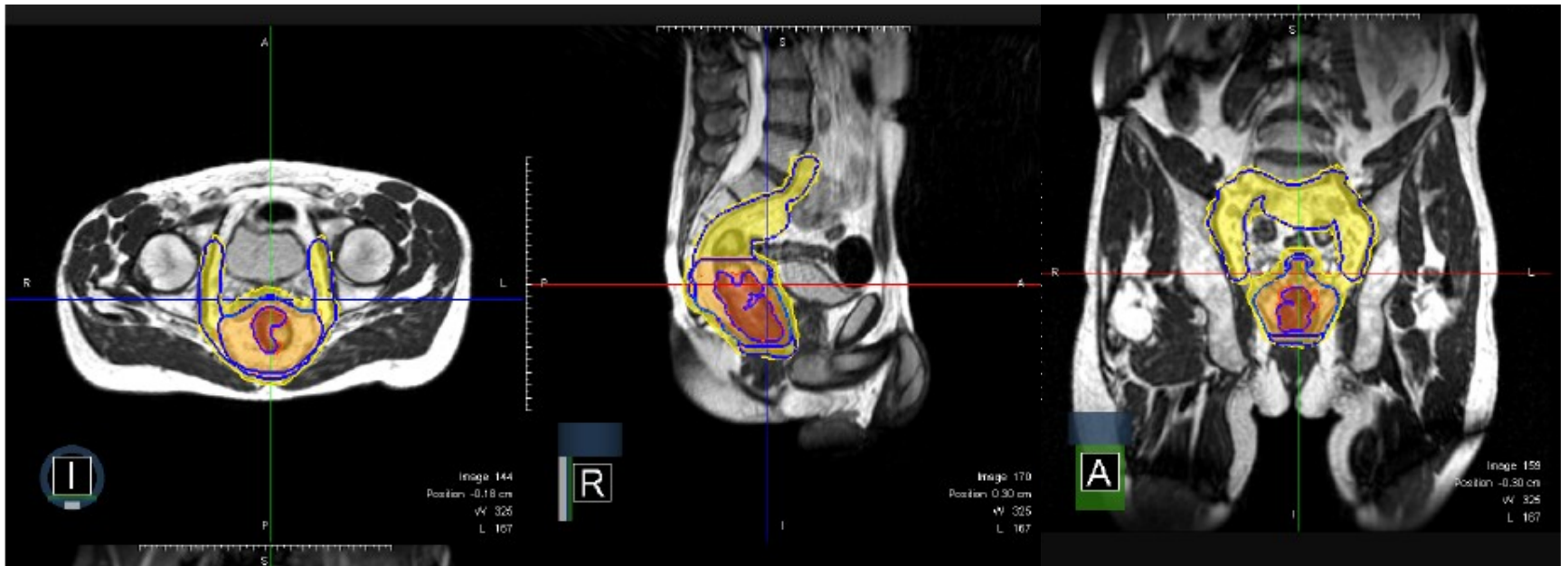
## Study endpoints

### The primary endpoints

- ↑CR as ypT0N0 (TME), ypT0ycN0 (LE), ycT0N0 (WW)
- Prospective validation of delta radiomics MRIgRT

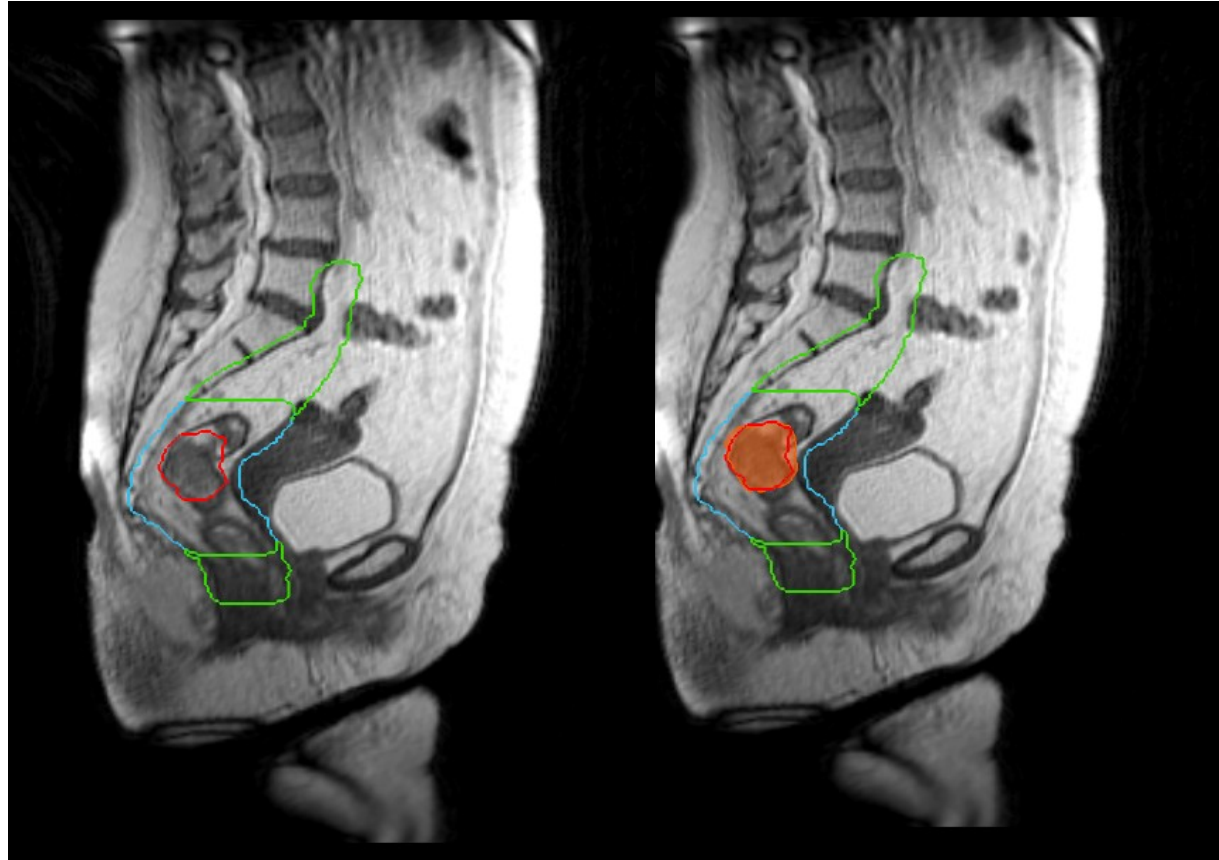
### The secondary endpoints:

- 3 years- LC, MFS, DFS and OS
- R0 resection rate
- TRG1, TRG 2, NAR score
- Sphincter preservation rate
- Organ preservation rate
- Rectal and sexual functions



## Interim analysis

41/63 patients enrolled,  
estimated by sample size  
calculation



**41 patients enrolled**

**39/41** completed RT treatment (**18/39** boost 46,2%)

**14/36\*** (**39%**) **complete response (CR)**

2 (6.1%) cases of acute G3 diarrhoea and proctitis

No toxicity differences in the boost patient group vs patients receiving conventional treatment



# Acknowledgements

## Gemelli ART MRIgRT Team

### RadOnc

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