Ductoscope's Future Bright for Breast Ca Diagnosis

The procedure can be done on an outpatient basis, is relatively inexpensive, and is minimally invasive.

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

ORLANDO — Light may soon take a place in the diagnostic and surgical armamentarium for breast cancer.

Researchers at the Technical University of Munich, Germany, have developed and are currently evaluating the world's first autofluorescence ductoscope, which has the potential to diagnose the earliest forms of intraductal breast cancer and guide surgical treatment, Dr. Volker Jacobs said at a meeting on laparoscopy and minimally invasive surgery.

The prototype chosen for study uses a 300-watt xenon lamp that emits white light; a foot switch adds a blue filter to change it to a fluorescent excitation light. Under this spectrum, healthy tissue shines brightly, reflecting 100% of the light, while dysplastic tissue reflects a reduced amount, or even none, and fades into blackness, said Dr. Jacobs, a research and clinical consultant in obstetrics and gynecology at the university.

This picture isn't optimal for diagnostic evaluation, however, he said in an interview. "We needed a more sophisticated way of viewing the information. So a complex data processing was performed to invert the picture [healthy areas diminish and suspicious areas are highlighted], and then we overlay it with an image from the red-violet spectrum to improve detection of potential lesions." In this final image, suspicious areas and potential intraductal lesions appear blue-violet.

The journal Clinical Breast Cancer has accepted Dr. Jacobs' technical feasibility study for publication. The paper describes five patients examined intraoperatively with this technique. All had either histologically confirmed ductal carcinoma in situ or papilloma that had been discovered with other imaging methods or fine-needle biopsies.

Diagnostic and autofluorescence ductoscopy were performed before segment or duct excision or lumpectomy. The additional time required for the ductoscopy was minimal, ranging from 5 to 15 minutes, and there were no associated complications. Since the procedure uses only light, there was no need for intravenous administration of any contrast agent.

The paper notes that areas of suspicion reflected distinctly different light values than did normal tissue. "The degree of blue-violet color appears to be proportional to the degree of alteration in this tissue, just as it is in bronchoscopy," Dr. Jacobs said at the meeting, sponsored by the Society of Laparoendoscopic Surgeons. "The more light we see, the more dysplastic the tissue should be."

This observation, if confirmed in prospective trials, could open the door to an impressive array of applications for autofluorescent ductoscopy, he said. "It could lead us to be able to intraoperatively differentiate between benign and nonbenign lesions, and maybe even to have semiquantitative visual differentiation that would allow us to make some instant conclusions about the lesion. This could really improve the diagnostic value of the procedure and might even allow earlier therapeutic intervention."

Similarly, he said, these color gradations could someday benefit women at high risk of breast cancer. "We might be able to develop this into an early screening procedure for these patients," Dr. Jacobs said. "This is hypothetical at this stage, but we are convinced it can be done."

Since the initial feasibility study included only five patients, there weren't enough data to characterize ductal lesions according to imaging color. But Dr. Jacobs hopes to publish a larger case series within a year; this study will include more data on color gradations, and compare the autofluorescent imaging to standard imaging techniques.

The most immediate application of autofluorescent ductal imaging would probably be surgical, he said. "If we could take a biopsy under autofluorescent visualization, we might be able to use the color as a guide to getting clear margins. This might cut down on the number of R1 resections, and also reduce the need for consecutive operations to ensure clear tumor margins."

In fact, Dr. Jacobs said, autofluorescent diagnostic ductoscopy would combine very well with interventional ductoscopy. The color gradations would guide the surgeon to the suspicious area, which could be treated endoscopically.

This type of interventional ductoscopy is under investigation in Europe. Miniature instruments only 0.8-0.4 mm in diameter are used in the procedures, passing through an additional working channel of the ductoscope.

Instruments include cytology brushes, microforceps, and a titanium basket for grabbing and removing intraductal papillomas. "All of these devices are either already in clinical use or are being investigated in Europe," Dr. Jacobs said. "But interventional ductoscopy is still an experimental procedure. We do not yet know, for example, if the removal of a papilloma by this means is as effective as the removal by traditional surgery. This needs further evaluation in trials."

