Healthy Blue

Medical Policy

Subject:	Breast Ductal Examination and Fluid Cytology Analysis		
Document #:	SURG.00044	**Publish Date:**	12/16/2020
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Description/Scope

This document addresses the examination of breast ducts via fiberoptic ductoscopy, and the analysis of breast ductal fluid via cytology, for the presence of hyperplasia. Fiberoptic ductoscopy provides direct visual examination of breast ducts by means of a small endoscope, whereas breast ductal fluid may be obtained for cytologic analysis by ductal lavage or nipple aspiration. Ductoscopy and cytologic analysis of breast ductal fluid have been proposed as diagnostic and risk assessment tools in individuals at high risk for breast cancer.

Position Statement

Investigational and Not Medically Necessary:

Cytologic analysis of breast ductal fluid, acquired invasively or noninvasively, is considered **investigational and not medically necessary** as a diagnostic or risk assessment tool for those considered at high risk for breast cancer, as well as for general population screening.

Breast fiberoptic ductoscopy is considered **investigational and not medically necessary** for the detection, diagnosis or treatment of breast cancer.

Rationale

Fiberoptic ductoscopy enables direct visual examination of the breast ducts using a small endoscope, advanced through an enlarged duct at the nipple. Breast ductal fluid may be obtained for cytologic analysis by ductal lavage or nipple aspiration. Utility of these techniques for the detection, diagnosis and treatment of breast cancer has not been demonstrated by randomized controlled studies. Public health agencies and both national medical and professional societies recommend mammography as the most effective method for detecting breast cancer in its earliest stages.

A multi-center, prospective clinical trial was conducted by Dooley and colleagues (2001) in which the diagnostic yield of ductal lavage was compared to that of nipple aspiration in 507 women considered at high risk of developing breast cancer but who were negative for mammographic abnormalities. High risk was defined as those with a 5-year Gail model risk of at least 1.7%, BRCA mutation positive, a personal history of breast cancer or previous diagnosis of lobular or ductal carcinoma *in situ (DCIS)*. A total of 57% of the participants had a prior history of breast cancer. All participants underwent nipple aspiration, followed by ductal lavage. Nipple aspiration produced adequate samples for analysis in 27% of women, compared to ductal lavage, which produced adequate samples in 78%. A total of 24% of ductal lavage samples revealed atypical cells, compared to 6% of fine needle

aspiration samples (Dooley, 2001). Treatment decisions and outcomes based on these findings have not been reported.

Other studies have found inconsistencies with cytological analysis. Visvanathan and colleagues (2007) found that the use of ductal lavage is limited by the technical challenges of duct cannulation, inconsistent nipple aspirate fluid production, a high rate of inadequate cellular material for diagnosis and fair cytologic reproducibility.

Supportive data for using results of ductal lavage as a risk assessment tool are based on studies that have shown that atypical hyperplasia (AH) is associated with an increased risk of cancer (Degnim, 2007; Fabian, 2000). Accurately identified AH can be significantly reduced with tamoxifen hormone therapy. However, whether the natural history of AH identified in mammographically normal women (that is, in the ductal lavage clinical study) confers the same degree of risk of AH associated with mammographic abnormalities (that is, in the tamoxifen cancer chemoprevention trial), and whether the two populations of participants respond similarly to tamoxifen, has not been answered. Additionally, since the sensitivity of ductal lavage is unknown, a negative test (that is, absence of AH) is not informative for the individual and does not contribute to decision-making regarding the initiation of tamoxifen therapy.

In a study designed to determine which histological lesions produce cellular atypia in lavage specimens and whether ductoscopy adds useful information for the evaluation of high-risk individuals with atypical lavage cytology, Cyr and colleagues (2011), prospectively studied 102 women who were 35 years or older and at high risk for developing breast cancer. All underwent ductal lavage. Women found to have atypia underwent ductoscopy-directed duct excision (group 1). Women without atypia were observed (group 2). The median follow-up was 80 months (range 5-90 months). Data included participant demographics, risk assessment, cytologic and histologic findings, and clinical outcomes. Descriptive statistics were utilized for data summary and were compared using Fisher's exact test. Overall, 27 (26%) had atypical lavage cytology (group 1), and 75 (74%) had benign cytology (group 2). Subsequent duct excision in group 1 revealed benign histology in 11 (44%), papillomas in 9 (36%), AH in 4 (16%), and DCIS in 1 (4%). At follow-up, 3 participants had developed breast cancer, including 1 participant from group 1, and 2 participants from group 2. There were no differences between groups 1 and 2 according to their demographics, Gail risk scores, or risk for subsequent breast cancer ($p>0.05$). The authors concluded that although 20% of high-risk women with ductal lavage atypia have AH or malignancy on subsequent excision, the majority do not. Atypia identified by ductal lavage was not found to be associated with a higher risk of developing subsequent breast cancer, even in this high-risk population.

