*Breast Cancer Research and Treatment* **18**: 179–188, 1991.


*Report*

# Duct endoscopy and endoscopic biopsy in the evaluation of nipple discharge

Masujiro Makita,[1,4] Goi Sakamoto,[1] Futoshi Akiyama,[1] Kiyoshi Namba,[1] Haruo Sugano,[1] Fujio Kasumi,[2] Mitsumasa Nishi[2] and Motoko Ikenaga[3]
[1] *Department of Pathology, Cancer Institute;* [2] *Department of Surgery, Cancer Institute Hospital;*
[3] *Department of Diagnostic Cytology, Cancer Institute Hospital;* [4] *Department of Surgery,*
*Tokyo Women's Medical College Daini Hospital, Japan*

*Key words:* breast cancer, duct endoscopy, galactography, intraductal biopsy of the breast, nipple discharge

**Summary**

Microdochectomy is usually performed on patients with nipple discharge caused by intraductal proliferative lesions, such as intraductal papilloma and carcinoma. But this operation often sacrifices large amounts of normal mammary gland even when the lesion is a benign intraductal papilloma a few millimeters in diameter. We have developed duct endoscopy for the mammary duct system, and have reliably performed biopsies for intraductal proliferative lesions intraductally. From June 1989 to April 1990, we examined 22 cases by duct endoscopy, and performed endoscopic biopsy in 16 cases. The method of endoscopic biopsy is as follows. First, a bougie is inserted, without anesthesia other than Xylocaine jelly, into the orifice of the duct to enlarge it. Second, the outer cylinder and the inner needle are inserted; then the inner needle is removed, and the endoscope is inserted. After examination, the outer cylinder is moved up to the lesion to be biopsied and the endoscope is taken out. Then a sample is taken into the outer cylinder by aspiration. We diagnosed 10 cases of benign lesion and 5 cases of malignant lesion by cytological and/or histological examination. In conclusion, endoscopic biopsy, aided by duct endoscopy, is a useful and harmless diagnostic procedure in the evaluation of nipple discharge.

## Introduction

Nipple discharge is an infrequent but important symptom of breast disease, because early stage breast cancer cases occur among patients with nipple discharge. When nipple discharge is caused by intraductal proliferative lesions (i.e. intraductal papilloma, intraductal carcinoma etc.), the evaluation of nipple discharge is clinically most important. Nipple discharge caused by intraductal proliferative lesions used to need surgical treatment, such as microdochectomy [1, 2]. However, ideally surgical damage to patients whose disease is benign should be made as small as possible. So, optimally, exploratory surgery for nipple discharge should be performed only if the lesion is highly suspected of being malignant. With this in mind we started to investigate a biopsy technique using a transnipple approach to intraductal proliferative lesions. When galactography showed filling defects or blockages in the ductal tree, and we could touch the lesions with an intraductally inserted bougie, we performed a blind intraductal biopsy of the breast (IDBB) [3]. In this way, we could diagnose intraductal papillomas and carcinomas without skin incision.

With the smallest lens attached to a rigid endoscope (i.e., not a fiberscope), we have begun to conduct endoscopy [4], and to perform endoscopic

*Address for offprints:* M. Makita, Department of Pathology, Cancer Institute, 1-37-1, Kami-ikebukuro, Toshima-ku, Tokyo 170, Japan

