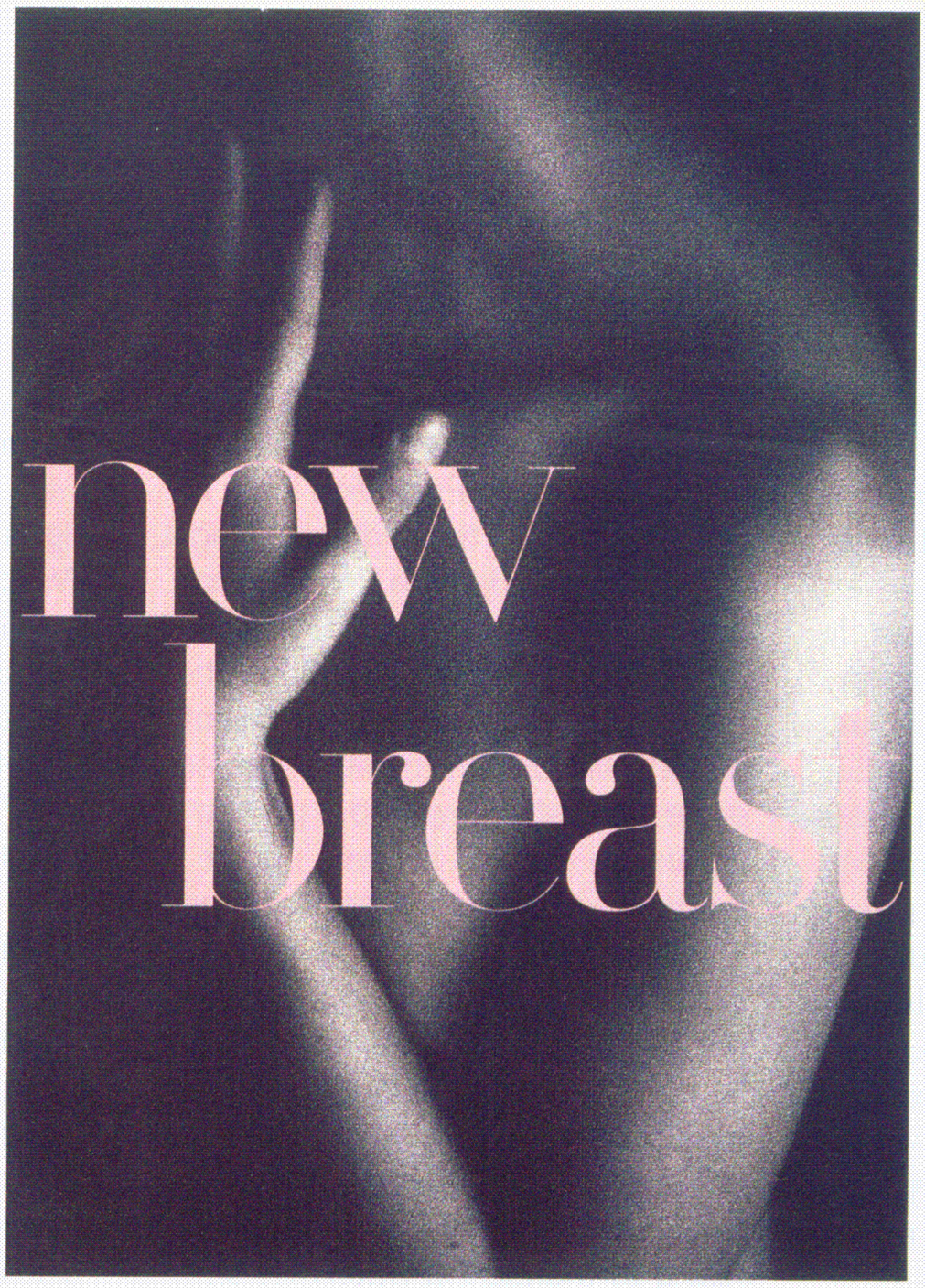
the new breast tests



FOUR TECHNOLOGIES ARE REVOLUTIONIZING THE EARLY DETECTION OF BREAST CANCER

BY KATHLEEN McAULIFFE

Though mammography remains the gold standard and is still indispensible, the test misses more than 15 percent of all breast cancers. That's why researchers have been aggressively pursuing better detection methods for years.

Now a quiet revolution is underway. Four technologies—some already in use, others on the horizon—offer important breakthroughs in early detection. Some transform mammograms into a far more accurate tool; others employ inventive methods for detecting precancerous changes in the breast. Here's what you need to know about the latest innovations.

BEFORE IT'S EVEN CANCER

Ductal lavage allows physicians to identify atypical cells in the breast that may develop into cancer years down the road. Currently, the technique is being used to assess the odds of breast cancer in high-risk women; if atypical cells are detected, these women may elect treatment to reduce their risk and even prevent the disease.

