

## Ductoscopy in the Evaluation and Management of Nipple Discharge

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### ABSTRACT

**Background.** Nipple discharge is a relatively common complaint among patients visiting specialized outpatient clinics for disease of the breast. With advancing technology, it became possible to diagnose and manage nipple discharge using minimally invasive procedures. The aim of this study is to report our experience with ductoscopic evaluation of patients with nipple discharge.

**Materials and Methods.** Between September 2005 and February 2009, 236 patients with complaint of nipple discharge were admitted prospectively into the study. All patients were evaluated with ductoscopy. Data concerning age, ductoscopic and postsurgical diagnosis, duration, and complications with the procedure were statistically analyzed.

**Results.** For 236 patients evaluated, there were 249 ductoscopic investigations. Of these, 39 patients were found to have intraductal solitary papilloma of which 24 were excised ductoscopically. Of the 24 ductoscopically excised solitary papillomas, it was possible to remove 17 completely, but 7 papillomas could be removed partially. For 13 patients with solitary papillomas large enough or unfavorably localized so that they could not be snare-excised and for 14 patients with multiple papillomas, we offered surgical removal of the lesions by limited excision of the ducts with the help of ductoscopic localization and marking. There were 35 patients who had debris within the canalicular system, and the debris was washed out. Ductoscopy revealed atypical ductal hyperplasia in 3 patients, ductal carcinoma in situ in 6 patients, and invasive carcinoma in 3 patients; all patients underwent surgery.

**Conclusions.** We believe that, as the technology quickly improves, ductoscopy will become more widely accepted and applied for breast disorders, not only as a diagnostic tool but also as a privileged therapeutic option for certain pathologies.

Nipple discharge is a frequent complaint (10%) after breast pain and lumps in the breast among women of reproductive age who apply to breast clinics.<sup>1,2</sup> Although most are physiologic, common pathologies include ductal ectasia, fibrocystic breast changes, intraductal papilloma, or papillomatosis (40–70%).<sup>3,4</sup> However, unilateral discharge may be an early sign of breast carcinoma of ductal origin. Breast cancer (10–13%) is thought to evolve from the lining of the milk ducts and lobules.<sup>5</sup>

Indirect imaging modalities (mammography, ultrasound, and magnetic resonance imaging), ductography, and smear of the discharge are commonly used for diagnostic purposes. Radiological imaging and cytological analysis of the discharge fluid usually fail to reveal the underlying pathology.<sup>6</sup> Surgery is indicated when diagnosis is suspicious. Because it provides a direct vision, the ability to biopsy, or a washing sample of the lesions for cytology, ductoscopy is gaining acceptance as another diagnostic method for equivocal cases.<sup>7–10</sup>

It is reported that ductoscopy is technically possible not only in dilated but also in normal caliber milk ducts.<sup>11</sup> It may help the surgeon to directly visualize the ductal epithelium and allow identification of early cytological changes.<sup>12</sup>

The study was designed to examine the efficacy of ductoscopy that was performed in the surgical clinic of Okmeydani Training and Research Hospital, Istanbul. We aimed to evaluate any potential applications and benefits of ductoscopy and report our initial experiences in the procedure.

## MATERIALS AND METHODS

From November 2005 to February 2009, 236 patients with nipple discharge were assessed by 249 ductoscopic investigations, and the results were collected prospectively. All patients were female, and an informed consent was signed by each patient. The study protocol was approved by the ethics committee.

The standard workup for patients with nipple discharge included complete history, physical examination, mammography (if present) and ultrasonography of the breast, and ductal lavage cytology. Ductography and magnetic resonance imaging of the breast when present were also included in the collected data.

### Fiber Optic Ductoscopy System

The ductoscopy system consists of a small and a large ductoscope LaDuScope S and T-flex (Polydiagnost GmbH, Pfaffenhofen, Germany), with outer diameters of 0.55 and 1.1 mm and resolutions of 3000 and 6000 pixels, respectively. The large ductoscope (LaDuScope T-flex) also has a second working channel, which accommodates a grasping basket (to excise papillary polypoid lesions with an endobasket), grasping forceps, and cytology brush or laser fiber. Both ductoscopes have a working length of 80 mm, with a 0° angle direct view and a field vision of 70°. The scopes are autoclavable and can also be sterilized with gas or plasma.

