Hematuria: From Cytology to Blue Light Cystoscopy

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Hamilton and Howd Chair of Urologic Oncology
Director, Center for Surgical Quality and Outcomes Research
Vanderbilt University Medical Center
Nashville, TN
Likelihood of most common diagnoses on evaluation of asymptomatic microhematuria

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Point estimate*</th>
<th>Confidence interval*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Cancer</td>
<td>3.3%</td>
<td>2.2-5.0%</td>
</tr>
<tr>
<td>Calculus</td>
<td>6.0%</td>
<td>3.8-9.2%</td>
</tr>
<tr>
<td>Benign prostatic enlargement</td>
<td>12.9%</td>
<td>6.3-24.6%</td>
</tr>
<tr>
<td>Urethral stricture</td>
<td>1.4%</td>
<td>0.6-3.2%</td>
</tr>
</tbody>
</table>

*Meta-analysis of studies from January 1980 to November 2011. Includes studies of screening in healthy populations, and evaluation in referral populations.

35-65% of patients with hematuria are diagnosed with a urologic or renal condition, many of which require treatment.
Malignancy in patients with microhematuria

- **Referral studies**: 4.0%
  - Higher in patients with risk factors (male, older, smoker, etc.)

- **Re-evaluation in referral studies**: 2.8%
  - Of whom initial (often incomplete) workup was negative

- **Screening studies**: 2.6%
  - Of the roughly 6.5% (95% CI: 3.4-12.2%)* found to have MH

*Probably lower in reality, since there were outlier studies.*
Grade I = Insufficient evidence to recommend
Evidence-based guidelines for evaluation of asymptomatic microhematuria
Asymptomatic Microscopic Hematuria in Adults: Summary of the AUA Best Practice Policy Recommendations

GARY D. GROSSFELD, M.D., University of California, San Francisco, School of Medicine, San Francisco, California
J. STUART WOLF, JR., M.D., University of Michigan Medical School, Ann Arbor, Michigan
MARK S. LITWIN, M.D., M.P.H., University of California, Los Angeles, Schools of Medicine and Public Health, Los Angeles, California
HEDVIG HRICAK, M.D., PH.D., Memorial Sloan-Kettering Cancer Center, New York, New York
CATHRYN L. SHULER, M.D., Kaiser Permanente, Portland, Oregon
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PETER R. CARROLL, M.D., University of California, San Francisco, School of Medicine, San Francisco, California

The American Urological Association (AUA) convened the Best Practice Policy Panel on Asymptomatic Microscopic Hematuria to formulate policy statements and recommendations for the evaluation of asymptomatic microhematuria in adults. The recommended definition of microscopic hematuria is three or more red blood cells per high-power microscopic field in urinary sediment from two of three properly collected urinalysis specimens. This definition accounts for some degree of hematuria in normal patients, as well as the intermittent nature of hematuria in patients with urologic malignancy. The Panel recommends the following approach to management of patients with asymptomatic microscopic hematuria: 1. Initial diagnostic evaluation with urinalysis, urine cytology, and appropriate imaging studies. 2. Follow-up evaluation with repeat urinalysis and imaging studies as clinically indicated. 3. Consider referral to a urologist for further evaluation if the urinalysis findings and other clinical findings are suggestive of underlying urologic disease. At this time, the Panel does not recommend active surveillance for the majority of patients with asymptomatic microscopic hematuria. 

American Urological Association (AUA) Guideline

DIAGNOSIS, EVALUATION and FOLLOW-UP OF ASYMPTOMATIC MICROHEMATURIA (AMH) IN ADULTS: AUA GUIDELINE

Definition of Microhematuria

- 3 or greater RBC/hpf on UA with micro…
  - Positive dipstick is sensitive, but insufficient to confirm diagnosis
  - UA with micro is required
  - One positive test sufficient

- Mimics of hematuria
  - Vaginal bleeding
  - Pigmenturia (myoglobinuria, beet-uria, dehydration)

- False negative UA if specific gravity < 308 mOsm
Ruling out Benign Causes

- Always gather evidence to support the presumed benign cause
  - UA with micro
  - Urine culture

- Always repeat the UA after resolution of the presumed benign cause
Prior treatments in patients with bladder cancer initially presenting with LUTS

