Prostate Cancer Staging

Indications for Imaging

DISTANT METASTASES?

LYMPHOGENOUS

Prostate Cancer Staging

Lymphatic Spread

• Lymph node invasion in about 10% of patients
  • EAU 2012: lymph node assessment only if
    • serum PSA 20 ng/ml or higher
    • cT2b or higher (TNM 2002)
    • Gleason score 7 or higher

• Gold standard: pelvic lymphadenectomy
  • most accurate staging test
  • disadvantages
    • invasive, morbidity
    • operating time, cost
  • Imaging?

Node positive when:

Oval node > 10 mm
Round node > 8 mm (i.e. short/long axis ratio > 0.8)

*Lahdollah, J Urol 2012;188:423
*Briganti, Eur Urol 2006;50:1006
*Jager, Am J Roentgenol 1996;166:1503
Node positive when:
- Oval node > 10 mm
- Round node > 8 mm (i.e. short/long axis ratio > 0.8)


---

Sensitivity for metastatic nodes: ~40%
- CT: 42% (range 5%-94%)
- MRI: 39% (range 6% - 83%)

Specificity: ~80%
- CT: 82% (range 80% - 83%)
- MRI: 82% (range 79% - 83%)

Hövels, Clin Radiol 2008;63:387

CT and MRI:
- perform equally well (or poor)
- most metastatic lymph nodes smaller than 10 mm
- only value of CT/MRI: high positive predictive value for lymph nodes > 1.5 cm = roadmap for PLD

---

IV injection of USPIO ("ultra small particles of iron oxide")

Nanoparticles
Ferumoxtran-10
Sinerem®
Combidex®
**Prostate Cancer Staging**

**Lymphatic Spread**

<table>
<thead>
<tr>
<th>Nodes 5-10 mm (n = 45)</th>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>28%</td>
</tr>
<tr>
<td>Specificity</td>
<td>78%</td>
</tr>
<tr>
<td>PPV</td>
<td>28%</td>
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<tr>
<td>NPV</td>
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</tr>
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*Harisinghani & Barentsz, N Engl J Med 2003;348:2491*

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<th>Nodes &lt; 5 mm (n = 17)</th>
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<tr>
<td>Sensitivity</td>
<td>0%</td>
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<tr>
<td>Specificity</td>
<td>100%</td>
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<tr>
<td>PPV</td>
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*Harisinghani & Barentsz, N Engl J Med 2003;348:2491*

**Prostate Cancer Staging**

**Lymphatic Spread**

- Much interest in USPIO as new standard of reference for lymph node staging
- However…

**FERUMOXTRAN IS NOT (CURRENTLY) COMMERCIALLY AVAILABLE!!!**

**Prostate Cancer Staging**

**Lymphatic Spread**

- Can we do better?
  - USPIO
  - DWI?

**Prostate Cancer Staging**

**Lymphatic Spread**

- Preliminary results in high risk patients*
  - Specificity : 98%
  - Sensitivity : 19% (43% if patient-based) (including micrometastases)

*Eiber, J Magn Reson Imaging 2011;33:1160
Beer, Med Imaging Biol 2011;13:352
Budiharto, Eur Urol 2011;60:125*
Prostate Cancer Staging
Lymphatic Spread

• DWI is feasible
• But, …

NOT READY FOR CLINICAL ROUTINE!!!

Prostate Cancer Staging
Lymphatic Spread

• Can we do better?
  – USPIO
  – DWI
  – PET?

Prostate Cancer Staging
Lymphatic Spread

• 18F-FDG-PET: no value
• 11C-acetate/18F-fluoroacetate: few reports
• 11C-choline/18F-fluorocholine

• 11C-choline
  – varying performance parameters
    • 60-80% sensitivity, 90-95% specificity*
    • 19% sensitivity, 95% specificity** (micrometastases!)
  – most promising tracer to date (recurrences!)
  – not widely available (cyclotron!)
• 18F-fluorocholine: promising alternative, but lower accuracy***

**Budiharto, Eur Urol 2011;60:125
***Poulson, BJUI, 2012;110:1666

Prostate Cancer Staging
Indications for Imaging

LYMPHOGENOUS
Pelvic Imaging
N1, N0

DISTANT METASTASES?

H1, H0

Prostate Cancer Staging
Indications for Imaging

LYMPHOGENOUS
Pelvic Imaging
N1, N0

HEMATOGENOUS

DISTANT METASTASES?

H1, H0
Prostate Cancer Staging

Hematogeneous Spread
- Usually bone metastases (lumbar spine, pelvic bones, femur, thoracic spine, ribs)
  - 80% osteoblastic
  - 5% osteolytic
  - 15% mixed osteoblastic/osteolytic
- Visceral metastases (lungs, liver, ...): very rare at initial diagnosis

Prostate Cancer Staging

Bone metastases
- EAU 2012: no skeletal assessment in asymptomatic patient with
  - serum PSA less than 20 ng/ml
  - Gleason 3+4 or lower
- Gold standard: bone scan

Prostate Cancer Staging

Indications for Imaging

LYMPHOGENOUS
- Pelvic Imaging
  - PLD
- Bone scan

HEMATOGENOUS
- Bone Metastases

DISTANT METASTASES?