Ductal lavage involves retrieving cells lining the milk ducts of the breast, where almost all breast cancers arise, and examining them under a microscope for certain aberrations. "We're trying to find breast cells that are thinking about becoming cancer when they grow up," says the physician instrumental in its development, Susan Love, M.D., a California-based researcher and author of *Dr. Susan Love's Breast Book* (Perseus Books Group, 2000). The principle, she adds, is similar to the Pap smear, which is typically used to detect precancerous changes in cervical cells.

To obtain breast-duct cells, a numbing cream is applied, then a suction device draws fluid into the nipple's six to nine ducts. Samples are taken from those that actually produce fluid (usually one to three ducts), since they are thought to be more likely to harbor abnormal cells. A hair-thin catheter is inserted, and more anesthetic and saline are infused to wash out cells for analysis.

If abnormal cells—known as atypical hyperplasia—are detected, the patient has a number of options. She can take the drug tamoxifen, which has been shown to reduce the risk of developing breast cancer by 50 percent in high-risk women. Or, she can wait and repeat the test, usually in three to twelve months, to see if further changes indicative of cancer occur; that's a reasonable strategy, since studies suggest that only about one third of women who have abnormal cells in the breast duct will develop cancer. If atypical cells are detected in women who carry the breast-cancer genes BRCA1 or BRCA2, the more drastic step of removing the breast might be considered.

The Food and Drug Administration cleared the equipment used in the ductal lavage procedure last year. For now, ductal lavage is available only to women at high risk for breast cancer (owing to a personal or family history of the disease) at more than 70 medical centers nationwide, at a cost of $400–$800. So far, only about 50 percent of cases have been covered by insurance. Though the technique is not yet recommended for women at average risk, Love is optimistic that could eventually change. "I can envision the day," she says, "when it will be common practice for women to get a Pap smear and their ducts washed."

A BETTER MAMMOGRAM?

You've probably read about the FDA's recent approval of digital mammography; the hope is that you'll soon see it at your local screening center. Rather than capturing X-ray images of the breast on film, as standard mammograms do, digital mammography converts those X rays into a digital image that can be manipulated via computer to highlight a hidden cancer. Doctors can enlarge a problem area and distinguish more shades of

PHOTO: GLEN ERLER/PHOTONICA.

gray, for example, which should enhance diagnostic accuracy.

At least that's the promise that digital mammography offers. According to a recent head-to-head comparison of traditional film and digital mammography (in a study involving nearly 5,000 women), there was no significant difference between the methods in detecting cancerous growths. Some experts remain hopeful that digital technology might yet surpass standard mammography as physicians gain experience and training with the newer method.

Digital mammography has other benefits that should lead to its quick dissemination. In the same study, fewer women who got digital mammography needed to be called back for retakes, partially due to doctors' ability to zoom in and manipulate the image. Digital pictures can also be zapped with the press of a button to other experts around the world for a second opinion—whereas transporting unwieldy film can be a time-consuming and frustrating process. In addition, digital mammography is more suited to be hooked up to other technologies (such as Computer-Aided Detection, described below) that are certain to improve breast-cancer detection in future.

Digital units were approved by the FDA for sale last November, and only a small number of medical facilities—an estimated 150—are equipped with them. Experts are hopeful that will soon change. The perks of digital mammography add up to a huge advantage, in

> "we're trying to find cells that are thinking about becoming cancer when they grow up"

the opinion of Carl D'Orsi, M.D., an investigator on the study and vice chairman of radiology at the UMass Memorial Medical Center in Worcester. "In the next three to four years," he says, "digital units will likely replace film screening everywhere."

CATCHING HARD-TO-SPOT TUMORS

When it comes to interpreting a mammogram, two sets of eyes may be better than one—especially if the second set belongs to a computer. That's the rationale behind ImageChecker, a computer system designed to double-check the results of standard mammograms. In a recent study presented last year at the Radiological Society of North America, the technology (known as Computer-Aided Detection, or CAD) increased cancer detection by 20 percent in nearly 13,000 women who received traditional film mammograms.

The computer is particularly adept at spotting certain cancers, such as those that are characterized by subtle calcium deposits, reports Timothy Freer, M.D., lead author of the study and director of the Women's Diagnostic & Breast Health Center in Plano, Texas. "It can see structures that are so small as to be nearly undetectable by the human eye," he adds.

The CAD system did increase the biopsy rate by 20 percent. However, the percentage of biopsies that turned out

to be benign was not any higher than with standard mammography.

The FDA approved the ImageChecker system in 1998. But due in part to the high cost of the system (some $200,000), only 120 or so CAD units are now in use in the U.S. But if these encouraging early results are confirmed, and if insurers start reimbursing for the procedure, it may prompt more institutions to invest in the equipment—particularly given that CAD and the newly approved digital mammography are considered extremely compatible. (The use of the two technologies together is currently in clinical trials.)