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Treatments for UTI and symptomatic treatments for voiding complaints and/or lower abdominal and bladder pain.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men, %</td>
</tr>
<tr>
<td>---------</td>
<td>--------</td>
</tr>
<tr>
<td>Treatments for UTI</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>81.5</td>
</tr>
<tr>
<td>1 or 2</td>
<td>14.6</td>
</tr>
<tr>
<td>≥3</td>
<td>3.8</td>
</tr>
<tr>
<td>Symptomatic treatments</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>81.0</td>
</tr>
<tr>
<td>1 or 2</td>
<td>16.2</td>
</tr>
<tr>
<td>≥3</td>
<td>2.9</td>
</tr>
</tbody>
</table>

Henning et al. BJUI, 2013
+Microhematuria

Repeat UA after treatment of confounding cause

Release from care

Rule out confounding causes of MH, such as infection

Consider concurrent nephrologic work up if proteinuria, red cell morphology or other signs indicate nephrologic causes

H+P Cysto Imaging (CTU)

Follow up with at least one UA/micro every 12 months for at least 2 years

Follow persistent MH with annual UA. Consider nephrologic evaluation. Repeat anatomic eval in 3-5 yrs or sooner if clinically indicated

Release from care

If unable to undergo CTU, options for imaging parenchyma and collecting system:
MR Urogram or MRI plus retrograde pyelograms

Treatment

Follow up as indicated by diagnosis. Repeat UA after resolution of identified condition.
Highlights of the Guidelines

• **Basic workup is cysto + imaging**
  – Cysto all pts > 35 and/or risk factors for malignancy
  – CT Urogram is the preferred imaging modality
  – Urine markers not part of the standard workup

• **Same workup for patients on anticoagulation**

• **Consider nephrologic referral for pts with renal insufficiency, proteinuria, cellular casts**
Cystoscopy: “The Gold Standard” in Bladder Cancer Diagnosis

• Good but not perfect
  – Small lesions sometimes missed
  – False positives occur (inflammation/edema)

• Repeated testing is costly
  – Frequent surveillance cystoscopy and imaging is required

• Cystoscopy often causes patient discomfort
  – Adherence to follow-up guidelines is poor
Can We Improve Upon (or Even Replace) Cystoscopy?

• Urinary Markers
  – Cytology
  – Protein based markers
  – Cellular markers
  – Genetic tests

• Endoscopic advances
  – Blue light cystoscopy
  – Narrow-band imaging
Cytology

Advantages
• High specificity in general
• Reasonably high sensitivity (33-95%) for high-grade disease

Disadvantages
• Low sensitivity (4-31%) for low-grade disease
• Will still miss up to 60% of high-grade tumors
• Operator dependent
• Results often equivocal

Lotan and Roehrborn, Urology, 2003
Karakiewicz, et al, BJUI, 2006
BTA Stat® and NMP 22®

PROTEIN-BASED MARKERS
BTA stat®

Detects the presence of human complement factor H related protein which is present in the urine of patients with bladder cancer

Advantages
- Point-of-care test
- Improved sensitivity (50-90%) compared to cytology
- FDA approved
- CLIA waived
- Inexpensive

Disadvantages
- Low specificity (50-73%)
  - Some benign cells shed complement factor H
- Not tested in general hematuria population

Lotan and Roehrborn, Urology, 2003
Karakiewicz, et al, BJUI, 2006
NMP22 BladderChek®
Dectes nuclear mitotic apparatus protein 22 which is a matrix protein more prevalent in cancer cells

Advantages
- Point-of-care test
- Improved sensitivity (47-90%) compared to cytology
- FDA approved
- CLIA waived
- Inexpensive

Disadvantages
- Moderate specificity (76-83%)
- Not tested in general hematuria population

Lotan and Shariot, AUA Update, 2011
CELLULAR MARKERS
ImmunoCyt®
Combines cytology with an immunofluorescence assay for CEA and two bladder cancer associated mucins

**Advantages**

- Improved sensitivity, even for small tumors < 1 cm

**Disadvantages**

- Performed in reference lab (requires a fluorescence microscope and trained personnel)
- Specificity inferior to cytology alone
  - False positives associated with immunofluorescence
- Expensive

