Initial Diagnosis of Bladder Cancer Using a Point-of-Care Assay

H. Barton Grossman, M.D.
and
the NMP22 Clinical Investigation Group
NMP22 Antigen

- Nuclear matrix proteins (NMP) make up the structural framework of the nucleus and are important in gene expression
- Malignant urothelial cells contain up to 80 times higher concentration of NMP22 antigen than normal urothelial cells and release it upon cell death
- Unlike urine cytology, detection of NMP22 antigen in urine is not dependent on recovery of intact cells
- Based on previous studies, an NMP22 test result $\geq 10$ U/ml in the urine is associated with a high probability of bladder cancer
Created to identify urine with NMP22 antigen ≥ 10 U / mL

- Can be performed by non-physician staff members (CLIA waived)
- Requires 4 drops of freshly voided urine
- Results available in 30 minutes
- Built-in quality control
- Positive result if NMP22 antigen level ≥ 10 U / mL
Study Design

- Prospective study: 23 facilities in 10 states; Academic, private practice and Veterans Hospitals
- September 2001 to May 2002: 1,331 patients scheduled for cystoscopy due to increased risk of bladder cancer such as hematuria, history of smoking, irritative voiding symptoms
- Voided urine sample for analysis of NMP22 antigen and cytology collected prior to diagnostic cystoscopy
- Cytology was performed per each site’s standard protocol
- NMP22 test: 4 drops of voided urine added to the test cassette and result read 30-50 minutes later
- Urologists were blinded to NMP22 test and cytology results while performing and reporting the result of cystoscopy
- Further work-up on clinical findings and results of cystoscopy and cytology; TCC diagnosis based on pathology

Grossman et al. JAMA 293:810-816, 2005
Demographics
Total Tested Population (1331) vs Patients with TCC (79)

TCC 79 / 1,331 (6%)
Sensitivity for Detecting TCC

NMP22 Test = 57%    Cytology = 16%
## Improved Detection with NMP22 BladderChek Test and Cystoscopy

<table>
<thead>
<tr>
<th></th>
<th>Muscle Invasive</th>
<th>All Cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystoscopy</td>
<td>91% (10/11)</td>
<td>94% (74/79)</td>
</tr>
<tr>
<td>&amp; NMP22 Test</td>
<td></td>
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<tr>
<td>Cystoscopy alone</td>
<td>55% (6/11)</td>
<td>86% (68/79)</td>
</tr>
</tbody>
</table>

Cancers not seen by cystoscopy but detected by NMP22 Test: Bladder CIS, T2, T3; Ureter T2; Renal Pelvis T1, T3

P = 0.014
## Specificity

<table>
<thead>
<tr>
<th></th>
<th>No GU Disease</th>
<th>No Cancer</th>
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</thead>
<tbody>
<tr>
<td><strong>NMP22 Test</strong></td>
<td>90%</td>
<td>86%</td>
</tr>
<tr>
<td></td>
<td>(512/567)</td>
<td>(1072/1249)</td>
</tr>
<tr>
<td><strong>Cytology</strong></td>
<td>99%</td>
<td>99%</td>
</tr>
<tr>
<td></td>
<td>(544/547)</td>
<td>(1198/1208)</td>
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The graph below illustrates the percentage of negative results for the conditions NED, BPH, Cystitis, and Calculi.
Conclusions

• Cystoscopy combined with the NMP22 BladderChek Test detected significantly more urothelial cancers than cystoscopy alone (P = 0.014)

• NMP22 test detected 3 upper tract TCC missed by cytology

• NMP22 test is significantly more sensitive than cytology in detecting cancer (P < 0.001)

• Test can be performed by clinic staff in any doctor’s office, results in 30 minutes, at half the cost of voided cytology
Collaborating Investigators

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