

CLINICAL LABORATORY TEST



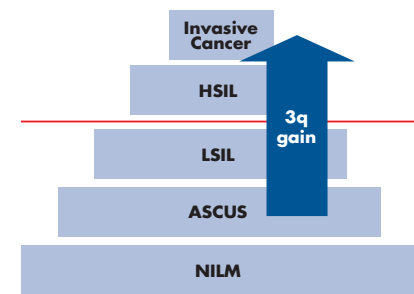
oncoFISH[®] cervical

A NEW TEST TO AID IN LSIL PATIENT MANAGEMENT

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CLINICAL LABORATORY

oncoFISH[®] cervical—a new test to aid in LSIL patient management

Which low grade squamous intraepithelial lesions (LSIL) will progress clinically to a higher grade? Which will regress to normal without treatment? Approximately 10% of patients diagnosed with LSIL will progress to HSIL, 60% will regress to normal, and 30% will remain LSIL¹. Historically, it has not been possible to identify which patients will progress or not. A more predictive tool to aid the clinician in managing an LSIL diagnosis is needed. Now the Ikonisys Clinical Laboratory (ICL) offers the oncoFISH[®] cervical test, to be used in conjunction with other testing, to better manage patients previously diagnosed with an LSIL result.



3q gain can aid in categorizing patients previously diagnosed with LSIL within the risk stratification.

Among the many chromosomal changes observed in cervical cancer, the most consistent abnormality is detected in chromosome arm 3q.² Studies have shown that at least 90% of invasive cervical cancer cases have a gain in the 3q arm.^{3,4} Additional research has demonstrated a correlation between the gain in the 3q26 copy number as the severity and stage of cervical disease progresses.^{4,5,6} Using this technology to look at the progression of individual patients, it has been shown that the sensitivity of the 3q26 loci for predicting progression from CIN1/CIN2 to CIN3 was 100% and the specificity, i.e., the prediction of regression, was 70%.⁶

Although several factors contribute to the progression of a precancerous lesion to malignancy, 3q26 gain is a marker that the medical professional can use, in conjunction with other tests, to aid in LSIL patient management.

Test Description

The oncoFISH cervical test from the Ikonisys Clinical Laboratory is a qualitative fluorescence *in situ* hybridization (FISH) test for determining the acquisition of specific chromosomal aneuploidies (within the 3q26 region) in cytological specimens revealing LSIL.

Until now, routine testing for 3q gain was not feasible, because assessment required analysis of a large number of stained, squamous cell nuclei—impractical for manual methods. By using the Ikoniscope[®] Digital Microscopy System to automate analysis, the oncoFISH cervical test makes testing for 3q gain a practical reality.

The test is performed on cervicovaginal cytology specimens, identical to those used for Pap and HPV testing. It assesses amplification of the 3q26 region by use of two FISH probes, one for the 3q26 locus and a control probe. Enumeration and

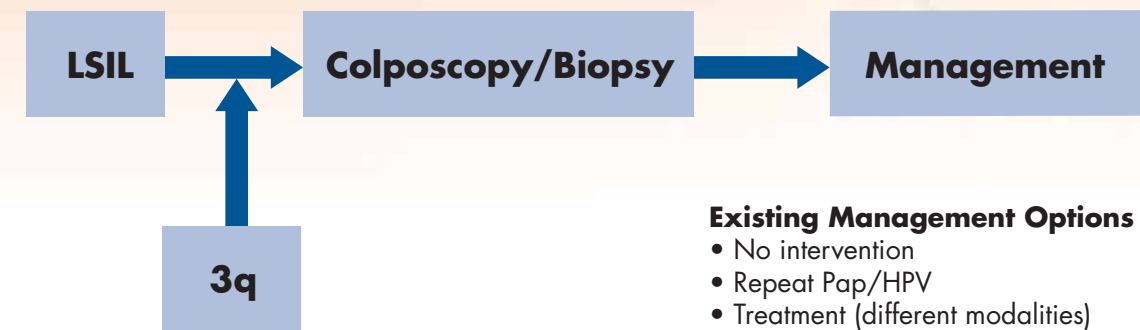
comparison of the 3q26 and control probes, in conjunction with the nuclear morphology, result in a 3q copy number for each of the nuclei analyzed.

Incorporating the oncoFISH cervical test into existing clinical practice guidelines

oncoFISH cervical results are to be used with other clinical findings for further evaluation and monitoring of cervical dysplasia in women with LSIL Pap results. The oncoFISH cervical test is not intended to replace or alter the current standards of practice used for the clinical management of women undergoing evaluation for cervical dysplastic lesions.