### Procedure

After cleaning the nipple-areola complex with povidine-iodine solution and alcohol, the ductoscopic

investigation was performed under local anesthesia using prilocaine HCl; the procedure is not fully comfortable for the patient without analgesia. Although patients with spontaneous nipple discharge have a somewhat dilated nipple orifice already, an expander system (SoLeX, soft lumen expander) was introduced into nipple orifice to reach the lactiferous ducts. The fiber optic scope then was introduced into the orifice.

Dilatation and introduction of the ductoscope is the most difficult part of the procedure; twisted and kinked ducts may easily be torn, and the ductoscope may slip into extraductal breast tissue. The major lactiferous ducts and segmental branches were visualized in an orderly fashion until the scope could not be advanced any further.

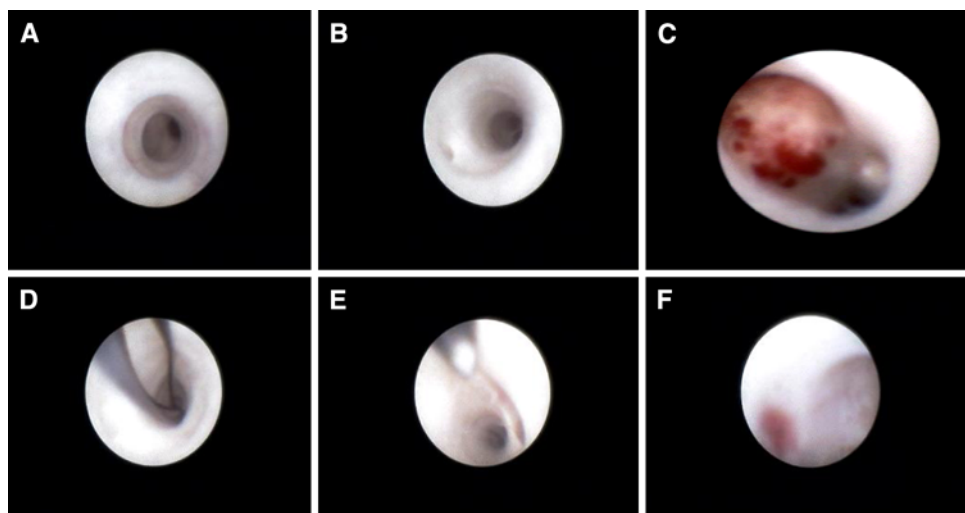
A smear of the nipple discharge and a ductal lavage from all patients were sent for cytology.

When the presence of any solitary papillomatous or polypoid (SP) vision was noted during ductoscopy, then the small-size ductoscope was replaced with the large one with a working channel. If it was technically feasible, an endoscopic excision (total or partial) transductal endoscopic polypectomy (EP) was performed (Fig. 1).

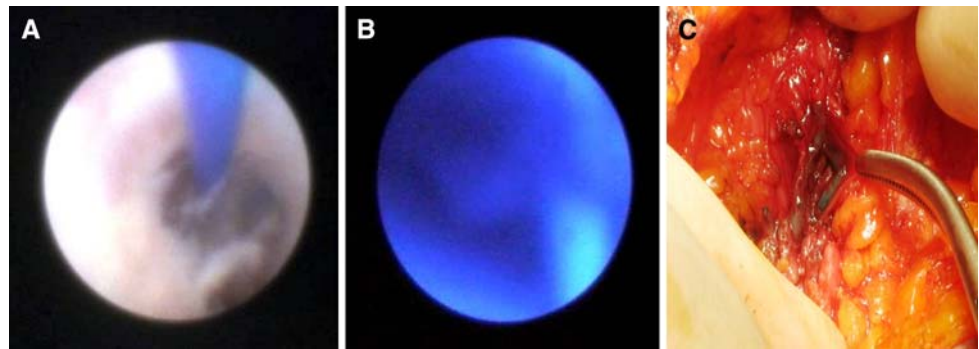
Patients with positive cytology (malignant cells, cells with atypical) and patients with negative cytology but SP or multiple papillomas (MP) that could not be completely excised underwent ductoscopy-assisted terminal ductal-lobular unit (TDLU) excision.

For TDLU excision, the duct that was to be cut out was marked either with isosulfan blue or with 00-polypropylene thread. When polypropylene thread was used, it was moved under direct vision 2–3 cm beyond the suspicious lesion, so that in surgery the tip of the thread was the distal end of the excised duct (Fig. 2). We found polypropylene thread marking to be more useful.

