

Detection and Diagnosis of Bladder Cancer

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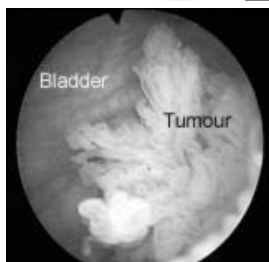


Cystoscopy

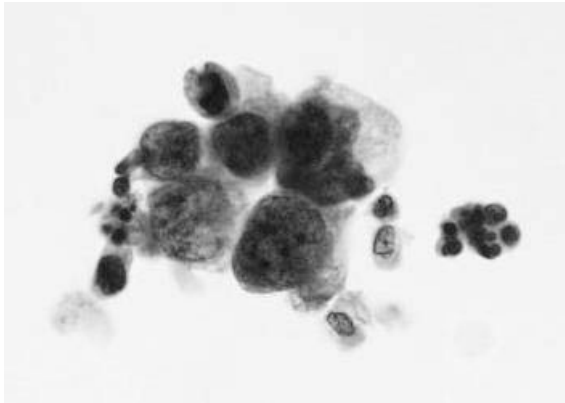
Rigid



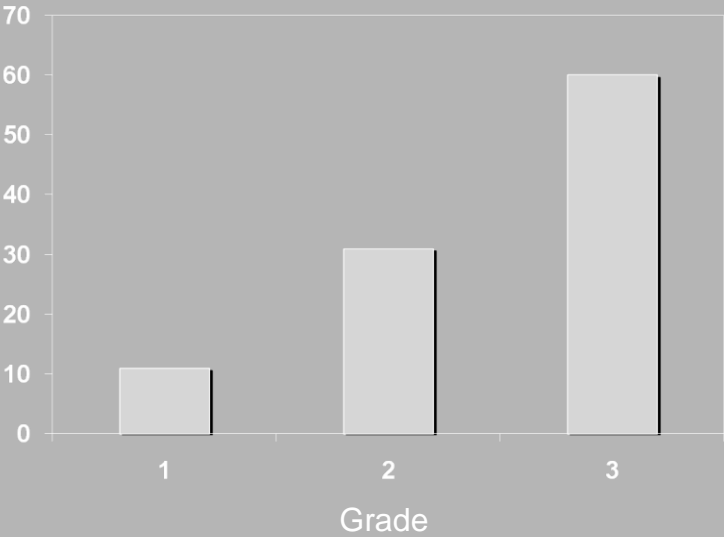
Flexible



Cytology



Cytology - Sensitivity



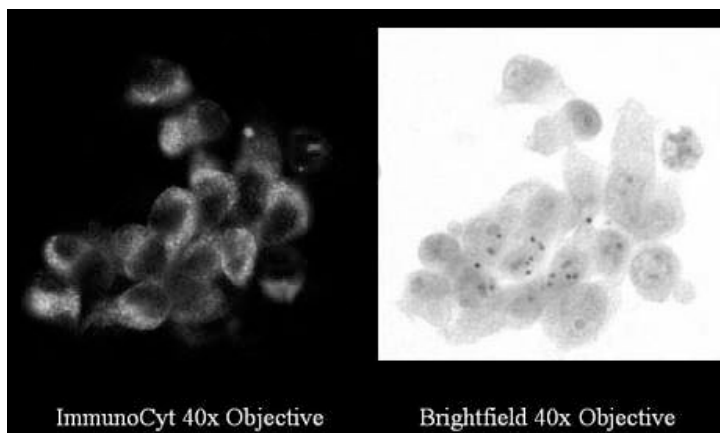
Immunocyt Improves Cytology

Cocktail of 3 fluorescently labelled
monoclonal Abs

Reacts with a mucin glycoprotein and CEA

High sensitivity

Immunocyt



BTA Stat / BTA TRAK Assays

BTA Stat is qualitative in - office test (urine pregnancy)

BTA TRAK is quantitative test - send out immunoassay

Detecting human complement factor H - related protein (hCFHrp)

