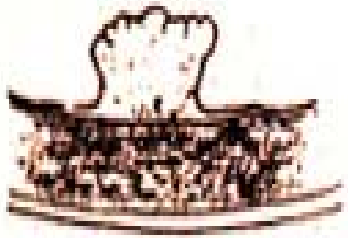
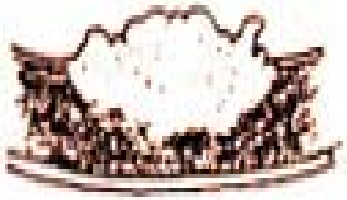
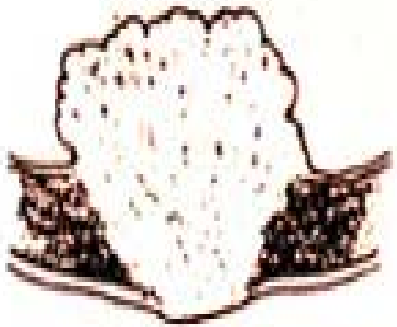
MSA Multi Center Trial for Bladder Cancer Detection

EDRN/NCI/Hopkins/FHCC

M. Schoenberg, J. Kagan, M. Thornquist, S. Srivastava

True or False?

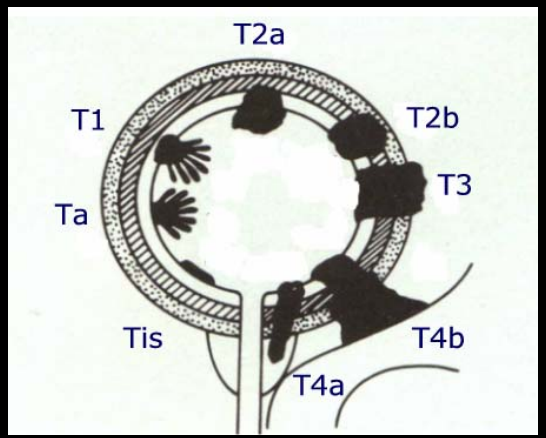
Group A	Group B	Group C
		
Submucosal infiltration	Muscular infiltration	Perivesical infiltration
No. of cases 3	No. of cases 15	No. of cases 89
Metastases 0	Metastases 1	Metastases 52
Perivesical lymph. only 0	Perivesical lymph. only 1	Perivesical lymph. only 6
Perivesical fixation only 0	Perivesical fixation only 0	Perivesical fixation only 8
Potentially curable 100%	Potentially curable 86.6 %	Potentially curable 24%

UCC:USA

- 60,000 new cases per year
- 12,000 cancer-specific deaths
- 90% transitional cell histology
- 75% non-muscle invasive tumors
- 70% recurrence rate

Non-Invasive UCC Treatment

- Ta, Tis or T1
- 75% disease burden
- Present w/ hematuria
- Standard workup
- TUR +/- drugs
  - MMC
  - BCG
  - IFN
  - others



- Success:
  - Ta 30%
  - T1 70%
- Progression
  - Low grade Ta: 2.4%
  - High grade T1: >50%
- Unresolved ??:
  - Follow-up
  - Early Intervention (T1)

