Preliminary experience of autofluorescence mammary ductoscopy

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Endoscopic examination through the milk ducts of resected breast tissue enables clear identification of a malignant tumor.

Mammary ductoscopy (MD) is a minimally invasive technique that uses a submillimeter endoscope inserted into breast ducts to directly visualize the ductal epithelium (lining) and to yield high-resolution white-light images of the tissue. Clinically, it has most commonly been used to manage pathological nipple discharge, as it allows therapeutic removal of intraductal papilloma and guides surgical excision during operations. MD has also been used as a diagnostic tool for ductal carcinoma, which is the most common form of cancer in the breast. However, to date, the approach was not deemed sufficiently advanced for detecting early-stage lesions.

Here, we describe our efforts to enhance the diagnostic accuracy of MD through the addition of autofluorescence imaging and diffuse reflectance and fluorescence point spectroscopies. Our goal was twofold: first, to assess the technical feasibility of autofluorescence to produce acceptable image quality in the ducts; and second, to find distinct changes between malignant and benign tissues that potentially can facilitate visualization of lesions that are not seen under conventional white-light ductoscopy. For simplicity, we used an existing autofluorescence-imaging system that was developed and optimized for gastrointestinal endoscopy. A priori, this approach is not necessarily optimal for ductoscopy. Consequently, we included the point fluorescence and reflectance spectroscopies to gain further data to aid interpretation of the imaging results as well as to optimize the imaging parameters.

Ten consenting mastectomy patients with a preoperative diagnosis of palpable invasive ductal carcinoma were recruited into the study between May 2005 and July 2008. This ex vivo pilot study was approved by the Research Ethics Board at the University Health Network, Toronto. All mastectomy specimens were examined within 1–1.5h after resection.

We investigated the first three cases using a 1.1mm-external-diameter ductoscope. However, we found that this size instrument limited access, and for the remaining seven cases we switched to a 0.7mm ductoscope. Both devices had a working length of 70mm, a field of view of 70°, and a depth of view of 1–10mm (rigid fiber ductoscope, model MS-611, Fibertech, Japan). The instrument was coupled through a standard eye-piece to a fluorescence endoscopic imaging system (OncoLIFE, Xillix Technologies Corp., Canada). The principle of operation and technical details are available elsewhere.

Figure 1 shows examples of ductoscopic images from the breast tissue of a 53-year-old woman who underwent a modified radical mastectomy for a 3.5cm invasive ductal...
Figure 2. (a) Diffuse reflectance spectra over regions of normal and tumorous tissue. (b) Autofluorescence spectra in the green band (G), together with some portions of blue (B-band) and red (R-band) reflectance from the excitation light. The sharp peaks within the blue (B) and red (R) bands are mercury lines from the arc lamp source. (Reproduced by permission.)

Carcinoma. Figure 1(a) and (b) shows images taken from a normal duct from the same patient in white-light and fluorescence modes, respectively. In white-light mode, the intraductal carcinoma appears as irregular protrusions into the ductal lumen, with color similar to the surrounding ductal tissue: see Figure 1(c). In fluorescence mode—see Figure 1(d)—the same intraductal carcinoma appears reddish compared to the surrounding ductal tissue, which is blue-green (cyan) in color. We noted that debris seen in the lumen of the normal duct—see Figure 1(a)—which can be misinterpreted as cancer, appropriately appeared blue-green in fluorescence mode, showing the ability of fluorescence ductoscopy to differentiate cancer from noncancerous tissue in this case.

Figure 2 provides an example of reflectance and autofluorescence spectra. The point spectroscopy and imaging gave qualitatively similar results. Because ductoscopy can access ducts about 6–10 cm from the nipple openings, it should make it possible to see >95% of breast cancers and papilloma with nipple discharge. It is important to reiterate that this work was performed in patients with frank tumor, whereas the ultimate major clinical impact will be in patients with early-stage lesions.

In summary, we have shown the technical feasibility of autofluorescence ductoscopy in an ex vivo setting. Although developed and optimized for other organs, the current imaging algorithm appears to provide discrimination between intraduc- tual tumor and normal ductal tissue. Our next step will be to carry out similar studies in vivo and in patients who do not have known malignancy, e.g., women presenting with abnormal nipple discharge.

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References