Produced directly from bladder cancer cells

NMP22 Bladder Check

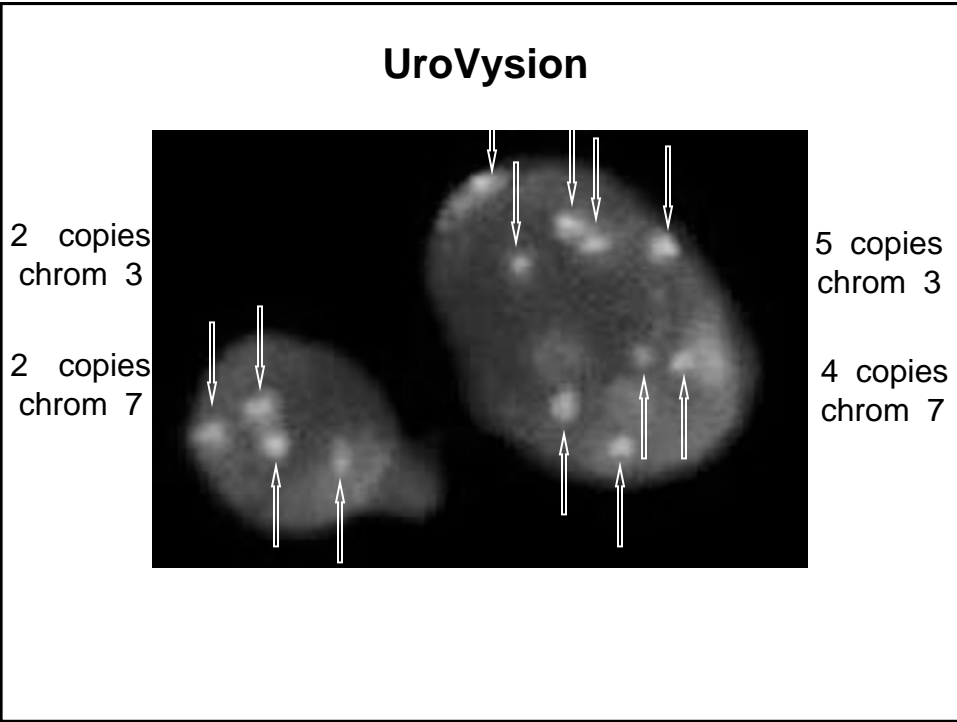


Nuclear matrix protein 22
In office testing

	NMP22 Assay		Voided Cytology	
	No. With Positive Test Result/Total No. With Bladder Cancer	Sensitivity, % (95% CI)	No. With Positive Test Result/Total No. With Bladder Cancer	Sensitivity, % (95% CI)
n = 79 cancers				
Grade				
Well differentiated	13/27	48.2 (28.7-68.1)	0/25	0 (0-13.7)
Moderately differentiated	9/18	50.0 (26.0-74.0)	3/18	16.7 (3.6-41.4)
Poorly differentiated	18/25	72.0 (50.6-87.9)	9/24	37.5 (18.8-59.4)
GX (grade unknown)	4/9	44.4 (13.7-78.8)	0/9	0 (0-33.6)

UroVysion

FISH - fluorescent in - situ hybridization
Chromosomes 3, 7, 17, 9p21
Changes in copy number



Relative Merit of Current Markers

Marker	Sensitivity %	Specificity %
Cytology	16 - 89	81 - 100
NMP22 blad chek	44 - 72	85
BTA stat	53 - 89	54 - 93
BTA TRAK	17 - 78	51 - 70
Immunocyt	39 - 100	73 - 84
UroVysion	73 - 81	96 - 100

Investigational Markers and Technology

Telomerase

High levels in rapidly proliferating cells

Rebuilds telomeres resulting in immortality

TRAP - telomeric repeat amplification protocol

Problems : unstable, costly assays,
reproducibility

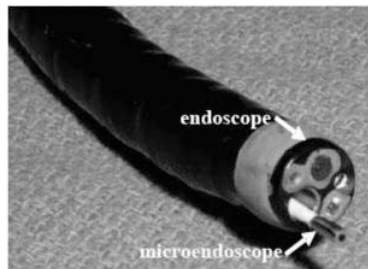
Urinary Micro - satellite Analysis

Assess for allelic loss at 20 different
highly polymorphic DNA loci on chrom
4, 8, 9, 11, 17, 18



Confocal Laser Endo - Microscopy

Intravenous or intravesical fluorescein
488 nm laser scanning unit : 8 - 12 frames / sec
60 micron depth of penetration



2.6 mm probe ↑

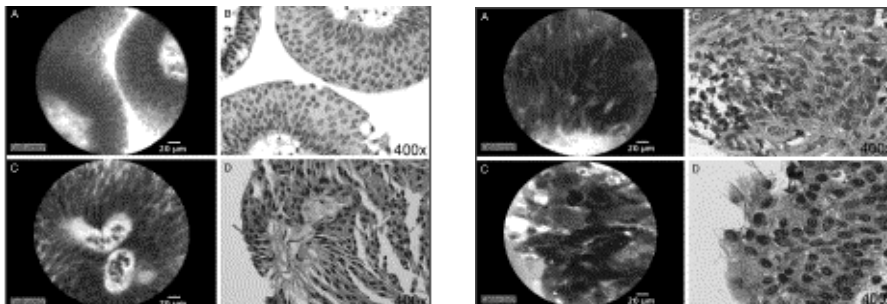
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Confocal Microscopy

