

EXPÉRIENCE PERSONNELLE/PERSONAL EXPERIENCE  
**THE FISH TEST FOR THE DIAGNOSIS, SURVEILLANCE, AND PROGNOSIS  
OF TRANSITIONAL CELL CARCINOMA OF THE BLADDER**

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Haddad FS. The FISH test for the diagnosis, surveillance, and prognosis of transitional cell carcinoma of the bladder. *J Med Liban* 2008 ; 56 (4) : 230-232.

**ABSTRACT • BACKGROUND :** A brief history of the fluorescence in situ hybridization (FISH) test and its use in the management of bladder tumors is outlined.

**METHODS & RESULTS :** After a brief review of the subject, between 1990 and the present, including sensitivity and specificity studies, a referenced list of the various uses of the FISH test is provided.

**CONCLUSION :** It is concluded that the FISH test has almost completely replaced cystoscopy, urine cytology and all other tests and markers for the diagnosis, surveillance, management, and prognosis of bladder tumors. It has completely changed and revolutionized our previous routine of managing bladder tumors.

#### INTRODUCTION

As early as 1992, it was surmised that anomalies of chromosome 9(-9) and others, which are commonly seen in bladder cancer, could be detected in urine and in bladder washings by the fluorescence in situ hybridization test (FISH) [1].

#### METHODS AND RESULTS

Clinically the FISH test for the detection of recurrent transitional cell carcinoma (TCC) of the bladder was first used on a patient (PF # 6110) in my service at the Veterans Administration Medical Center, Phoenix, in 1990 [2]. I soon found that it was a most helpful test especially in the detection of bladder cancer recurrence. I found that sometimes we had a positive FISH test when cystoscopy had been negative. If cystoscopy were repeated, the cancer would be found behind the pubic bone. Here is an example case.

#### Case

PF # 6110 had his first tumors (two kissing tumors) first resected on 90 11 18 (they were Grade I). The tumor

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**RÉSUMÉ • HISTORIQUE :** Après un bref résumé de l'histoire de l'hybridation in situ de la fluorescence (FISH), l'emploi de ce test dans le traitement des cancers de la vessie est détaillé.

**METHODS & RÉSULTATS :** Après une revue de la littérature entre 1990 et 2008 et un sommaire des études de sensibilité et de spécificité, une liste de références des différents emplois du test FISH est dressée.

**CONCLUSION :** Il apparaît que le test FISH a presque totalement remplacé la cystoscopie et la cytologie urinaire ainsi que toutes les autres épreuves et marqueurs dans le diagnostic, le contrôle, le suivi et le pronostic des tumeurs de la vessie. Cette technique a complètement révolutionné notre ancienne routine du contrôle des tumeurs de la vessie.

recurred and was fulgurated on 91 03 07. Despite the intravesical instillation of thiotepa, the tumor recurred again on 92 01 22, 04 03 and on 07 17 ; cystoscopies were negative on 92 10 16 and on 93 01 20, but the FISH test was positive on 93 04, so the patient was cystoscoped again on 04 12 and found to have a tumor recurrence [2].

#### DISCUSSION

This experience was repeated over 300 times. The FISH test proving, time and again, that it usually detects tumor recurrence much earlier than cystoscopy ; it is a quick, inexpensive, accurate, sensitive, and relatively specific method for the detection of chromosomal anomalies [3].

I learned, early on, that the FISH test was a simple test with objective clear end point, which did not depend on the expertise of the cytologist. Particularly when used on urine or bladder washings, the FISH test is a very useful tool in the diagnosis, early detection, and management of bladder cancer (Fig. 1) [4].

Others have confirmed our results and concluded, from a study of 23 cases of TCC (in Holland [5] and in Switzerland [6], TCC is also called "urothelial cell carcinoma," UCC) of the bladder, that the FISH test can be reliably applied for the detection of numerical chromosome 9 aberrations [7] and other chromosome anomalies.

