Magnetic Resonance Imaging alone should not be considered as a stand-alone test for disease reclassification of men in Active Surveillance.

Roscigno M.[1], Stabile A.[2], Lughezzani G.[3],Pepe P.[4], Galosi A.B.[5], Nicolai M.[1,] La Croce G.[1], Manica M.[1] ,Naselli A.[6], Guazzoni G.[7], Briganti A.[8], Balzarini L.[9], Montorsi F.[10] , Sironi S.[11], Da Pozzo L.F.[12]

Introduction & objectives: Multiparametric Magnetic Resonance Imaging (mpMRI) and ultrasound (US) fusion biopsy are increasingly used in the management of patients with clinically low-risk prostate cancer (PCa), despite their role has not yet been established definitively. The aim of the study is to evaluate whether mpMRI alone could be used as a stand-alone test suggesting risk of reclassification in men in AS.

Materials & methods: We retrospectively evaluated 340 pts undergoing confirmatory or follow-up biopsy according to PRIAS protocol, from January 2016 to September 2018. All patients were submitted to mpMRI on a 1.5 T or 3T magnet, using triplanar high-resolution T2-w, axial DWI, and 3D T1-w dynamic contrast-enhanced sequences after injection of paramagnetic contrast agent. Pts with negative (-) mpMRI subsequently underwent systematic random biopsy. Pts with positive (+) mpMRI (PI-RADS-V2 score ≥3) underwent targeted fusion prostate biopsies (3 cores) + systematic random biopsies (12-18 cores). Multivariate logistic regression analyses (MVA) was used to create three model predicting the probability of disease reclassification, defined as presence of PCa GS≥3+4 (GG2) at prostate biopsy: a basic model including only clincial variables (age, PSAD and number of positive cores at baseline); a MRI model including only PI-RADS score; a full model including both the previous ones. The predictive accuracy (PA) of each model was quantified using the AUC. The clinical net benefit deriving from the use of each model was assessed with the use of decision curve analysis.

	PIRADS 1-2	PIRADS 3	PIRADS 4	PIRADS 5	P value
Age yrs Mean (95% CI)	67.2 (65.7 – 68.7)	65.7 (64.0 – 67.6)	66.6 (65.5 – 67.7)	68.7 (66.1 – 71.3)	0.191
PSA ng/mL Mean (95% CI)	6.19 (5.30 - 7.08)	6.78 (4.96 - 8.59)	7.82 (6.79 - 8.85)	10.0 (7.46 – 12.55)	0.010
PSAD Mean (95% CI)	0.12 (0.10 – 0.14)	0.13 (0.11 -0.15)	0.14 (0.13 – 0.16)	0.21 (0.17 – 0.25)	< 0.001
PSAD # (%) < 0.10 0.10 – 0.19 ≥0.20	 43 (51.2) 30 (31.7) 11 (13.1)	 28 (39.4) 32 (45.1) 11 (15.5)	 58 (39.7) 56 (38.4) 32 (21.9)	 7 (17.9) 15 (38.5) 17 (43.6)	0.002
csPCa (GG2) # (%) No Yes	 70 (83.3) 14 (16.7)	 47 (66.2) 24 (33.8)	 92 (63.0) 54 (37.0)	 18 (46.2) 21 (53.8)	< 0.001

Patient characteristics according to PI-RADS score

Results: Median patient age and PSA was 67 yrs and 6.3 ng/ml, respectively. Median PSA density was 0.12 ng/ml/cm3. Median number of positive cores at initial biopsy was 1 (IQR:1,2). Eighty-four pts (24.7%) had mpMRI(-); out of 256 pts with mpMRI (+), 71 (20.9%) had PI-RADS 3, 146 (42.9%) PI-RADS 4, and 39 (11.5%) PI-RADS 5 lesions. At a median follow up of 12 months, 113 patients (33.2%) were reclassified and switched to active treatment. In pts with mpMRI(-) the rate of reclassification was 18%. In mpMRI(+), the overall rate of reclassification, at target + random biopsies, was 28%, 40% and 50% according to PI-RADS 3, 4 and 5, respectively.

Predictors	Multivariable analysis	
	OR (95% CI)	p-value
Age	1.03	0.08
PSAD	66.4	0.001
N. of positive cores at baseline	2.22	<0.001

In the basic model, PSAD and the number of positive cores at baseline biopsy were independent predictors of risk of reclassification (p=0.001; OR 66.4 and p<0.001; OR 2.2, respectively), with an AUC of 69%.

Predictors	Multivariable analysis	
	OR (95% CI)	p-value
PI-RADS 1 2 3 4 5	 Ref 0.60 2.07 2.18 4.76	 0.40 0.12 0.07 0.002

In the MRI model, PI-RADS 5 was predictor of reclassification (p=0.002; OR 4.76) and the PA was lower than in the basic model (AUC 62%).

Predictors	Multivariable analysis	
	OR (95% CI)	p-value
Age	1.03	0.09
PSAD	28.6	0.01
N. of positive cores at baseline	2.20	<0.001
PI-RADS 1 2 3 4 5	 Ref 0.55 2.07 2.21 3.60	 0.33 0.14 0.07 0.02

The full model, that includes clinical variables and MRI results, had the best AUC of 72%. PSAD (p=0.01; OR 28.6), number of positive cores at baseline (p<0.001; OR 2.20) and PI-RADS 5 (p=0.02; OR 3.6) were independent predictors of reclassification.

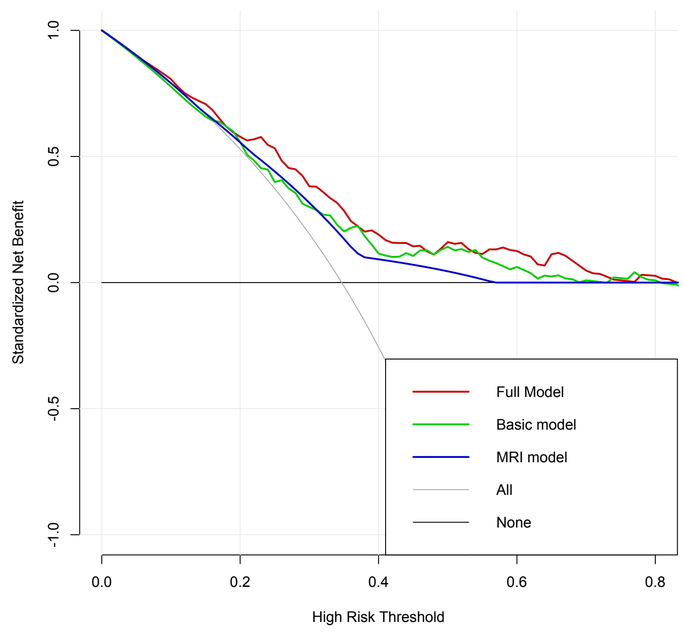

Fig.1 Depicts clinical net benefit deriving from the use of the three evaluated models

Conclusions: MRI alone should not be used in clinical practice as a stand-alone trigger for disease reclassification. The combination of MRI and other clinical variables still represents the most accurate approach to patients on AS.

Sistema Socio Sanitario
Ospedale di Bergamo
Regione Lombardia
ASST Papa Giovanni XXIII