Intravenous fluorescein preferred - green urine
Stains extracellular matrix, doesn't enter cell
Cannot see muscularis propria (too deep)

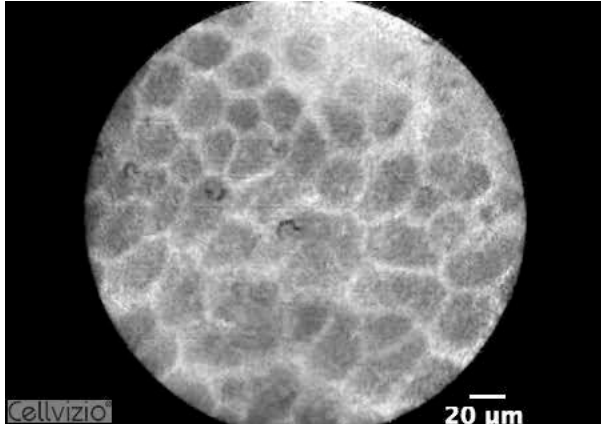
Low grade Ta

High grade Ta



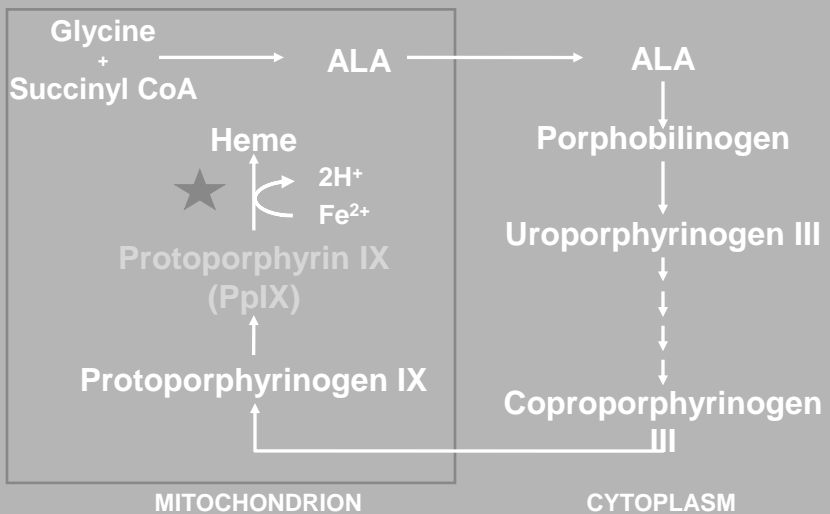
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Confocal Microscopy