Messing, et al, J Urol 2005
UroVysion®

GENETIC TESTS
UroVysion®

Fluorescence in-situ hybridization assay that detects increased numbers of chromosomes 3, 7 and 17 as well as loss of the 9p21 locus

**Advantages**

- Relatively high sensitivity (52-100%) and specificity (62-83%)
- Sensitivity for upper tract tumors
- FDA-approved for use in bladder cancer and hematuria

**Disadvantages**

- Expensive
- Requires a reference lab
- Still has a false positive rate of 15-20%
- 11% of tests are inconclusive

Prospective analysis of sensitivity and specificity of urinary cytology and other urinary biomarkers for bladder cancer

Faysal A. Yafi, M.D.\textsuperscript{a}, Fadi Brimo, M.D.\textsuperscript{b}, Jordan Steinberg, M.D.\textsuperscript{a}, Armen G. Aprikian, M.D.\textsuperscript{a}, Simon Tanguay, M.D.\textsuperscript{a}, Wassim Kassouf, M.D., F.R.C.S.(C).\textsuperscript{a,*}

<table>
<thead>
<tr>
<th></th>
<th>Number of studies</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytology</td>
<td>29</td>
<td>10.3–84.6</td>
<td>78.0–100</td>
</tr>
<tr>
<td>Hematuria dipstick</td>
<td>6</td>
<td>47.0–92.6</td>
<td>51.0–84.0</td>
</tr>
<tr>
<td>BTA Stat</td>
<td>8</td>
<td>52.5–78.0</td>
<td>69.0–87.1</td>
</tr>
<tr>
<td>ImmunoCyt</td>
<td>7</td>
<td>63.3–84.9</td>
<td>62.0–84.7</td>
</tr>
<tr>
<td>NMP22 BladderChek</td>
<td>9</td>
<td>49.5–65.0</td>
<td>40.0–89.8</td>
</tr>
</tbody>
</table>
Sensitivity of Urinary Markers Stratified by Tumor Grade and Aggressiveness

**Table 2: Sensitivity of cytology and commercially available markers based on tumor grade**

<table>
<thead>
<tr>
<th>Marker</th>
<th>No. Studies</th>
<th>Grade 1</th>
<th>% Median (95% CI)</th>
<th>Grade 2</th>
<th>Grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytology</td>
<td>8</td>
<td>12 (4-31)</td>
<td>26 (17-37)</td>
<td>64 (38-84)</td>
<td></td>
</tr>
<tr>
<td>Cytology</td>
<td>9</td>
<td>17</td>
<td>34</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>BTA stat</td>
<td>8</td>
<td>47 (38-56)</td>
<td>73 (59-83)</td>
<td>94 (55-99)</td>
<td></td>
</tr>
<tr>
<td>BTA stat</td>
<td>7</td>
<td>45</td>
<td>60</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>NMP22</td>
<td>3</td>
<td>41</td>
<td>53</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>NMP22</td>
<td>7</td>
<td>61 (35-81)</td>
<td>71 (41-90)</td>
<td>79 (63-89)</td>
<td></td>
</tr>
<tr>
<td>ImmunoCyt 95</td>
<td>1</td>
<td>78</td>
<td>90</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>FISH (UroVysion)</td>
<td>2</td>
<td>56</td>
<td>78</td>
<td>95</td>
<td></td>
</tr>
</tbody>
</table>

**Table 4: Sensitivity of cytology and commercially available markers, and association with tumor aggressiveness**

<table>
<thead>
<tr>
<th>Marker</th>
<th>Median % Less Aggressive/Lower Risk pTa, G1, G2 (range)</th>
<th>Median % More Aggressive pT1, G3, CIS (range)</th>
<th>Median % CIS (range)</th>
<th>Total No. Pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytology</td>
<td>27 (0-93)</td>
<td>69 (0-100)</td>
<td>78 (0-100)</td>
<td>12,566</td>
</tr>
<tr>
<td>NMP22</td>
<td>50 (0-86)</td>
<td>83 (0-100)</td>
<td>83 (0-100)</td>
<td>7556</td>
</tr>
<tr>
<td>FISH (UroVysion)</td>
<td>65 (32-100)</td>
<td>95 (50-100)</td>
<td>100 (50-100)</td>
<td>2164</td>
</tr>
<tr>
<td>ImmunoCyt</td>
<td>81 (55-90)</td>
<td>90 (67-100)</td>
<td>100 (67-100)</td>
<td>2502</td>
</tr>
</tbody>
</table>

Data from meta-analyses.