N1

N0

M1

High sensitivity for osteoblastic mets
Whole body scan +/- SPECT

Bone Scintigraphy

Prostate Cancer Staging

Gold standard: bone scan

Prostate Cancer Staging

Bone metastases
- EAU 2012: no skeletal assessment in asymptomatic patient with
  - serum PSA less than 20 ng/ml
  - Gleason 3+4 or lower
- Gold standard: bone scan

Pelvic Imaging
- PLD

Bone scan

Prostate Cancer Staging

Distal metastases?

LYMPHOGENOUS
- Pelvic Imaging
  - PLD

HEMATOGENOUS
- Bone Metastases

DISTANT METASTASES?

N1

N0

M1
Prostate Cancer Staging

Bone Scan
- Bone scan images secondary effects of marrow metastases in skeleton
  - false positives (degenerative disease, inflammation, Paget, trauma, ...)

Targeted Imaging

Plain Film
- > 50% change BMD
- < 18m later than Tc-scan

CT
- also finds lytic lesions

MRI
- Assessment of bone marrow!

Indications for Imaging

DISTANT METASTASES?

LYMPHOCENOUS

HEMATOCENOUS

Pelvic Imaging
- PLD

Bone scan
- PSA > 50 ng/ml and bone pain

RX/CT/MR

N1
N0
M1
M0

DISTANT METASTASES?
Prostate Cancer Staging

Bone metastases
• Gold standard: bone scan + targeted imaging
• MRI?

Prostate Cancer Staging

Bone Scan
• Bone scan images secondary effects of marrow metastases in skeleton
  – false positives (degenerative disease, inflammation, Paget, trauma, …)
  – lag time between marrow involvement and bone scan positivity

66 high-risk patients | Sensitivity | Specificity
<table>
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<tbody>
<tr>
<td>BS + RX/CT/MRI</td>
<td>83</td>
<td>100</td>
</tr>
<tr>
<td>MRI</td>
<td>100</td>
<td>88</td>
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Prostate Cancer Staging

MRI?

• Higher sensitivity:
  – “MRI detects cells seeded into the normal hematopoietic marrow and its fat cells, thus identifying “bone” metastases before osteoblastic reaction becomes visible on BS and/or targeted imaging”

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<th>Sensitivity</th>
<th>Specificity</th>
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<td>BS + RX/CT/MRI</td>
<td>86</td>
<td>98</td>
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<tr>
<td>MRI</td>
<td>96.100</td>
<td>98.100</td>
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Prostate Cancer Staging

Whole-body MRI?

• Unclear issues
  – reproducibility?
  – economic impact?
• Multicenter trial underway

Prostate Cancer Staging

Bone metastases

• Gold standard: bone scan + targeted imaging
• Axial MRI?
• PET?

Prostate Cancer Staging

Bone metastases

• $^{18}$F-FDG-PET: no value
• $^{11}$C-choline, $^{18}$F-fluorocholine, $^{18}$F-fluoride, $^{11}$C-acetate, and $^{11}$C-methionine-PET: promising, but overall performance remains unclear

*Langsteger, Semin Nucl Med 2006;36:73
Bauman, Prostate Cancer Prostatic Dis 2012;15:45
Prostate Cancer Staging
Indications for Imaging

DISTANT METASTASES?

LYMPHOGENOUS

HEMATOGENOUS

Pelvic Imaging

Bone scan

Visceral Metastases

RX/CT/MR

N1

N0

N1

N0

Visceral Metastases

• Usually bone metastases (lumbar spine, pelvic bones, femur, thoracic spine, ribs)
• Visceral metastases (lungs, liver, ...): very rare at initial diagnosis

Prostate Cancer Staging
Visceral Metastases

• Only in symptomatic patients (clinically or biochemically)!
Prostate Cancer Staging

Indications for Imaging

DISTANT METASTASES?

LYMPHOGENOUS

HEMATOGENOUS

Pelvic Imaging

PLD

Bone scan

Chest XR

Chest + Abd CT

RX/CT/MR

N1

N0

M1

M0

LOCAL DISEASE?