The usefulness of the FISH test has been extended to other fields besides urology. By 1994, it had been used

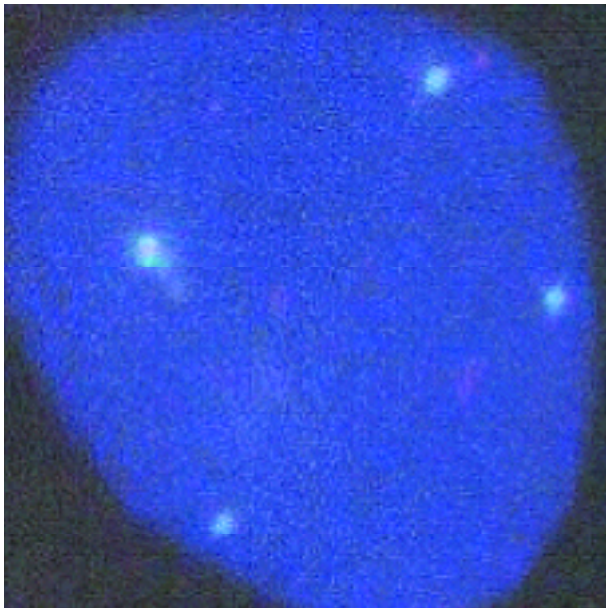


FIGURE 1. FISH test showing trisomy and tetrasomy of chromosomes 7 and 8, pt # 22 [4].

for prenatal diagnosis on amniotic fluid in over 10 000 cases [3].

The sensitivity and specificity of the FISH test have been studied in several series (Table I).

The use of the FISH test in the management of bladder tumors has spread around the world with lightening speed and has already reached many countries including Austria, Denmark, Germany, India, Japan, Sweden, Switzerland and The Netherlands.

The FISH test has been used in the following situations :

- For the diagnosis of bladder cancer [9, 14, 17-18].
- For the monitoring of postoperative tumor recurrence [8-10].
- To select patients for cystoscopy [13].
- To determine the length of the surveillance period in the follow-up of patients with bladder cancer [16].

- To monitor the response to intravesical therapy [15].
- To get a fair idea of the prognosis [16].

The FISH test should be used more frequently in the postoperative follow-up of bladder tumors ; it should be relied upon to alert the urologist to the probability of tumor recurrence, which should then be investigated by cystoscopy, which is an invasive procedure that should be reserved for patients who have a positive FISH test.

In conclusion, I can say with Krause (2006) [19] that *“the FISH test showed very high sensitivity, higher even than cytology, in detecting bladder tumors ... The use of this test in everyday clinical urology can be a very useful decision ... FISH analysis is currently the most sensitive marker for bladder tumors.”* Urine cytology is no longer the gold standard for the non-invasive detection of bladder carcinoma [9-10], it has been replaced by the FISH test

N.B. There are a few kits available on the market for the FISH test ; UroVysion, from Abbott, is one of them [13, 15, 19].

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**TABLE I**  
SPECIFICITY AND SENSITIVITY OF THE FISH TEST

YEAR	Author	Reference	Country/City	Number of Pts	Specificity	Sensitivity
1999	Jung	8	New York	061		
2001	Ishiwata	9	Japan	077	95%	85%
2002	Sarosdy	10	Switzerland	126	94.5%	71%
2003	Mian	11	Austria	–		96%
2003	Friedrich*	12	Hamburg	103	89%	69%
2004	Varella-Garcia	13	Denver, CO	019		87%
2004	Toma*	14	Hamburg	126	89.1%	68.8%
2005	Kipp	15	Rochester, MI	037		
2005	Bollmann	16	Bonn	047		

\* These two reports are the result of the same study.

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#### إختبار الفلورية تم التآلقته بالتهجين الموضعي (إختبار فش)

موجز : بعد تلخيص تاريخ التهجين الموضعي للتآلق (إختبار فش) فإن إستعمال هذه التجربة لمعالجة سرطانات المثانة وضعت بشكل مفصل.

بعد مراجعة المنشورات الطبية من ١٩٩٠ لغاية ٢٠٠٨ وموجز عن الدراسات الحسية والنوعية، وضعنا قائمة بالمراجع المتعلقة بجميع إستعمالات إختبار زفشرز

والخلاصة : تبين إن هذه التجربة جاءت بشكل تام عوضاً عن تنظير المثانة وفحص الخلايا من البول وكذا جميع التجارب والواسمات لأجل التشخيص والمراقبة لبقاء واندثار أورام المثانة فكانت هذه الطريقة "ثورة" عوضاً عن الطريقة السابقة لمراقبة أورام المثانة.