Lotan and Shariot, AUA Update, 2011
Urinary Markers Alone CANNOT Replace or Avoid Cystoscopy

• Current AUA guidelines recommend AGAINST the use of urinary biomarkers in the routine work-up of patients with asymptomatic microscopic hematuria
  – Current AUA guidelines make no recommendations concerning the use of urinary markers in the follow-up of NMIBC

• Current EAU guidelines suggest that “positive urine test results have a positive impact” on the quality of follow-up cystoscopy in NMIBC
  – While they don’t specify which test to use, they mention that patients with negative cystoscopy and positive cytology should undergo guided bladder biopsy

Davis, et al, AUA guideline, 2012
Hall, et al, AUA guideline, 2010
Babjuk, et, EAU guideline, 2015
Blue-Light Cystoscopy and Narrow-Band Imaging

ADVANCES IN CYSTOSCOPY
Enhancing Cystoscopy with Photodynamic Diagnosis

• Hexaminolevulinate (HAL, Cysview®)
  – Lipophilic hexyl ester of 5-ALA which results in increased uptake of protoporphyrin IX in neoplastic tissue
  – Illumination with blue-violet light (380-440 nm) results in red fluorescence from malignant tissue

• Used with the Karl Storz D-Light C Photodynamic Diagnostic (PDD).

• Not for repetitive use and is not a replacement for random bladder biopsies or other procedures used in the detection of bladder cancer.
Cysview- Papillary lesion
Cysview - CIS

Courtesy of Ashish Kamat, MD
US Pivotal Cysview (HAL) FDA registration study

Stenzl A et al. J Urol 2010
HAL Pivotal Study – Detection

- 286 patients: Ta or T1 bladder cancer
  - 16.4% of patients had one or more Ta or T1 tumor with Cysview only (p=0.001)
- 41 patients: CIS
  - 32% of patients (13/41) had CIS detected with Cysview only (p<0.0001)
- No difference in number of false positive results

Burger M et al. EAU 2012.
HAL Pivotal Study – Recurrence

- Tumor recurrence rates over 9 months were 47% and 56% for the HAL and white light groups respectively (p=0.026)
- Relative reduction in recurrence rate was 16%
- Number of recurrences were lower at each timepoint (3, 6 and 9 months) in the BLC with HAL group compared with the white light group

Stenzl A et al. J Urol 2010
Burger M et al. EAU 2012.
HAL Meta-analyses

• Prior meta-analysis were conflicting
  – Kaush et al noted significant reduction in recurrence and improved tumor-free survival
  – Shen et al noted the same reduction in recurrence rates but did not show an advantage in tumor-free survival

• Both meta-analyses had limitations
  – Both studies included studies with HAL and 5-ALA
  – Shen et al did not include key studies of HAL

• Recent meta-analysis from Burger et al overcomes these limitations

Kaush et al. Eur Urol, 2010
Meta-analysis included 2212 patients who underwent blue light cystoscopy.