Prostate Cancer Staging

Extraprostatic tumor extension

• EAU 2012: T-staging only indicated if it affects the management of the patient

Prostate Cancer Staging

Extraprostatic tumor extension

• EAU 2012: T-staging only indicated if it affects the management of the patient

Prostate Cancer Staging

Extraprostatic tumor extension

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Prostate Cancer Staging

Extraprostatic tumor extension

• EAU 2012: T-staging only indicated if it affects the management of the patient

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<tr>
<td>Primary EBRT (+/- ADT)</td>
<td></td>
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<tr>
<td>T1 – T2 “small” T3a</td>
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<tr>
<td>T1 – T4</td>
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</table>
Prostate Cancer Staging
Extraprostatic tumor extension

- Gold standard?
  - Clinical Predictors:
    - Clinical stage (DRE)
    - Gleason score
    - Serum PSA (PSA-density)
    - Transrectal core needle biopsy variables:
      - % involved cores among total number > 15%
      - % tumor in involved cores
      - presence of perineural invasion

Prostate Cancer Staging
Extraprostatic tumor extension

- Gold standard?
  - Integration into nomograms…
    - Partin’s tables (ECE and SVI)*
    - Kattan nomogram (SVI)**
  - … or formulas
    - Roach and Diaz formula (ECE and SVI)***

* Makarov, Urology 2007;69:1095
** Koh, J Urol 2003;170:1203

Prostate Cancer Staging
Extraprostatic tumor extension

- Gold standard?
  - Result: % chance of T3-T4 disease
  - Accuracy in predicting ECE and SVI: ROC 0.79-0.82*
  - Drawbacks:
    - only a %, no individual information
    - no anatomical information (side? size??)

  Wang, Radiology 2006:238:597
** Wang, Radiology 2004;232:133

Prostate Cancer Staging
Definitely intracapsular tumor

iT2a

Prostate Cancer Staging
Extraprostatic tumor extension

Only if (among others)

<table>
<thead>
<tr>
<th>Treatments</th>
<th>cT1 – cT2</th>
<th>cT1c – cT2a</th>
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Prostate Cancer Staging
Extraprostatic tumor extension

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Prostate Cancer Staging
Definitely extracapsular tumor

Extracapsular extension = irregular capsular bulge OR infiltration of periprostatic fat OR neurovascular bundle asymmetry

Prostate Cancer Staging
Definitely extracapsular tumor

- Undulation/blurring of capsule
- Obliteration of rectoprostatic angle
- Tumor contact > 1.5 cm with capsule
- Low signal intensity in periprostatic area

Prostate Cancer Staging
Definitely extracapsular tumor

Seminal vesicle invasion = abnormally low signal intensity within lumen/ focal thickening of seminal vesicle wall

Prostate Cancer Staging
Extraprostatic tumor extension

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<td>Slight capsular irregularity</td>
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Prostate Cancer Staging

Doubtful cases

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More aggressive therapy, but no worse outcome

Radical prostatectomy

Primary EBRT (+/- ADT)

More aggressive therapy, but better outcome (no undertreatment)

• Aggressive reporting:
  - 84% sensitivity (for ECE)
  - 89% specificity (for ECE)
### Prostate Cancer Staging

#### Doubtful cases

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**Patient spared unnecessary (R1) surgery**

**Usually obvious on MRI!**

**No potentially curative surgery, more unnecessary side-effects**
Prostate Cancer Staging
Doubtful cases

- Only if (among others) Imaging
- Radical prostatectomy: cT1 – cT2
  - “small” cT3a
  - “big” ipT3-ipseT4
- Primary EBRT + ADT

Patient spared unnecessary (R1) surgery

Prostate Cancer Staging
Doubtful cases

- Talk to the surgeon:
  - where is the potential ECE?
  - broader margin → more R0!
- Conservative reporting:
  - 55% sensitivity (for ECE)
  - 96% specificity (for ECE)

Cornud, Eur J Radiol 2012;81:e591

Prostate Cancer Staging
Summary

MRI-staging in cT1-cT2:
- if definite iT1-iT2: no management change
- if definite iT3-iT4: upstaging and more aggressive therapy
- if doubtful:
  - for AS, focal therapy or EBRT without ADT: aggressive reporting
  - for RP: conservative reporting + alert surgeon about location of possible margin involvement!

Prostate Cancer Staging
Indications for Imaging

DISTANT METASTASES?
- LYMPHOGENOUS
- HEMATOGENOUS
- ECI
- SVI
- M1
- M0
- T1-T2
- T3-T4

LOCAL DISEASE?
- Pelvic Imaging
- PLD
- Bone scan
- Chest XR
- Chest + Abd CT
- RX/CT/MR

Prostate Cancer Staging
Take home messages

- First look for lymphogenous metastases
  - if PSA > 20 ng/mL, > T2b, or Gleason score 3+4 or higher
  - do pelvic imaging (CT or MRI) as adjunct to pelvic lymph node dissection

Take home messages

- First look for lymphogenous metastases
  - if PSA > 20 ng/mL, > T2b, or Gleason score 3+4 or higher
  - do pelvic imaging (CT or MRI) as adjunct to pelvic lymph node dissection
Take home messages

• Then look for hematogenous metastases
  – except in asymptomatic patients with
    • serum PSA less than 20 ng/ml
    • Gleason 3+4 or lower
  – do bone scan (+ targeted imaging)
  – don’t look for visceral metastases in absence of clinical or biochemical abnormalities

Take home messages

• If no distant metastases are found, do local staging
  – use MRI for assessing
    • capsular perforation
    • seminal vesicle invasion

References

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