In a retrospective review, Fisher and colleagues (2011) reviewed the clinical outcomes of those who underwent ductoscopy by the same surgeon for pathologic nipple discharge at one institution from 2006-2010. Data included imaging characteristics, indications, operative findings, and pathologic outcomes. Descriptive statistics were used for data summary. A total of 121 participants underwent ductoscopy and directed duct excision for pathologic nipple discharge, including 66 (55%) with bloody discharge. Breast imaging (mammography, ultrasound, and/or magnetic resonance imaging [MRI]) revealed Breast Imaging Reporting and Data System (BIRADS) category I/II/III findings in 112 (93%) women, BIRADS category IV findings in 6 (5%) women, and was unknown in 3 (2%) women. Final pathology revealed papillomas in 64 (53%) participants, duct ectasia and associated benign findings in 48 (40%) participants, DCIS in 7 (6%) participants, and atypical ductal hyperplasia in 2 (1%) participants. The authors acknowledged that the majority of those with pathologic nipple discharge had benign nonproliferative

findings or benign papillomas. In this study, atypia and malignancy were diagnosed in 7% of those who underwent ductoscopy for pathologic nipple discharge; however, there were no routine imaging findings indicative of these diagnoses preoperatively.

A study by Ohlinger and colleagues (2014) investigated the sensitivity and specificity of ductoscopy compared to standard diagnostic tests including breast sonography, mammography, MRI, ductography and less conventional diagnostic methods such as cytological nipple swab and ductal lavage in 214 women with pathologic nipple discharge. Sonography had the highest (82.9%) sensitivity, followed by MRI (82.5%), ductography (81.3%), ductoscopy (71.2%), lavage cytology (57.8%), mammography (57.1%), and nipple swab (22.8%). Nipple swabs had the highest (85.5%) specificity, followed by lavage cytology (85.2%), ductoscopy (49.4%), ductography (44.4%), mammography (33.3%), sonography (17.9%), and MRI (11.8%). This study lacked a control group and randomization. In addition, a large number of women either elected or were unable to undergo certain procedures; data on their characteristics are not reported thus study biases cannot be ruled out.

In another assessment of the diagnostic capability of ductoscopy in identifying intraductal breast neoplasms (Zielinski, 2015), ductoscopy was performed in a total of 168 women; 128 with pathologic nipple discharge and 36 with a known presence of breast cancer. Using post-operative histopathological examination the sensitivity of ductoscopy in this study was determined to be 68.1%, specificity 77.3%, positive predictive value 90.4%, and negative predictive value 44.1%. This study lacked randomization, a control group and a comparative component to assess the diagnostic utility of ductoscopy relative to standard methods of breast cancer screening and diagnosis.

The American Cancer Society (ACS, 2020) does not mention fiberoptic ductoscopy or the analysis of breast ductal fluid via cytology as diagnostic or risk assessment tools in breast cancer screening.

The 2020 National Comprehensive Cancer Network® (NCCN) Clinical Practice Guidelines in Oncology®, Breast Cancer Screening and Diagnosis Guidelines states that current evidence does not support the routine use of ductal lavage as a screening procedure and states that, "The FDA [Food and Drug Administration] has issued a safety alert stating that ductal lavage should not be a replacement for mammograms."

Background/Overview

Breast cancer is the most common female malignancy worldwide (excluding skin cancers) and the second leading cause of cancer death in women in the United States (U.S.). According to ACS predictions, approximately 276,500 new cases of invasive breast cancer will be discovered in the United States in 2020, and roughly 42,000 women will die of the disease. About 95% of breast cancers originate in the ducts, and abnormal cells found there may be associated with a significant increased risk of breast cancer. Early detection based on established and effective screening programs, a high degree of awareness of the disease in the population, and aggressive multi-modality therapy have led to a decline in mortality from breast cancer in the developed world.