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of patients recruited</th>
<th>Design</th>
<th>Study arms</th>
<th>Tumour types</th>
<th>Detection/Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jichlinski et al. [22]</td>
<td>52</td>
<td>Within-patient comparison; WL then BL</td>
<td>–</td>
<td>Ta, T1, CIS</td>
<td>D</td>
</tr>
<tr>
<td>Schmidbauer et al. [12]</td>
<td>286</td>
<td>Within-patient comparison; WL then BL</td>
<td>–</td>
<td>Ta, T1, CIS</td>
<td>D</td>
</tr>
<tr>
<td>Grossman et al. [19]; Fradet et al. [18]</td>
<td>298</td>
<td>Within-patient comparison; WL then BL</td>
<td>–</td>
<td>Ta, T1, CIS</td>
<td>D</td>
</tr>
<tr>
<td>Jocham et al. [8]</td>
<td>162</td>
<td>Within-patient comparison; WL then BL</td>
<td>–</td>
<td>Ta, T1, CIS</td>
<td>D</td>
</tr>
<tr>
<td>Stenzl et al. [21]</td>
<td>814</td>
<td>Detection: within-patient comparison; WL then BL</td>
<td>Group 1: WL plus TURB; Group 2: WL plus BL plus TURB</td>
<td>Ta, T1, CIS</td>
<td>D, R 9 mo</td>
</tr>
<tr>
<td>Hermann et al. [24]</td>
<td>233</td>
<td>Comparison of randomised parallel groups</td>
<td>Group 1: WL plus TURB, Group 2: WL plus TURB, then BL plus TURB</td>
<td>Ta, T1, CIS</td>
<td>D, R</td>
</tr>
<tr>
<td>Burgués et al. [23]</td>
<td>305</td>
<td>Within-patient comparison; WL then BL</td>
<td>–</td>
<td>Ta, T1, CIS</td>
<td>D</td>
</tr>
<tr>
<td>Drăgoescu et al. [25]</td>
<td>44</td>
<td>Comparison of randomised parallel groups</td>
<td>Group 1: WL plus TURB, Group 2: WL plus BL plus TURB</td>
<td>Not specified</td>
<td>D, R</td>
</tr>
<tr>
<td>Ray et al. [26]</td>
<td>18</td>
<td>Within-patient comparison; WL then BL</td>
<td>–</td>
<td>Ta, T1, CIS</td>
<td>D</td>
</tr>
<tr>
<td>Total</td>
<td>2212</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

BL = blue light; CIS = carcinoma in situ; D = detection; R = recurrence; TURB = transurethral resection of the bladder; WL = white light.

### Meta-analysis: Ta/T1 tumor Detection Results

<table>
<thead>
<tr>
<th>Group</th>
<th>Patients N(%) in whom at least 1 Ta/T1 was detected with BL and not WL</th>
<th>Event rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>168/790 (21.3%)</td>
<td>21.9%, p&lt;0.001 (0.139-0.247)</td>
</tr>
<tr>
<td>Initial BC</td>
<td>68/346 (16.8%)</td>
<td>17.3%, p&lt;0.001 (0.123-0.239)</td>
</tr>
<tr>
<td>Recurrence BC</td>
<td>110/444 (24.8%)</td>
<td>26.1%, p&lt;0.001 (0.213-0.294)</td>
</tr>
<tr>
<td>High risk</td>
<td>83/377 (22%)</td>
<td>22.9%, p&lt;0.001 (0.188-0.276)</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>79/237 (33.3%)</td>
<td>34.1%, p&lt;0.001 (0.282-0.406)</td>
</tr>
<tr>
<td>Low risk</td>
<td>6/176 (3.4%)</td>
<td>4.6%, p&lt;0.001; (0.022-0.097)</td>
</tr>
<tr>
<td>Prior intravesical treatment</td>
<td>48/192 (25%)</td>
<td>25.3%, p&lt;0.001; (0.196-0.319)</td>
</tr>
<tr>
<td>No prior intravesical treatment</td>
<td>88/434 (20.3%)</td>
<td>20.9% p&lt;0.001; (0.173-0.291)</td>
</tr>
</tbody>
</table>

High risk: TaG3, T1  
Medium risk: Multiple TaG1/G2  
Low risk: Single TaG1/G2  

## Meta-analysis: CIS Detection Results

<table>
<thead>
<tr>
<th>Group</th>
<th>Patients (%) in whom CIS was detected with BL and not WL</th>
<th>Event rate, p-value, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>61/256 (23.8)</td>
<td>24.6, p&lt;0.001 (0.196-0.304)</td>
</tr>
<tr>
<td>Initial BC</td>
<td>30/110 (27.3)</td>
<td>23.8, p&lt;0.001 (0.205-0.378)</td>
</tr>
<tr>
<td>Recurrent BC</td>
<td>31/146 (31.2)</td>
<td>21.8, p&lt;0.001 (0.168-0.294)</td>
</tr>
<tr>
<td>Prior intravesical treatment</td>
<td>14/74 (18.9)</td>
<td>19.7, p&lt;0.001 (0.120-0.307)</td>
</tr>
<tr>
<td>No prior intravesical treatment</td>
<td>29/128 (29.7)</td>
<td>27.4, p&lt;0.001 (0.196-0.369)</td>
</tr>
</tbody>
</table>

