

OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

R. Autorino

OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

DIAGNOSTIC IMAGING IN ONCOLOGY



Radiomics-based prediction of two-year clinical outcome in locally advanced cervical cancer patients undergoing neoadjuvant chemoradiotherapy

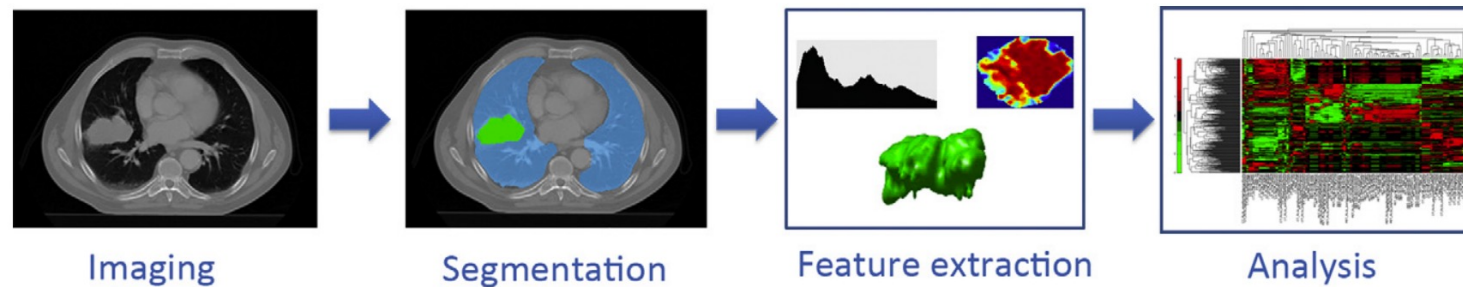
Rosa Autorino¹ · Benedetta Gui¹ · Giulia Panza²  · Luca Boldrini¹ · Davide Cusumano^{1,3} · Luca Russo¹ · Alessia Nardangeli¹ · Salvatore Persiani² · Maura Campitelli¹ · Gabriella Ferrandina¹ · Gabriella Macchia⁴ · Vincenzo Valentini^{1,2} · Maria Antonietta Gambacorta^{1,2} · Riccardo Manfredi^{1,2}

OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

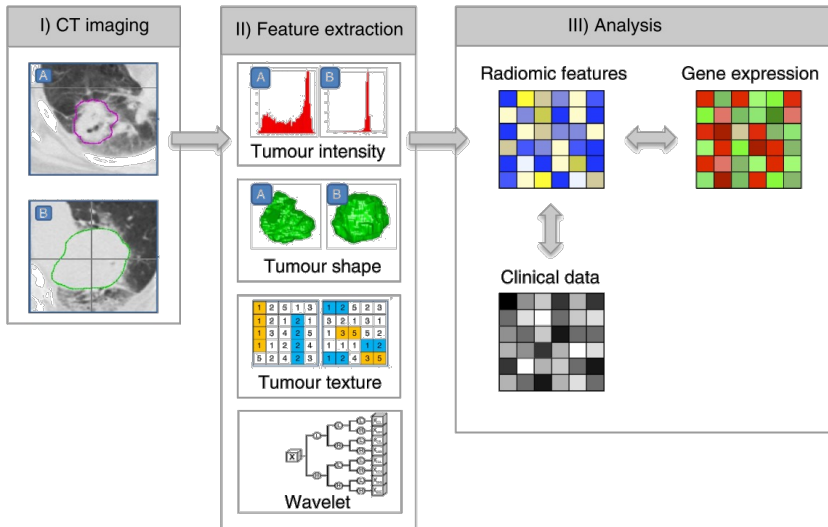
Radiomics is the process of extraction of **quantitative features** from **standard radiological imaging** for **clinical decision making tool**

Texture Analysis, Hystogram Analysis and **Morphometric Analysis** represent the three main approaches for **Features extraction**

Dedicated **software** needed



OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

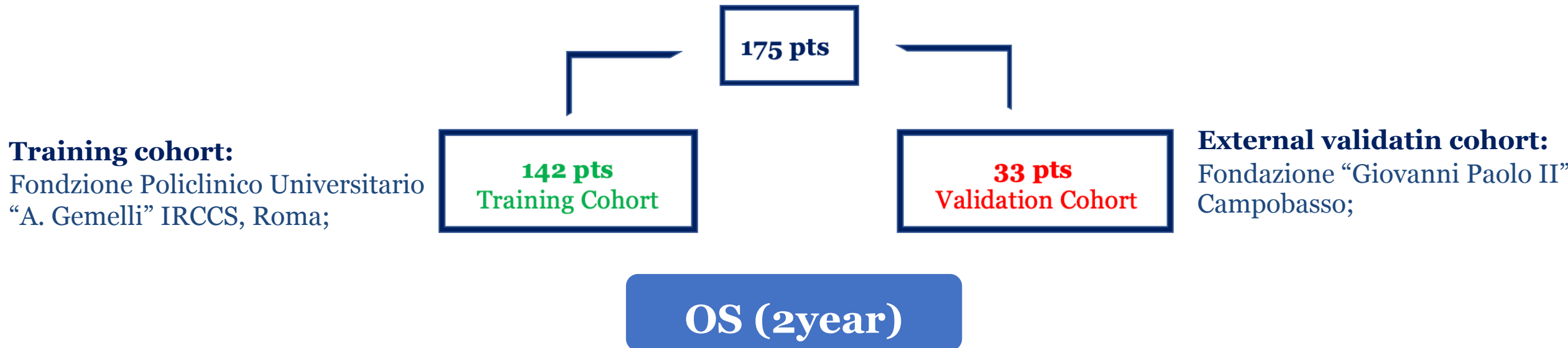


Radiomics features from T2-weighted 1.5 T MR images could **predict 2yOS** in patients with LACC **before NACRT?**

OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

Retrospective study

Patients with **Cervical Cancer** stage FIGO **IB2-IVA** without distant metastasis (cMo) treated with **NACRT** + radical hysterectomy +/- pelvic and/or lombo-aortic lymphadenectomy



OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

Treatment workflow

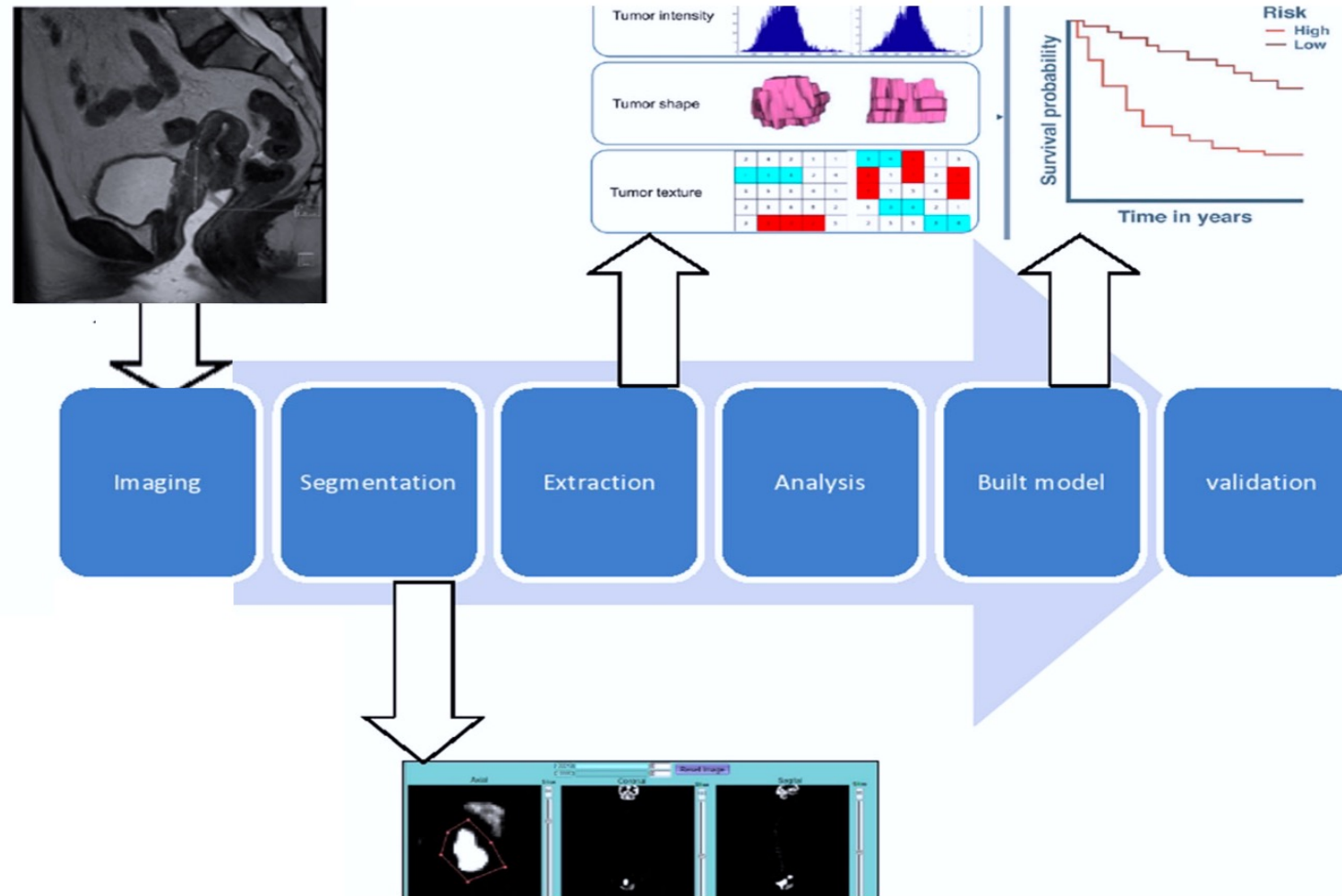
→ All patients underwent **NACRT** followed by **surgery**

