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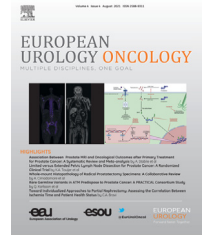
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# Assessing the Clinical Value of Positive Multiparametric Magnetic Resonance Imaging in Young Men with a Suspicion of Prostate Cancer

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## Abstract

**Background:** There is a lack of evidence on the ability of magnetic resonance imaging (MRI) of the prostate to detect clinically significant prostate cancer (csPCa) in young patients.

**Objective:** We hypothesised that the diagnostic performance of MRI for csPCa varies according to patient's age. To address this, we assessed the variation in the csPCa detection rate of MRI targeted biopsy (MRI-TBx) versus systematic random biopsy (SBx) across different patient ages.

**Design, setting, and participants:** We retrospectively identified 930 patients who underwent prostate MRI and subsequent biopsy at two referral centres between 2013 and 2018. The Prostate Imaging Reporting and Data System (PI-RADS) was used for MRI reporting.

**Intervention:** A lesion with a PI-RADS score of  $\geq 3$  detected at MRI received an MRI-TBx in addition to an SBx during the same session.

**Outcome measurements and statistical analysis:** The outcome of our study was the relationship between age and csPCa detection rate at MRI-TBx and SBx, respectively. Clinically significant prostate cancer (PCa) was defined as the presence of PCa with Gleason score  $\geq 3 + 4$ . Multivariable logistic regression analyses (MVAs) predicting csPCa detection were assessed for both MRI-TBx and SBx. Covariates were age, prostate-specific antigen density, PI-RADS score, previous biopsy status, digital rectal examination, and the number of targeted and systematic cores. The hypothesis that MRI accuracy in detecting csPCa differed by age was finally tested with a nonparametric loess analysis.

**Results and limitations:** The overall rate of csPCa was 54% ( $n = 506$ ). Overall, 325 (35%) and 461 (50%) patients had csPCa at SBx and MRI-TBx, respectively. The median numbers of SBx and MRI-TBx cores were 12 (interquartile range [IQR]: 10–13) and 5 (IQR: 4–7), respectively. At MVA, age at biopsy was an independent

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predictor of csPCa at MRI-TBx only (odds ratio: 1.05), after accounting for confounders. In men aged less than roughly 50 yr, SBx had a higher probability of detecting csPCa relative to MRI-TBx (25% vs 16% at 40 yr). Conversely, in patients aged >50 yr, the probability of csPCa was higher in MRI-TBx than in SBx, reaching the highest difference for very elderly patients (48% vs 68% at 80 yr). The main limitations were the retrospective design and the small number of young patients.

**Conclusions:** In this study, we reported the performance of MRI and MRI-TBx in detecting csPCa changes according to patients' age.

**Patient summary:** In young patients, the performance of a systematic random biopsy in detecting clinically significant prostate cancer (csPCa) is higher relative to magnetic resonance imaging targeted biopsy (MRI-TBx), reflecting the lower accuracy of MRI in younger men. Conversely, in older patients, MRI-TBx showed a clinical benefit with a higher csPCa detection rate compared with SBx, suggesting an increase of MRI accuracy with the increase of age.

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## 1. Introduction

Prostate cancer (PCa) still represents the most common solid organ malignancy after skin cancer worldwide, with one out of nine men developing this disease during the lifetime [1,2]. Although PCa has historically been considered as a disease affecting older men, a non-negligible proportion of newly diagnosed PCa cases are found in young men. Indeed, the incidence of PCa in men aged 45–49 yr was 39.5 per 100 000 men between 2001 and 2006 [3], with over 10% of the new diagnoses occurring in men aged ≤55 yr [4].

Interestingly, young men diagnosed with PCa seem to have worse prognosis, in terms of cancer-related mortality, compared with their older counterparts [5,6]. This, taken together with a reported slight increase over time in the incidence of PCa in young men not explained by the change in the use of screening tools (ie, prostate-specific antigen [PSA]) [3], increases the need for improvement in the diagnostic assessment of PCa in this population.