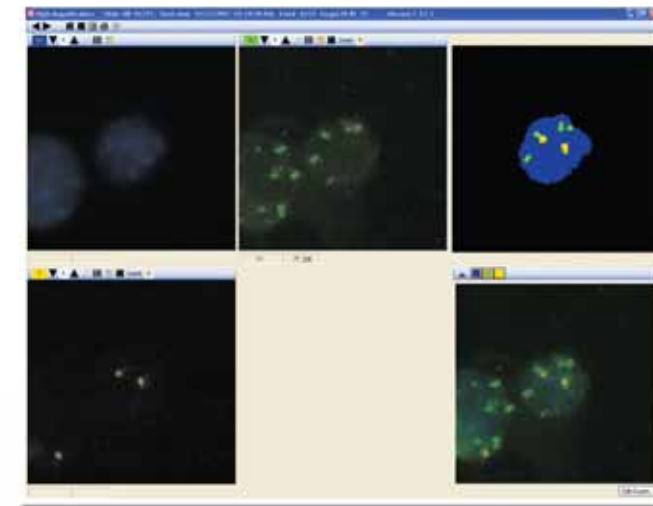
The results should be considered by the clinician in the context of other testing when formulating clinical management.

oncoFISH cervical provides information for the clinical assessment of dysplasia prior to colposcopy



Existing Management Options

- No intervention
- Repeat Pap/HPV
- Treatment (different modalities)



Ikonisys Clinical Laboratory uses the Ikoniscope Digital Microscopy System to analyze hundreds of nuclei. Automated enumeration of the aqua (3q26) and gold (CEP7) probes produces images for review. Images are generated and a test result is provided in a comprehensive, easy-to-read report.

“... the detection of 3q gain and amplification of *TERC* in routinely collected Pap smears can assist in identifying low grade lesions with a high progression risk and in decreasing false-negative cytological screenings.”

Genomic Amplification of the Human Telomerase Gene (TERC) in Pap Smears Predicts the Development of Cervical Cancer. Kerstin Heselmeyer-Haddad, et al, American Journal of Pathology, 2005, 166:1229-1238.

For more information about incorporating the oncoFISH cervical test into your patient management algorithm, please visit us at www.ikonisys.com/cervical or call us at 888.445.6652.

ORDERING INFORMATION oncoFISH cervical ■ Test Order Code: 1003 ■ CPT Code*: 88367 x 2, 88275 x 2, 88291

*The CPT codes provided are based on AMA guidelines and are provided solely for informational purposes.

Ikonisys Clinical Laboratory

ADVANCING TESTING FOR CANCER AND GENETIC DISORDERS

The Ikonisys Clinical Laboratory (ICL) is a fully licensed, CAP-accredited clinical laboratory offering testing for early cancer and genetic disorder screening. Specializing in FISH, our menu includes both established assays and a growing family of new, unique FISH tests for rare and abnormal cell detection.

FISH procedures are performed using our Ikoniscope Digital Microscopy System that provides fully automated FISH scoring and preliminary analysis. This greatly reduces subjectivity compared to manual processing. The combination of automation and our scientific/medical expertise provides our clients with highly objective, accurate results.

More Than a Clinical Laboratory

ICL is part of Ikonisys, Inc., a leader in automated FISH testing. Ikonisys is at the forefront of developing novel FISH applications to detect rare and abnormal cells. Through the Ikonisys Clinical Laboratory, Ikonisys provides clients with early access to these new, high-value test solutions, enhancing patient diagnosis and management. The synergy between ICL and the Ikonisys applications development group creates unique opportunities for improved patient care.

The ICL staff has exceptional expertise in FISH technology. Reproducible, accurate results with excellent turn-around time, and a demonstrated commitment to providing uniquely personalized service for our clients and their patients, define the Ikonisys Clinical Laboratory.

References

- ¹ American Society for Colposcopy and Cervical Pathology (ASCCP) Practice Recommendations. [Updated July 24, 2008.] Available from <http://www.asccp.org/edu/practice/cervix/premalignant/epidemiology.shtml>.
- ² Heselmeyer K, et al. 1997. Advanced-stage cervical carcinomas are defined by a recurrent pattern of chromosomal aberrations revealing high genetic instability and a consistent gain of chromosome arm 3q. *Genes Chromosomes Cancer*. 19(4):233-40.
- ³ Heselmeyer K, et al. 1996. Gain of chromosome 3q defines the transition from severe dysplasia to invasive carcinoma of the uterine cervix. *PNAS*. 93(1):479-84.
- ⁴ Caraway, NP, et al. 2008. Gain of the 3q26 region in cervicovaginal liquid-based Pap preparations is associated with squamous intraepithelial lesions and squamous cell carcinoma. *Gynecol. Oncol.* 110(1):37-42.
- ⁵ Heselmeyer-Haddad, K, et al. 2003. Detection of genomic amplification of the human telomerase gene (TERC) in cytologic specimens as a genetic test for the diagnosis of cervical dysplasia. *Am J Path.* 163(4):1405-1416.
- ⁶ Heselmeyer-Haddad, K, et al. 2005. Genomic amplification of the human telomerase gene (TERC) in Pap smears predicts the development of cervical cancer. *Am J Path.* 166(4):1229-1238.

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