**FIG. 1** a, b Normal ductoscopic appearance, c papilloma within the duct, d basket, e papilloma in the basket, f duct after papillectomy



**FIG. 2** a Marking of the duct with polypropylene thread, b isosulfan blue, c Intra-operative view of the duct



## RESULTS

From November 2005 to February 2009, 249 ductoscopic investigations were performed for 236 female patients with nipple discharge. The results are presented concerning the procedure number.

The median patient age was 43 years (range, 14–80 years); 162 patients were of reproductive age, while 87 patients were in menopause.

The duration of the symptom was 10 days to 120 months (mean, 17.5; median, 8 months; SD 25, 3). The nipple discharge was from the right breast in 118 patients and from the left breast in 131 patients. The color of the discharge was classified according to patients' description as dark-brown (bloody, 82 patients), yellowish-light brown (serous/serosanguinous, 103 patients), whitish (milky, 26 patients), and other (38 patients).

In 249 ductoscopic investigations, we failed to introduce the device into the ductal orifice in 5 patients with inverted nipples. In addition, in 1 patient with ulceration around the nipple, in 1 with discharge from an ectopic mammary duct, and in 2 patients with intolerable pain, ductoscopy could not be performed. In 9 patients, the ductoscopy failed as the probe went out of the ductal system (rupture) into the mammary tissue. Additionally, in 25 patients who were found to have narrow channels, the ductoscope could not be advanced further than 3 cm in to the canalicular system (Table 1).

Consequently, 206 out of 249 ductoscopic investigations (83%) were completed and evaluated in the study. The

mean examination duration was 25.5 minutes (SD 14.4 minutes; range, 7–120 minutes). In 102 examinations, the ductal system was found to be normal. In 1 patient, hairlike foreign material was found and washed out. In 35 cases, there was intraductal debris that was cleared and reported in cytology as condensed intraductal lavage containing many macrophages.

In 52 ducts, we observed lesions protruding into the lumen, 38 of which was solitary and 14 multiple. We were able to completely remove 17 of 38 solitary papillomas by ductoscopy, using the grasping basket through the working channel of the endoscope. In 7 cases, papillomas could only be excised partially; the remnant lesions were about 1/3 of the original mass. The average distance from the orifice of the nipple to the lesion was 3.1 cm (range, 1–8 cm). Complete endoscopic papillomectomy was successfully performed in patients containing papillomas with very thin peduncles.

Of the solitary papillomas, 6 were large enough so that the snare could not be manipulated to remove the lesions. In 4 cases, papillomas were located in such narrow ducts that the large caliber endoscope reached the lesions, but the grasping basket could not be opened. We failed in 2 cases because of the technical problems (sharp angularity, basket tear, etc.) and in another 2 patients because at the very beginning of the study we were just aiming a diagnostic approach and endoscopic removal of the lesions was not attempted. As a result, a total of 14 patients underwent TDLU surgery.

We applied surgery for the lesions in 11 of 14 multiple papilloma cases, and pathology proved the presence of multiple lesions. There were 3 patients scheduled for surgery but the surgery was not performed during the period of study.

We operated on 9 patients with suspicious color or structural appearances in the ducts. Pathology revealed carcinoma in situ in 5 patients, and 1 patient had invasive carcinoma. Also, 2 patients were shown to harbor atypical ductal hyperplasia, and 1 was diagnosed as having mastitis.

Normal ductal system was diagnosed in 1 patient, but cytology of the ductal lavage revealed malignant cell that

**TABLE 1** Causes of failure in ductoscopy

Cause	No.
Rupture	9
Inverted nipple	5
Nipple ulcer	1
Pain	2
Ectopic canal	1
Narrow canal	25
Total	43

was later proven to be carcinoma in situ. Another patient with same ductoscopic result was reported as possessing atypical ductal hyperplasia by the cytologist.

Ductography suggested a papilloma in 1 patient, but it could not be investigated by ductoscopy because of narrow channels. The duct was removed surgically, and the diagnosis was reported as solitary papilloma. In another patient, ductography showed dilated channels, but endoscopy was normal, and pathology confirmed the presence of dilated duct only.

Mammography of 1 patient resulted in the radiologist reporting the presence of microcalcifications. We did not find any abnormality in the endoscopy, but the excision of the lesion showed the presence of invasive ductal carcinoma. The patient had to be reoperated on because the borders were positive.