Introduction of multiparametric magnetic resonance imaging (MRI) of the prostate in the diagnostic pathway of PCa has significantly improved the ability to detect clinically significant PCa (csPCa), with the potential advantage to spare a proportion of men from receiving a prostate biopsy [7–9]. The use of MRI and eventual subsequent targeted biopsy (MRI-TBx) in addition to the traditional systematic biopsy (SBx) has been demonstrated to be the most accurate and efficient approach for PCa diagnosis [10–12].

Nonetheless, the diagnostic performance of MRI and MRI-TBx in relationship to patients' age has been assessed poorly. Gielchinsky et al. [13] published the only study in this field, retrospectively comparing the sensitivity of MRI in detecting csPCa in two cohorts of men aged <50 and ≥55 yr. The authors reported significantly reduced sensitivity of MRI in the young group compared with the older group (49% vs 72.5% for Prostate Imaging - Reporting and Data System [PI-RADS] score ≥4) [13].

Our hypothesis is that the diagnostic accuracy of MRI varies according to the age of patients, and this is reflected

in the variation in the detection rate of significant disease at MRI-TBx.

In the current study, we aimed at assessing the diagnostic performance of MRI according to patient's age, specifically comparing csPCa detection rate of MRI-TBx versus that of SBx across different patient ages.

## 2. Patients and methods

### 2.1. Study population

Between January 2013 and February 2018, 1208 consecutive patients underwent MRI of the prostate with subsequent targeted fusion (MRI-TBx) and concomitant SBx at two tertiary care referral centres (San Raffaele Hospital, Milan, Italy, and Mayo Clinic Hospital, Rochester, MN, USA). All clinical and pathological data were prospectively collected from the first case performed within a review-board-approved database. For the purpose of the present study, we excluded patients with MRI reporting areas scored as PI-RADS <3 ( $n = 58$ ). Further exclusion criteria included presence of missing values for PSA, prostate volume, clinical stage, and biopsy history ( $n = 220$ ). These selection criteria resulted in a final population of 930 patients.

### 2.2. Multiparametric MRI

All patients underwent a 1.5-T MRI study (Achieva and Achieva dStream; Philips Medical Systems, Best, the Netherlands) or a 3-T MRI study (Discovery; GE Healthcare, Chicago, IL, USA) with phased array surface coil and endorectal coil (BPX-15; Bayer Medical Care, Indianola, PA, USA). According to the European Society of Urogenital Radiology guidelines [14], the imaging protocol consisted of multiplanar T2-weighted images, diffusion weighted imaging (with  $b$  values of 50–800–1600 s/mm<sup>2</sup> in the San Raffaele Hospital cohort and 100–800–1600 s/mm<sup>2</sup> in the Mayo Clinic Hospital cohort; apparent diffusion coefficient [ADC] maps were automatically elaborated), dynamic contrast-enhanced MRI, and delayed T1-weighted images with fat suppression. In both centres for patients who had previously received one or more sets of biopsies, all MRI scans were performed at least after 4 wk from prostate biopsy, and precontrast T1-weighted images were performed to rule out postbiopsy haemorrhagic artefacts. The MR images were scored and reported according to the PI-RADS version 1 [14] and, from 2015 onwards, the subsequent PI-RADS version 2 [15]. Experienced radiologists analysed the MRI findings.

### 2.3. Prostate biopsy

Each patient underwent firstly a software registration targeted biopsy (MRI-TBx) of the lesion detected at MRI. During the same session, each patient underwent subsequently to an SBx (median number of cores 12), according to the current guidelines [16,17]. All biopsies were performed with a transrectal approach. Systematic random biopsies were performed using a Flex Focus 500 machine with a biplanar transducer (BK Medical, Herlev, Denmark) in both centres. Software registration targeted biopsies were performed using the BioJet fusion system (D&K Technologies, Barum, Germany) at San Raffaele Hospital and the UroNav fusion system (Invivo Corp., Gainesville, FL, USA) at Mayo Clinic Hospital. The technical data and usage of BioJet and UroNav fusion systems have been described previously [18–20]. Software registration biopsies were carried out by five experienced urologists overall. All prostate biopsy specimens were analysed by a dedicated uropathologist.