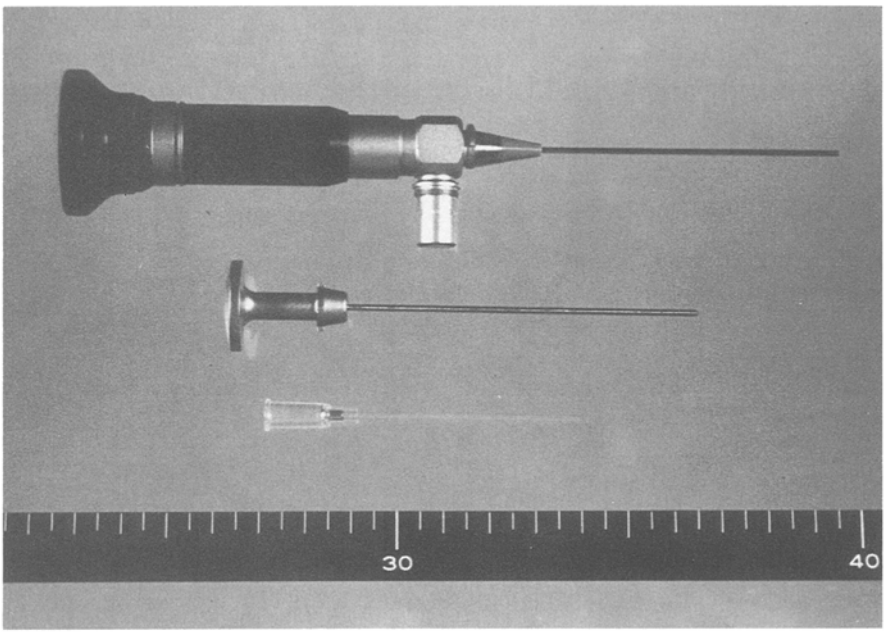


*Fig. 1.* Instruments used in duct endoscopy. Endoscope (above; OES Selfoscope A-7001, Olympus Optical Co.), inner needle (middle), outer cylinder (bottom; disposable 16 gauge Surflo intravenous catheter).

biopsy [3, 5], aided by duct endoscope, to get a tissue sample more reliably. Up to April 1990, there have been 15 specimens successfully obtained by endoscopic biopsy. This report is an account of this duct endoscopy and endoscopic biopsy. Relationships between endoscopic findings and pathological diagnosis of the intraductal proliferative lesions are reviewed.

## Material and method

Duct endoscopy is currently performed at the Cancer Institute Hospital, Tokyo. There were 22 cases from June 1989 to April 1990, and in 16 of these cases, we performed endoscopic biopsies.

The duct endoscope consists of an inner needle, an endoscope (OES Selfoscope A-7001, Olympus Optical Co.) and an outer cylinder (a 16 gauge Surflo intravenous catheter, Telmo Co.) (Fig. 1). The endoscope is similar to an arthroendoscope in appearance, but is smaller in size. The endoscope is fitted with its smallest lens, so the endoscope diameter is 1.25 millimeters. The length of the effectively inserted portion is 66 millimeters. The visual field of the endoscope is 45°, and we can see directly ahead. The endoscope has a connection for a light-guide. The inner needle has a blunt, round tip.

The method of using the duct endoscope is as follows: First, a bougie is inserted (we use the same bougie as for a lacrimal duct) with Xylocaine jelly into the discharging pore to enlarge the ostium of the mammary duct. Second, the rounded inner needle, which is inserted into the outer cylinder, is inserted in the same way as was the bougie. Then the inner needle is taken out leaving only the outer cylinder in the duct. A small amount of air is blown into the outer cylinder to make the duct patent, and the endoscope is inserted into the outer cylinder. Throughout this process, we need no anesthesia other than the formerly mentioned Xylocaine jelly. The intraductal smooth surface is clearly visible and we can easily orient our instruments in the direction in which we want to insert them along the duct (Fig. 2).

As for the method of endoscopic biopsy, after examination of the duct, the endoscope, with the

outer cylinder (a disposable 16 gauge Surflo intravenous catheter, used for containing the tissue sample), is inserted into the location of the intraductal proliferative lesion through the ostium of the duct. Under endoscopic observation, the outer cylinder is brought just up to the lesion. If the lesion is papillary, we can draw the lesion successfully into the outer cylinder by rolling it like a screw. After confirming that the lesion is inside the outer cylinder, we take out the endoscope and aspirate through the outer cylinder using an inserted syringe, so we can get the lesion, as a small tissue bit or a fluid sample, inside the outer cylinder. If the specimen is large enough to embed, it is put into a bottle of 10% formalin for pathological examination. If the specimen is not large enough to embed, we put the outer cylinder as a whole into saline for subsequent cytological examination (Fig. 3).

