Prostate Cancer
— Facts, Diagnosis, Use of Medical Images in Guiding Biopsy and Improving Cancer Detection

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Outline

• Prostate
• Prostate Cancer
• Diagnosis of Prostate Cancer
• Biopsy Strategies
• Imaging/Image Analysis to aid diagnosis
1. Prostate

Fig 1. Sagittal view of prostate and peripheral organs[1].

Fig 2. Prostate zonal anatomy[2].

Fig 1. Sagittal view of prostate and peripheral organs[1].
2. Prostate Cancer (1)

- Definition: adenocarcinoma (glandular cancer)
- Symptoms: urination & ejaculation problems

Normal\(^3\)

Infection\(^3\)
(Benign Prostate Hyperlasia)

Enlargement\(^3\)

Cancer\(^4\)
2. Prostate Cancer (2)

- Causes: unknown
- Epidemiology
  - age\(^5\),
  - genetics (race\(^5\), family history)
  - diet, lifestyle, medication, etc.
- Risk
  - metastasis \(^8\)
2. Prostate Cancer (2)

- Causes: unknown
- Epidemiology
  - age\[^5\],
  - genetics (race\[^5\], family history, diet, lifestyle, medication, etc.
- Risk
  - metastasis \[^8\]
2. Prostate Cancer (2)

- Causes: unknown
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  - age\(^{[5]}\),
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  - metastasis \(^{[8]}\)
2. Prostate Cancer (2)

- Causes: unknown
- Epidemiology
  - age, genetics (race, family history)
  - diet, lifestyle, medication, etc.
- Risk
  - metastasis
2. Prostate Cancer (3)

Incidence Rate [5]  

Fatality Rate [5]

Cancer Statistics[5]. 2007
3. Diagnosis of Prostate Cancer

- No symptom at early stage
- Prostate-specific antigen (PSA) test
- Digital rectal exam (DRE)
- Biopsy
- Staging
- Imaging for diagnosis and staging
3.1 Prostate-Specific Antigen (PSA) test

- Antigen
- PSA
- PSA test \(^1\) (unit: ng/ml)
  - < 4 (or, < 6.5 for 65 or older): normal
  - 4-10: 25% chances
  - >10: 50 chances
- Problem
3.2 Digital Rectal Exam (DRE)\cite{6}

- Check the size, shape and texture of the prostate
- Able to find cancers in men with normal PSA
- However, DRE only find advanced cancer – no effect in early diagnosis
3.3 Biopsy

- The only test to confirm diagnosis

Trans-Rectal UltraSound (TRUS) guided biopsy[7]
3.4 Prostate Cancer Grading/Staging

- Conducted if prostate cancer confirmed in biopsy
- Tumor/Nodes/Metastases (TNM) system, T1-T4
- Gleason System, score 2-10

Staging by TNM system. [7]
3.5 Imaging

TRUS, sagittal

CT

MRI, T2-weighted, fast spin-echo. 1.5T. Left to right: Axia/Coronal/Sagittal

4. Biopsy Strategies

• Motivation

To optimize the needle biopsy placement with
1) maximum prostate cancer detection rate
2) minimum number of biopsy cores
4. Biopsy Strategies

4.1 Random Systematic Method

The most increasing point is 10-core biopsy. [9]

Noguchi et al, 2006
4.2 Computerized Biopsy Strategies

  - divide the prostate into 48 (or 64 in Mazal’s work) boxes
  - analyze statistical cancer occurrence in those boxes
  - place needles in a subset of those boxes
  - voxel-wise registration by AFDM
  - search $k$ independent locations with maximum statistical cancer occurrence

They are all based on statistical cancer distribution of a large number of prostate specimens, or, population-based cancer information.
4.3 Possible improvement

- Patient-specific biopsy protocols
- How?
  a) suspicious cancer tissues in a patient’s own image
     -- patient-specific cancer information
  b) statistical cancer distribution in a large number of prostate specimens
     -- population-based cancer information
- So, patient-specific + population-based information
- Challenge:
  Can we detect prostate cancer in images and achieve desirable accuracy?
5. Imaging/Image Analysis to aid diagnosis

• Imaging Modalities
  - T2-Weighted (T2W)
  - Diffusion Weighted Imaging (DWI)
  - Dynamic Contrast Enhanced Imaging (DCE)
  - MR Spectroscopy (MRS)

• Image Analysis literature
5.1.1 T2-weighted image

Figure 5: Images in 45-year-old man with prostate cancer stage pT2b and presurgical PSA level of 5.1 ng/mL. (a) Transverse, (b) coronal, and (c) sagittal unenhanced T2-weighted fast spin-echo (repetition time msec/echo time msec of 5000/96[effective]) MR images demonstrate a low-signal-intensity area (arrow) in the peripheral zone of right posterolateral midgland and apex. Tumor appears confined to the gland, as outer margin in all planes is smooth.

