Developing a Multidisciplinary Prostate MRI Program in a Community –based Health System:

Essential Initial Activities and Clinical Outcomes

Crystal Farrell[1,2] & Sabrina L. Noyes[2], Joe Joslin[2], Manish Varma[2,3], Andrew Moriarity[2,3], Christopher Buchach[2,3], Leena Mammen[2,3], Brian R. Lane[2,4]

[1]Grand Rapids Medical Education Partners/MSU Radiology Residency, Grand Rapids, MI
[2]Spectrum Health, Grand Rapids, MI
[3]Advanced Radiology Services, PC, Grand Rapids, MI
[4]Michigan State University College of Human Medicine, Grand Rapids, MI

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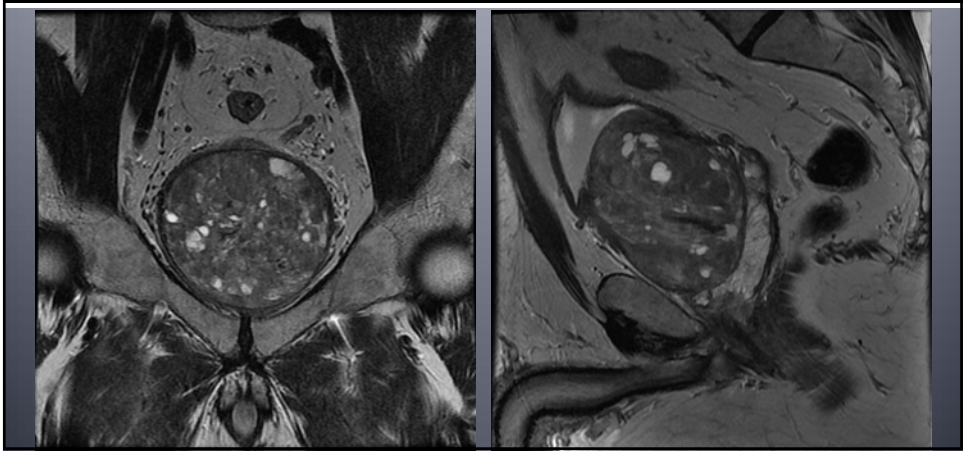


Prostate Cancer (PCa) Background

- PCa is the 2nd most common cancer (behind skin cancer) for men in the U.S. [1]
- PCa is the 2nd leading cause of cancer death (behind lung cancer) for men in the U.S[1]
  - ~180,890 new PCa cases; ~26,120 deaths from PCa
    - 1/7 men will be diagnosed with PCa in their lifetime
    - 1/39 men will die from it
- 5-year PCa-specific survival rates are nearly 100% [1]
  - 10-year survival ~98% when including all stages of PCa

[1] American Cancer Society (2016)

PCa Screening Controversy

- Risks of over-diagnosis and over-treatment
  - Increased morbidity without mortality benefit for treating "dormant malignancies"
  - Grade D recommendation for routine PSA testing by the USPSTF*[2] in 2012
  - Differentiation between clinically-significant and indolent PCa is becoming recognized to be of paramount importance
- New approaches to PCa screening and risk stratification are needed!

*United States Preventative Services Task Force

[2] Moyer VA et al. *Ann Intern Med* 157(2): 120-134, 2012

Prostate Magnetic Resonance Imaging (PMR)

- Initially T1 and T2 weighted sequences only
  - Locoregional staging
- Multiparametric PMR now includes:
  - Diffusion Weighted Imaging (DWI) &
  - Apparent Diffusion Coefficient (ADC) maps
  - Dynamic Contrast Enhancement (DCE)
- Expansion of clinical applications
  - Lesion detection and localization
  - Risk stratification
  - Active surveillance
  - Evaluation for disease recurrence
  - Image guidance for biopsy, surgical planning, and focal therapy

Barriers to Adoption of PMR

- Excessive variability in the use and application of PMR
  - Interpretation subjective, complex, low reproducibility
- Publication of Prostate Imaging Reporting and Data System (PI-RADS) in 2012[3] and PI-RADS v2 in 2015[4]
  - Increased standardization of acquisition protocols, interpretation methods, and reporting systems worldwide