J Urol 182: 1299, 2009

Heme Biosynthetic Pathway



Hexvix® Cystoscopy Protocol

Hexyl aminolevulinate 85 mg

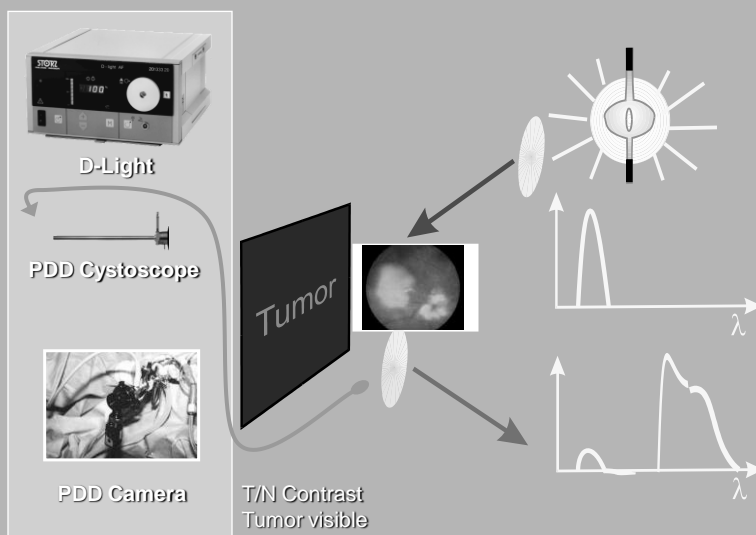
Solvent 50 ml

Bladder instillation 1 hour

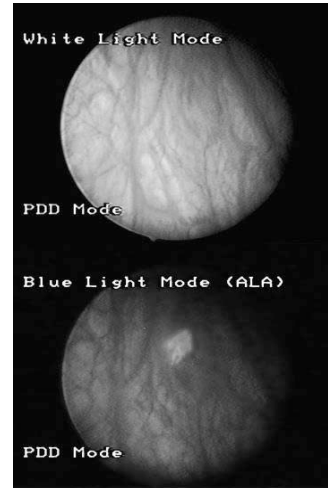
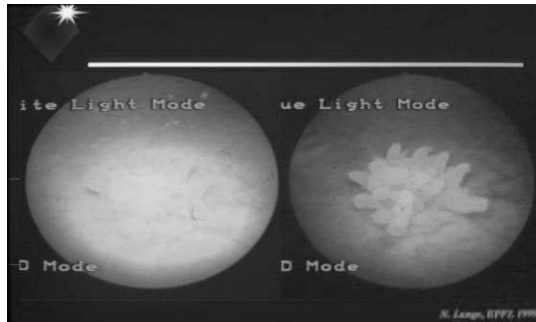
Bladder evacuation followed by white
and blue light inspection

Bladder resection under white and blue
light

Photodiagnosis Light Source



Hexaminolevulinate Fluorescent Cystoscopy Facilitates Cancer Detection



Initial Study Population Entry Criteria

Positive cytology

Multiple tumors

Tumor > 3cm.

Recurrence within 3 months

Study Design

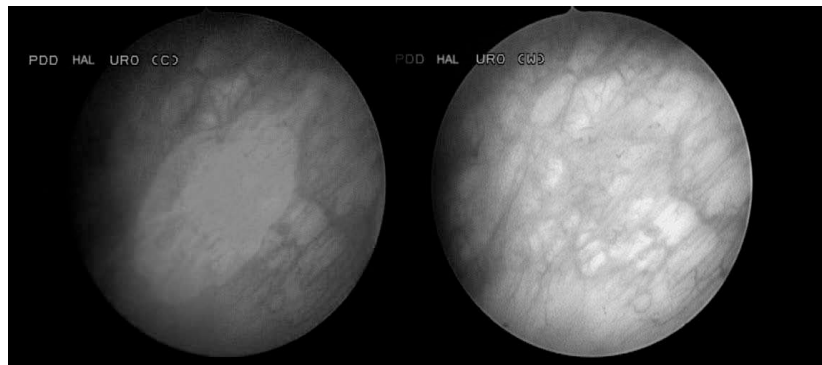
Compare detection rates of white light and blue light cystoscopy

All lesions mapped first under white light and then blue light (within - patient design)

