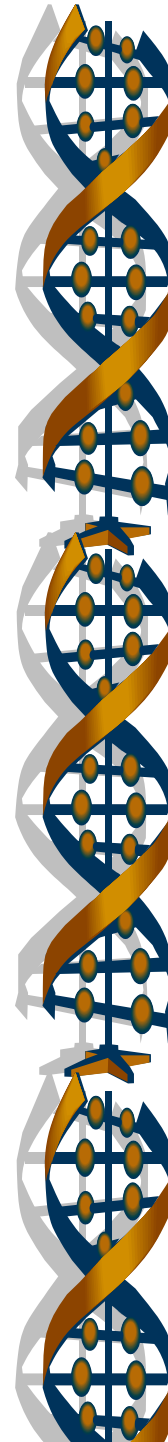




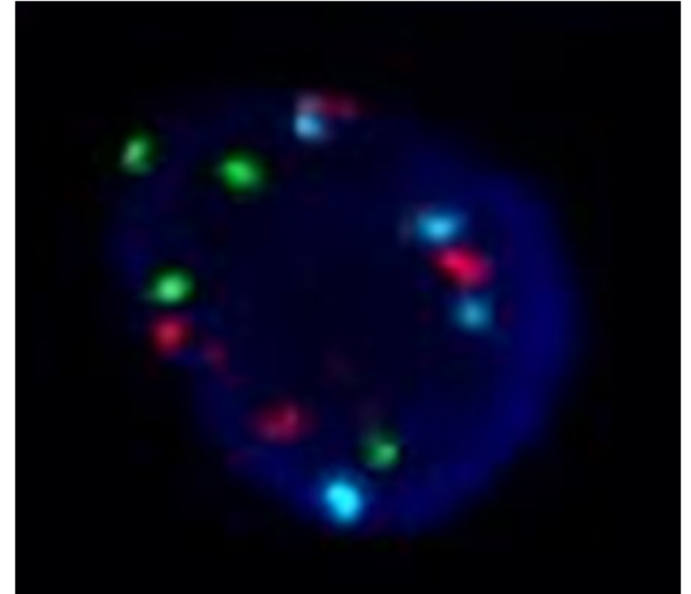
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FISH Testing for Bladder Cancer



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Clinical Use:

- Detects chromosomal abnormalities associated with the development and recurrence of bladder cancer.
- Delivers definitive results (positive/negative) in suspicious cystoscopes or atypical cytology cases.
- Show greatest clinical sensitivity (100%) among the most severe tumors (T2 and Tis), when compared to cystoscopy/histology.
- Delivers an 81% Negative Predictive Value for detection of bladder cancer recurrence versus cystoscopy/histology.

Clinical Background:

Bladder cancer is the fourth most common cancer in men and the twelfth in women, with a combined estimate of 67,160 new cases in the U.S. in 2007. Non-invasive, superficial cancers can usually be cured, especially when well differentiated. Many bladder cancers, however, will recur despite complete tumor resection, about 66% of patients will have a recurrence within 5 years and 88% within 15 years. Frequent monitoring (up to four times per year) for early detection of recurrence is key to increased survival of these patients. Traditionally, cystoscopy-guided biopsy, followed by histology, has been used for initial diagnosis, and cystoscopy and voided urine cytology (VUC) have been used for monitoring.

Fluorescence in situ hybridization (FISH) is a state of the art DNA test which can detect abnormalities of chromosomes 3, 7, and 17 and deletion of the 9p21 locus in urine specimens. In a study of 497 patients with blood in the urine the FISH test showed a diagnostic sensitivity of 69% and specificity of 78% compared with cystoscopy followed by histology. The positive and negative predictive values were 27% and 95%, respectively (prevalence, 10.8%). Thus, FISH test appears useful for the diagnosis of bladder cancer in patients with blood in the urine.

Researchers have found that increased DNA instability and aneuploidy, such as that detected by the FISH test, are characteristic of bladder cancer. Due to its high specificity (~96%) and increased sensitivity (Figure 1), the FISH test is useful for early detection of bladder cancer recurrence when used in conjunction with cystoscopy. When the FISH test is positive and the cystoscopy is

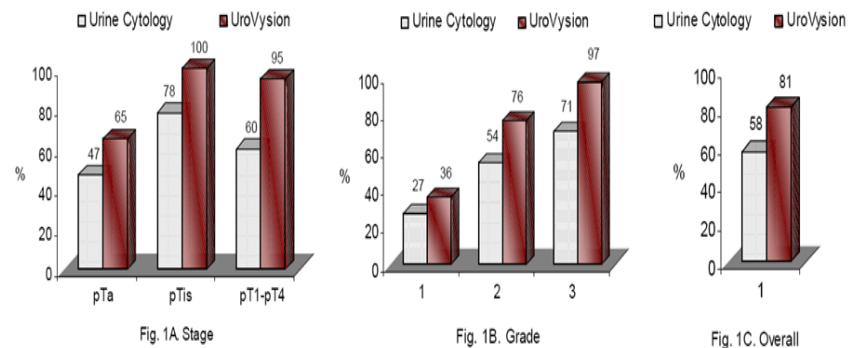


Figure 1. Sensitivity of the Vysis UroVysion test as compared to that of urine cytology.

Figure 1A shows sensitivity for tumor stages pTa, pTis, and pT1-pT4; Figure 1B shows sensitivity for tumor grades 1, 2, and 3; and Figure 1C shows overall sensitivity. Reference: Halling KC, et al. *J Urol*. 2000;164:1768-1775.

negative, cancer recurs on average 4 months earlier than when both tests are negative: thus, a positive FISH test may indicate a need for increased surveillance in these cases.

Method:

In this fluorescence in-situ hybridization (FISH) method, a mixture of CEP3, CIP7, CEP17, and LSI p16 probes, each labeled with a different fluorochrome is used to analyze DNA within cells and to enumerate chromosomes 3, 7, 17 and detect the 9p21 locus deletion on chromosomes.

Interpretive Information:

A positive result is consistent with a diagnosis of bladder cancer or bladder cancer recurrence, either in the bladder or in another site within the urinary system. A negative result is suggestive of the absence of bladder cancer but does not rule it out.

Specimen Requirements:

- 50 mL room-temperature urine
- Collect urine in a sterile screw-cap container
- Abnormal tests and those with insufficient cellular yield should be repeated.