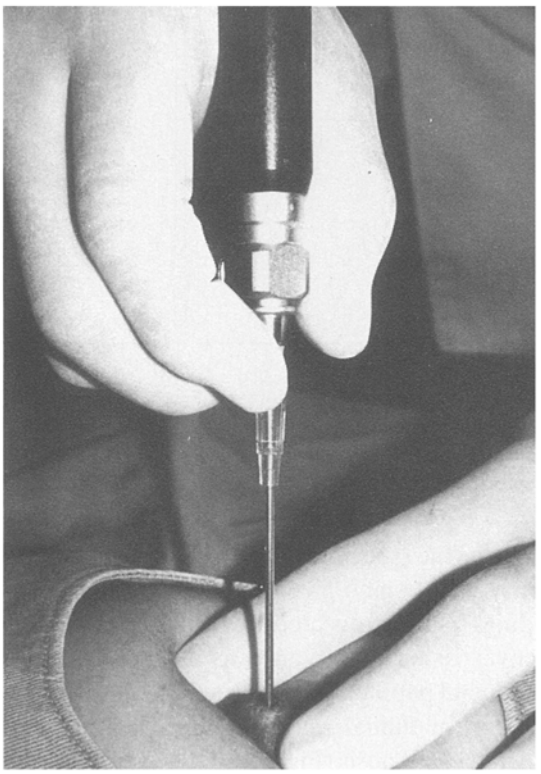

*Fig. 2.* Duct endoscopy. The duct endoscope was inserted in the mammary duct.

## Results

We performed endoscopic biopsy on 16 cases, and were able to take samples for pathology and/or cytology in 15 cases. (In one case, insufficient specimen material for proper examination was taken because of poor sampling technique.)

Table 1 shows 10 cases which we are now following after performing endoscopic biopsy. Six of these cases proved, from their endoscopic biopsy specimens, to be histologically benign intraductal papillomas (cases No. 1, 4, 5, 8, 9, and 10), and 2 cases (cases No. 2 and 3) were diagnosed as benign, i.e. Class II, cytologically. These 8 cases did not need further biopsy and are now being followed. The remaining 2 cases (cases No. 6 and 7) were suspected to be malignant, i.e. Class IV or V, cytologically, but had no palpable tumors, and no evidence of malignancy both in mammography and in ultrasonography. Therefore, following endoscopic biopsy, we could not avoid performing segmental resection of the discharging lobes. One proved to be a benign intraductal papilloma (case No. 6) and one to be a border-line malignancy (case No. 7) histologically. We make it a rule not to further excise lesions that are proved to be benign, and we are now following these 10 cases carefully.

Table 2 shows 6 cases diagnosed as breast cancer in which mastectomies were performed. In all of the breast cancer cases, we could not get enough specimen to examine histologically. But five of these cases were diagnosed as malignant, i.e. Class IV or V, cytologically (in case No. 1, we could not get a sample because of poor technique). These cases were then biopsied after endoscopic biopsy, and diagnosed as malignant. These 6 cases were mastectomized and proved to be in the early stage of breast cancer pathologically.

Endoscopic findings of benign intraductal papilloma were apt to indicate a single localized polypoid lesion (Fig. 4). Endoscopic findings of malignant cases revealed various features. Fig. 5 shows an intraductal view of a breast cancer case (case No. 1, Table 2), which looks like cancer is creeping along the wall of the mammary duct.

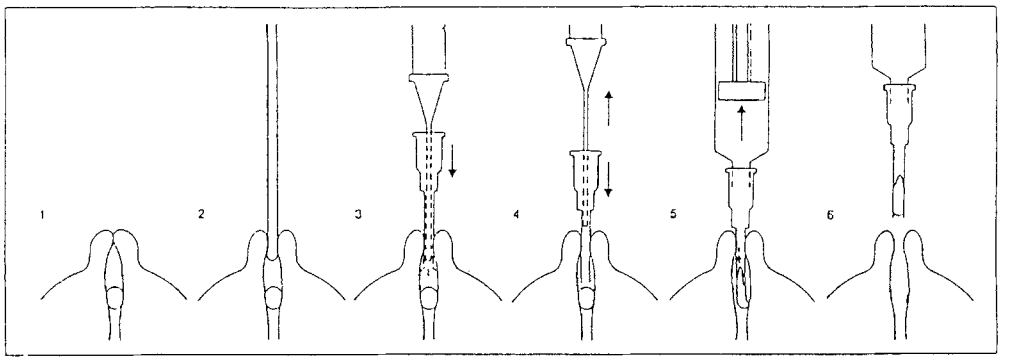


*Fig. 3.* Method of endoscopic biopsy. 1: Papillary lesion located in the mammary duct. 2: Inserting bougie to dilate the orifice of the duct. 3: Duct endoscopy. After examination, outer cylinder (16 gauge Surflo intravenous catheter) is moved adjacent to the lesion. 4: Removing the endoscope from the outer cylinder. 5: Aspiration through the outer cylinder. 6: The sample in the outer cylinder being taken out from the duct.