### 2.4. Variable definition

All patients had complete clinical data consisting of age at biopsy, PSA values (ng/ml), prostate volume defined at MRI (cc), digital rectal examination (DRE; normal vs abnormal), PI-RADS (3 vs 4 vs 5), number of SBx cores, number of MRI-TBx cores, and previous biopsy history (biopsy naïve vs repeat biopsy). Primary and secondary Gleason scores were available separately for all cores taken at MRI-TBx and SBx.

### 2.5. Outcomes

The outcome of our study was the relationship between age and csPCa detection rate at MRI-TBx in comparison with SBx corrected for the main confounders. Clinically significant PCa was defined as the presence of PCa with Gleason score  $\geq 3 + 4$ .

### 2.6. Statistical analysis

Our statistical analyses consisted of three main steps. First, the median and interquartile range, and the frequency and proportion were reported for continuous and categorical variables, respectively. A Mann-Whitney *U* test and a Kruskal-Wallis test were used to test the statistical significance of differences between continuous and categorical variables, respectively. Second, two multivariable logistic regression analyses were used to assess the relationship between csPCa detection rate and age at MRI-TBx and SBx, while accounting for different covariates. The following covariates were tested for both MRI-TBx and SBx csPCa detection rates: PSA density (ng/ml/ml), PI-RADS (3 vs 4 vs 5), DRE (normal vs abnormal), and previous biopsy history (biopsy naïve vs repeat biopsy). We also adjusted for either the number of MRI-TBx cores or the number of SBx cores within the two different multivariable logistic regression analyses. Third, the multivariable probability of the csPCa detection rate of MRI-TBx and SBx according to age was graphically depicted using a nonparametric loess analysis [21]. All statistical tests were performed using the RStudio graphical interface v.1.1.383 for R software environment v.3.4.2 (R Foundation, Vienna, Austria). All tests were two sided, with a significance level set at  $p < 0.05$ .

## 3. Results

Descriptive characteristics of the population are reported in Table 1. Overall, 930 men received prostate MRI and subsequent MRI-TBx and SBx in this study. Median age was 67 (interquartile range [IQR]: 61–72) yr, median PSA was 7 (IQR: 5.1–10.3) ng/ml, and 85% had a DRE scored as

normal. Overall, detection rates of PCa and csPCa were 75% (693/930) and 54% (506/930), respectively. The median numbers of MRI-TBx and SBx cores were 5 (IQR: 4–7) and 12 (IQR: 10–13), respectively. Multiparametric MRI reported PI-RADS scores of 3, 4, and 5 in 35%, 45%, and 21% of patients, respectively.

Detection rates of csPCa at MRI-TBx in patients aged  $\leq 50$  and  $>50$  yr were 24% and 52% ( $p < 0.001$ ), respectively. Detection rates of csPCa at MRI-TBx for men aged  $\leq 50$  versus  $>50$  yr for PI-RADS 3, 4, and 5 lesions were 9% versus 29% ( $p = 0.006$ ), 39% versus 56% ( $p = 0.02$ ), and 67% versus 79% ( $p = 0.34$ ), respectively (Table 2).

At the multivariable logistic regression analysis predicting csPCa detection at SBx (Table 3), the presence of a lesion scored as PI-RADS 4 (odds ratio [OR]: 3.78; 95% confidence interval [CI]: 2.65–5.47;  $p < 0.001$ ), presence of a lesion scored as PI-RADS 5 (OR: 4.00; 95% CI: 2.57–6.27;  $p < 0.001$ ), PSA density (OR: 2.93; 95% CI: 1.38–6.73;  $p = 0.008$ ), abnormal DRE (OR: 1.89; 95% CI: 1.28–2.81;  $p = 0.001$ ), the number of SBx cores (OR: 1.06; 95% CI: 1.01–1.11;  $p = 0.01$ ), and the presence of a previous prostate biopsy (OR: 0.43; 95% CI: 0.32–0.58;  $p < 0.001$ ) were independent predictors of the outcome.

