ORIGINAL ARTICLE

Breast Ductoscopy and the Evolution of the Intra-Ductal Approach to Breast Cancer

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■ **Abstract:** Interest in breast endoscopy came from Oriental investigators in the early 1990s where bloody nipple discharge is a more common presentation of breast cancer. The early techniques using a single microfiber scope without ductal distension was successful in navigating only the first 1–3 cm of the ducts and fraught with technical problems such as scope breakage and poor image quality. In spite of these barriers there has been increasing use of this technology in Japan and more widespread acceptance as the technology of scope design improved. Dooley and others tested a new method of obtaining a rich cytologic specimen from the ducts of high-risk women known as ductal lavage recently. The success of this procedure was that it detected severe cytologic and malignant atypia in clinically and radiographically normal breasts. Reproducibly, the same breast duct could be cannulated and severely atypical cytology obtained. The problem arose in identifying the lesion within the breast, which was the source for the atypia. New American multi-fiber microendoscopes were applied to solve this problem in an initial series of patients with abnormal cytology to identify the lesions. Success of that series lead to wider application of the imaging technology and eventual adoption of this imaging modality help to guide during all non-mastectomy breast surgery where fluid could be elicited from the nipple to identify the duct connecting to the lesion for which surgery was being performed. Initial reports have demonstrated the types of operative findings in certain sub-populations early in the use of this technology. ■

Key Words: breast cancer, breast ductoscopy, nipple discharge

BACKGROUND

In the early 1990s surgeons in Japan, where nipple discharge is a more common complaint amongst new breast cancer patients, began to experiment with endoscopes less than 2 mm in diameter (1). The initial effort was successful at identifying the cause of symptomatic bloody nipple discharge in a majority of patients. Unfortunately the technology was cumbersome and expensive which limited its early widespread use. However, mammography has been a poor tool for diagnosis of breast cancer because of small breast size and high breast density in the Oriental population. Persistent efforts in the 1990s with ductoscopy in Japan, Korea and Hong Kong began to show increasing success and developed a loyal following of surgical advocates as equipment improvements made this more practical (2–7).

The Oriental technique of breast endoscopy was to identify the ductal orifice draining blood, dilate the orifice, and introduce an optical fiber rigid scope with a chip camera mounted at a distance of about 6 inches. The fiber carried both light and the image and a very small working channel allowed air insufflation to distend the ducts (1,7,8). The air distension led to bubbles within a fluid-secreting duct, which then appeared as glistening reflective balls in the image. Clearly this limited exposure until the duct was either cleared of bubbles. Lesions seen were collapsed to the sidewall from the intra-luminal air distension but the bleeding source could usually be recognized easily and resection guided by transillumination thru the skin. Further refinements of this technique have allowed cyst puncture and cystoscopy directly through the puncture tract (9–11).

American efforts to perform ductoscopy began with experimentation with single fiber much smaller and very flexible scopes (12). These were even harder to direct and manipulate through the ductal system than their Oriental rigid counterparts. No working port was available so that active distension of the ductal system during endoscopy was not feasible. To achieve the distension needed pre-scope distension of the duct with saline afforded some increase in manipulation room.

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While participating in the initial ductal lavage trial, I recognized the problem of identifying a single ductal orifice which could be reliably multiply lavage for cancerous cells without any lesion being found clinically or radiographically (13,14). Aware of both the prior Oriental and American experiences with ductoscopy I sought to find a semirigid sub-millimeter scope through which I could perform saline distension of the ductal tree. Further to avoid the torque issue of the camera at the end of a long lever arm, I wanted an optical fiber long enough and flexible enough to not interfere with driving the scope down the ducts. The Acueity 9 mm microendoscope fit these criteria and I began a small pilot series to identify the cause of malignant and severe atypia from ductal lavage or nipple aspiration fluids. Quickly it became apparent that the scope identified both the source of abnormal cells or bleeding from the intraluminal inspection (15,16). As cancer patients were examined more closely it also became apparent that a small volume of fluid could be elicited from the duct connecting to the tumor in a majority of patients. Even where this fluid did not contain cytologically detectable cancer cells, fragments of cancer cell DNA could be identified and when endoscoped the cancerous lesion and proliferative disease around it could be often identified (17).

Expanding the use of breast endoscopy, first I used it to direct investigations and biopsies for bloody nipple discharge (18). I found that the most proximal intraductal lesion was often not the source of the blood and results suggested that multiple lesions are much more common than previous blind retro-areolar duct excisions had suggested. Next when fluid could be elicited from cancerous breasts, those ducts were endoscoped at the time of surgical lumpectomy (19). The majority of cancers were seen and the ductoscopy proved to be a very reliable way of both documenting the presence or absence of extensive intraductal carcinoma (EIC) and directing complete resection at first attempt at lumpectomy.