When the specimen taken by an endoscopic biopsy was a small piece of tissue, its histological findings usually revealed two cell layers and connective tissue stroma and we diagnosed it as an intraductal papilloma (Figs. 6 and 7). Atypical cells included in fluidal samples played an important role in the diagnosis (Fig. 8). In such cases, biopsies were performed, and the intraductal carcinomas were revealed on their histologic slides.

## Discussion

Diagnosis of nipple discharge has been made more accurate through galactography [6–8], discharge smear cytology [7–9], carcinoembryonic antigen (CEA) measurement of nipple discharge [10], and duct wash cytology [11]. But, for final pathological diagnosis, unneccessarily wide excisions frequently sacrificed healthy mammary gland, even though nipple discharge was caused by only a tiny benign intraductal papilloma. We have tried to research diagnostic methods that are successful in diagnosis and less harmful than excisional biopsy. We estab-

*Table 1.* Cases being followed

| No. | Endoscopic findings | Endoscopic biopsy specimen | |
|---|---|---|---|
| | | cytological diagnosis | histological diagnosis |
| 1. | Localized polypoid, duct obstructed, whitish yellow | – | Intraductal papilloma |
| 2 | Localized papillary, reddish white | Class II | Not available |
| 3 | Localized polypoid, duct obstructed, reddish white | Class II | Not available |
| 4 | Localized polypoid, duct obstructed, dark red | Class III | Intraductal papilloma |
| 5 | Localized polypoid, duct obstructed, yellowish white | Class II | Intraductal papilloma |
| 6 | Broad based papillary, with spotty erosion, white | Class V | Not available (intraductal papilloma*) |
| 7 | Erosive rough surface, duct obstructed, yellow & green spots | Class IV | Not available (border-line case**) |
| 8 | Localized polypoid, duct obstructed, yellowish white | Class II | Intraductal papilloma |
| 9 | Localized polypoid, duct obstructed, yellowish white | Class II | Intraductal papilloma |
| 10 | Localized polypoid, duct obstructed, yellowish gray | Class I | Intraductal papilloma |

* followed by excisional biopsy (final histological diagnosis).

** followed by excisional biopsy (histological diagnosis = severely atypical papillary lesion).

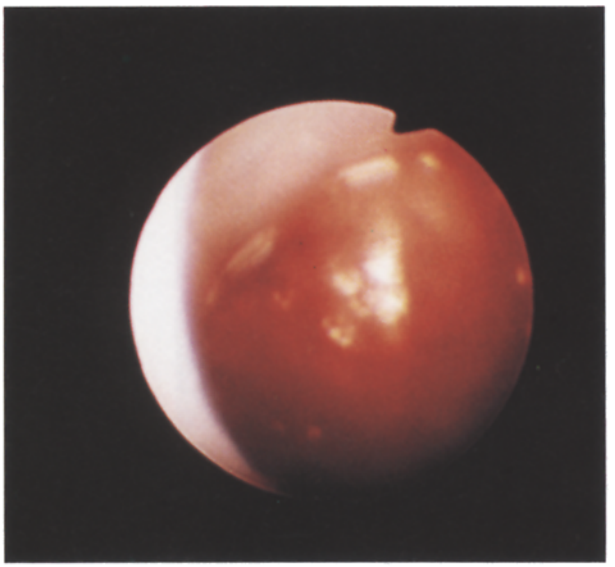

*Fig. 4.* Endoscopic picture of an intraductal papilloma (case No. 1, Table 1). Localized polypoid appearance, without luminal change around the tumor.

