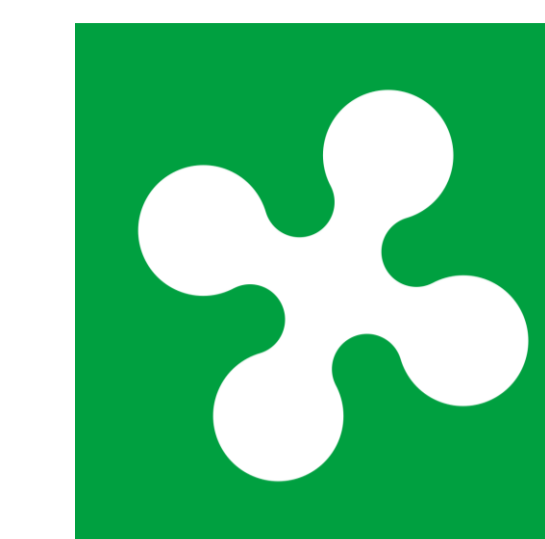


# Modified TGR: a new strong radiological marker to accurately predict early response to PRRT in GEPNETs

\*F. SCALORBI (1), G. CALARESO (1), EM. GARANZINI (1), G. ARGIROFFI (1), V. FUOCO (1), M. BACCINI (2), L. GHERARDINI (2), A. MARCHIANO' (1), E. SEREGNI (1), M. MACCAURO (1)

(1) IRCCS Foundation, National Institute of Tumor, Milan, Italy; (2) Department of Statistics, Computer Science, Applications (DiSIA), University of Florence, Florence, Italy

\*Corresponding author: federica.scalorbi@gmail.com, MD, PhD student - Open University (UK)



## AIM

To investigate the added value of modified TGR (tumor growth rate) as radiological predictor of early response to PRRT, in GEPNET patients.

## MATERIALS AND METHODS

Progressive metastatic G1-G2 GEPNET patients treated with PRRT (177 Lu-DOTATATE 4 administrations, 7.4 GBq/each) at our centre from 04/2019 to 10/2020 were considered. Inclusion criteria were 3 CT/MRI scans per patient: one (i) performed within 3 months before PRRT to assess disease burden and confirm radiological progression, one (ii) interim evaluation after 2 PRRT administrations and one (iii) within 4 months after the end of treatment to assess early response, according to RECIST1.1. All the scans were centrally re-evaluated by 2 dedicated radiologists. **TGR was calculated in 2 ways: assuming that the volume of the lesions can be calculated applying the volume of a sphere formula (TGR\_sphere, classical TGR formula, Dromain, BMC 2019) or the volume of an elliptical cylinder (TGR\_elliptical\_cylinder, new model).**

In both cases, to assess TGR, baseline versus interim evaluations were compared and the values were expressed as % increase/month. Patients were subdivided as responders (CR, PR, SD) and non-responders (PD), according to RECIST. Performance status was evaluated by ECOG v.5, lines of previous therapies were calculated as possible confounders. Chi/Fisher and K-Wallis test were applied to assess independence between response to treatment and patient characteristics. Logistic regression was performed to determine predictability of both TGR models and clinical features for disease progression. ROC analysis was applied to assess the performance of the two models and evaluate optimal TGR\_sphere and TGR\_elliptical\_cylinder cut-off.

PATIENT CHARACTERISTICS (N=27)		
GENDER	female	15 (55.6%)
	male	12 (44.4%)
AGE	mean	63.9
	range	37-80
	SD	10.8
LOCALISATION	midgut	15 (55.6%)
	foregut	12 (44.4%)
ECOG	0	24 (88.8%)
	1_2	3 (11.2%)
PRRT LINE of ADMINISTRATION	second	18 (66.6%)
	further	9 (33.4%)
RECISTI CRITERIA 1.1	non-responders	4 (14.8%)
	responders	23 (85.2%)

Tab. 1: Patient characteristics.