39.6 Gy @ 1.8 Gy/fr at whole pelvis
+
50.6 Gy @ 2.3 Gy/fr at primary tumor

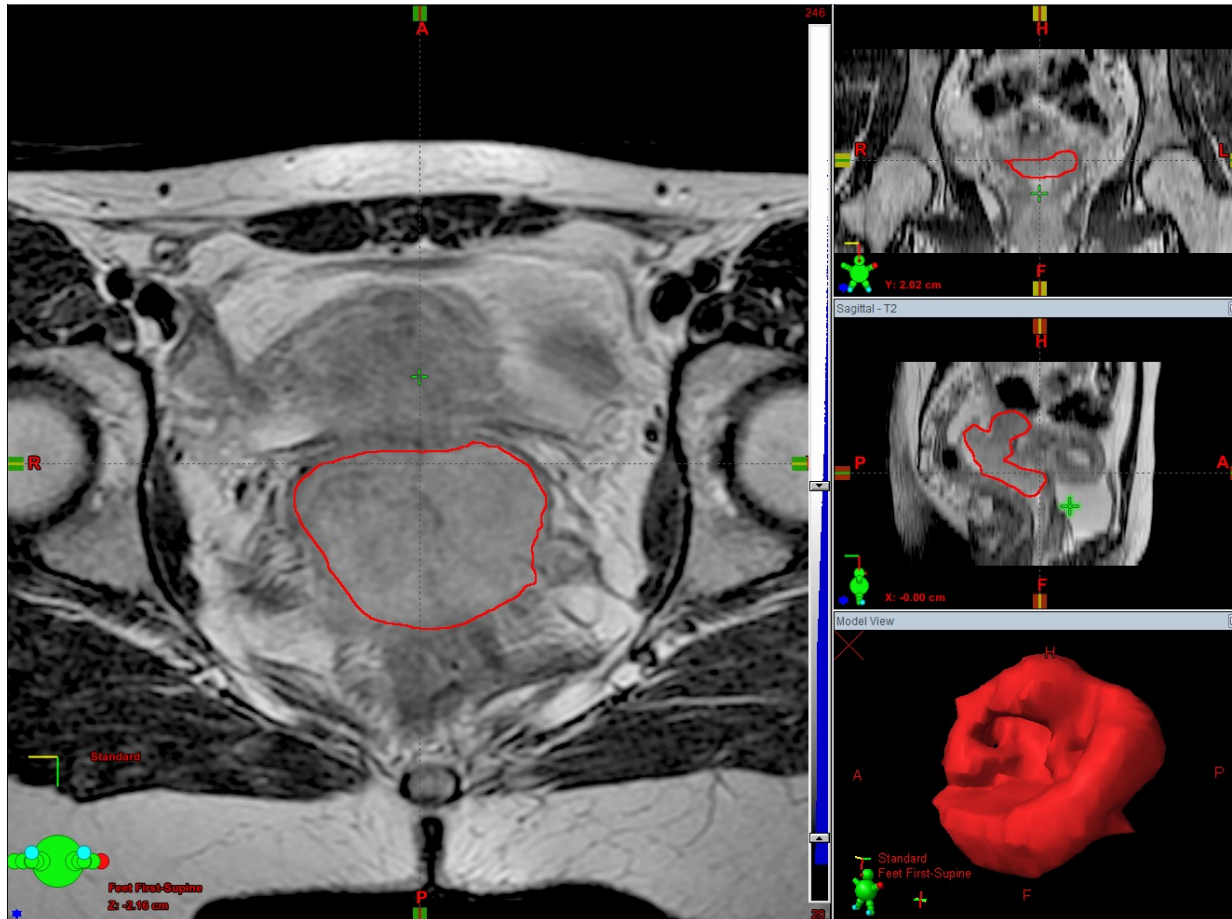
with CDDP weekly

OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

Radiomic Model Workflow



OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN



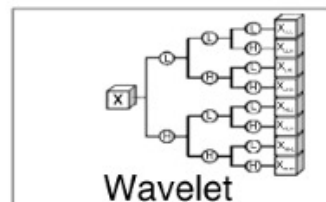
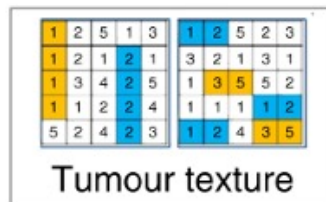
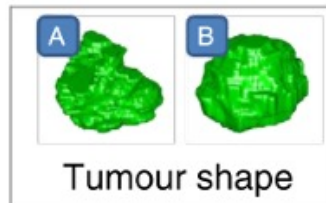
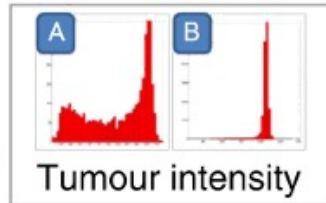
Staging MR:

- 1.5T T2 HR
- (Para)axial slices
- section thickness: 3 mm

GTV delineation:

- A RO and a Radiologist delineated the **primary GTV** excluding the lumen (no nodes)

OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN



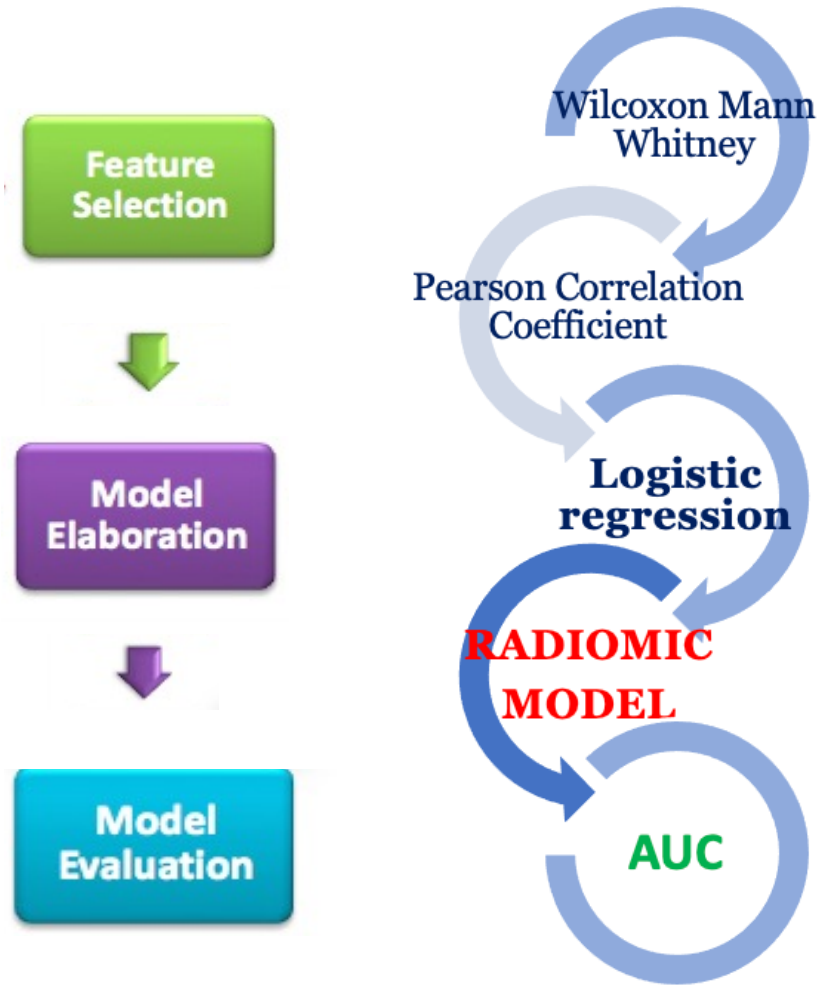
Feature extraction

1557 Radiomics Features
from pre-treatment MRI


Belonging to 3 families

- Statistical
- Textural
- Morphological

OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN



→ **Statistical analysis to build a model**

 Radiomics analysis performed by in-house produced software: **MODDICOM** *

**Dinapoli N, et al. Conf Proc. Eng Med Biol Soc IEEE. 2015;2015:771–4.*

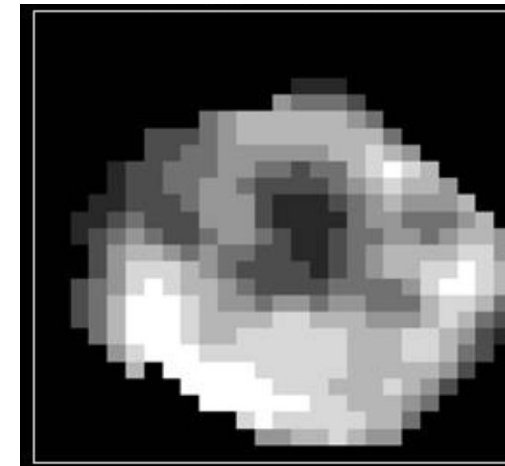
OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

	features.name	all.pvalues	padj
726	F_cm.corr_0.7	0.001097667	0.4943522
751	F_cm_merged.corr_0.7	0.001151189	0.4943522
505	F_cm.corr_0.6	0.001455952	0.4943522
530	F_cm_merged.corr_0.6	0.001831808	0.4943522
947	F_cm.corr_0.8	0.002193120	0.4943522
972	F_cm_merged.corr_0.8	0.002504824	0.4943522
1168	F_cm.corr_0.9	0.002617229	0.4943522

46 features showed significance ($p < 0.5$) at the univariate analysis

25	F_morph.comp.1	0.019439588	0.9746422
257	F_morph.sph.dispr_0.5	0.021562861	0.9746422
259	F_morph.asphericity_0.5	0.021562861	0.9746422
478	F_morph.sph.dispr_0.6	0.021562861	0.9746422
480	F_morph.asphericity_0.6	0.021562861	0.9746422
699	F_morph.sph.dispr_0.7	0.021562861	0.9746422
701	F_morph.asphericity_0.7	0.021562861	0.9746422
920	F_morph.sph.dispr_0.8	0.021562861	0.9746422
922	F_morph.asphericity_0.8	0.021562861	0.9746422

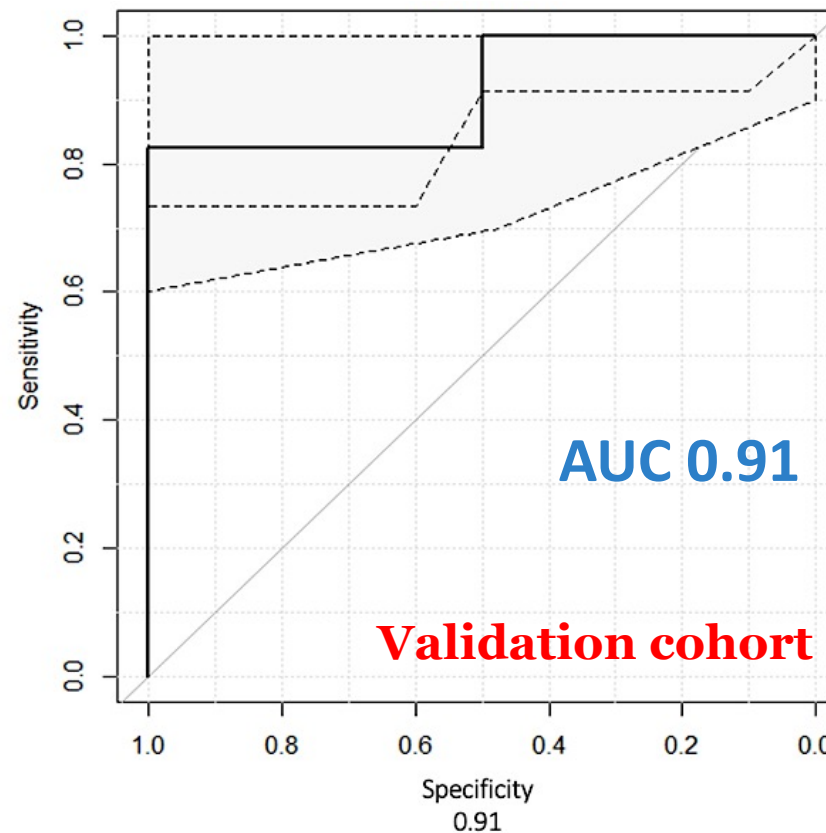
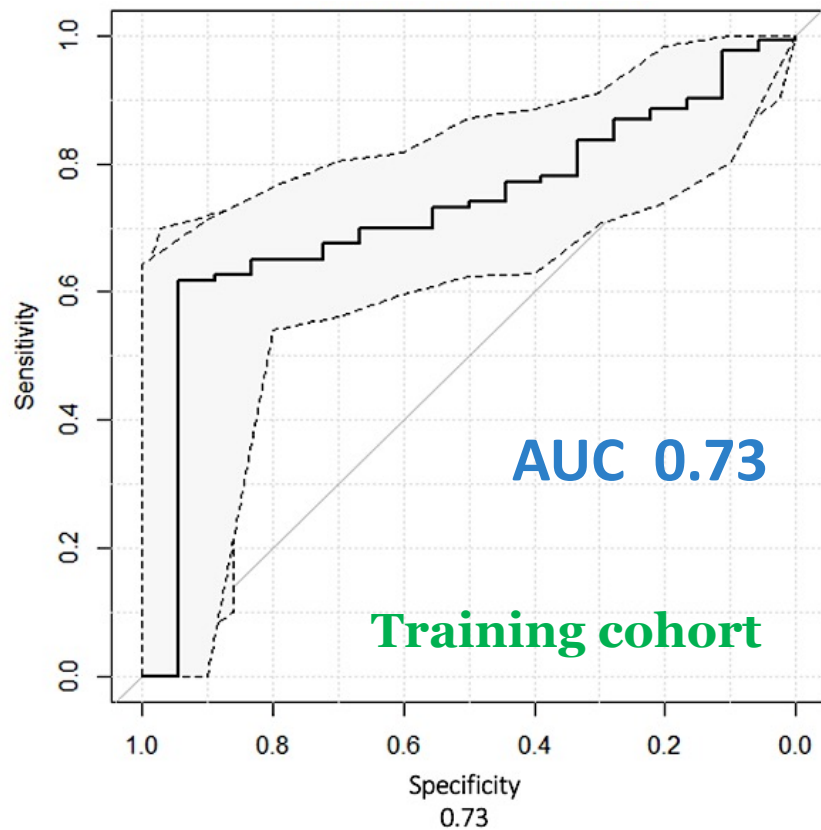
Grey-Level Co-occurrence Matrix (GLCM)