[3]Barentsz JO et al. *Eur Radiol.* 22(4): 746-757, 2012
[4]Weinreb JC et al. *Eur Urol* 69(1): 16-40, 2016

Current State of PMR Programs

- Growing experience at academic centers, but delayed implementation in community settings
  - 89% of the academic institutions performed PMR
  - 60% of large private practice groups
  - compared to 30% of community groups[5]
    - 38% of groups have been performing PMR <5 years
    - 41% between 6 and 10 years[5]
- No current literature on outcomes of PMR programs in community settings
  - Results from "mature" academic programs may not reflect the "learning curve" of program development

[5]Leake et al . *J. Am Coll. Radiol. 11(2): 156-160,* 2014

Purpose

- To describe our >5-year experience developing a community-based PMR program, including:
  - Diagnostic and staging accuracy of PMR over time
    - Based on available biopsy and prostatectomy findings
  - Clinical impact of multidisciplinary PMR meetings
    - Quality and process improvement
    - Changes in patient management

Methods

- IRB approved, retrospective review of a database of all PMR studies performed between August 2010 and December 2015
- Data recorded and analyzed included:
  - Patient demographic information
  - Clinical history
  - PMR interpretations
  - Available biopsy/surgical pathology results
  - Patient specific management plans

Methods

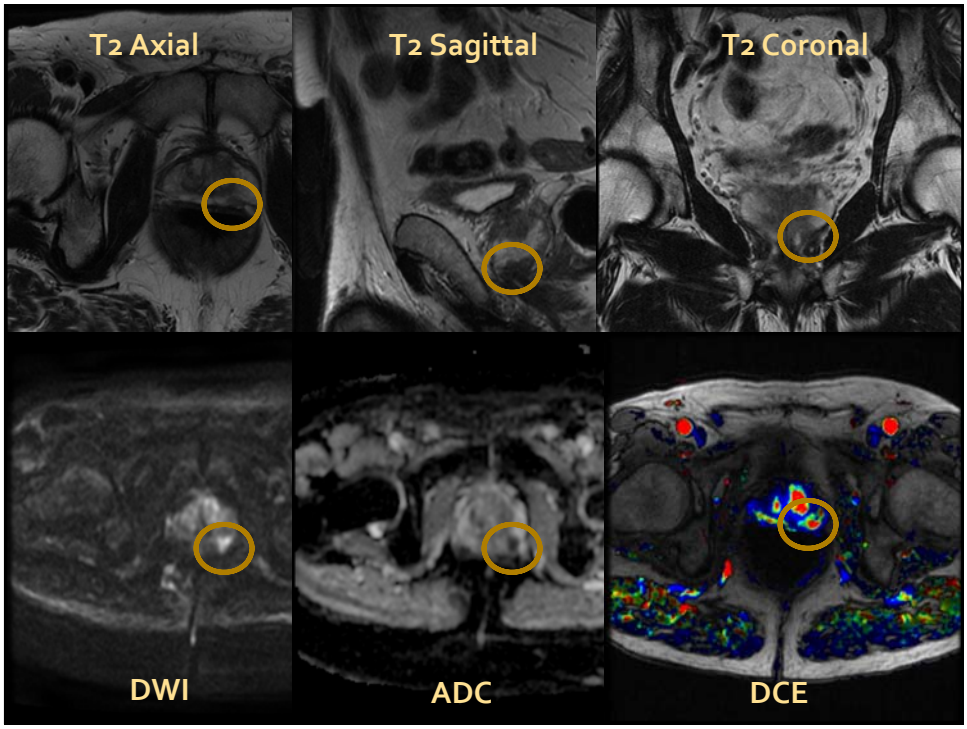
- The overall lesion suspicion level on PMR was correlated with patient pathology results
  - Suspicion level assigned as low, intermediate, or high
- Outcomes were compared across three different reporting experience eras:
  - **Early**: August 2010 – May 2014
    - Presence or absence of suspicious nodules reported
  - **Mid**: June 2014 – February 2015
    - Standardized reporting system- suspicion level based on number of positive parameters out of: T2W, DCE, and DWI
  - **PIRADSv2**: March 2015 – December 2015
    - Implementation of the PI-RADSv2 system