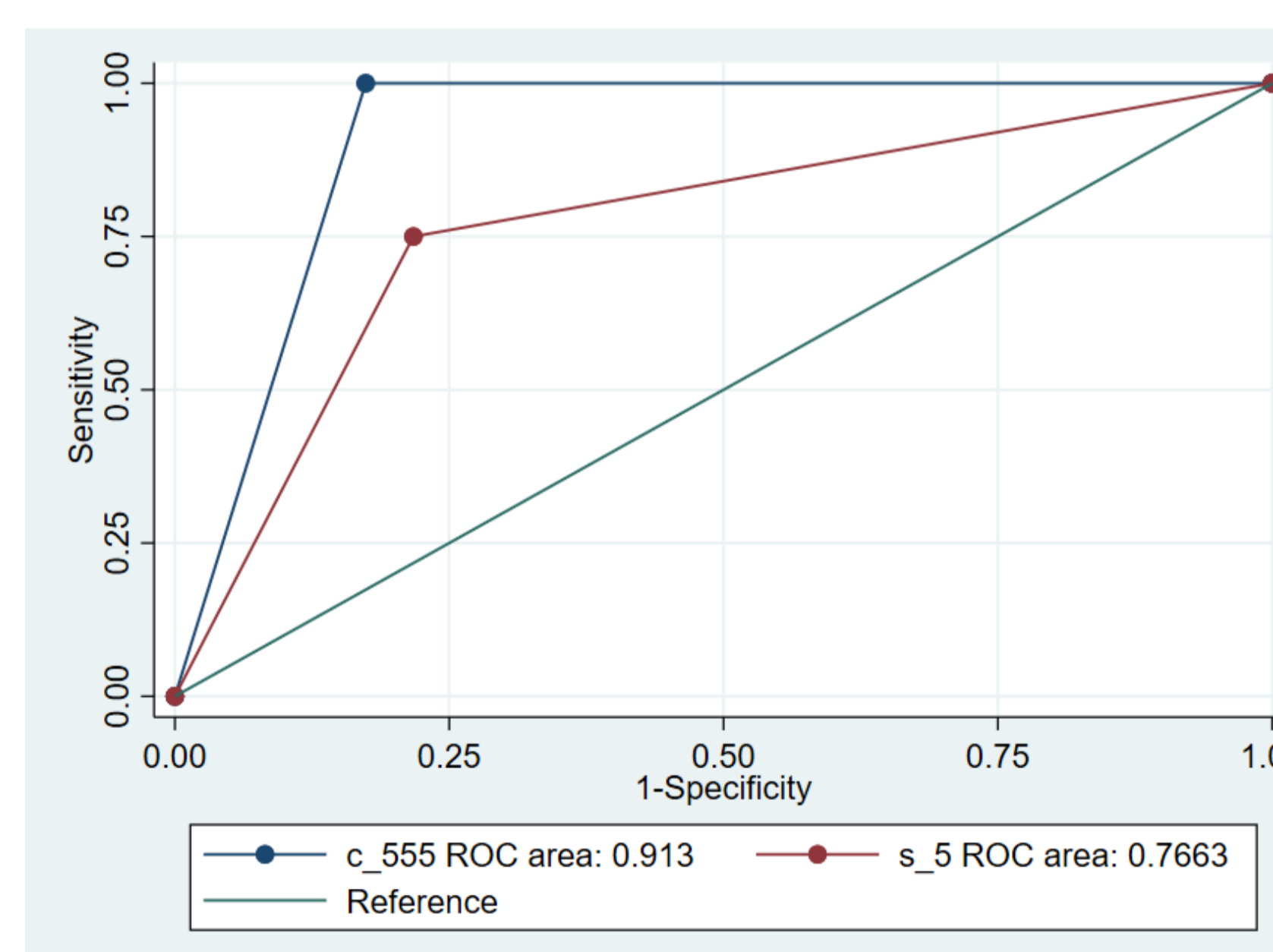


Fig 1: ROC area, TGR\_elliptical model (blue), TGR\_spherical model (red)

## RESULTS

According to inclusion criteria, 27 patients (12 males, 15 females, mean age 63.9, range 37-80, SD 10.8) were analysed. Fifteen (55.6%) were midgut, 12 (44.4%) foregut, 24 (88.8%) ECOG 0, three (11.2%) ECOG 1 or 2. PRRT was applied in second line in 18 (66.6%), in third or further in 9 (33.4%) in patients. Considering RECIST, 4 (14.8%) patients were non-responders (**Tab 1**). Chi/Fisher and K-Wallis test didn't show statistical significance. **Logist regression showed OR equal to 5.9 (SE 9.4) with AUC 0.95 (Sensitivity 75%, Specificity 95%) for TGR\_elliptical model and OR 1.05 (SE 0.07) with AUC 0.75 (Sensitivity 25%, Specificity 75%), for TGR\_spherical model.** The optimal cut-off value for progression prediction was 5.5% volume increase/month for TGR\_elliptical\_cylinder (Sensitivity 100%, Specificity 86.4%) and 5% /month for TGR\_sphere (Sensitivity 75%, Specificity 81.8%). **Fig 1** shows the ROC curves for TGR-spherical model and TGR-elliptical model highlighting how the area under the curve is optimal (0.95) for the TGR modified model (c\_555 ROC area).

## CONCLUSIONS

Interim TGR\_elliptical\_cylinder is a strong and accurate predictor of early progression of GEPNET disease after PRRT. **The optimal TGR\_elliptical\_cylinder cut-off value to predict early progression is 5.5% /month, with optimal sensitivity and specificity.** External validation is on course.

**CONFLICT OF INTEREST and FINANCIAL TRASPERENCY:** The authors have nothing to declare and the didn't receive any founding to develop the study

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