At the multivariable logistic regression analysis predicting csPCa detection at MRI-TBx (Table 3), patient age (OR: 1.05, 95% CI: 1.03–1.07;  $p < 0.001$ ), presence of a lesion scored as PI-RADS 4 (OR: 3.24; 95% CI: 2.36–4.49;  $p < 0.001$ ), presence of a lesion scored as PI-RADS 5 (OR: 5.32; 95% CI: 3.47–8.24;  $p < 0.001$ ), PSA density (OR: 56; 95% CI: 30–69;  $p < 0.001$ ), abnormal DRE (OR: 1.97; 95% CI: 1.30–3.00;  $p = 0.001$ ), and presence of a previous prostate biopsy (OR: 0.65; 95% CI: 0.48–0.86;  $p = 0.003$ ) were independent predictors of the outcome.

The multivariable predicted probability of the csPCa detection rate at MRI-TBx and SBx according to age is depicted in Fig. 1. Age was positively correlated with the probability of detecting csPCa in both the biopsy approaches, namely, MRI-TBx and SBx. Nonetheless, age is statistically significantly related only to the probability of detecting significant disease at MRI-TBx (Table 3). The MRI-TBx curve is steeper than the SBx curve, ranging from 16% to 68% for men aged 40 and 80 yr, respectively. Notably, under the age of 50 yr, the predicted probability of detecting csPCa with MRI-TBx becomes lower as compared with SBx (16% vs 25% at 40 yr), even after accounting for all confounders. Conversely, in patients aged  $>50$  yr, the probability of detecting csPCa was higher at MRI-TBx than at SBx, reaching the highest difference for very elderly patients (48% vs 68% at 80 yr). Positive predictive values of MRI were 24% and 52% for men aged  $\leq 50$  and  $>50$  yr, respectively.

## 4. Discussion

During the last few years, significant improvements have been made for the diagnosis of PCa. These improvements are mostly due to the introduction of MRI of the prostate together with the possibility to perform MRI-TBx [9,10]. These tools considerably helped in increasing the

**Table 1 – Descriptive characteristics of 930 patients with positive prostate MRI receiving MRI-TBx and SBx**

Variables	Overall (n = 930)	Age ≤50 (n = 82)	Age >50 (n = 848)	p value
Age at biopsy (yr)				<0.001
Median	67	48	68	
IQR	61–72	43–49	63–73	
PSA value (ng/ml)				<0.001
Median	7.0	5.4	7.3	
IQR	5.1–10.3	4–7	5.3–10.5	
Prostate volume (ml)				0.002
Median	46	42	47	
IQR	35–66	30–53	35–68	
DRE				
Normal	794 (85.4)	75 (91.5)	719 (84.8)	0.3
Abnormal	136 (14.6)	7 (8.5)	129 (15.2)	
PSAd (ng/ml/ml)				0.5
Median	0.1	0.1	0.1	
Range	0.1–0.2	0.1–0.2	0.1–0.2	
Biopsy history				
Biopsy naïve	423 (45.5)	41 (50)	382 (45)	0.67
Repeat biopsy	507 (54.5)	41 (50)	466 (55)	
Number of SBx cores				
Median	12	12	12	0.43
IQR	10–13	11–12	10–13	
Number of MRI-TBx cores				0.07
Median	5	5	5	
IQR	4–7	3–6	4–7	
PI-RADS				
3	322 (34.6)	47 (57.3)	275 (32.4)	
4	416 (44.7)	26 (31.7)	390 (46)	0.012
5	192 (20.6)	9 (11.0)	183 (21.6)	
Overall detection of PCa	693 (74.5)	45 (54.9)	648 (76.4)	<0.001
Overall detection of csPCa	506 (54.4)	23 (28)	483 (57)	<0.001
Detection of csPCa at SBx	325 (34.9)	18 (22)	307 (36.2)	0.01
Detection of csPCa at MRI-TBx	461 (49.6)	20 (24.4)	441 (52)	<0.001

csPCa = clinically significant prostate cancer; DRE = digital rectal examination; IQR = interquartile range; MRI = magnetic resonance imaging of the prostate; MRI-TBx = MRI targeted biopsy; PCa = prostate cancer; PI-RADS = Prostate Imaging Reporting and Data System; PSA = prostate-specific antigen; PSAd = PSA density; SBx = systematic random biopsy.

