MRI and MRSI of Prostate Cancer

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Disclosures

Choi receives research support from GE Healthcare.

Ma is an inventor of United States patents that are licensed to GE Healthcare and Siemens AG. He also receives research support from GE Healthcare and Siemens AG.

Contents

1. Clinical aspect of prostate cancer
2. Radiological aspect of prostate cancer
3. Technical considerations in prostate MRSI
4. Clinical application of spectroscopy
5. Discussion and summary
Introduction

- The most commonly diagnosed visceral cancer
- The second most common cause of cancer death in American men
- Up to 15-30% of men over age 50: Indolent

Normal Anatomy

- Histology: glandular + non-glandular
- Model by McNeal: 4 zones
  - Peripheral zone (PZ; 70-80%)
  - Central zone (CZ; 20%)
  - Transitional zone (TZ; 5%)
  - Anterior fibromuscular stroma (AFS)

Prostate Cancer

- Site: PZ 70%, TZ 20%, CZ 10%
- Histopathology
  95% - Adenocarcinoma - acini of prostate duct
  5% - small-cell carcinoma: most common mucinous adenocarcinoma squamous carcinoma sarcomatoid carcinoma TCC adenoid basal cell tumors malignant mesenchymal tumors etc.
Diagnosis of Prostate Carcinoma

- Digital rectal examination (DRE)
- PSA: <4ng/ml
- Trans-rectal ultrasound (TRUS): “Gleason score”

Clinical challenges in detection

- PSA
  - 70-80% of patients with PSA >4ng/ml DO NOT have prostate carcinoma
  - Normal PSA (<4ng/ml) in nearly 20% of biopsy proven prostate carcinoma
- DRE
  - Underestimate local extent up to 40-60%

Imaging Techniques

- Systemic disease
  - CT
  - Bone scan
  - MRI

- Local disease
  - MRI

Cancer Imaging 144,2000
**Clinical management**

- Diagnosis
- Staging and Risk Assessment
- Detection
- Treatment
- Follow-up

**T Primary tumor**

- **T1** Clinically inapparent tumor, not palpable, not visible on TRUS
- **T2** Clinically localized within the prostate
- **T3** Clinically locally invasive beyond the capsule
  - T3a Extracapsular extension
  - T3b Tumor invades the SV
- **T4** Clinically locally invasive involving the adjacent organs (e.g. rectum, bladder, levator ani)
Treatment planning – Rad Onc

MRI-CT coregistration

Treatment planning

Simulated IMRT planning with a boost
Challenges in Image interpretation

- Post-biopsy change
- Post-biopsy hemorrhage
- Prostatitis
- Hormone
- Radiation
- Atrophy
- etc.

Multimodal MRI

<table>
<thead>
<tr>
<th>Image</th>
<th>Technique</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>eMRI</td>
<td>Anatomy</td>
<td>High resolution (e.g. 3mm)</td>
<td>Universal Consistent</td>
</tr>
<tr>
<td>DWI</td>
<td>Diffusion Cell density</td>
<td>ADC map</td>
<td>Short scan time</td>
</tr>
<tr>
<td>DCE-MRI</td>
<td>Perfusion Angiogenesis</td>
<td>Degree, Rate of enhancement</td>
<td>Specific in the setting of RP or post treatment</td>
</tr>
<tr>
<td>Hi-MRSI</td>
<td>Prostate Metabolism</td>
<td>Cho, Po, Cr, Ci</td>
<td>Specific to the prostate cancer</td>
</tr>
</tbody>
</table>

MR Spectroscopy

- A technique to provide metabolic or biochemical information of tissue

- $^1$H, $^3$P, $^{13}$C, $^{19}$F, $^{23}$Na, $^7$Li, $^{39}$K, $^{15}$N, $^{17}$O
Normal prostate

- **Citrate**: (substantially high)
  - Essential end-product of epithelial cells
  - \(24-130 \text{ mM} = x \times 240-1300 \text{ of blood level}

- **Choline**:
  - Essential nutrient for cell membrane synthesis
  - Compounds involving the phospholipid synthesis and hydrolysis (e.g. choline, phosphocholine)

