FISH TO DETECT URINARY AND OTHER CANCERS: DO IMAGING SYSTEMS HELP?

G. D. Smith1 and J. S. Bentz1,2

1ARUP Institute for Clinical and Experimental Pathology®, ARUP Laboratories, Salt Lake City, UT, USA

2Department of Pathology, University of Utah, Salt Lake City, Utah, USA

Abstract

Introduction: Cytological abnormalities are associated with a variety of pathologic alterations, including dysplasia, atrophy, and the detection of malignancy. The UroVysion FISH kit detects these alterations by fluorescence in situ hybridization (FISH). Because the manual interpretation and documentation of UroVysion FISH in the laboratory is time consuming, we investigated image processing and automated cell classification techniques to improve the turnaround time. This study evaluated the BioView Duet imaging system as an aid to the interpretation of UroVysion FISH slides. We compared it to manual review. We additionally evaluated the BioView false targets. Target FISH.

Materials and Methods: UroVysion FISH cases that were reviewed in the ARUP laboratory were reviewed manually and with the aid of a BioView Duet imaging system. Manual and BioView-aided interpretations were compared with respect to accuracy, between-run precision, and the time required to perform it.

For Target FISH, BioView was used to capture target cell images from Pap stained slides, which were then destained and evaluated before carrying out UroVysion FISH. The BioView instrument was used to relocate the original target cells, and FISH signals were evaluated.

Results: Fifty percent of the UroVysion cases could be interpreted as clearly positive or negative, with some cases showing 9p21 aneuploidy, and others showing 8q24 aneuploidy, between the manual and BioView-aided interpretations. Two cases judged to be BioView-positive, but manual negatives, were controlled to be positive, and three manual negative FISH signals. Thirty percent of the manual cases showed non-specific DNA or nuclear dye, and the remaining 17% of the slides were unsatisfactory for the BioView interpretation because of low cellularity or excessive clumping. The total time required for pathologist evaluation was 15 minutes with the aid of the BioView, compared to 30 minutes for a manual interpretation.

Conclusions: For Target FISH, it is important to fully destain the slides before FISH was carried out, and some cell loss occurred during the procedure. Brightfield cells did not demonstrate the same quality as the recent cases, with some non-specific DNA signals and high background cells. The BioView classification of manual negatives was excellent, with targets in near-perfect resolution or location in the field of view.

In the study, the BioView-aided interpretations were at least equivalent to manual interpretations, but 2 manual negative false signals did not match the aid of the BioView Duet imaging system. To work optimally, cell distribution on the slide must be high quality. The image generated are of excellent quality for archiving. The system permits interactive review of abnormal cells, as well as the ability to evaluate the same cells for brightfield cytology followed by UroVysion FISH (Target FISH).

Why do we need image processing/analysis for Urovysion FISH?

• FISH. Why images should be processed and analyzed.
  - manual interpretation was requiring 50 minutes/case. Could image processing reduce false negatives?
  - Patient care – Could image processing reduce false positives?
  - Images for CAP archiving requirements – Could an imaging system provide quality images for archiving?
  - Locations of cells – Could an imaging system track the locations of cells for re-examination?
  - New tool for advancement of cytology and expanded role for trained cytotechnologists

Imaging Systems Have Some Advantages Over the Human Eye

• Humans do not see too dim light
• Image capture and processing can be used to adjust for variations in signal strength and background

Concordance between Manual and BioView Aided Interpretations for Clearcut + or - Cases

<table>
<thead>
<tr>
<th>Sample Type</th>
<th>BioView Negative</th>
<th>Manual Positive</th>
<th>Percentage Concordant</th>
</tr>
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<tbody>
<tr>
<td>Non-Urine</td>
<td>11 TP</td>
<td>16 TP</td>
<td>88.5%</td>
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</table>

Overall Summary and Conclusions

- BioView aids at least equivalent to Manual Interpretation. Valuable tool:
  - Great clinically – minimizes false negatives!
  - Intuitive review of abnormal cells
  - Image enhancement of weak signals
  - Great training tool!

- Pathologists time (30 min manual vs 4 min BioView); Cytotechnologist 15+2 min. Total 30 vs 21 min.

- Multiple cases of good quality for archiving (CAP)

- Segregated cases – 13%. Tumors/normality or purity.

- Precision study – excellent reproducibility

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- Image capture and processing can be used to adjust for variations in signal strength and background

Conflict of Interest: The authors declare that no conflict of interest relationship exists.