Methods

- Primary outcome:
  - How did the relative proportion of low/int/high suspicion PMR studies compare with the number of positive PCa biopsies over time?
- Secondary outcome:
  - How did staging information on PMR correlate with prostatectomy outcomes over time?
    - Extra-prostatic extension (EPE), seminal vesicle invasion (SVI), lymph node metastasis (LN), or other metastases

Methods

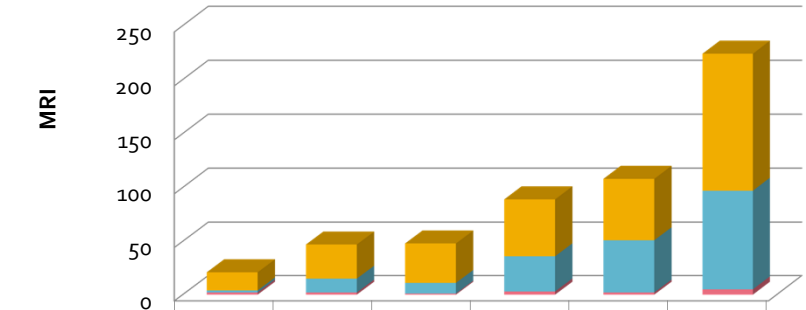
- All statistical analyses were performed using SAS/JMP version 10.0
  - Continuous variables are reported as the median with the interquartile range (IQR; 25^{th}, 75^{th} percentile) or as the mean ± SD
  - Categorical variables are reported as the frequency (%)
- Differences between quantitative variables were analyzed using the t-test, while differences for categorical variables were determined using the chi-square test
  - Statistical significance was assessed at $p < 0.05$



Results

- Timeframe: Between 8/2010 and 12/2015
- 537 PMR studies were performed, increasing in volume every year
- Patient demographics:
  - Median age: 65 years (IQR: 59, 69)
  - 93% of patients were Caucasian
  - 21% had a positive family history of PCa
  - Median PSA prior to PMR was 6.1 ng/ml (IQR: 4.0, 10.0)

PMR Studies



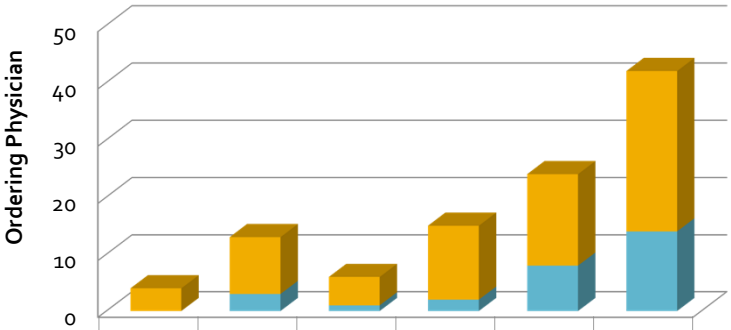
	2010	2011	2012	2013	2014	2015
PCa	17	32	37	53	57	127
PCa screening	2	13	10	33	49	92
Other	2	2	1	3	2	5

Figure 1. Number of PMR studies by diagnosis by year

Results

- Indications:
  - PCa evaluation/staging (60%, n=324)
  - PCa screening (37%, n=198)
    - Including negative prior and no prior biopsies
  - Other prostatic/pelvic disease (2.8%, n=15)
    - The percentage of PCa screening patients more than quadrupled from 9.5% to 41% over 5 years
- Significant increase in the number of ordering physicians occurred in both Mid and PiRADSv2 eras
  - Additional urologists, radiation oncologists, and medical oncologists ordering PMR exams once the program became more established

Ordering Physicians



	2010	2011	2012	2013	2014	2015
Urologist	4	10	5	13	16	28
Other physician	0	3	1	2	8	14

Figure 2. Number of PMR by ordering physician by year

Multispecialty Meetings

- Multispecialty meetings initiated in July 2014
  - Radiologic-pathologic correlation
  - Technical improvements in image quality
  - Selected cases reviewed in detail