**Table 2 – Clinically significant PCa detection rate at MRI-TBx in men aged ≤50 and 50 yr, according to PI-RADS score**

PI-RADS	Age ≤50 % (n/N)	Age >50 % (n/N)	p value
3	8.5 (4/47)	28.7 (79/275)	0.006
4	38.5 (10/26)	55.6 (217/390)	0.02
5	66.7 (6/9)	79.2 (145/183)	0.34

MRI-TBx = magnetic resonance imaging targeted biopsy; PCa = prostate cancer; PI-RADS = Prostate Imaging Reporting and Data System.

diagnostic accuracy for csPCa, while giving the possibility to better select patients with a low probability of harbouring a disease that would deserve a treatment [10,12].

Given the incidence of PCa among young populations [3,4] and the importance of further improving the PCa diagnostic pathway in young men, in the current study, we aimed at assessing the diagnostic accuracy of MRI across different ages, considering MRI-TBx as the reference test, compared with SBx.

Indeed, young men benefit most from an efficient PCa diagnostic pathway, receiving a radical treatment when necessary but sparing unnecessary potential side effects (ie,

erectile dysfunction and urinary incontinence) when possible, choosing a less aggressive approach (ie, active surveillance).

According to our knowledge, Gielchinsky et al. [13] carried out the only study evaluating the diagnostic accuracy of MRI according to patients' age. The authors suggested that MRI sensitivity decreased in men aged <50 versus ≥55 yr (49% vs 72.5% for PI-RADS ≥4 and 80.3% vs 84.3% for PI-RADS ≥3). Nonetheless, this study [13] is limited by the small cohort, and most importantly, it is not clear how lesions detected at MRI were matched with the final pathology at radical prostatectomy. To overcome this issue, we relied on MRI-TBx results assessing the variation in csPCa detection rate according to the age of patients in order to evaluate the variation in MRI accuracy at different ages. Moreover, we compared this with the variation in the SBx csPCa detection rate according to patients' age.

First, we demonstrated that age was statistically significantly related to csPCa detection at MRI-TBx. At multivariable logistic regression analyses, the age of a patient was significantly related only to the csPCa detection rate at MRI-TBx (Table 3) but not with the csPCa detection at SBx (Table 3), after accounting for several confounders. This supports our hypothesis, according to which MRI accuracy in



**Table 3 – Multivariable logistic regression model predicting csPCa detection at SBx and MRI-TBx**

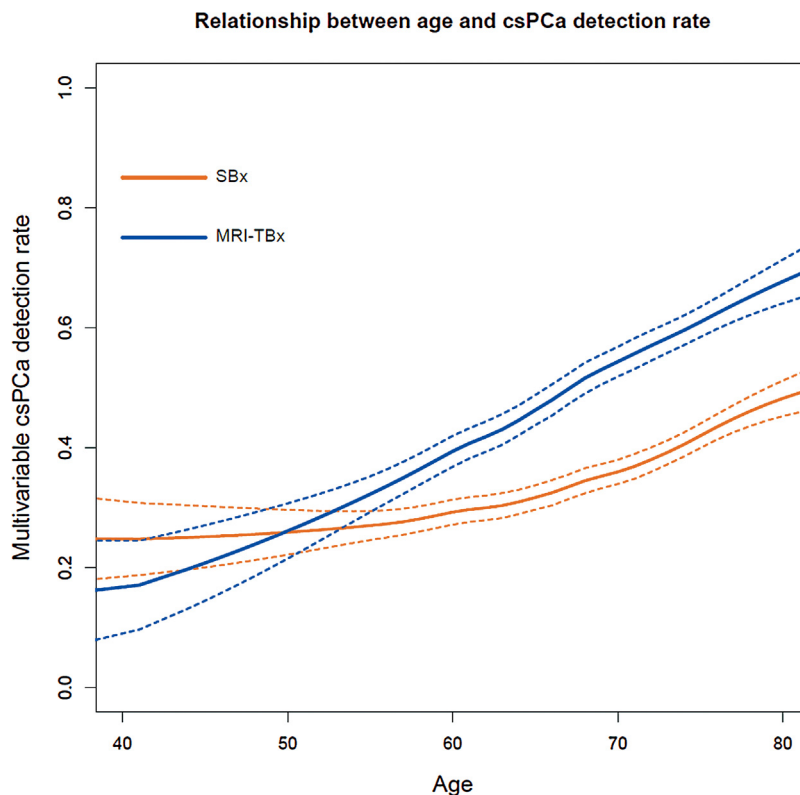
Predictors	Multivariable analysis	
	OR (95% CI)	p value
<b>csPCa detection at SBx</b>		
Age at biopsy	1.01 (1.00–1.03)	0.09
PSAd	2.93 (1.38–6.73)	0.008
DRE		
Normal	Ref.	–
Abnormal	1.89 (1.28–2.81)	0.001
Biopsy history		
Biopsy naive	Ref.	–
Repeat biopsy	0.43 (0.32–0.58)	<0.001
Number of SBx cores	1.06 (1.01–1.11)	0.01
PI-RADS		
3	Ref.	–
4	3.78 (2.65–5.47)	<0.001
5	4.00 (2.57–6.27)	<0.001
<b>csPCa detection at MRI-TBx</b>		
Age at biopsy	1.05 (1.03–1.07)	<0.001
PSAd	56 (30–69)	<0.001
DRE		
Normal	Ref.	–
Abnormal	1.97 (1.30–3.00)	0.001
Biopsy history		
Biopsy naive	Ref.	–
Repeat biopsy	0.65 (0.48–0.86)	0.003
Number of MRI-TBx cores	1.00 (0.95–1.05)	0.8
PI-RADS		
3	Ref.	–
4	3.24 (2.36–4.49)	<0.001
5	5.32 (3.47–8.24)	<0.001
CI = confidence interval; csPCa = clinically significant prostate cancer; DRE = digital rectal examination; MRI = magnetic resonance imaging; MRI-TBx = magnetic resonance imaging targeted biopsy; OR = odds ratio; PI-RADS = Prostate Imaging Reporting and Data System; PSAd = prostate-specific antigen density; Ref. = reference; SBx = systematic random biopsy.		