Hricak et al, Radiology. 2007
5.1.1 T2-weighted image (cont.)

Table 1 - Studies using unenhanced T2-weighted magnetic resonance imaging and whole-mount histology correlation to detect intraprostatic disease

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of patients (no. of tumours assessed), no. of segments used for analysis</th>
<th>Coil type</th>
<th>Study design and exclusions</th>
<th>Sensitivity (specificity) and further findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifkin 1990 [72]</td>
<td>186 (259)</td>
<td>Body coil</td>
<td>Incidental cancers &gt;0.5 cm in diameter included Prospective</td>
<td>60% for &lt;1 cm, 71% for &gt; 1 cm</td>
</tr>
<tr>
<td>Parivar 1991 [73]</td>
<td>12 (26)</td>
<td>Endorectal</td>
<td>All cancers included Prospective</td>
<td>77%</td>
</tr>
<tr>
<td>Quint 1991 [20]</td>
<td>26 (54)</td>
<td>Body coil</td>
<td>All cancers included Prospective</td>
<td>54% for cancers &gt;0.1 ml 37% if all included</td>
</tr>
<tr>
<td>Carter 1991 [74]</td>
<td>53 (84) 4 segments</td>
<td>Not stated</td>
<td>All cancers included Retrospective</td>
<td>96% for the clinically palpable tumors 58% (43%) for the impalpable 85% sensitivity for posterior impalpable tumours 15% for anterior 50% 79% of missed tumours were at least partly anterior 62% 78/79 anterior gland cancers were missed</td>
</tr>
<tr>
<td>Quinn 1994 [75]</td>
<td>69 (134)</td>
<td>Endorectal</td>
<td>All cancers included Prospective</td>
<td>50%</td>
</tr>
<tr>
<td>Ellis 1994 [24]</td>
<td>330 (484)</td>
<td>Body coil</td>
<td>Incidental cancers &gt;0.5 cm in diameter included Prospective</td>
<td>79% of missed tumours were at least partly anterior 62% 78/79 anterior gland cancers were missed</td>
</tr>
<tr>
<td>Hricak 1994 [21]</td>
<td>71 (126 positive halves) 2 segments (see note in text)</td>
<td>Endorectal and pelvic phased array</td>
<td>TZ cancers not included</td>
<td>96% (98%) endorectal coil 92% (21%) pelvic phased array 67% 14/18 missed tumours were in the central zone (sensitivity 92% for peripheral) 60% (83%) overall 53% (67%) anterior gland 77% (38%) posterior gland 77% (61%) reader 1</td>
</tr>
<tr>
<td>Jager 1996 [53]</td>
<td>34 (52)</td>
<td>Endorectal</td>
<td>All cancers included Prospective</td>
<td>67%</td>
</tr>
<tr>
<td>Ikomen 1988 [25]</td>
<td>51 (324 positive segments) 10 segments</td>
<td>Endorectal</td>
<td>All cancers included Retrospective</td>
<td>53% (67%) overall 77% (38%) posterior gland 77% (61%) reader 1</td>
</tr>
<tr>
<td>Schellhammer 1999 [19]</td>
<td>53 (155 positive segments) 6 segments</td>
<td>Endorectal and pelvic phased array</td>
<td>TZ cancers not included</td>
<td>81% (46%) reader 2</td>
</tr>
</tbody>
</table>

Only studies including incidental tumours are included.
TZ = transitional zone.

Kirkham et al, European Urology. 2006
5.1.2 Diffusion Weighted Image (DWI)

Conclusion: T2W+DWI > T2W

5.1.3 Apparent Diffusion Coefficient (ADC)

Conclusion from 33 patients: ADC values are significantly lower in malignant area than normal area.

Figure 3. Box plot comparing ADC values in malignant peripheral zone (PZ), central gland (CG) and non-malignant PZ.