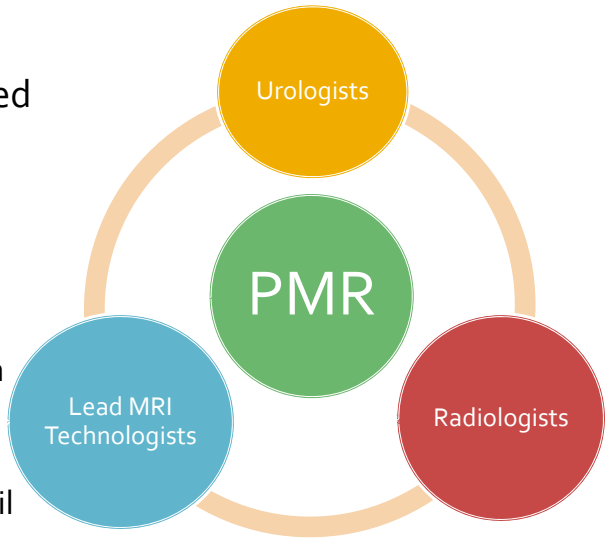
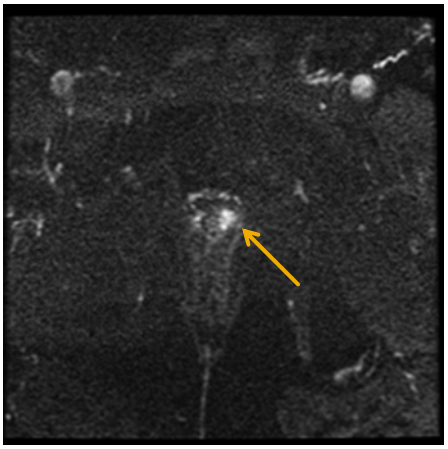
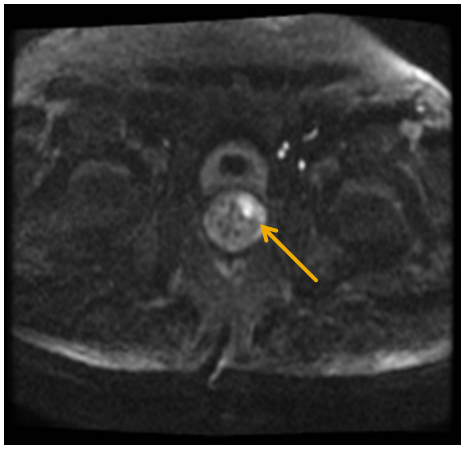


Image Quality: DWI



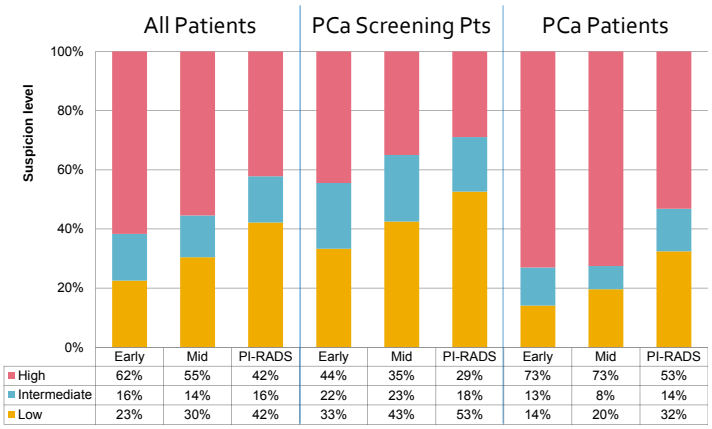


(2012) Same patient (2015)

Impact of Multispecialty Review

- 67 patients reviewed (14%) for clinical, radiographic, and pathologic information
- 51% of reviewed cases subsequently had change in management
  - Different PI-RADSv2 score assigned (n=6)
  - Treatment advised rather than continue on active surveillance (AS) (n= 5)
  - AS without an immediate biopsy (n= 4)
  - Approach to biopsy selected for difficult scenarios (anterior lesions, patients without a rectum) (n=4)
  - Surgical technique changed based on PMR findings (n= 4)

Suspicion Level by Era



	Early	Mid	PI-RADS	Early	Mid	PI-RADS	Early	Mid	PI-RADS
High	62%	55%	42%	44%	35%	29%	73%	73%	53%
Intermediate	16%	14%	16%	22%	23%	18%	13%	8%	14%
Low	23%	30%	42%	33%	43%	53%	14%	20%	32%

Figure 3. Suspicion level on PMR by era.