Texture analysis is concerned with the spatial distribution of gray level variation within an image

OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

2ys OS

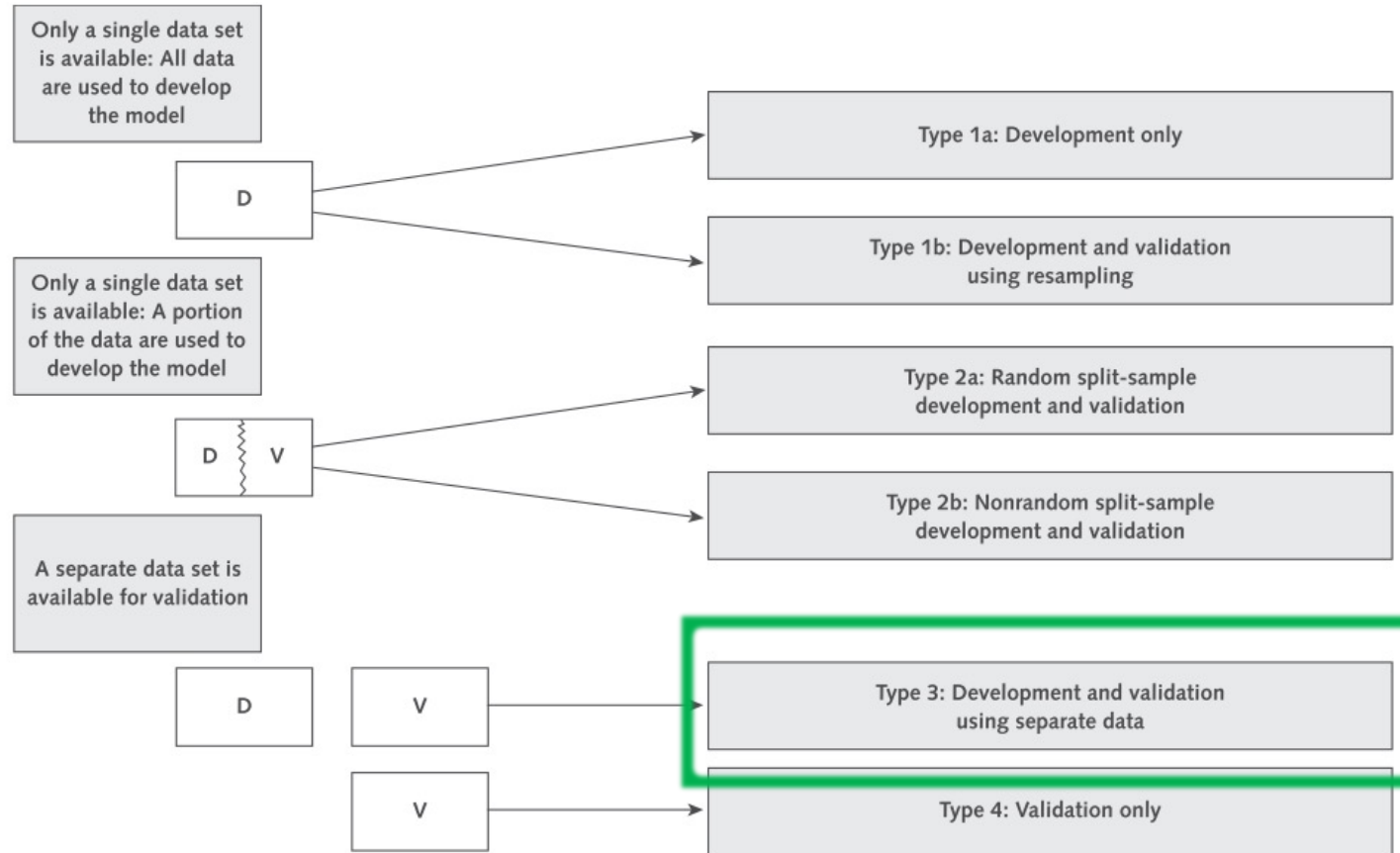


OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

□ Strenght points

→ **TRIPOD 3**

- Sound Methodology
- External validation studies



«Development of a prediction model using one data set and an evaluation of its performance on separate data»

Collins GS, et al. the TRIPOD statement. Ann Intern Med 2015.162:55–63.

OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

□ Limit of the study

- NACRT is **not** standard treatment
- **Lack** of a **biological interpretation** (clinical, histopathological and **molecular data**) of the significant features limits the translational value of this experience, even if this issue is not considered mandatory for radiomics study

OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

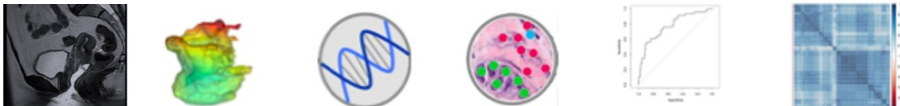
→ The proposed **Radiomic Model** showed promising performances in predicting **2yOS before NACRT**.

→ **Larger studies** with a consistent external validation are mandatory

→ Integration with **clinical, histopathological and molecular data**, which would allow to build **multi-omics predictive models**

«An accurate outcome prediction before or during oncological treatments could be an added clinical value to provide a guidance for clinicians in their decision-making process to adapt and tailoring treatment.»

→ Potential tools to **clinical practice**



OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN



ELSEVIER

Contents lists available at [ScienceDirect](#)

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com



Original Article

Evaluation of early regression index as response predictor in cervical cancer: A retrospective study on T2 and DWI MR images



Davide Cusumano^{a,b}, Luca Russo^a, Benedetta Gui^a, Rosa Autorino^a, Luca Boldrini^{a,*}, Luca D'Erme^a, Salvatore Persiani^a, Francesco Catucci^b, Sara Broggi^c, Giulia Panza^d, Alessia Nardangeli^a, Maura Campitelli^a, Gabriella Ferrandina^a, Gabriella Macchia^e, Claudio Fiorino^c, Vincenzo Valentini^{a,d}, Giovanni Scambia^{a,d}, Riccardo Manfredi^{a,d}, Maria Antonietta Gambacorta^{a,d}

OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

EARLY REGRESSION INDEX

$$ERI = -\ln \left[\left(1 - \left(\frac{V_{mid}}{V_{pre}} \right) \right)^{V_{pre}} \right]$$

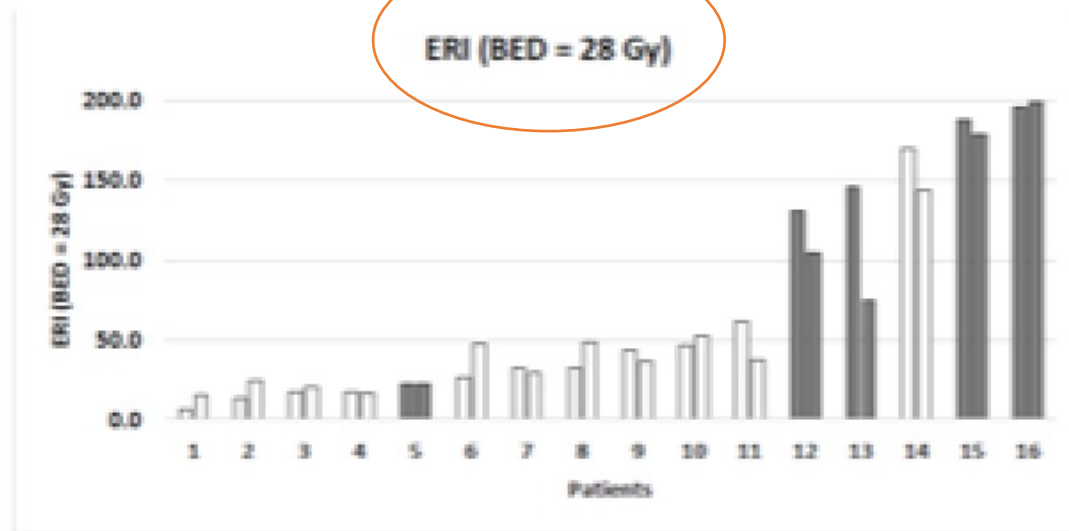
Vpre GTV volume during simulation
Vmid GTV volume at the mid of therapy

Fiorino et al, A TCP-based early regression index predicts the pathological response in neo-adjuvant radio-chemotherapy of rectal cancer, *Radiotherapy and Oncology* 128 (2018) 564-568

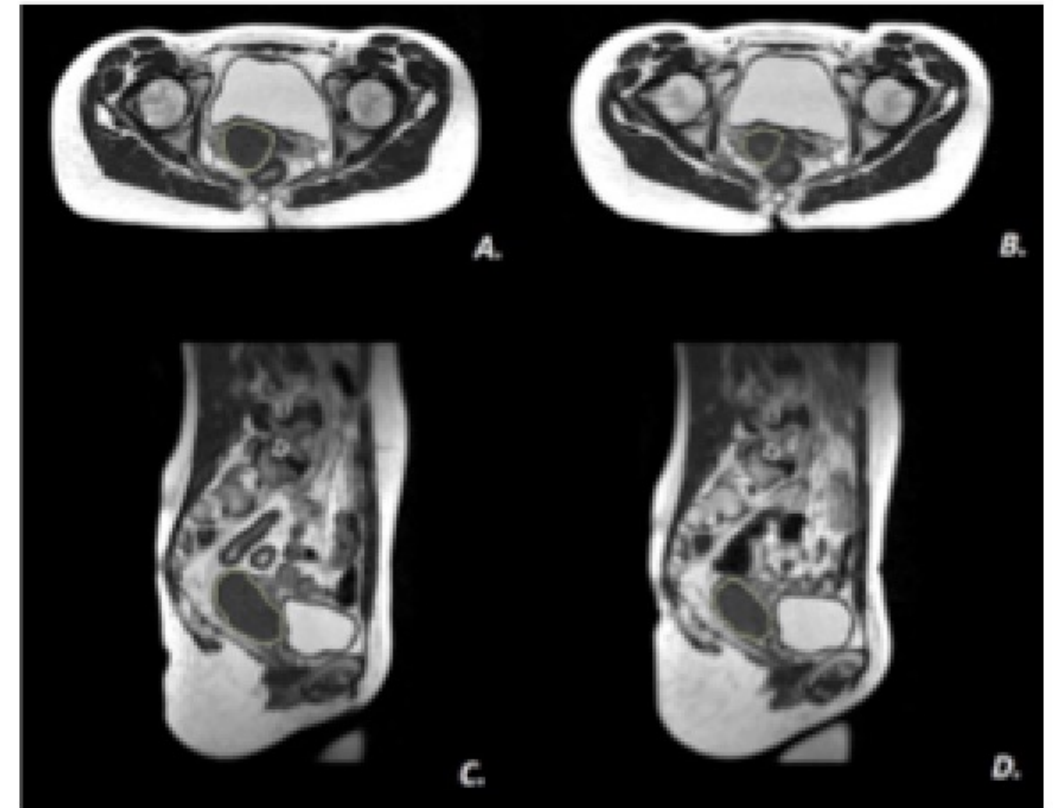
OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