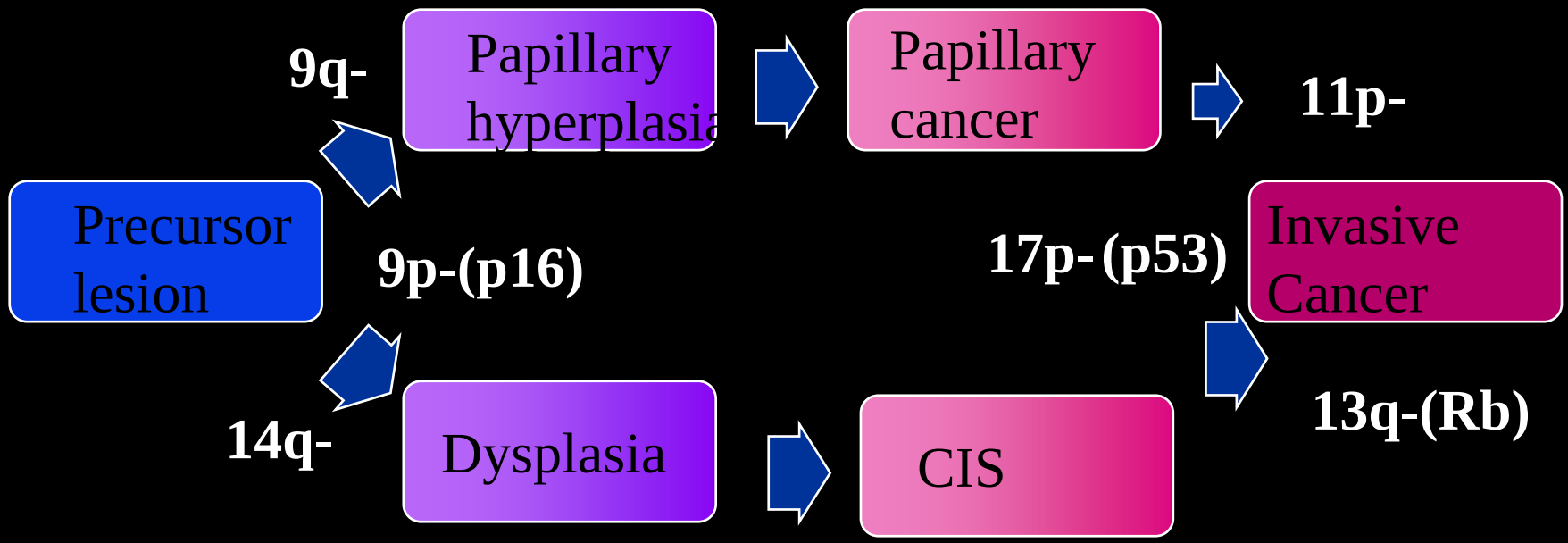
Standard Clinical Experience

- Hematuria (70%)
- Cystoscopy, CT/IVP, urinary cytology
- Biopsy diagnostic and therapeutic
- Followup (not evidence-based)

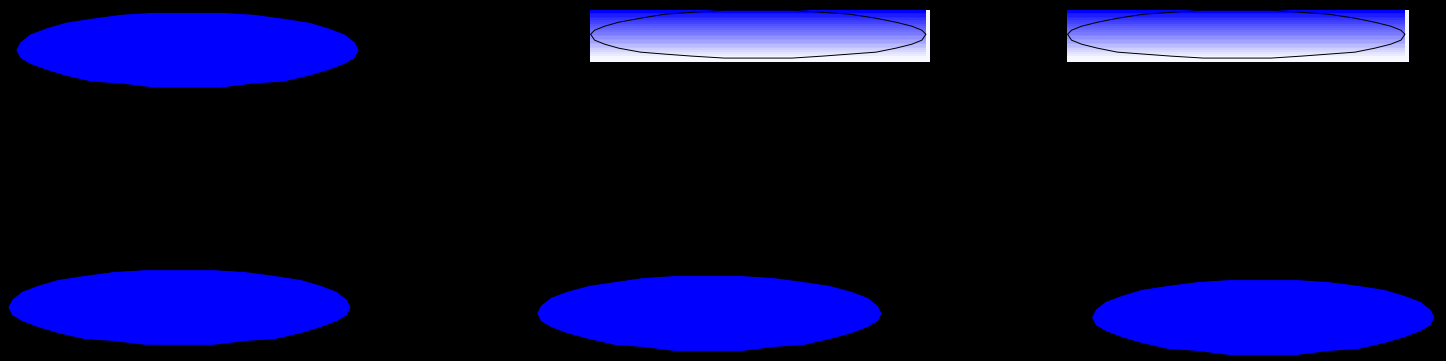
Diagnosis and Followup: Expensive

- Non-invasive UCC a chronic disease
- Average age Dx: 65
- Prevalence 600,000 USA
- Bottman et al (Pharmacoeconomics, 2000)
  - Most expensive solid tumor
  - Alteration of monitoring pattern could positively alter economics of care