Suspicion Level by Era

- As the number of low suspicion studies increased, the rate of cancer detection following biopsy also increased
- Patients that underwent biopsy for suspicious lesions had cancer:
  - **Early**: 30 of 61 (49%)
  - **Mid**:6 of 20 (30%)
  - **PI-RADSv2**: 15 of 24 (63%) (p=0.09)

Biopsy Results

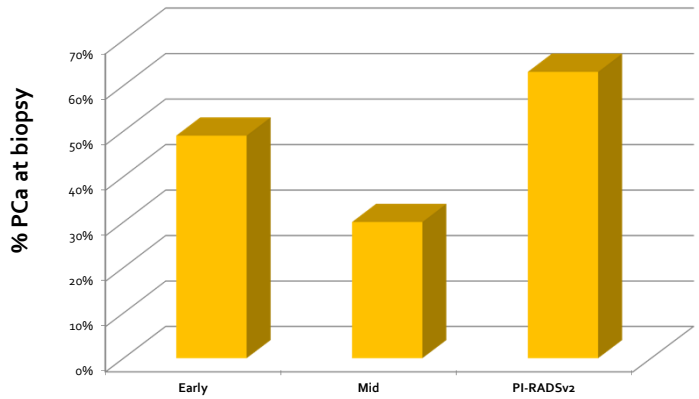


Figure 4. Percentage of biopsies positive for PCa across eras.

Biopsy Results

- 105 pts underwent bx for PMR detected lesions:
  - 7 (7%) following "Low"
  - 25 (24%) following "Intermediate"
  - 73 (70%) following "High" suspicion studies
- PCa detection rates increased according to PMR level of suspicion, with PCa confirmed in
  - 29% (2 of 7) of "Low"
  - 36% (9 of 25) of "Intermediate"
  - 55% (40 of 73) of "High" suspicion studies

Biopsy Results

- PCa rates at biopsy during PI-RADSv2 era were
  - 40% for PI-RADS 3
  - 77% for PI-RADS 4
  - 86% for PI-RADS 5 studies
- Biopsy pathology included
  - Gleason 4+5 (n=3), 4+4 (n=1), 4+3 (n=7), 3+4 (n=21), 3+3 (n=18)
  - Atypical small acinar proliferation (n=10)

PMR Staging: All Patients

All Patients	Overall (n=535)	Early (n=253)	Mid (n=92)	PI-RADSv2 (n=190)	P-value
Extraprostatic extension (EPE)*	17% (87)	18% (43)	17% (15)	16% (29)	0.87
Seminal vesical invasion (SVI)*	7.3% (37)	7.9% (19)	8.0% (7)	6.1% (11)	0.74
Lymph node involvement	6.9% (37)	7.9% (20)	7.6% (7)	5.3% (10)	0.53
Other metastasis	4.1% (22)	3.6% (9)	6.5% (6)	3.7% (7)	0.44

*Of the 537 PMR, EPE and SVI were not evaluable in 26 patients s/p prostatectomy, 1 with hemorrhage from biopsy 3 weeks prior, and 2 with claustrophobia, leaving 508 for analysis. LN involvement and metastasis was assessed in 535 patients (all but the 2 with claustrophobia).

Table 1. Percentages of all patients with locally-advanced or metastatic PCa based on PMR findings.