Also, 1 patient with nipple discharge was found to have a lump in the breast during physical examination. Ductoscopy showed a narrow orifice and angulation only, but surgical removal of the lump revealed invasive ductal carcinoma. The characteristics of patients diagnosed as cancer were indicated in Table 2.

For patients who had any ductal pathologies that were ductoscopically or surgically shown to be cancer, intraductal papilloma, atypical ductal hyperplasia, or very dilated duct, the color of the nipple discharge according to the patients' definition was compared. Of 66 patients, 31 had dark-bloody and 24 patients had light-colored discharge. Patients' definitions as light-colored discharge are noteworthy in positive pathological results. Patient

characteristics according to the color of the discharge are presented in Table 3.

## DISCUSSION

Nipple discharge is a commonly encountered complaint in outpatient settings that causes great worry for the patients. It refers to the spontaneous escape of the fluid from the ducts of the breast and makes up 3–6% of symptoms presented to the breast specialty clinics.<sup>12</sup> Although in the majority of cases the etiology is benign, the surgeon must carefully evaluate the signs and symptoms because it may be a sign of malignancy.

Until a couple of decades ago, the routine evaluation of nipple discharge was composed of the cytological examination of the discharge, radiological visualization (e.g., mammography, ultrasonography) of the breast ducts, and ductography (galactography).<sup>8</sup> The sensitivity of cytological examinations from the nipple discharge is reported to be around 15%.<sup>9,10,12</sup> Additional tools are inevitable for the differential diagnosis.

The desire to directly visualize and biopsy the lesions led to the development of the ductoscopic investigations. After initial blind intraductal biopsy experiences, rigid endoscopes were developed. With the efforts of researchers in the early 1990s, it became possible to directly visualize inside the breast ducts.<sup>12–17</sup> In 1988, Teboul used a 1.7 mm rigid endoscope (ductoscope) and ultrasonography to observe the ductal cavity.<sup>12</sup> Ductoscopy helped to limit the extent of surgery and provided a tissue-conserving approach.<sup>18,19</sup>

**TABLE 2** Characteristics of patients with cancer

Patient no.	Age	Mammography results	Ultrasonography results	Physical examination	Ductoscopic results	Cytology of the ductal lavage	Pathological diagnosis
1 LU	42	Unremarkable	Dilated ducts	Spontaneous/serosanguinous	Irregular ductal wall and color	Suspicious (mastitis?)	Ductal carcinoma in situ
2 GÇ	42	Unremarkable	Dilated ducts	Spontaneous/bloody	Ductal wall irregularity	Negative	Invasive ductal carcinoma
3 NK	48	Unremarkable	Dilated ducts	Spontaneous/serous	Irregular ductal wall and color	Atypical epithelial cells	Ductal carcinoma in situ
4 SG	32	Stable bilateral calcifications	Dilated ducts	Spontaneous/bloody	Irregular ductal wall and color	Negative	Ductal carcinoma in situ
5 SS	58	Distortion	Normal	Spontaneous/bloody	Irregular ductal wall and color	Atypical epithelial cells	Ductal carcinoma in situ
6 AU	65	Normal	Normal	Spontaneous/bloody	Irregular ductal wall and color	Atypical epithelial cells	Ductal carcinoma in situ
7 EÖ	63	Normal	Normal	Spontaneous/bloody	Irregular ductal wall and color	Negative	Ductal carcinoma in situ
8 MZ	73	Calcifications	Normal	Spontaneous/serosanguinous	Normal	Negative	Invasive ductal carcinoma
9 FN	57	Normal	Papilloma	Spontaneous/bloody	Normal	Negative	Invasive ductal carcinoma

**TABLE 3** Patients' characteristics according to the color of the discharge

Ductoscopic appearance or pathological diagnosis	The color of the nipple discharge according to the patient					Total
	Bloody	Serosanguinous	Serous	Milky	Others	
Normal	23	26	18	11	24	102
Ductal carcinoma in situ	4	2	0	0	0	6
Invasive ductal carcinoma	2	1	0	0	0	3
Atypical hyperplasia	2	0	1	0	0	3
Papilloma	21	8	9	1	0	39
Multiple papilloma	9	1	3	1	0	14
Mastitis	1	0	0	0	0	1
Debris	9	8	8	5	5	35
Cystic dilatation	1	0	0	0	0	1
Fungal infection	0	0	1	0	0	1
Foreign body	1	0	0	0	0	1
Perforation	2	2	1	2	2	9
Total	75	48	41	20	31	215