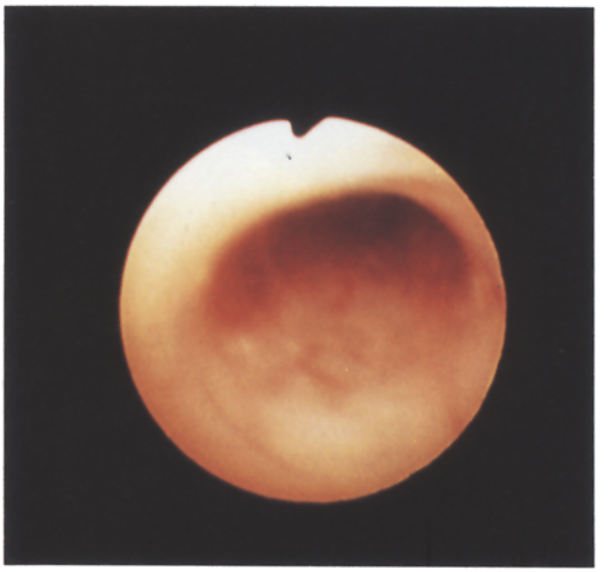

*Fig. 5.* Endoscopic picture of an intraductal spread of breast cancer (case No. 1, Table 2). Flat elevations continuously from the periphery.

lished IDBB (Intra-Ductal Biopsy of the Breast) [3], through which we can take enough samples for diagnosis from intraductal lesions by using a sure-cut needle. There has been another effort in which transnipple intraductal biopsy was performed using a curette [5]. But, because these procedures are done blindly, and without any guide, operators have to rely solely upon their sense of touch to guide the sure-cut needle or curette to the lesion. With this in mind we investigated intraductal biopsy under endoscopic examination. Teboul had already used an endoscope (Olympus Selfoscope 1717-K, mainly used for arthroendoscopy) in order to examine intraductal lesions of the mammary duct [12, 13]. According to this procedure, using a narrower lens attached to the endoscope, we have developed duct endoscopy especially for the mammary duct system [4].

*Table 2.* Breast cancer (mastectomized) cases

| No. | Endoscopic findings | Endoscopic biopsy specimen examination | Final histological diagnosis |
|---|---|---|---|
| 1 | Yellowish-white, continuous rough flat elevation | Not available | Invasive ductal carcinoma (node negative) |
| 2 | White flat elevation and papillary lesion at the distal branch | Cytology only: Class V | Apocrine carcinoma (node negative) |
| 3 | Localized polypoid and small granular plaque | Cytology only: Class IV | Noninvasive ductal carcinoma & intraductal papilloma (node negative) |
| 4 | Scattered, yellow flat elevations and rough surface | Cytology only: Class V | Noninvasive ductal carcinoma (node negative) |
| 5 | Scattered, yellow papillary or fungal lesions | Cytology only: Class V | Invasive ductal carcinoma (2 nodes positive) |
| 6 | Yellow polypoid lesions and white plaques; duct obstructed | For cytology: Class V<br>For pathology: Not available* | Invasive ductal carcinoma (4 nodes positive) |

* A small sample was taken, but disappeared during fixation.

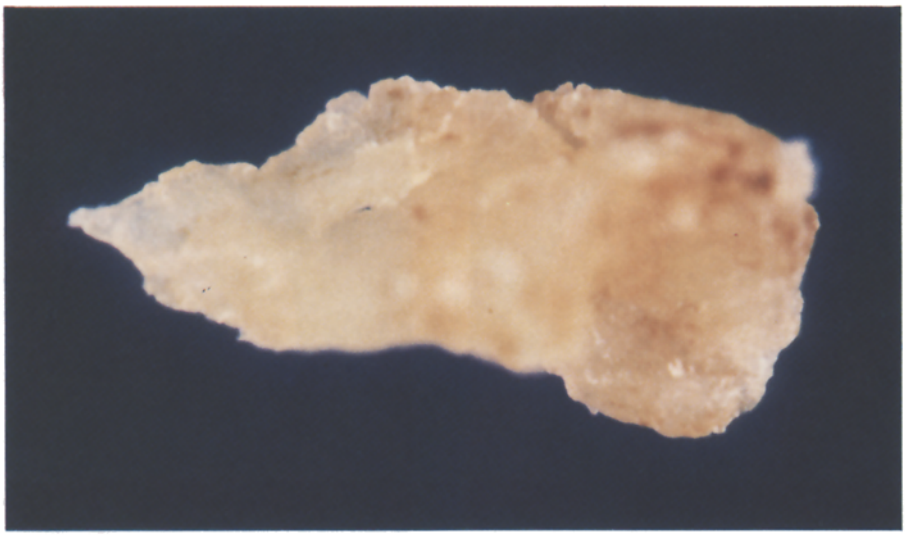

*Fig. 6.* Macroscopic picture of an endoscopic biopsy specimen (case No. 1, Table 1). A small piece of tissue was taken by endoscopic biopsy.