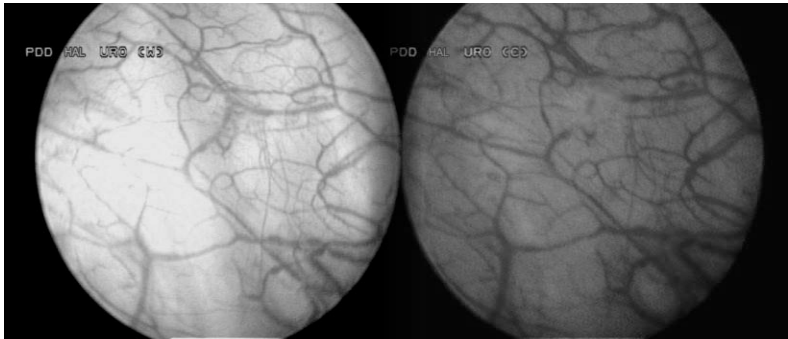
Blinded central pathologist

196 patients evaluated

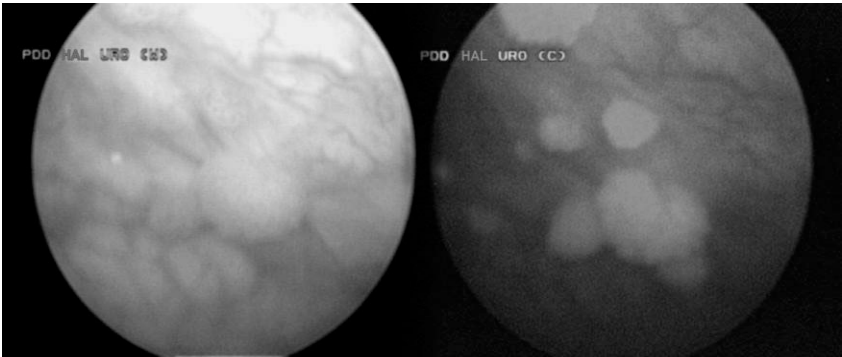
Tis Detected with Hexvix Imaging Only



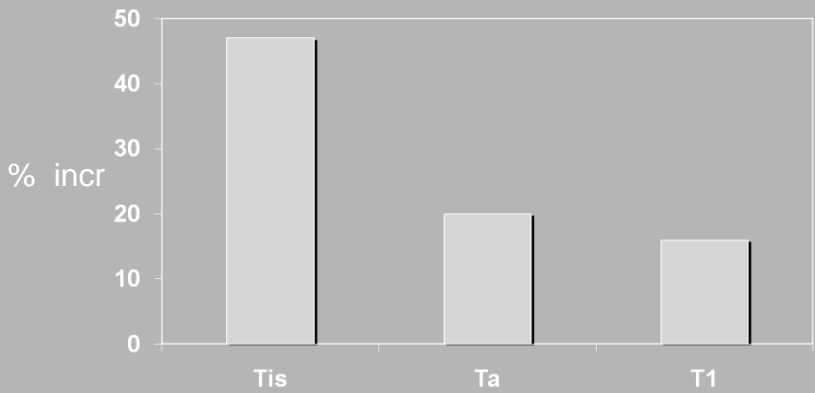
Ta Detected with Hexvix Imaging Only



Hexvix Imaging Multiple Ta Tumors

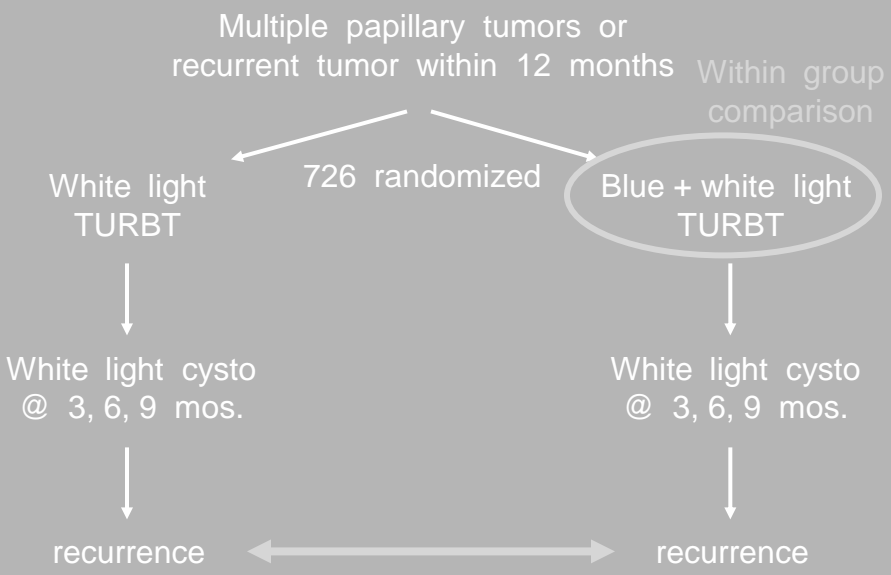


Improvement in Tumor Detection Rate with Hexvix

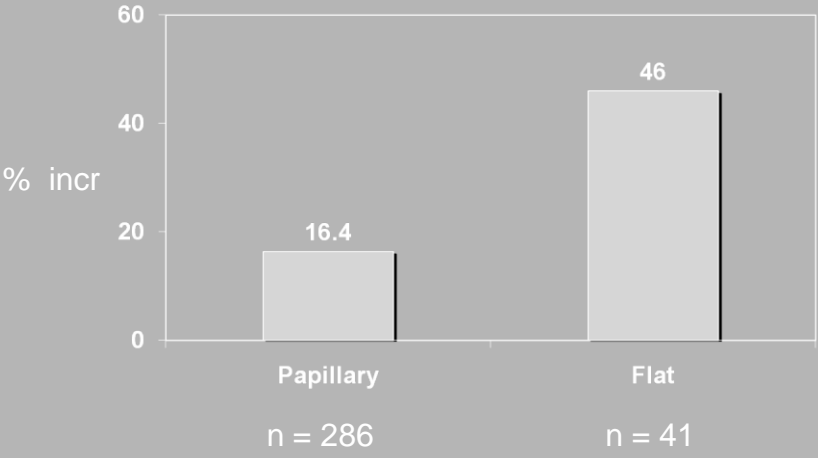


J Urol 178: 62, 2007

Schema for Recurrence Trial



Hexaminolevulinate Fluorescent Cystoscopy Increases Cancer Detection Rates



Hexaminolevulinate Fluorescent Cystoscopy Results in Lower Recurrence Rates