- **Polyamine**:
  - Highly concentrated in epithelial cells
  - Regulate epithelial cell proliferation, differentiation, and growth of epithelial cells

*No significant change in peripheral zone citrate and choline levels with age*

Prostate \(^1\)H-MR Spectroscopy
Prostate carcinoma

- **Citrate:**
  - Change in epithelial cellular function and structure
  - Transformation of epithelial cells to citrate-oxidizing cells that may be essential in process of malignancy and metastasis

- **Choline:**
  - Inc. rate of cell proliferation
  - Inc. cell density
  - Change in cell membrane composition

- **Polyamine:**
  - Overexpression of ornithine decarboxylase, a polyamine biosynthesis enzyme
### Interpretation of MRSI

- Primary score based on Ch+Cr/Cit ratio:

<table>
<thead>
<tr>
<th>SDs from Normal</th>
<th>0-1</th>
<th>1-2</th>
<th>2-3</th>
<th>3-4</th>
<th>4+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

- Initial adjustment:
  - Ch/Cr > 2:1 or 3 to 4
  - Ch/Cr < 2:1 or normal polyamines - 4 to 3, 5 to 4

- Final adjustment:
  - SNR < &: 4 to 3, 5 to 4

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### Technical considerations for high-quality prostate MRSI

- Technical overview of prostate MRSI
- Patient selection, preparation, and setup
- Prescribing prostate MRSI
- Automatic and manual prescan tuning
- Patient communication and cooperation
Basic building blocks of MRSI

- PRESS-CSI
- Outer volume signal suppression
- CHESS for water suppression

PRESS-CSI

- Slice selective excitation and refocussing RF pulses in orthogonal directions → define inner volume
- CSI: phase encode each step in all directions → long acquisition time
- Dual-band spectral spatial refocusing pulses or BASING pulse used for water and lipid suppression

Outer volume signal suppression

- Very selective spatial saturation (VSS) RF pulses
  - 2ms 11kHz or 7kHz
- 6-12 repetitively applied pulses to help conform to a volume of interest (VOI)
- Progressive flip angles
  - B1 homogeneity
  - TG accuracy
CHESS for water suppression
• Repetitively applied to knock down water signal
  – Based on the same principle as FatSat pulses (excitation + spoiling)
  – Subject to the same pitfalls when B₀ and B₁ are inhomogeneous or inaccurate
  – Small residual water signal is used as reference

Patient selection
• Post biopsy
  – Wait 4-6 weeks for blood clots to resolve
• Patients with brachytherapy seeds
• Patients with hip or other metal implants

Patient preparation and Setup
• Nurse and technologist’s experience in placing endorectal coil

L/R  S/I
Prescribing prostate MRSI

- Recognizing anatomy in all three planes

Automatic and Manual prescan

- After auto prescan (APS), look for:
  - FWHM (<15Hz at 1.5T)
  - Water suppression (>98%)
  - TG (with scanner limit)

- Repeat APS or Adjust graphic prescription and repeat APS

- Manual spectro prescan
  - B0 shimming
  - TG may need adjust at 3T
Bo Shimming

before

after

Patient communication

Communicate to the patient that the next scan is about 15 minutes, and it is very important that he breathes nice and easy and try not to move during the scan.
Clinical Applications of MRSI

- Detection
- Staging
- Surveillance

Tumor behavior

Non-specific low T2

Post biopsy hemorrhage
Detection Accuracy

<table>
<thead>
<tr>
<th></th>
<th>MRI Reader 1</th>
<th>MRI Reader 2</th>
<th>MRSI</th>
<th>MRI+ MRSI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>77</td>
<td>81</td>
<td>63</td>
<td>95</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>61</td>
<td>46</td>
<td>75</td>
<td>91</td>
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</table>