CERVICAL CANCER

- 16 patients, Long Course MRI-guided Radiochemotherapy
- 50.6 Gy @2.3 Gy/fr
- 2 observers
- pCR prediction



AUC = 0.84



OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

To evaluate the feasibility of using this parameter in the context of

Locally Advanced Cervical Cancer (LACC),

evaluating its ability in predicting

pCR starting from T2 and diffusion weighted images (DWI)

OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

- **88 patients** retrospectively enrolled
- Locally advanced cervical cancer (**LACC**)
- FIGO stage **IB2 – IVA**
- Histologically proven

All patients underwent **NACRT followed by surgery**

39.6 Gy @ 1.8 Gy/fr at whole pelvis +
50.6 Gy @ 2.3 Gy/fr simultaneous integrated boost

OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

MRI IMAGES:

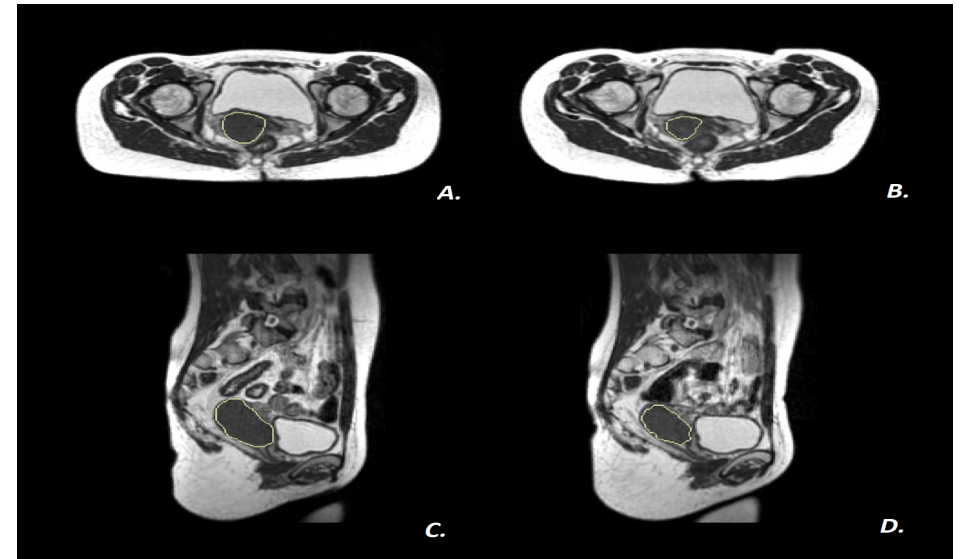
- ✓ 1.5T T2 High Resolution MRI
- ✓ GE Medical System MR
- ✓ Pixel spacing: 0,39 – 1,17 mm
- ✓ Para-axial slices
- ✓ section thickness: 3-5 mm

<u>Image Parameter</u>	T2-weighted	DWI
<u>Sequence</u>	FSE	FSE
<u>Echo time (ms)</u>	16	16
<u>NEX</u>	2	2
<u>Repetition time (ms), TR</u>	470	470
<u>No. of sections</u>	30	30
<u>Receiver bandwidth (kHz)</u>	31,25	31,25
<u>Echo train length</u>	3	3
<u>Field of view (mm), FOV</u>	24	24
<u>Section thickness (mm)</u>	4	4
<u>Section spacing (mm)</u>	0,5	0,5
<u>Spatial Resolution (mm)</u>		
<u>b Value (s/mm²)</u>	---	---
<u>Phase direction</u>	A/P	A/P

Staging and at fraction 10

OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

- ❑ **GTV** was delineated on simulation CT imaging and at fraction 10 in axial (A and B) and sagittal plan (C and D) using the MR supporting images.
- ❑ **CTV1** = GTV
- ❑ **CTV2** = entire cervix, uterus, parametria, vagina and the corresponding drainage nodal
- ❑ **GTV** was retrospectively delineated by two radiologists blinded with respect the outcome of the therapy.
- ❑ **ERI** was calculated for T2 and DWI images