As the duct endoscope (OES Selfoscope A-7001) does not have fibers, but has a small slender lens, its visual area is wide and endoscopic image is excellent. We can get a clear view of the mammary duct system because we blow air into the duct to make the ductal lumen patent. We can see the luminal surface of the duct as if viewing by bronchoscopy. The endoscope is slenderer than the 16 gauge Surflo intravenous catheter (1.3 mm in inner diameter, 1.7 mm in outer diameter). Because we can dilate the orifice of the duct so as to insert a 16 gauge Surflo intravenous catheter into it, this ex-

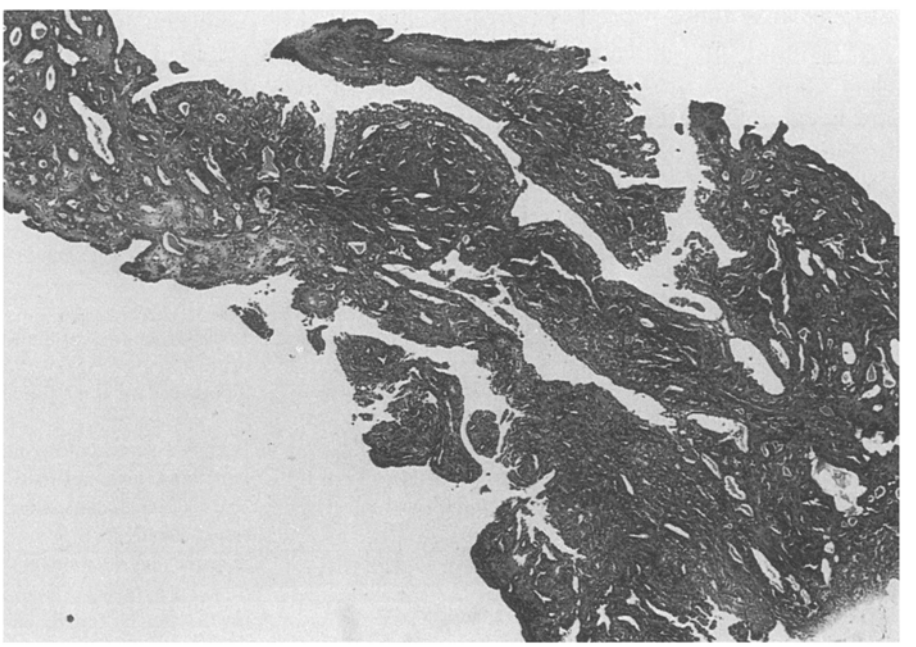

*Fig. 7.* Microscopic picture of an endoscopic biopsy specimen (case No. 1, Table 1). Intraductal papilloma, diagnosed histologically.