In contrast to initial rigid ductoscopes with a diameter of more than 1.5 mm, today the rapidly developing technology through the decade gave us the opportunity to use fiber-optic ductoscopes with smaller diameters (the instruments used in our series have 0.55–1.1 mm diameters). The optical instruments gained higher resolution, and working channels were developed that allow the surgeons perform direct biopsies (Fig. 1).<sup>13,15,20–22</sup>

Ductoscopy is not technically challenging and usually easy to perform. It is possible to apply outpatient or day surgery with minimal risks and complications.<sup>23</sup> It is a routine investigation for nipple discharge in Japan and China; a positive predictive value of 83% is reported.<sup>24</sup>

Intraductal papilloma is the most frequent cause of nipple discharge (40–70%). For symptomatic patients with nipple discharge who were evaluated with radiology, the most reliable approach is surgical excision of the affected ducts to confirm the diagnosis and relieve the discharge. However, minute papilloma are rarely found in gross pathologic examination. That gives a false positive ratio of 17% for the radiological evaluation of the nipple discharge.<sup>8</sup> The intraductal papillomas may be fragile and exfoliate easily. For these lesions, ductoscopic removal can be managed with ease. We were able to completely remove 17 of 38 solitary papillomas, and in 7 cases papillomas could be excised partially. No malignancy was detected, and the patients were protected from unnecessary surgery. In the literature, a similar but multicentric study by Kapenhas-Valdes et al. was performed to further discover if ductoscopy would be any of any benefit in decreasing unnecessary investigations or biopsies.<sup>17</sup>

We found cancer in 9 patients, of whom 8 did not have any suspicious signs on mammography or ultrasonography. When the discharge patterns were evaluated, in addition to

spontaneous and dark fluids, light-colored clear discharges are also noteworthy. The 25 of 88 patients with clear discharge and the 38 of 75 patients with dark discharge were found to have a kind of pathological problem (papilloma, carcinoma in situ, etc.) that required further intervention. A light-colored clear discharge cannot rule out cancer.

It is sometimes not possible to introduce the ductoscopy into narrow ductal channels or into narrower terminal channels and have biopsies or remove the lesions. In addition to radiological evaluation, it is wise to add ductal lavage cytology in evaluation of every patient with nipple discharge so that the diagnosis becomes more reliable.<sup>25</sup>

During ductoscopy, even when all the images are recorded, the decision about which canal should be followed or about a suspicious lesion requires experience. It is highly performer dependent, and there is a learning curve. The ductoscopy procedures were performed by 2 attending surgeons and 3 fourth-year surgery residents. A minimum of 10 and a maximum of 15 procedures were required to achieve the experience to introduce the ductoscope to a point that was limited by the length of the endoscope or by the diameter of the cannulated canal. Zagouri et al. reported that the number of procedures required for the proficiency was between 9 and 17 among 10 breast fellows, and the mean number that 50% of the trainees successfully competent was 13.<sup>26</sup> In addition to the need of experience to perform ductoscopy, the surgeon also needs a knowledge to comment on the images recorded during the procedure. Beyond gross morphological abnormalities such as papillomas, no specific data are present about the endoscopic imaging of the ductal system. Thus, the more we perform ductoscopy, the more we become proficient to comment on the endoscopic images.

Another limiting point is that if the possibility of cancer development from the distal ductal units is taken into account, it is not always possible to reach the very narrow distal channels using current endoscopes. The peripheral distributions of the lesions result in a false negative ratio of 18% for ductoscopy.<sup>8</sup> Consequently, although it is beneficial as a diagnostic tool, it has limitations and should not be used alone in the clinical evaluation. It is a cost-effective tool. The cost given by the Turkish Medical Association for the ductoscopy is 420 TL (an equivalent of US \$290). In another study, the approximate all-inclusive cost was given as US \$330.00.<sup>7</sup> With developing technology, we think that it will be possible in the near future to use ductoscopy such as vital microscope ductoscopy with a stick type of objective lenses that produce a real-time hundreds of power imaging of the lesions clearly.

In conclusion, we experienced that mammary ductoscopy is well tolerated, not very difficult to perform, and may have a role in the diagnosis and treatment of intraductal papillomas. Even if one cannot remove a papilloma endoscopically, one can limit the extent of surgery.

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