PMR Staging: PCa Patients

- There were no statistically significant differences in staging information across eras
- As expected, there were slightly higher rates metastatic disease in known PCa patients

PCa Patients	Overall (n= 325)	Early (n= 163)	Mid (n= 51)	PI-RADSv2 (n= 111)	P-value
EPE*	24% (73)	24% (36)	28% (13)	24% (24)	0.87
SVI*	10% (30)	9.9% (15)	11% (5)	10% (10)	0.74
LN	8% (26)	9.8% (16)	8.7% (4)	5.4% (6)	0.53
Other mets	5.6% (18)	4.3% (7)	9.8% (5)	5.4% (6)	0.4

Table 2. Percentages of PCa patients with locally-advanced or metastatic PCa based on PMR findings.
*See footnote on previous slide

Staging Accuracy at Prostatectomy

	EPE (n=77)	SVI (n=77)	LN (n=78)
Sensitivity	56.3%	58.3%	75.0%
Specificity	77.8%	90.8%	98.5%
Positive predictive value	64.3%	53.4%	90.0%
Negative predictive value	71.4%	92.2%	95.6%

EPE, extraprostatic extension; SVI, seminal vesicle invasion; LN, lymph node metastasis
Based on 78 patients who underwent prostatectomy and lymph node dissection after PMR;
1 study was indeterminate for EPE and SVI and thus excluded.

Table 3. Diagnostic accuracy of PMR in patients with pathologic confirmation at prostatectomy.

Discussion

- Staging information was consistent throughout all eras, even early in the program
  - Sensitivities/Specificities within range of published literature[6]
- There was a high false positive rate for lesion characterization and risk stratification in the Early and Mid eras
- Cancer detection rate increased during the PI-RADSv2 era to 63%
  - Improved image quality
  - Standardized interpretation and reporting methods
  - Multidisciplinary collaboration

[6]Bonekamp D et al . *Radiographics 31(3): 677-703*, 2011

Limitations

- PI-RADS not adopted until version 2 published in 2015
  - Early and Mid eras not based on validated scoring system
- Biases
  - Only selected cases discussed at Multidisciplinary meetings
  - Image quality improved in later eras
- Pathologic correlation
  - Many patients (predictably) did not undergo biopsy or surgery after PMR
  - Rad-Path correlation not performed on a per nodule basis
- Sample size
  - Subset to determine sensitivity and specificity for PCa detection was smaller than the overall cohort
  - 24 patients managed by an outside physician and/or lost to follow-up

Future Directions

- UroNav results on first 42 patients:
  - Prostate cancer detected:
    - 30 of 42 patients (71%)
  - Cancer in target lesion:
    - PIRADS 4/5: 19 of 31 (61%)
    - PIRADS 3: 2 of 10 (20%)
    - 73% were high-grade cancer
      - Gleason 4 +4 (2), 4+3 (1), 3+4 (13), 3+3 (6)

Conclusion

- PMR is a powerful up and coming tool for prostate disease evaluation and management
- Staging information is accurate, even early in the program
- There is a "learning curve" for identifying and characterizing clinically significant PCa lesions
  - Improved with PI-RADSv2 criteria and reader experience
  - Aided by regular multidisciplinary meetings with radiologic/pathologic correlation

Conclusion

- Regular multidisciplinary meetings
  - Increase PMR reliability and reputation
  - Maximize clinical impact and patient outcomes
  - Foster interdepartmental collegiality and cooperation
- A successful community-based PMR program depends on:
  - Strong interdisciplinary communication
  - Cooperation
  - Trust
    - All of which require time and effort to build

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- Betz Family Endowment for Cancer Research through the Spectrum Health Foundation
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THANK YOU!!

References

1. American Cancer Society. (2016) Cancer Facts & Figures 2016. Atlanta.
2. Moyer VA, U.S. Preventative Services Task Force. (2012) Screening for prostate cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med 157(2):120-134.*
3. Barentsz JO, Richenberg J, Clements R, et al. (2012) ESUR prostate MR guidelines 2012. *Eur Radiol 22(4):746-757.*
4. Weinreb JC, Barentsz JO, Choyke PL, et al. (2016) PI-RADS Prostate Imaging - Reporting and Data System: 2015, Version 2. *Eur Urol 69(1):16-40.*
5. Leake JL, Hardman R, Ojili V, et al. (2014) Prostate MRI: access to and current practice of PMRI in the United States. *J Am Coll Radiol 11(2):156-160.*
6. Bonekamp D, Jacobs MA, El-Khouli R, et al. (2011) Advancements in MR imaging of the prostate: from diagnosis to interventions. *Radiographics 31(3):677-703.*