Marín-Aguilera et al [1] report a sensitivity rate of 76.7% for detecting upper tract urothelial carcinoma, significantly better compared to 36% sensitivity for urinary cytology. They analyzed samples from 53 patients; 23 were excluded from the analysis for different reasons, 9 of them due to lack of cells in the sample.

Moonen et al [2] compared the UroVysion test with cytology in surveillance of non–muscle-invasive bladder cancer and found a sensitivity of 39.1%, not different from cytology.

An intriguing assumption was raised in the editorial to this article by Nieder et al [3], who questioned the cost effectiveness and usefulness of the UroVysion test and indicated enthusiasm for this method has passed beyond its zenith. They pointed out the low overall reliability of fluorescence in situ hybridization (FISH) and high reliability of cytology in the study by Moonen et al [2] and their own experience.

We would like to comment on those apparently discrepant findings in light of our 2-yr experience with clinical use of the UroVysion test, which is available to practicing urologists in our institution. The use of the test is based on the urologists’ discretion for cases where they suspect the results may help them in their clinical decision-making. Altogether, 153 urine samples were sent for FISH testing; sensitivity was 75%. We included in our analysis as true positives only those that were histologically confirmed in the 3 mo after FISH testing.

In our series, 32 (21%) samples were reported as “no cells,” which we clinicians are not used to and found very annoying. From the viewpoint of practicing clinicians, a test for cancer that does not find the disease in a patient with cancer is considered a false-negative result, regardless of the reason. We see this as an important factor in the discrepancies reported for test characteristics in different studies.

For example, sensitivity in the report by Marín-Aguilera et al [1] decreased from 76.7% (23 of 30) to 59.0% (23 of 39), assuming “empty samples” from cancer patients to be false negatives. Comparing the two reports after this adjustment, one predominantly high-grade cancers [1] and the other [2] mostly Ta cases, the sensitivity of the two reports does not differ greatly.

Considering reports of “no cells,” we observed an interesting finding in our series; there were 71 samples collected from women, 6 of them “no cells” (9%) and 82 samples collected from men, 26 of them “no cells” (32%). We found significantly more men with “empty samples” (p = 0.001). This may indicate imperfect urine sampling and contamination from epithelial cells to be quite frequent in samples from women.

Considering conclusions from Nieder et al [3], we should point out that cytology results differ greatly among institutions, with those of Herr, Soloway [3], and Witjes [2] being some of the best, because cytology relies greatly on the knowledge and experience of the interpreter. In our experience, of 15 true positive FISH cases, cytology was negative in 5 cases (although repeated 3 times, whereas each FISH sample was sent only once) and we were not able to identify a single case where cytology would be positive and the FISH test negative. Our cytology results are even worse compared with those from Marín-Aguilera et al [1]. FISH is much more objective. However, for FISH tests it is also important that results should be interpreted by an observer with a great deal of experience in interphase FISH. Furthermore, the criteria for FISH results are still debatable. Especially, the cases with a low number of available cells from voided urine samples should be interpreted with caution. Evaluation of positive cells that do not reach the criteria for the FISH positive results (≥ 4 cells according to UroVysion instruction, ≥ 10 cells in study by Zellweger et al [4]) should be considered as borderline cases.

Although the FISH test is (with probes supplied from Vysis) undoubtedly a very expensive examination, cost comparisons are not automatically the same between pathology and genetics laboratories in the United States and other parts of the world. Cytology requires a physician to interpret the results, whereas FISH test results in our health system are evaluated and issued by geneticists.

We do agree with Nieder et al [3] that FISH should not be incorporated into rigid schemes of clinical decision-making for every patient with a suspected urothelial tumor and everyone should be aware of its restrictions. However, for those of us who do not have access to reliable urinary cytology, it has proven to be a great tool.

We think along the same lines as those expressed in the comments by Hajdinjak et al regarding the use of fluorescence in situ hybridization (FISH) for the detection of urothelial carcinoma (UC). However, when comparing UroVysion sensitivity and specificity between the findings of Moonen et al [1] and our work on FISH for detection of UC in the upper urinary tract [2], the discrepancies obtained in sensitivity (39.1% vs. 76.7%, respectively), in our opinion, are exclusively due to the different populations of UC studied. In the Moonen et al study only 28% (18 of 64) of samples correspond to G3 samples, whereas in our study 73.3% (22 of 30) of samples studied were from high-grade tumours. Opposite figures can be found in the proportion of Ta tumours in both studies: 68.8% (44 of 64) and 16.7% (5 of 30), respectively.

It would be more appropriate to compare the results of Moonen et al with a recently published study by our group on the utility of UroVysion in detecting specifically non–muscle-invasive UC of the bladder [3]. In our study, higher sensitivities in the detection of UC were found. For instance, T1 sensitivity was 85% and 60%, respectively, and for G1 52.8% versus 22.2%, respectively. Of note, overall sensitivity of urinary cytology in both reports were very similar (47.3% vs. 40.6%, respectively).

Hajdinjak et al raise a question regarding the cases with “no cells” that consequently cannot be evaluated by FISH. We think that probably it is not fair to compute those cases as false negatives because in our case those samples without an appropriate cellularity were not considered for hybridization (due to the high cost of the test). On the other hand, although we cannot prove it statistically because of the low number of women in our series, we also noticed a trend toward getting fewer cells from men’s urines than from women’s samples.

As regards using the UroVysion test for clinical practice, we also agree with the comments by Nieder et al and Hajdinjak et al about not incorporating the FISH test in rigid schemes of clinical decision-making for every suspected urothelial tumour case. However, we do think that FISH can helpful in the diagnosis of upper urinary tract UC [1], in the case of predicting recurrence after bacillus Calmette-Guérin therapy [4], and in the case of suspicious cytology [5] and could probably also be of help in reducing the number of cystoscopies performed during monitoring of good-prognosis non–muscle-invasive UC of the bladder.

Finally, we would like to state that the investigation for new molecular markers in urine is open as well as their clinical indications for use. Most current tests imply the study of single proteins resulting from genetic alterations, DNA alterations, or the combination of a few numeric chromosome alterations, still with unsatisfactory results, far from the desirable 90% specificity and sensitivity. Thus, in our opinion future studies should search for a combination of multiple markers in a single test