detecting significant disease changes with patient's age, regardless of any other clinical feature. Moreover, we observed an increase in the csPCa detection rate at SBx according to age (Fig. 1), albeit with a weak correlation (OR: 1.01;  $p = 0.09$ ; Table 3). This result was expected as age is a well-known risk factor for PCa, even though in our analysis its effect is made weaker by the introduction of other strong confounders (ie, PI-RADS). Second, PI-RADS score is related to the csPCa detection rate of both MRI-TBx and SBx. This result is confirmed by our previous findings where we reported that PI-RADS score is significantly related to csPCa multifocality; thus, the higher the PI-RADS score, the higher the probability of finding significant disease in the prostatic tissue surrounding the lesion detected at MRI through systematic sampling [22]. Third, when the multivariable relationship between age and csPCa detection rate at MRI-TBx and SBx was graphically represented (Fig. 1), the MRI-TBx curve was higher than the SBx curve for a wide range of ages; specifically, there was an overall decrease of csPCa detection towards younger men. Nonetheless, the curve related to the MRI-TBx detection rate was steeper and decreased more quickly than the SBx curve. The csPCa detection rate at MRI-TBx became even lower than that at SBx for men aged <50 yr. Therefore, while in older men with positive MRI, MRI-TBx is significantly superior to SBx in detecting csPCa, in very young patients (aged <50 yr), the

performance of MRI/MRI-TBx seems to decrease. Finally, when looking specifically at the csPCa detection according to the PI-RADS score (Table 2), we observed that, given the same score, detection of significant disease at MRI-TBx was higher in older patients, even though only statistically significant for PI-RADS 3 and 4, further confirming our results.

These findings bring two main reflections: (1) an MRI-TBx should be considered in men referred for a suspicion of PCa with positive MRI (ie, PI-RADS  $\geq 3$ ) particularly in those aged >50 yr. In this range of age, MRI-TBx is superior to SBx in detecting csPCa. (2) In very young patients (aged <50 yr), the performance of MRI-TBx and therefore the performance of MRI seem to decrease, particularly for lesions scored as PI-RADS 3 and 4. Therefore, according to our results, positive MRI in patient aged <50 yr might overestimate the risk of the patient to harbour a significant disease compared with the same MRI in older men. Fig. 1 shows that men aged 40 yr with positive MRI have 84% risk to receive a useless MRI-TBx, detecting either no cancer or insignificant disease. In this context, in order to improve risk stratification, the use of further tools might be useful. Several risk calculators, which include age among variables considered, have been developed over the last years [23,24]. These risk tools should be used to identify, among young men with positive MRI, those with a higher risk, in order to minimise unnecessary prostate biopsy and the risk of overdiagnosis.