UCSF, Radiol 1999; 213:473-480

Detection: T2 vs. DCE, MRSI

<table>
<thead>
<tr>
<th></th>
<th>SE</th>
<th>SP</th>
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<tbody>
<tr>
<td>T2</td>
<td>73/42*</td>
<td>89/83*</td>
</tr>
<tr>
<td>DCE</td>
<td>42/18*</td>
<td>97/96*</td>
</tr>
<tr>
<td>MRSI</td>
<td>26/13*</td>
<td>99/97*</td>
</tr>
</tbody>
</table>

Turkbey, et al. Radiol, 2010
Surveillance

T2a, G6, PSA 4.2
6-year post EBR, PSA 2.1

Surveillance

H+EBR 10/03  T1c, G7, PSA 4.6 ng/ml → PSA 0.9 ng/ml

Monitoring: Hormone Treatment

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Detectable (Cho+Cr)/Cl</th>
<th>Undetectable Cl, detectable (Cho+Cr)</th>
<th>Metabolic atrophy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Untreated (n=30)</td>
<td>100%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>&lt;6 weeks (n=18)</td>
<td>94%</td>
<td>6%</td>
<td>0%</td>
</tr>
<tr>
<td>7-16 weeks (n=18)</td>
<td>61%</td>
<td>33%</td>
<td>6%</td>
</tr>
<tr>
<td>&gt;16 weeks (n=32)</td>
<td>31%</td>
<td>44%</td>
<td>25%</td>
</tr>
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</table>

Monitoring: Hormone Treatment

- Follow-up MRSI within 4 months following hormone deprivation therapy
- Similar accuracy in localizing prostate cancer using combined MRI/3D-MRSI

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<td>92</td>
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<tr>
<td>Specificity (%)</td>
<td>48</td>
<td>60</td>
<td>80</td>
<td>92</td>
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Radiol 2001, 221:380-390

Aggressiveness of tumors

- Tumor volume: MRSI predictor of extraprostatic disease (EPD)
  - < 1 voxel: 6% risk
  - > 4 voxels: 80% risk for extracapsular disease

Radiology 1999, 213; 481-488

- Tumor metabolism: MRSI
  - Citrate
  - Choline

Aggressiveness

- Tumor grade
- Transformation of epithelial cells
- Membrane Phospholipid
- Citrate
- Choline

Significance of Ch+Cr/Ci ratio

Challenges in MRS Imaging

- Tumor detection sensitivity
  - Patient factors
  - Technical factors
    Spatial resolution
    Spectral resolution
    Field inhomogeneity
- Scan time
**Perfluorocarbon (PFC) compound**

- PFCs = (carbons + fluorine atoms) without hydrogen atoms.

- **Physical Characteristics**
  - Magnetic susceptibility matches with that of human tissue.
  - No signal on MRI
  - Chemically inert
  - Immiscible with water
  - Low surface tension, high specific gravity
  - Tasteless, odorless, virtually non-toxic

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**57-year-old, T2c, G 7(3+4), PSA 4.2 ng/ml**

Air, 16 Hz  

PFC, 6 Hz

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**Linewidth with Air vs. PFC**

![Graph showing linewidth comparison between Air and PFC](image)
To be further explored

• Spectral resolution
• Spatial resolution
• Scan time
• Use of endorectal coil

Summery

• MRSI evaluates the metabolic status, specifically Cho, Po, Cr, and Ci of prostate tissue at the cellular level.
• MRS improves the specificity in tumor detection but with limited sensitivity.
• Limited sensitivity are related to patient and technical factors.
• Technical challenges remain to be further improved.

Thank you.
Monitoring: Hormone Treatment

- Effect of hormone deprivation: MRI
- 42-224 days (mean 103 days)

Results:
- Detection accuracy: 74%
- Staging accuracy: 68%
- Overestimation of presence of tumor: 24%

AJR 1996, 166: 1157-1163

T2a

T2c

74Y, Hx of 3 negative biopsies, Rising PSA 13.8 ng/ml
Local Staging: MRSI

- Tumor volume = voxel count \( \propto \) ECD
- MRSI: strict criteria on MRI + voxel count

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<th>MRS</th>
<th>MRSI</th>
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R1 = reader 1, R2 = reader 2

Radiol 1999; 213:481-488