Multifocality of Prostate Cancer based on Magnetic Resonance Imaging: Implications for Focal Therapy

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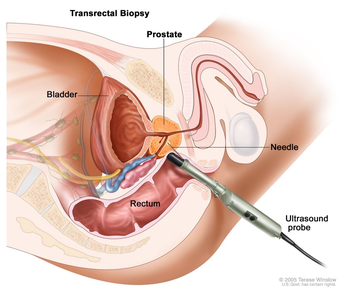
Introduction

- Prostate cancer (PCa) is the most commonly diagnosed cancer in American men and a leading cause of malignancy related deaths.[1]
- Multiparametric magnetic resonance imaging (mpMRI) can identify suspicious lesions, increase the detection of clinically significant PCa, provide information on clinical stage, and help risk-stratify patients on need for biopsy.[2]
- mpMRI has a potential application in guiding focal therapies of the prostate over traditional whole-gland treatments.



"Transrectal Biopsy" by Terese Winslow / U.S. Govt.

- mpMRI limitations exist in detecting smaller low-grade lesions and even high-grade non-index lesions, especially in the apex of the prostate. These findings have brought up uncertainties in the ability of mpMRI to fully depict the multifocality of PCa.[3,4,5]
- Data suggest up to 60% to 90% of PCa are multifocal, but there are a limited number of studies on detection of multifocality on mpMRI proven by biopsy pathology.[6]
- Inadequate information on focality prior to intervention. Thus, definitive whole-gland treatments are utilized, which carry inherent morbidity including incontinence, impotence, and risk of surgical complications.[7]
- Further investigation is needed to understand the efficacy of mpMRI in detecting multifocality in PCa which is directly relevant for planning and implementing focal therapies.

Objectives

- Identify male patients (biopsy-naïve or prior negative biopsy) who have undergone mpMRI and MRI/US fusion-guided biopsy.
- Compare lesions identified on mpMRI to MRI/US fusion-guided targeted biopsy results to calculate prevalence of multifocality along with demographic and clinical variables associated with multifocality.
- Evaluate predictors (demographic and clinical including age, PSA, PIRADS score, location, clinical stage) of contralateral cancer on systematic biopsy among patients with single mpMRI biopsy-confirmed lesions (mpMRI misclassification).
- Estimate the proportion of patients who would be potential candidates for true targeted (focal) therapy, hemigland therapy, whole-gland therapy, or no treatment.

Methods

- Study included biopsy-naïve and prior biopsy-negative men who received mpMRI, fusion-targeted biopsy, and systemic biopsy from the Prospective Loyola University mpMRI (PLUM) Prostate Biopsy Cohort since 2015.
- Tabulated demographic information and clinical characteristics of PCa prior to biopsy for each patient. mpMRI, fusion targeted biopsy, and systemic biopsy findings were analyzed.
- Patients with a single targeted biopsy-confirmed grade group 2 lesion and concordant systemic biopsy finding were considered FT candidates.
- Statistical analysis:
  - Baseline demographics and clinical characteristics were compared by focality (no cancer vs. unifocal vs. multifocal) using appropriate statistical tests (t-test for continuous variables and chi-squared tests for categorical variables).
  - A multivariable logistic regression (MVLR) model evaluated predictors of contralateral PCa on systematic biopsy among men with single mpMRI biopsy-confirmed lesions.

Results

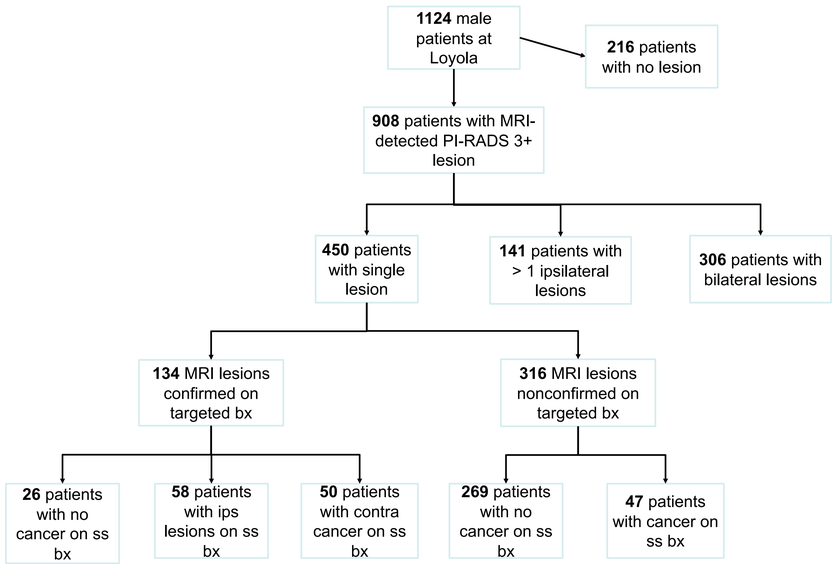


Figure 1. Simplified flow chart of 1124 male patients in PLUM Prostate Biopsy Cohort based on mpMRI, targeted biopsy, and systemic biopsy: 897 men (11 lost due to no laterality data) were included. 450 (50.2%) had a single lesion, 141 (15.7%) had multiple unilateral lesions, and 306 (34.1%) had contralateral lesions. The rate of targeted-biopsy confirmed single lesion and multifocal PCa was 257/897 (28.7%; 167/503 (33.2%) biopsy-naïve subset) and 93/897 (10.4%; 80/503 (15.9%) biopsy-naïve subset), respectively.