5.1.4 Dynamic Contrast Enhanced MR

- Four parameters on time-concentration curve:
  - start of enhancement (onset)
  - time to peak enhancement
  - peak enhancement
  - washout time
- Challenge: Spatial-temporal tradeoff

Futterer et al, Radiology, 2005
Conclusion: T2W+DCE > DCE > T2W

Futterer et al, Radiology, 2005
### 5.1.3 DCE-MR (cont.)

#### Table 2 – Studies using dynamic magnetic resonance scans and whole-mount histology correlation to detect intraprostatic disease

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of patients (no. of tumours assessed)</th>
<th>Sensitivity, (specificity) and further findings</th>
<th>Study design</th>
<th>No. of slices</th>
<th>Temporal resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jager 1997 [17]</td>
<td>57 (102 positive segments) 4 segments</td>
<td>57% (80%) T2 73% (81%) with dynamic contrast 6 patients: major improvement in detection or staging with contrast</td>
<td>Incidental cancers included Prospective</td>
<td>One slice, 1.25, 2.5 s</td>
<td></td>
</tr>
<tr>
<td>Ogura 2001 [35]</td>
<td>38 (85 positive segments) 7 segments</td>
<td>59% (88%) PZ: 81% (79%) TZ: 37% (97%)</td>
<td>Incidental cancers included Prospective</td>
<td>Gland covered, 30 s</td>
<td></td>
</tr>
<tr>
<td>Preziosi 2003 [29]</td>
<td>11 (17) 7 segments</td>
<td>76% (one 5-mm anterior lesion and three 1-mm lesions missed) 9 patients had PZ tumour, 4 TZ 2/9 cases did not have an equivalent low-density T2 area</td>
<td>Incidental cancers included Prospective</td>
<td>Gland covered, 30 s</td>
<td></td>
</tr>
<tr>
<td>Schlemmer 2004 [32]</td>
<td>28 (28)</td>
<td>79% T2 (PZ) 68% dynamic (PZ) 89% (both) Signal enhancement started earlier in high-grade tumors</td>
<td>Incidental and TZ cancers not included Retrospective</td>
<td>10 slices, 13 s</td>
<td></td>
</tr>
<tr>
<td>Nakashima 2004 [50]</td>
<td>95 (186)</td>
<td>58% (85% for &gt;1-cm diameter tumours)</td>
<td>Incidental cancers included Prospective</td>
<td>Not stated</td>
<td></td>
</tr>
</tbody>
</table>

All studies used endorectal coils. TZ = transitional zone; PZ = peripheral zone.

Kirkham et al, European Urology. 2006
5.1.5 MR Spectroscopy (MRS)

- MRS provides metabolic information of tissues.
- It displays relative concentration of citrate, creatine, choline and polyamines for each voxel.
- \(\frac{(\text{Cho} + \text{Cr})}{\text{Cit}}\)
5.1.6 Multi-modality Analysis

Conclusion:
T2W+DEC+spectroscopy

Futterer et al, Radiology. 2006
Conclusion: T2W+DWI+ADC+DCE > each separately

Tanimoto et al, J. MRI. 2007
5. Imaging Modalities (cont.)


• • •
5.1 Imaging Modalities - Summary

• Available modalities
  - functional MR: \textit{DCE + DWI/ADC + Spectroscopy}
  - structural MR: \textit{T2W}
  - functional + structural MR

• Research Trends
  - Information fusion + automated cancer detection
  - which modality is more important
  - Multi-modality used in cancer staging
  - 1.5T or 3T?
5.2 Image Analysis in Prostate Cancer Diagnosis

Prostate Cancer Detection in *ex vivo* T2 MR images
- Texture feature: GLCM + Gabor
- Tissue Classification
- Average 42.35% detection accuracy

Madabhushi et al, TMI. 2005
5.2 Image Analysis in Prostate Cancer Diagnosis (cont.)

Feature: GLCM + DCT
Classifier: FLD or SVM
Ground Truth: manual + biopsy validation

Training scheme

Probability Map

6. Summary

- Prostate cancer is a big issue
- Early diagnosis is very important
- Biopsy is the gold-standard to confirm diagnosis
- To optimize biopsy, patient-specific and population-based cancer info. can be utilized
- Multi-channel MR (T2W+DWI+ADC+DCE+MRS) has stronger differentiation ability than single MR modality
Reference

[6] American Cancer Society: How is prostate cancer found?