Latest research in prostate cancer: ProtecT and PROMIS

Hayley C. Whitaker
Molecular Diagnostics and Therapeutics Group

Twitter: @TheWhitakerLab
@HayleyWhitaker

Web: www.whitakerlab.org
1. Diagnosis
2. Risk
3. Treatment
Clinically indolent cancers are identified by chance

Clinically significant lesions are missed

Important cancers are incorrectly classified as unimportant

Men undergo whole-gland treatment which carries harm
PROMIS objectives

To assess the ability of Multi-Parametric prostate MRI prior to first biopsy to,

Identify men who can safely avoid unnecessary biopsy

Reduce over-diagnosis of clinically insignificant cancer

Improve the detection of clinically significant cancer defined as Gleason $\geq 4+3$ and/or cancer core length $\geq 6$mm
Eligible, consenting patients with clinical suspicion of prostate cancer

Visit 1: Registration

Visit 2: MP-MRI (1.5 Tesla)

Visit 3: Combined biopsy (under general anaesthetic)
- 1st: TPM-biopsy
- 2nd: TRUS-biopsy

Visit 4: End of study
Results given to patients

576 patients
Standard test: 12 core systematic TRUS-biopsy

Index test – multiparametric MRI with gadolinium contrast

LIKERT scoring 1 to 5

SCORE 1 2 3 4 5

1=highly unlikely to harbour significant cancer  5=highly likely to harbour significant cancer
Reference Test - Template Prostate Mapping (TPM)

Excellent diagnostic accuracy

Prostate biopsies every 5mm

Requires general anaesthetic
Are image guided biopsies better at diagnosing cancer than TRUS biopsies?

MP-MRI score

<table>
<thead>
<tr>
<th>MP-MRI score</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23</td>
</tr>
<tr>
<td>2</td>
<td>135</td>
</tr>
<tr>
<td>3</td>
<td>163</td>
</tr>
<tr>
<td>4</td>
<td>120</td>
</tr>
<tr>
<td>5</td>
<td>135</td>
</tr>
</tbody>
</table>

% by status of disease

- Significant cancer
- Insignificant cancer
- No cancer
## MP-MRI compared to TRUS-biopsy

<table>
<thead>
<tr>
<th>Test attribute</th>
<th>TRUS-biopsy</th>
<th>MP-MRI</th>
<th>Odds ratio* [95% CI]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>48%</td>
<td>93%</td>
<td>0.06 [0.02-0.12]</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Specificity</td>
<td>96%</td>
<td>41%</td>
<td>0.02 [0.003-0.05]</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>PPV</td>
<td>90%</td>
<td>51%</td>
<td>8.2 [4.7-14.3]</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>NPV</td>
<td>74%</td>
<td>89%</td>
<td>0.34 [0.21-0.55]</td>
<td>p&lt;0.0001</td>
</tr>
</tbody>
</table>
PROMIS- summary

Image guided biopsies are almost twice as sensitive as standard TRUS biopsies.

This could reduce the number of men requiring a biopsy by 27%.

Up to 18% more cases of clinically significant cancer could be detected.

5% fewer insignificant cancers would be detected.
Medical genetics and risk profiling?

99% of human DNA is the same…but 1% is different.

Small differences, known as single nucleotide polymorphisms (SNPs) make up the other 1%
Prostate Testing for Cancer and Treatment - ProtecT

Is localised prostate cancer, detected by community based PSA testing, better treated with radical prostatectomy, radiotherapy or active monitoring?

Took 10 years to complete.

Recruited from across the UK

Published October 2016, The New England Journal of Medicine, Hamdy et al.
How was the trial conducted?

228,926 men were invited for PSA testing

82,429 men had a PSA test (1999-2009)

~10% of those tested had a raised PSA

~85% of men with a raised PSA were given a biopsy

2,664 were diagnosed with localised prostate cancer

Men with a PSA of >20ng/ml were excluded
Diagnosed with prostate cancer (2,664)

Randomised (1,643)
- Surgery
- Radio-therapy
- Active monitoring

Personal preference (919)
- Surgery
- Radio-therapy
- Active monitoring

Annual check-up for all groups

- Which group survive longer?
- Which group have the lowest levels of disease progression?
- Which is the best treatment for patients?
Active monitoring

Based on serum PSA

50% rise in PSA over 12 months triggered surgery/radiotherapy

Measured every 3 months in year 1

6-12 months thereafter

Radiotherapy

Treated for 3-6 months with hormone therapy before and during treatment

Given 74 Gy in 37 fractions

PSA rise of 2ng/ml above nadir triggered review – options; monitoring, more testing, salvage therapy or palliative

Surgery

PSA measured every 3 months post-op in year 1

Every 6 months for 2 years

Then annually

Adjuvant or salvage radiotherapy discussed for +ve margins, extracapsular disease, PSA >0.2ng/ml
Which patients were more likely to undergo intervention?
Which patients were more likely to progress?
Which treatment resulted in the best survival?
ProtecT - summary

More likely to require intervention and have progression on active monitoring.

No difference in overall survival with any treatment option.

Earlier treatment

Possible side effects

Limited to localised disease, largely white Caucasian population
Active monitoring has been improved in the last 10 years
Summary

How we diagnose and treat prostate cancer is undergoing a revolution

New research can provide information for patients to make informed choices based on their individual risk

Patients can be reassured by the current research, the work is robust and reliable