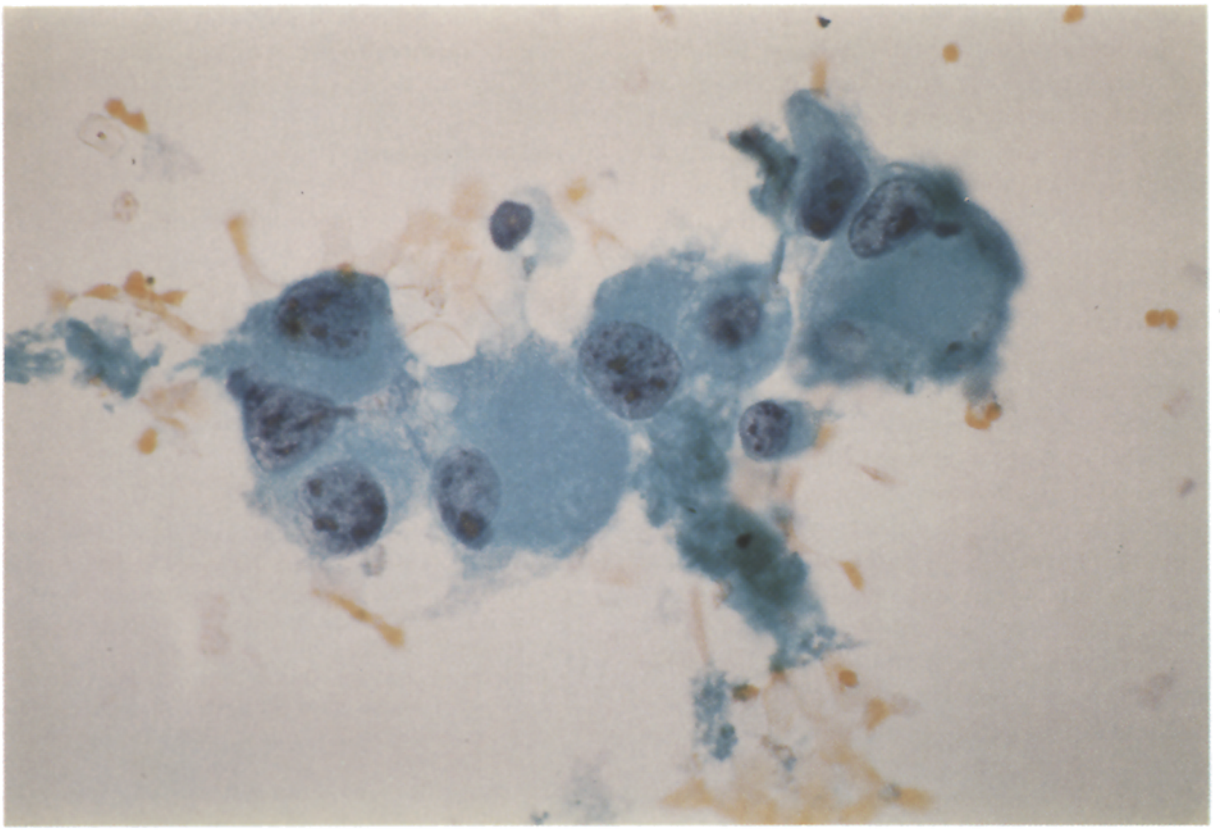

*Fig. 8.* Cytological picture of an endoscopic biopsy specimen (case No. 4, Table 2). Atypical cells with hyperchromatic nuclei were revealed. Cytological diagnosis was malignant, class V.

amination actually needs no anesthesia other than Xylocaine jelly. This apparatus (the endoscope, Surflo intravenous catheter and light guide) is very light and compact, so that we can operate it easily and orient it in the direction in which we want to insert it. We think that its use is indicated for all cases whose galactographic findings show filling defects and blockages in the relatively large mammary ducts, and where we suspect intraductal proliferative lesions.

Through the use of the duct endoscope, a reliable method has been established for the biopsy of intraductal proliferative lesions, as described above. The principle of endoscopic biopsy is aspiration, but sometimes we were unable to get enough tissue for a diagnosis, and could only get fluid samples. In order to take samples reliably, we used disposable Surflo intravenous catheters as containers. By using these, we can also precisely take samples located somewhat ahead from the tip of the endoscope. If the samples are very small, the whole catheter is sent for histological and/or cytological examination to prevent loss of material.

The endoscopical findings of scattered, flat elevations observed in the breast cancer case are consistent with the irregularity of the caliber in galactography [11]. Endoscopical findings of multiple scattered papillary or fungal projections in the ductal surface were observed in the breast cancer cases. These are consistent with the findings of multiple filling defects in galactography, which are thought by Ciatto *et al.* [8] to be suspicious of malignancy. These findings, i.e., a continuous rough surface and multiple scattered projections, indicate that carcinoma spreads intraductally and continuously, as proved pathologically by Gallager and Martin [14]. Benign intraductal papillomas are usually isolated, steeply standing polypoid lesions,

even if they are large. There is no change in the wall of the duct surrounding the papilloma. A benign, intraductal papilloma grows individually and expansively at the site where the lesion occurs, while breast cancer spreads on the luminal surface of the mammary duct forming scattered papillary or flat-elevated lesions. In other words, benign intraductal proliferative lesions are different from malignant ones in their growth characteristic. These are considered to be the most valuable points concerning the endoscopical diagnosis of intraductal proliferative lesions.

There was an interesting case (case No. 3, Table 2) in which breast cancer spread into the peripheral region behind an intraductal papilloma located near the nipple in the same duct system. This case supports the theory, suggested by Wellings *et al.* [15], that intraductal papillomas occur in the larger ducts, and cancers occur in the region of TDLU (terminal ductal lobular unit). Therefore, when intraductal carcinoma has spread and reached into the larger ducts, it can be diagnosed by duct endoscopy. Although these endoscopically diagnosed breast carcinomas had spread over a distance in the duct system, these cases seemed to be early stages of breast cancer, because almost all the cancer foci were within the ducts, rarely invading the surrounding mammary tissue.