The instrument combines an autofluorescence light source and camera already approved in Europe for diagnostic bronchoscopy with a 1.3-mm diameter ductoscope. Like autofluorescence bronchoscopy, it operates on the principle that healthy and dysplastic tissues reflect different percentages of light, Dr. Jacobs said.

Light-induced fluorescence bronchoscopy has been used for several years to identify early lung lesions: A helium cadmium blue laser stimulates the lining of the bronchi to autofluoresce in a range of colors. Normal, healthy tissue is shown as being bright green, and suspicious tissue looks reddish-brown.

A summary of studies with this technique concluded that it can increase the detection rate of premalignant lesions by up to six times, compared with conventional, white-light bronchoscopy (Lung Cancer 2004;45[suppl. 2]:S29-37). "We wondered if we could use a similar technique to identify early breast lesions," Dr. Jacobs said.

In 2003, he and Dr. Stefan Paepke began investigating the scientific and clinical potential of autofluorescence ductoscopy. "Transferring this technology from large-lumen bronchoscopy to small-lumen endoscopy seemed technically feasible. We were soon able to get our first prototypes developed and start a clinical evaluation," he said.

Neither investigator claims a financial interest in either the procedure or the unit.

Although many of autofluorescence ductoscopy's benefits are still theoretical, some are immediate and proven, Dr. Jacobs said. The procedure can be done on an outpatient basis. It's relatively inexpensive (about 10 times cheaper than an open biopsy in Germany), minimally invasive, and eliminates the need for sedation or contrast agents—all important considerations for a procedure with the potential to enter into widespread use.

"Its long-term clinical impact is still unproven at the present time," he said. "It's a target on the horizon. But we are convinced it's a target we can reach." ■

COURTESY DR. VOLKER R. JACOBS

Dr. Volker Jacobs displays images obtained with his prototype autofluorescence ductoscope.

Experimental Breast Cancer Vaccine Cuts Recurrences in Half

BY BRUCE JANCIN
Denver Bureau

SAN ANTONIO — A novel anti-HER2 breast cancer vaccine reduced recurrences by 50% in a phase II clinical trial involving high-risk patients, Col. George E. Peoples, MC, USA, said at a breast cancer symposium sponsored by the Cancer Therapy and Research Center.

Based on these encouraging results, a large phase III randomized trial is planned, added Dr. Peoples, a surgeon at Brooke Army Medical Center, San Antonio.

The vaccine, called NeuVax, is built on the E75 peptide from the extracellular domain of human epidermal growth factor 2 (HER2), the oncogene targeted by trastuzumab (Herceptin). HER2 is overexpressed in one-quarter of breast cancers.

Other attempts at developing peptide vaccines for breast cancer have proved largely disappointing.

However, those vaccines were designed to treat metastatic disease. In contrast, the new E75 vaccine is a preventive therapy for patients who have been treated for breast cancer and have a high risk of recurrence but no evidence of breast cancer following multimodal treatment. The mechanism of action involves overcoming tolerance through repeated administration of large quantities of a single purified antigen.

At 24 months, 8.3% of the vaccine group had developed recurrent disease, compared with 16% of controls, a difference that missed statistical significance because of the small sample size.

Dr. Peoples reported on 101 patients who received monthly intradermal injections of the vaccine mixed with granulocyte-macrophage colony-stimulating factor and 85 controls who did not. All participants had lymph node–positive, HER2-positive breast cancer or high-recurrence-risk, node-negative, HER2-positive cancer and no evidence of disease.

At 20 months the recurrence rate was 5.7% in the vaccine group and 14.1% in controls.

At the latest update at 24 months, 8.3% of the vaccine group had developed recurrent disease, compared with 16% of controls, a difference that just missed statistical significance because of the small sample size, according to the surgeon.

Mild cutaneous, delayed-type hypersensitivity reactions to the vaccine were extremely common. There was no significant systemic toxicity.

The vaccine project was initially sponsored by the Department of Defense and conducted through the Uniformed Services University of the Health Sciences Cancer Vaccine Development Laboratory, Bethesda, Md. It has been taken over by Apthera, which is also developing the drug as a prostate cancer vaccine. ■