At present the clinical use of ductoscopy is limited because of steep learning curves to successfully cannulate, distend and navigate the ductal branches. Further since the number of intraductal photographs with pathologic correlates is still small, the learning curve also includes building up your own personal repertoire of pathologic correlates. Equipment prices continue to fall and the technology is becoming more affordable as multiple manufacturers of sub-millimeter endoscopes worldwide are adapting there technologies to breast duct applications. A number of intraductal biopsy tools are beginning to appear to allow biopsy through these sub-millimeter scopes. Unfortunately the specimen size is often <0.1 mm and would be more appropriately characterized as "chunky cytology" than a true histopathologic specimen. Pathologists will have to modify their approach to such specimens to try to give meaningful and precise answers with such small tissue samples.

INDICATIONS

Mammary ductoscopy is a surgical tool which allows identification of intra-ductal intra-luminal growths and mapping of the branching patterns of the mammary ductal systems in vivo. Most successful breast endoscopists use sub-millimeter scopes and distend the ductal system in some way. The most obvious indication is naturally one of diagnostic and therapeutic direction of excisional biopsy for bloody or pathologic nipple discharge. Papillomas account for a large percentage of these underlying lesions for this indication. Many of these papillomas will be present in the first 20 mm of the breast duct and can be easily identified for removal. Techology of completely removing these large central papillomas from within the limitations of a sub-millimeter ductoscope is evolving. Simple transillumination of the skin in the central breast can easily direct a minimal access approach to removing these lesions. Deeper proliferative lesions causing pathologic nipple discharge are much more likely to reveal pre-malignant or frankly malignant changes. These lesions are almost always found within the larger ductal branches. This raises the important questions of were these branches larger before the lesions arose or did they just dilate since the lesions were making fluid. Since these worrisome lesions are in the most dilated ductal branches, scoping down the largest ducts usually finds the most suspicious pathology.

Ductoscopy can be used in other ways as an adjunct to a planned surgical breast resection. Here ductoscopy allows mapping of the involved ductal tree and identification of intraluminal growths down to about 1/100 mm. This resolution is far below external imaging techniques as mammography, ultrasound and MRI. Unfortunately, there is a large visual overlap in the appearance of some malignant/pre-malignant and benign lesions. Trans-scope biopsy techniques are still in their infancy so until these are available all intraluminal growths must be assumed to be proliferative

and therefore potentially important to sample or excise. In the case of DCIS or T1 breast cancers, about 60% have very small fields or zones of surrounding proliferation. The remaining 40% however seem to have a field defect within the ductal tree leading to widespread proliferative changes at frequently several stages of development. It is these cases that give rise to the EIC (extensive intraductal component), and multi-focality or multi-centricity seen in pathologic mapping of breast cancers and as secondary cancers in MRI and advanced imaging cases. Ductoscopy of a fluid producing duct in the same quadrant of the breast as the known cancer will >85% of the time reveal a direct connection to the cancer and allow the surgeon to determine the presence or absence of associated proliferative changes. By mapping out these changes, using skin transillumination, the surgeon can then do an entire ductal tree or sub-segment resection to incorporate the allied proliferative disease. My prospective but nonrandomized series has shown a dramatic fall in positive margin at initial resection (arguably because of larger resections when associated proliferative disease) and a dramatic reduction of local failure rate of traditional breast conservation. As more surgeons become facile with breast endoscopy, hopefully these results can be proven even more conclusively in a prospective randomized multicenter trial.

PREOPERATIVE PLANNING

The most important aspect of successful breast endoscopy is being able to reliably identify the correct duct and reproducibly be able to get fluid from it for successful cannulation in the operating room. First, you need to develop the skill of expression of nipple fluid during your clinical exams. The La Leche League has an excellent video primer on expression of milk during lactation. The techniques they explain in detail are excellent for expressing the microliters of ductal fluid in nonlactating women with underlying proliferative breast disease. Most series report high expression of nipple fluid using such techniques in those with strong breast cancer history or high Gail model risk.

Next is reproducibly being able to find the offending duct between your clinic exam and the operating room. You can draw a clock face on the areola and take a picture. Cannulating the duct with a soft suture such as a 2–0 prolene can further assist in correct duct identification. With a little practice, using a grid much as in the child's game Battleship with letters on the *x*-axis and numbers on the *y*-axis, you can code position on the nipple and be able to find the ducts without the added picture step. Remember for the ducts to produce fluid the patient will need to be well-hydrated. To some extent consumption of methyl zanthines such as caffeinated drinks will stimulate some additional ductal secretion and assist. Clearly being NPO for 12 hours prior to the operating room can make fluid more difficult elicit from the nipple. I encourage women to "super-hydrate for at least a couple of days before." Giving liberal IV fluids on the day of surgery and keeping the nipple warm prior to trying to elicit fluid are important.