Meta-analysis: Pooled Recurrence Rates

<table>
<thead>
<tr>
<th>Study</th>
<th>M-H Risk Ratio</th>
<th>p</th>
<th>Relative Weight</th>
<th>Risk Ratio and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hermann et al [24]</td>
<td>0.805</td>
<td>0.250</td>
<td>24.82</td>
<td></td>
</tr>
<tr>
<td>Stenzl et al [21]</td>
<td>0.790</td>
<td>0.053</td>
<td>63.75</td>
<td></td>
</tr>
<tr>
<td>Drăgoescu et al [25]</td>
<td>0.504</td>
<td>0.065</td>
<td>11.43</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>0.761*</td>
<td>0.006</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Cochran Q test for Heterogeneity

1.413 (p = 0.493) 0.000

*Weighted overall results from the fixed effects meta analysis.

Fig. 4 – Meta-analysis: recurrence rates up to 12 mo. BL = blue light; CI = confidence interval; M-H = Mantel-Haenszel (test); WL = white light.
Enhancing Cystoscopy and TURBT with Narrow-Band Imaging

• Optical imaging technology (Olympus) enhances visibility of vessels on mucosal surfaces.
• Filters the white light into specific light wavelengths that penetrate only surface of human tissue are absorbed by hemoglobin.
• Bluish light enhances superficial capillary network and greenish light enhances deeper vessel visibility.
White light cystoscopy vs. NBI

Herr and Donat, BJUI, 2008
White light cystoscopy vs. NBI

Herr and Donat, BJUI, 2008
Initial Results with NBI

<table>
<thead>
<tr>
<th>Cystoscopy</th>
<th>Biopsied</th>
<th>With tumour recurrence</th>
<th>No tumour recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>WL + NBI+</td>
<td>136</td>
<td>90</td>
<td>46</td>
</tr>
<tr>
<td>WL + NBI−</td>
<td>0</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>WL – NBI+</td>
<td>26</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>WL – NBI−*</td>
<td>265</td>
<td>0</td>
<td>265</td>
</tr>
<tr>
<td>Totals</td>
<td>427</td>
<td>103</td>
<td>324</td>
</tr>
</tbody>
</table>

*Patients not biopsied.

TABLE 2
Cystoscopy and biopsy results in 427 patients

Herr and Donat, BJUI, 2008
NBI may improve TURBT and reduce recurrence rates

- Cauberg et al, World J U, 2011
  - Residual tumor after white light WL = 30%
  - Residual tumor after narrow band imaging NBI = 15%
  - p=0.03

- Naselli et al, EU, 2012
  - 1 yr Recurrence Rate after NBI = 33%
  - 1 yr Recurrence Rate after WL = 51%
  - p=0.01
RCT of White Light TUR vs. NBI TUR
254 pts with NMIBC total- 127 to each arm

Fig. 1 – Two-year tumor recurrence-free survival after restaging transurethral resection by narrow-band imaging (NBI) or white-light imaging (WLI) cystoscopy.

Fig. 2 – Two-year progression-free survival after transurethral resection by narrow-band imaging (NBI) or white-light imaging (WLI) cystoscopy.
Narrow-band Imaging for Upper Urinary Tract Transitional-Cell CA

- Significant improvement in cancer detection and changes in management in 23% of patients.
  - Additional tumor detection (14%)
  - Extended limits of ablation (9%)
  - 11% - traditional white light imaging MISSED the cancer

Traxer, J Endourol 2011
Take-Home Messages

• Cytology is a useful adjunct to but not a replacement for cystoscopy
  – You must be willing to biopsy patients in whom cytology is positive but cystoscopy is negative

• The role of other urinary markers in bladder cancer is unclear
  – I personally do not use any of these
  – Most guidelines do not recommend their use
Take-Home Messages

• Enhanced cystoscopy with photodynamic diagnosis methods is very promising

• Both HAL (Blue light) and NBI have been shown to improve detection and reduce recurrence in studies

• HAL should not be used in all patients
  – Useful in patients with CIS or high-grade disease, particularly after intravesical therapy
  – Useful in patients with negative cystoscopy and positive cytology