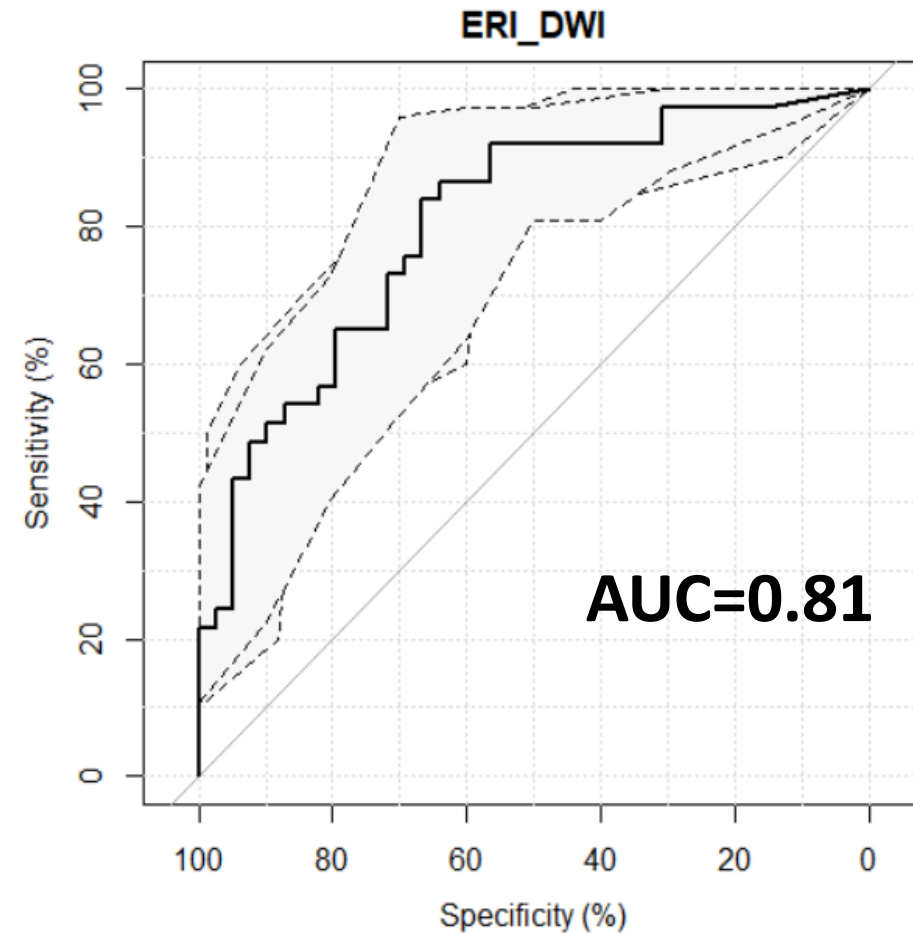
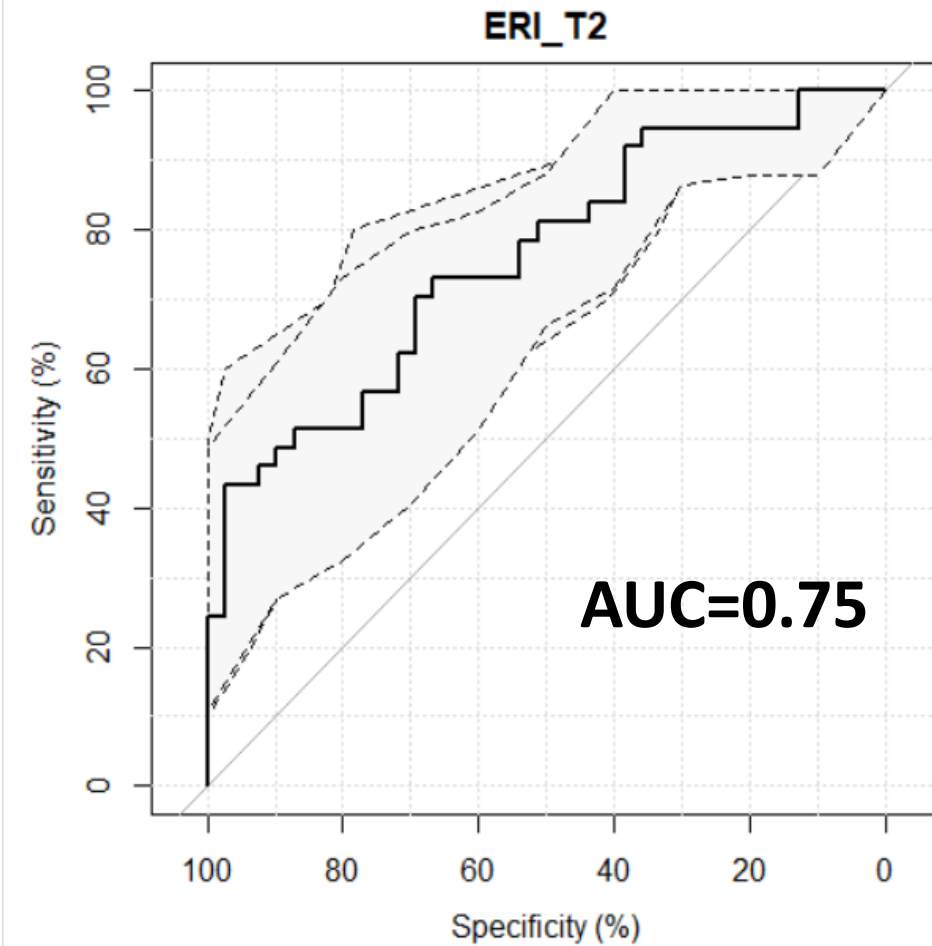


OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

Clinical Characteristics

Number of patients	88
Age (Mean)	22-76 (50.2)
Histology	
Squamous cell carcinoma	86 (97.7%)
Adenocarcinoma	2 (2.3%)
FIGO Stage	
IB2	6 (6.8%)
IIA	8 (9.0%)
IIB	63 (71.5%)
IIIA	2 (2.2%)
IIIB	8 (9.0%)
IVA	1 (1.5%)
Nodal status	
N0	41 (46.5%)
N1	47 (53.5%)
Pathological Response	
pR0	37 (42.0%)
pR1	28 (31.8%)
pR2	23 (26.2%)

OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN



	Sensitivity	Specificity	Threshold	J_index	AUC	Low_AUC	High_AUC
ERI_T2	43.24324	97.43590	5.007381	0.4067914	75.74498	64.95075	86.53920
ERI_DWI	86.48649	64.10256	18.247302	0.5058905	80.38808	70.52463	90.25153

OMICS GUIDED RADIOTHERAPY PRESCRIPTION: GYN

- ERI-TCP** as a good biomarker also in case of LACC, especially if calculated considering DWI
- Personalized Treatments
- Cure Strategy Optimization