Molecular Progression of Bladder Cancer



Molecular Detection

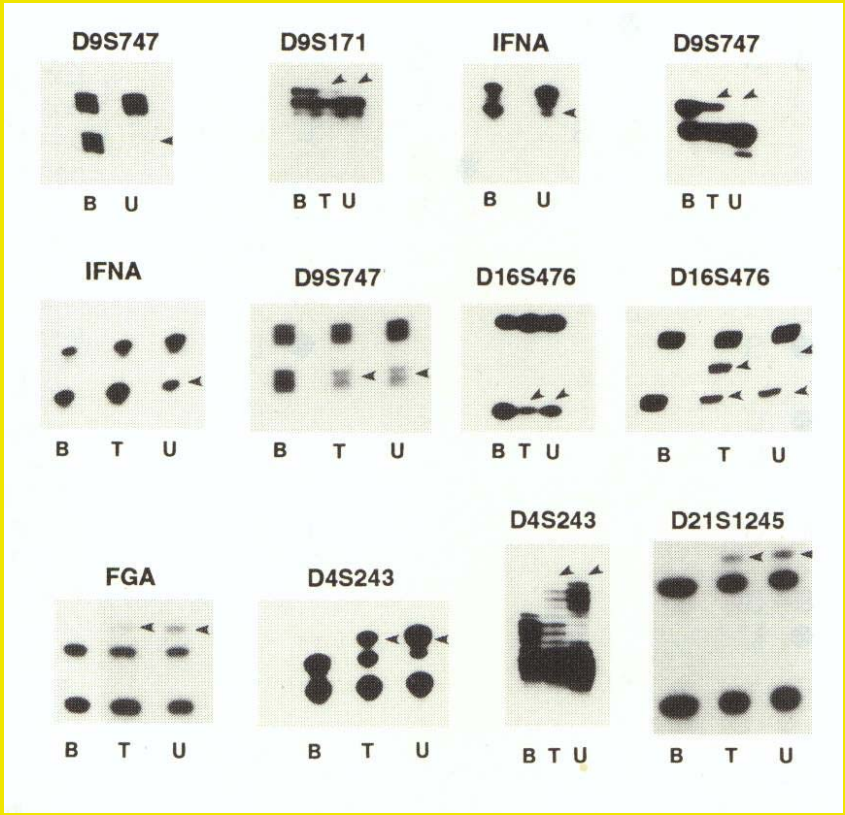


Normal **Tumor** **Sample**

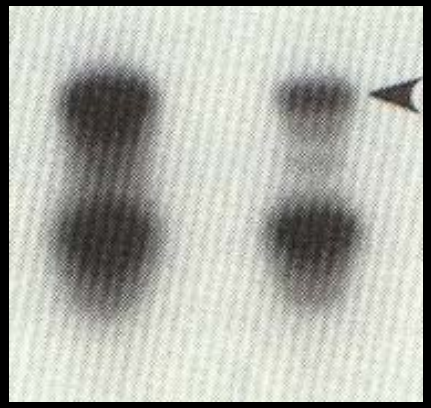
MSA

- Mao et al. (Science, 1996)
  - LOH/MIS demonstrated in urine of UCC pts
  - Small sample (n=25)
- Steiner et. Al. (Nat Med., 1997)
  - MSA used in monitoring after TUR of UCC
  - Detects > 90% tumors
  - Some detected 6-9 months before (+) cysto