Third is being sure that keratinous debri and crusty dried secretions do not limit your ability to find the duct of interest. I have found most useful some minimally abrasive facial exfollient and a 4×4 gauze pad as the most expeditious way to scrub off the plateau of the nipple papilla for this purpose.

Finally is the massage in the OR prior to prepping the patient. Using the La Leche techniques and hand lotion the breast is kneaded from chest wall toward nipple to push deep pockets of fluid into the lactiferous sinuses behind the nipple. After prepping, simple radial compression of the sinuses allows easy identification of the ducts producing fluid.

SURGERY

Ductal Identification

Cannulate fluid producing duct—in case of pathologic discharge, use a 2–0 prolene cut to a gentle taper; for breast cancer cases, the orifice will be smaller and produce much less fluid. In these cases inject Lymphazurin and local anesthetic in the region around the tumor first to be better able to select the correct low volume duct. Cannulate with the 2–0 prolene if possible or when needed more rigid introducers such as the smallest larcimal duct dilators or stents. Then, progressively dilate in Seldinger fashion using 24G and 22G angiocaths. With each size Angiocath inject 1–5 ccs of local anesthetic into duct for distension.

Ductoscopy—Diagnostic

The scope sheath is introduced in Seldinger fashion with the hollow introducer being removed and replaced by the scope. It is important to have the scope well-focused and white balanced before introduction into the breast ducts. The duct then can be distended by saline or local anesthetic while preventing leakage by compress-

ing nipple papilla against scope with thumb and index finger. The scope is advanced as distension is obtained. Distraction of the nipple outward and gentle motion of the underlying breast mound back and forth can be used to negotiate the varying branches. The scope sheaths all come with markings help to keep track of depth. When you come to multiple branches, the largest diameter branch usually takes you to the most proliferative lesion.

To find position of scope tip if an abnormality is seen that needs excisional biopsy, turn off all the overhead lights in the OR and use the transillumination from the scope tip to identify your site for biopsy. The scopes can all be readily seen with ultrasound so that minimal access biopsy devices can be used to same lesions near the scope tip using percutaneous ultrasound directed techniques.

Ductoscopy—Therapeutic

In the case of directing breast cancer procedures, remember that the volume of expressed fluid may be small and the ductal cannulation may be substantially more challenging. Do not perforate the ductal system or efforts to distend the ducts will fail. Be gentle and expect that distension may take longer.

The ductal orifice chosen should usually be within 100°–110° radially from the nipple papilla of the known lesion position in the breast. Always scopes down largest branches first since these are more likely to connect to tumor. Once obstructing tumor is found, mark position on the skin by transillumination. Work your way backwards scoping each smaller branch and mark each site of intraductal luminal defects by transillumination on breast surface.

Leave scope at the most proximal extent of nippleward progression of intraluminal disease or replace it with a prolene suture. Design your excision of the sub-segmental quadrant to include from scope tip to a pie shaped wedge to the periphery of the breast from the known tumor. The width of this wedge is determined by the intraluminal disease foci you identified in side branches. Most resections can be easily adapted to one of the newer oncoplastic incisions to hide the resection defect.

POSTOPERATIVE MANAGEMENT

These patients require no different care than after any surgical breast tissue excision. It is normal for bloody fluid to drain from the nipple for several days following ductoscopy. I encourage women to avoid tape on the sensitive breast skin and wear a feminine napkin strategically placed within a bra to catch the nipple fluid which may drain.

COMPLICATIONS

Perforation of the lactiferous sinus in the immediate retro-areolar space is common. There are no known or described complications of that now. The most disturbing aspect is that it may limit your ability to find the distal segment of duct to scope. As soon as a perforation is seen or suspected from soft tissue infiltration in the retro-areolar space, stop instilling any fluid through the scope. Careful circular motion of the scope will usually allow you to find the cresent like collapsed distal duct. If you can manipulate the scope to engage this remanent, regular scoping with saline distension can resume after getting 10–15 mm down this segment.

Most patients will drain fluid from the nipple for 1–5 days after the procedure and this is normal.

CONCLUSIONS

Ductoscopy can currently be used as an aid to identification of the root causes of pathologic nipple discharge. Its role in the management of early stage breast cancer is evolving but clearly directs us toward the goal of anatomic resection of proliferative disease instead of the more traditional non-anatomic lumpectomy. Perhaps the greatest importance however of ductoscopy is the ready access to the ductal epithelium in vivo for research purposes. Just as the polyp model of colon cancer with its sequence of genetic alterations, the ability to visualize, repeatedly sample and monitor chemoprevention efforts will direct us in unlocking the secrets of breast cancer carcinogenesis and prevention. Development of molecular markers might even allow us to screen for the precancerous stages and prevent breast cancer instead of waiting till there is an invasive cancer in the majority of patients.

Disclosure

WCD has developed a new breast microscope for Luminus Technologies.

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