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

Essential Initial Activities and Clinical Outcomes

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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.S¹
  - ~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
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

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


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

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

All statistical analyses were performed using SAS/JMP version 10.0
- Continuous variables are reported as the median with the interquartile range (IQR; 25th, 75th 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

Figure 1. Number of PMR studies by diagnosis by year

<table>
<thead>
<tr>
<th>Year</th>
<th>PCa</th>
<th>PCa screening</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>17</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>2011</td>
<td>32</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>2012</td>
<td>37</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>2013</td>
<td>53</td>
<td>33</td>
<td>3</td>
</tr>
<tr>
<td>2014</td>
<td>57</td>
<td>49</td>
<td>2</td>
</tr>
<tr>
<td>2015</td>
<td>127</td>
<td>92</td>
<td>5</td>
</tr>
</tbody>
</table>

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**

![Graph showing the number of PMR by ordering physician by year]

**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
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)
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*)

*Figure 3. Suspicion level on PMR by era.*
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

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

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

*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 of metastatic disease in known PCa patients

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

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

<table>
<thead>
<tr>
<th></th>
<th>EPE (n=77)</th>
<th>SVI (n=77)</th>
<th>LN (n=78)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>56.3%</td>
<td>58.3%</td>
<td>75.0%</td>
</tr>
<tr>
<td>Specificity</td>
<td>77.8%</td>
<td>90.8%</td>
<td>98.5%</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>64.3%</td>
<td>53.4%</td>
<td>90.0%</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>71.4%</td>
<td>92.2%</td>
<td>95.6%</td>
</tr>
</tbody>
</table>

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
- 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


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
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)

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

Acknowledgments

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- All the MRI techs who helped obtain images

THANK YOU!!