		Cancer Location on Systematic Biopsy				
		None or Ipsilateral		Contralateral		p-value
		Median/N	IQR/(%)	Median/N	IQR/(%)	
N		165	-	92	-	
Age		66.8	61.7-72.6	65.5	61.7-70.9	0.8
Family History of Prostate Cancer	Yes	36	(21.8)	21	(22.8)	0.9
	No	129	(78.2)	71	(77.2)	
Race	Caucasian	112	(67.9)	54	(58.7)	0.1
	Hispanic	7	(4.2)	9	(9.8)	
	Asian	6	(3.6)	1	(1.1)	
	African-American	26	(15.8)	15	(16.3)	
	Other/Unknown	14	(8.5)	13	(14.1)	
DRE	Negative	139	(84.2)	66	(71.7)	0.03
	Positive	13	(7.9)	17	(18.5)	
	Unknown	13	(7.9)	9	(9.8)	
Prior Negative Biopsy	Yes	65	(39.4)	25	(27.2)	0.05
	No	100	(60.6)	67	(72.8)	
PSA	(ng/mL)	7.2	5.2-10.4	7.5	5.3-12.7	0.01
Prostate Volume	(cc)	41.1	31.8-58.0	45.0	34.0-63.2	0.7
Highest PI-RADS Lesion	3	20	(12.1)	7	(7.6)	0.5
	4	74	(44.8)	44	(47.8)	
	5	71	(43.0)	41	(44.6)	
Total Number of PI-RADS Lesions	1	84	(50.9)	50	(54.3)	0.4
	2	55	(33.3)	33	(35.9)	
	3	23	(13.9)	9	(9.8)	
	≥4	3	(1.8)	0	0.0	
Grade Group on Targeted Cores	1	50	(30.3)	26	(28.3)	0.005
	2	65	(39.4)	36	(39.1)	
	3	26	(15.8)	11	(12.0)	
	4	19	(11.5)	5	(5.4)	
	5	5	(3.0)	14	(15.2)	

IQR = interquartile range; DRE = digital rectal exam; PSA = prostate-specific antigen; PI-RADS = Prostate Imaging-Reporting and Data System

Table 1. Demographic, clinical, and pathologic characteristics of patients with a single mpMRI-fusion targeted biopsy confirmed lesion stratified by laterality of cancer on systematic biopsy. Prospective Loyola University mpMRI Prostate Biopsy Cohort, 2015-2021

MVLR predictors of contralateral PCa on systematic biopsy:
Positive DRE (OR 3.26 (95%CI 1.38-7.72), PSA (OR 1.98 (95%CI 1.24-3.14), Prior Negative Biopsy (OR 0.50 (95%CI 0.27-0.93)

Results (cont'd)

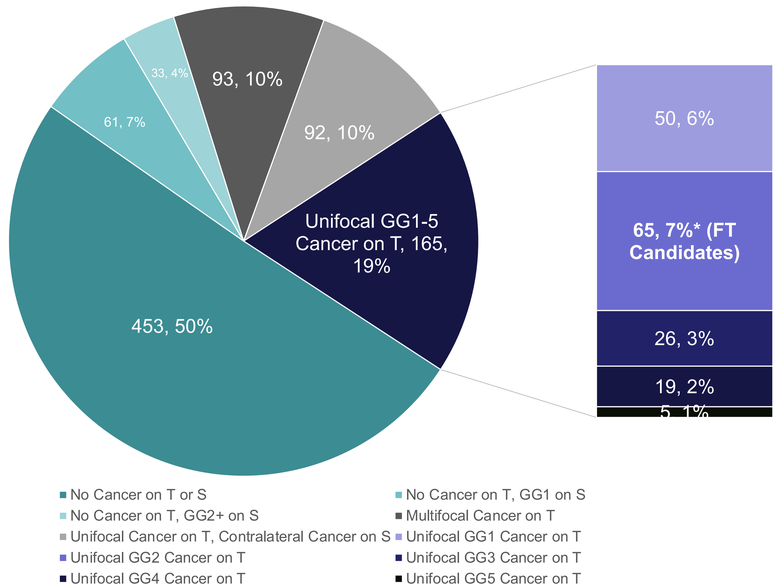


Figure 2. Categorization of men with mpMRI lesion in treatment groups: After comparison with systematic biopsy, the 897 men were categorized into treatment groups based on concordance between mpMRI, fusion targeted biopsy, and systemic biopsy. 165/897 (18.4%; 100/503 (19.9%) biopsy-naïve subset) remained FT candidates. After further restrictions, 61/897 (6.8%) remained potential FT candidates based on having GG2 PCa (61/450 (13.6%) with single lesion on mpMRI).

Conclusion

Prevalence of multifocal and focal PCa

- **28.7%** of men with clinical suspicion of PCa on mpMRI-fusion targeted prostate biopsy had single targeted-biopsy confirmed lesion.
- **10.4%** of men had biopsy-confirmed multifocal cancer on mpMRI, but an additional **10.3%** were multifocal based on contralateral detection on systematic biopsy (mpMRI misclassification).
- After restrictions**, 6.8%** of all men had unifocal GG2 PCa and may be potential candidates for FT.

Considering Focal Therapy

- **Prior biopsy history, DRE status, and PSA** may be potential selection factors for FT inclusion criteria in future clinical trials and treatments.
- Additional studies are necessary to **define strict criteria for FT candidacy** and prevent undertreatment of clinically significant PCa due to mpMRI and biopsy misclassification of multifocality.

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Acknowledgements

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