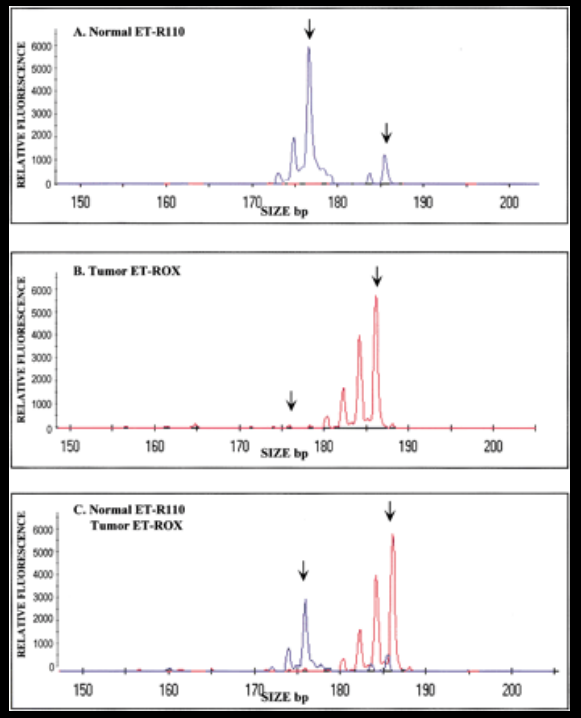
MSA Urine, Mao et al. (1996)



Microsatellite Analysis



32-P Isotopic technique



Fluorescent technique

MSA Trial

- North American validation study
  - 12 USA
  - 1 Canada
  - 300 cases (Ta, Tis, T1)
  - 200 controls
- EDRN/NCI sponsored
- Partnered with Cangen, Inc.
- Virtual data monitoring system (Fred Hutch CC)
  - FDA Compliant

Accrual by Center

Final Group Status

Site Name	Healthy	BPH	Foreign Bodies	Hematuria	Infection	Bladder Ca	Site Total
112 - Memorial Sloan-Kettering	4	0	0	0	0	25	**29**
114 - University of Toronto	0	0	0	0	1	2	**3**
115 - University of Michigan	11	1	1	2	0	23	**38**
116 - Baylor College of Medicine	0	1	0	3	0	11	**15**
117 - University of Rochester Medical Center	20	2	3	8	2	9	**44**
118 - Stanford University	10	3	3	2	2	15	**35**
119 - University of Chicago Urology Center	2	0	1	5	1	22	**31**
120 - University of Alabama at Birmingham	2	1	14	3	1	8	**29**
121 - Johns Hopkins University	36	4	1	1	0	39	**81**
122 - M.D. Anderson Cancer Center	0	0	0	0	0	12	**12**
124 - University of Texas Health Science Center San Antonio	7	4	2	2	0	11	**26**
125 - Washington University	7	6	0	4	3	30	**50**
136 - CURC/Carolina Urologic Research Center	1	6	1	6	2	23	**39**
221 - Brigham and Women's Hospital	0	0	0	0	0	10	**10**
222 - The Urology Group	0	0	0	0	0	0	**0**
223 - Harborview Medical Center	0	0	0	0	0	2	**2**
226 - LURN-Orange City	0	0	0	0	0	8	**8**
227 - LURN-Daytona Beach	0	0	3	0	0	12	**15**
228 - LURN-New Jersey	0	0	0	0	0	0	**0**
280 - Mayo Clinic-Jacksonville	1	0	0	0	0	0	**1**
287 - The Fe/Male Health Clinic	0	0	0	0	0	0	**0**
288 - Burlington Urology	0	0	0	0	0	0	**0**
298 - The Male Health Centre	0	0	0	0	0	0	**0**
299 - Urotec	0	0	0	0	0	0	**0**
310 - The Male/Female Health and Research Center	0	0	0	0	0	0	**0**
Total	**201**	**28**	**29**	**36**	**12**	**262**	**468**

EDRN/MSA Trial: current status

- Accrual completed (DQMB confirmed)
- Study centers monitoring for recurrence
- Biomarker lab (CBI) and QA lab (UM) completing internal assessments
- Coordinating Center (JHMI) tracking compliance

Thank you

- S. Srivastava, J. Kagan EDRN/Biomarkers
- David Sidransky, Ian Thompson
- Cangen, Inc., CBI, University of Maryland
- Mark Thornquist (DMCC/FHCC)
- Abigail Booker (JHMI)
- Colleagues at clinical centers