Analysis of epithelial cells found in ductal fluid has been studied as an early indicator of breast cancer. These cells, if atypical, might indicate the possibility of future breast cancer. Breast ductal fluid can be obtained by ductal lavage or nipple aspiration via suction or random periareolar fine needle aspiration (RPFNA). Ductal lavage is an

invasive procedure that obtains ductal fluid by the cannulation of the breast milk ducts via the nipple. RPFNA, also considered invasive, is a procedure in which a fine gauge needle with suction capabilities is introduced into a duct in the nipple area. Gentle suction is applied for fluid acquisition. Aspirated fluid from these procedures is analyzed for abnormal cytology.

The HALO® Breast Pap Test (Halo Healthcare, Inc, Irvine, CA) is an FDA approved, noninvasive device that is positioned on the nipple and acquires ductal fluid by applying heat, cyclic compression and suction. This device is discussed in one small study funded by the manufacturer and concludes that although the device can collect the duct fluid noninvasively, well-designed randomized controlled studies are required to determine the utility of cytological analysis of breast ductal fluid (Proctor, 2007).

In general, each of the aforementioned techniques are problematic in that not all ducts produce fluid, or if fluid is found, the quantity may not be sufficient for testing. Furthermore, ducts producing fluid may not be the source of the atypical cells associated with early stages of cancer. These inconsistencies compromise any analysis of ductal fluid for early identification of breast cancer. There are ongoing clinical studies investigating the clinical utility of mammary duct fluid cytology.

In 2017 the FDA reaffirmed this warning to the public:

> …the FDA is unaware of any valid scientific data to show that a nipple aspirate test, when used on its own, is an effective screening tool for any medical condition, including the detection of breast cancer or other breast disease. .

Fiberoptic ductoscopy has been developed for structural examination of the breast duct. The procedure involves the enlargement of the duct at the nipple with small metal wires. A ductoscope, which is a small tube with a camera attached, is passed into the duct and advanced into the breast. Water may be injected through the scope into the duct to allow easier passage of the scope. Fluid may be collected through the scope and examined and a very thin wire probe may be passed up to several inches into the breast to sample any abnormalities that might be found. Fiberoptic ductoscopy is currently being studied in clinical trials.

Definitions

BIRADS: The Breast Imaging Reporting and Data System is a tool used to categorize results of breast mammography, ultrasound and magnetic resonance imaging (MRI). It is divided into the following levels:

BIRADS 0: Assessment incomplete. Additional imaging evaluation
BIRADS 1: Negative. Routine follow-up for age
BIRADS 2: Benign finding. Routine follow-up for age
BIRADS 3: Probably benign. Short-term follow-up (usually in 6 months)
BIRADS 4: Suspicious abnormality. Tissue sampling
BIRADS 5: Highly suspicious of malignancy. Tissue sampling

Cannula: A tube for insertion into a duct or cavity.

Duct: A duct is a passageway with well-defined walls, especially a tube for the passage of excretions or secretions.

Ductal: Relating to a duct.

Gail Model: A computer program that uses personal and family history to estimate a woman's chance of developing breast cancer.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time for service to determine coverage or non-coverage of these services as it applies to an individual member.

When services are Investigational and Not Medically Necessary:
When the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

CPT

19499	Unlisted procedure, breast [when specified as catheter lavage of a mammary duct or fiberoptic ductoscopy]

ICD-10 Diagnosis

All diagnoses

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Government Agency, Medical Society, and Other Authoritative Publications:

1. NCCN Clinical Practice Guidelines in Oncology®. © 2020 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on August 24, 2020.
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Acueity System breast
Ductal Lavage
Ductoscopy, Fiberoptic
FirstCyte® Aspirator
FirstCyte® MicroCatheter
FirstCyte® MicroDilator DucPrep™ Breast Aspirator
HALO® Breast Pap Test
Mammary Aspirate Specimen Cytology Test
Pro-Duct Catheter

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

Status	Date	Action
Reviewed	11/05/2020	Medical Policy & Technology Assessment Committee (MPTAC) review. Updated Rationale, Background/Overview, References, and Websites sections.
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Reviewed	03/08/2007	MPTAC review. References updated.
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Revised	04/28/2005	MPTAC review. Revision based on Pre-merger Anthem and Pre-merger WellPoint Harmonization.

Pre-Merger Organizations	**Last Review Date**	**Document Number**	**Title**
Anthem, Inc.	04/28/2004	SURG.00044	Ductal Lavage and Fiberoptic Ductoscopy
WellPoint Health Networks, Inc.	12/02/2004	3.01.27	Ductal Lavage
WellPoint Health Networks, Inc.	09/23/2004	2.01.23	Breast Duct Endoscopy (Ductoscopy)