The phenomenon according to which MRI accuracy changes with age might be due to some factors: First, architectural changes in prostatic tissue that occur with ageing (eg, young men are more likely to have smaller prostates with a more represented peripheral zone). Second, radiologists reporting MRI of a young patient referred for a clinical suspicion of PCa might be biased towards higher PI-RADS scores, resulting in an increased rate of false positives in this population. This could also be partially explained by the fact that the highest and most significant difference in the false positive rate between young and old men referred to indeterminate lesions (ie, PI-RADS 3; 91 vs. 71%; Table 2). An ambiguous lesion in a young patient referred for PCa is presumably more likely to be scored as PI-RADS 3 rather than being scored as non-suspicious. This bias is potentially due to a less specific and more sensitive approach by the radiologist in reporting MRI in young men, although this point should be addressed in a prospective way relying on a cohort that includes men with both positive and negative MRI. Third, differences in sexual activity between young and old populations might affect the quality of MRI sequences. It has been demonstrated that the ejaculatory status influences the ADC at prostate MRI, and more specifically, ejaculation determines a significant reduction in whole-gland ADC, which represents one of the key sequences included in the PI-RADS scoring system [25,26]. This effect may lead to a reporting bias towards higher PI-RADS scores in the population with a higher prevalence of sexual activity, which is justified by the thought that it may be represented by the young cohort. Further experimental studies attempted to address this topic [27–29], reporting a variation in the ADC in prostates at different ages [29].



**Fig. 1 – Multivariable csPCa detection rate of MRI targeted biopsy (MRI-TBx) and systematic random biopsy (SBx) according to patients' age. csPCa = clinically significant prostate cancer; MRI = magnetic resonance imaging.**

We recognise a few limitations of this report. First, this is a retrospective study with a quite long study period. During this time frame, in 2015, PI-RADS score has been updated to version 2 [15]. Since our population included patients of both pre- and post-PI-RADS updates, radiologists might have been affected by changing reporting flowchart, even though the diagnostic performance of PI-RADS versions 1 and 2 seems to be similar [30]. The effect of the use of two different reporting systems across the study period may be even more pronounced on our findings, considering the aforementioned reported effect of age (and sexual activity) on some MRI sequences (eg, ADC) together with the slightly different role of these sequences in PI-RADS versions 1 and 2. Second, even though our results took into account all the potential confounders, differences in PCa prevalence between young and old patients might affect the trend in PCa detection rate according to age. Third, in this study, we used MRI-TBx as a reference test to assess MRI accuracy in detecting csPCa. Limitations of this choice include the presence of a well-known learning curve effect [31,32] in performing MRI-TBx; as a result, this is a not completely reliable reference test. Further prospective studies on radical prostatectomy specimens are needed to confirm our results. Fourth, only men with positive MRI have been included in the current study. This prevented us from assessing the whole diagnostic performance of MRI at different patient ages (ie, sensitivity, specificity, and negative predictive value) and might have introduced some selection bias. Finally, the sample size was rather small in

the very young group; still the high number of patients included overall allowed carrying out of predictive analyses.

## 5. Conclusions

In this study, we reported the performance of MRI and MRI-TBx in detecting csPCa changes according to the age of patients. Specifically, in young patients, the performance of SBx in detecting csPCa is higher than MRI-TBx, reflecting the lower accuracy of MRI in younger men. Conversely, in older patients, MRI-TBx showed a clinical benefit with a higher csPCa detection rate compared with SBx, suggesting an increase of MRI accuracy with the increase of age.

**Author contributions:** Armando Stabile had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Stabile, Briganti.

**Acquisition of data:** Stabile, Soligo, Dell'Oglio, Brembilla.

**Analysis and interpretation of data:** Stabile, Dell'Oglio, Briganti.

**Drafting of the manuscript:** Stabile.

**Critical revision of the manuscript for important intellectual content:**

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