In our experience, benign papillary-shaped lesions can probably be taken out successfully by aspiration. But in cancer cases, we were unable to take in enough of a sample to examine histologically. These cases were suspected to be malignant only after cytological examination. The reason for this difference was that the papilloma usually has prominent connective tissue stroma, but papillary carcinoma usually has delicate or no connective tissue stroma, as reported by Kraus and Neubecker [16].

We think that endoscopic biopsy is not only a useful diagnostic procedure but also a therapeutic one. We are now following patients whose lesions were completely removed to see if nipple discharge may disappear. Perhaps it will be possible to treat benign intraductal papillomas without incision of the breast.

In conclusion, we think that endoscopic biopsy aided by duct endoscopy is a helpful diagnostic procedure. It is probably also a harmless therapeutic method for use in nipple discharge.

**Acknowledgement**

We thank Olympus Optical Co. for offering the endoscope to use.

**References**

1. Urban JA: Excision of the major duct system. Cancer 16: 516–520, 1963
2. Atkins H, Wolff B: Discharges from the nipple. Brit J Surg 51: 602–606, 1964
3. Namba K, Sakomoto G, Akiyama F, Makita M, Sugano H, Yoshimoto M, Watanabe S, Kasumi F, Nishi M: Intraductal biopsy of the breast (IDBB) for intraductal lesions – a case of breast cancer diagnosed by IDBB. Jpn J Breast Cancer 4: 253–258, 1989
4. Makita M, Sakamoto G, Namba K, Akiyama F, Iwase T, Sugano H, Yoshimoto M, Watanabe S, Kasumi F, Nishi M: Nyukannaishikyo (in Japanese). Jpn J Breast Cancer 4: 571–575, 1989
5. Leborgne RA: The Breast in Roentgen Diagnosis. Constable & Co, London, 1953, pp 14–19
6. Hicken NF, Best RR, Hunt HB, Harris TT: The roentgen visualization and diagnosis of breast lesions by means of contrast media. Am J Roentgenol Rad Therapy 39: 321–343, 1938
7. Gregl A: Color atlas of galactography. F.K. Schattauer Verlag, Stuttgart-New York, 1980, pp 43–53, pp 139–199
8. Ciatto S, Bravetti P, Berni D, Catarzi S, Bianchi S: The role of galactography in the detection of breast cancer. Tumori 74: 177–181, 1988
9. Ishii Y, Fujii M, Wakabayashi T, Chyodo K, Sakuma I, Tomono T, Hagiwara K, Nagao M, Kato K: Cytology of nipple discharge with a cell concentration method – comparative study with a direct smear method. J Jpn Soc Clin Cytol 28: 389–393, 1989
10. Namba K, Sakamoto G, Akiyama F, Sugano H, Yoshimoto M, Watanabe S, Kasumi F, Nishi M: Diagnostic value of CEA measurement of nipple discharge in breast carcinoma – utilization of 'film method'. Jpn J Breast Cancer 3: 295–304, 1988
11. Okazaki A, Watanabe Y, Okazaki M, Sato H, Mikami T, Toda K, Okazaki Y, Nabeta K, Asaishi H, Hayasaka H, Narimatsu E: Diagnosis of nonpalpable breast cancer by ductography – Histological study compared with ductographic findings. Jpn J Breast Cancer 4: 587–594, 1989
12. Teboul M: A new concept in breast investigation: echohistological acino-ductal analysis or analytic echography. Biomed Pharmacother 42: 289–296, 1988

13. Teboul M: Echo-histological 'acino-ductal analysis', Preliminary results. Ultrasound in Med. & Biol. 14: 89–95, 1988
14. Gallager HS, Martin JE: Early phases in the development of breast cancer. Cancer 24: 1170–1178, 1969
15. Wellings SR, Jensen HM, Marcum RG: An atlas of subgross pathology of the human breast with special reference to possible precancerous lesions. JNCI 55: 231–273, 1975
16. Kraus FT, Neubecker RD: The differential diagnosis of papillary tumors of the breast. Cancer 15: 444–455, 1962