REDUCE THE ANXIETY OF BIOPSIES

When a mammogram is hard to interpret, 3-D ultrasound imaging could potentially take the worry out of waiting for biopsy results, by allowing doctors to immediately determine whether a lump is benign or cancerous. This experimental technique uses sound waves and state-of-the-art computer equipment to precisely measure the speed and volume of blood flowing in the vessels in and around a suspicious mass (cancer needs extra blood flow to spread)—and to see that area in 3-D. These advances should make it superior to gray-scale breast ultrasonography, the method that is commonly used today.

The technique may turn out to be particularly suited to women who have dense breasts—including postmenopausal women taking hormone replacement therapy—which tend to appear white or opaque on mammograms, according to Marilyn Roubidoux, M.D., a radiologist and associate professor who is developing the method at the University of Michigan School of Medicine in Ann Arbor.

Currently, only a few institutions offer 3-D ultrasound imaging for research purposes. (Investigators are also testing this method to evaluate how breast-cancer patients are responding to chemotherapy.) But with further progress over the next five years, says Roubidoux, it could become a standard tool in selective cases. ■

Kathleen McAuliffe is a health writer and a **more** *contributing editor.*

princess caroline

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A year later, at the end of 1983, Caroline married Stefano Casiraghi, the heir of a Milanese oil-refining family. Monaco's eldest princess had, it seemed, found happiness at last. The couple had three children—two boys and a girl—who, like their father, were unencumbered by titles and protocol. They lived, claims one acquaintance, in "a place of well-being and strength, replenishment and renewal"—a phrase straight out of Princess Grace's *My Book of Flowers*, published in 1980.

But in 1990, tragedy struck again when Casiraghi was killed in a powerboat accident. Left alone to raise her three children, 33-year-old Caroline retreated from the public life she had so recently embraced, moving to a renovated stone farmhouse some two hours north of Monte Carlo in the French village of St-Rémy-de-Provence. There, the former party girl did her own shopping, played with her children and sought comfort in a simpler way of life. "For personal reasons, she wanted to move away from the gossip and hoopla of Monaco," her brother, Prince Albert, explained.

As Caroline's mourning period came to an end, she occasionally began to come out of her self-imposed exile. For five years, she was involved with French actor Vincent Lindon, whom many considered to be more down-to-earth than her previous husbands; the relationship ended in 1995. "Vincent wanted an upside-down fairy tale in which the princess is turned into a shepherdess," sniffed *Paris Match*.

The fairy tale was quickly righted. Soon after her breakup with Lindon, Caroline was spotted in Bangkok with Prince Ernst August of Hanover—the very suitor Grace had hoped she would marry 18 years before. Though the prince was considerably less eligible, having been married for the past 16 years to Swiss pharmaceutical heiress Chantal Hochuli, the two began to appear together with increasing frequency in the world's most exotic cities. Ernst remained at her side when Caroline reportedly battled a bout of alopecia, a stress-related scalp condition that left her temporarily bald. When the affair could no longer be denied, Ernst's wife filed for divorce; the couple married in 1999, and their daughter, Alexandra, was born six months later.

But many in her circle have, once again, questioned Caroline's taste. Her latest husband, known for his violent temper, has lashed out in public, breaking the nose of a cameraman who tried to videotape him in 1998 and beating up a nightclub owner in 2000. Prince Rainier, said a friend of the couple's, was "not happy; he doesn't like scandals." Ernst's widely reported exploits can be bizarre: last June, he was spotted urinating near the Turkish pavilion at Hanover's Expo 2000. "Caroline's taste in men has always been capricious, but Ernst is in a class of his own," said a friend.

But for all his eccentricities, Caroline's new husband has in some way brought her life full circle. With the new title he has bestowed—Her Royal Highness Caroline, Princess of Hanover, Duchess of Brunswick and Lüneburg—he has caused his wife to outrank everyone in her immediate family except Rainier. Although by right of primogeniture the title will ultimately pass to her brother, Albert—whose durable bachelorhood has spawned rampant rumors that he is gay—there are many in Monaco who would like to see Caroline take over the family's multimillion-dollar business when the time comes. "She's modern, forthright, smart as a whip, and an icon of Monaco's glamour," says a former courtier. "She would make a wonderful head of state."

But perhaps a more pressing question is whether Caroline has truly put her demons behind her. Her life, filled with as much tragedy as privilege, is compelling evidence for the so-called "curse of the Grimaldis," which has plagued the family with recurring bouts of bad luck since the 13th century. Or perhaps, like the Windsors, Caroline is in some way paying the price of being a princess in modern times. "You don't get used to people looking at you all the time," she told *Harper's Bazaar* in a rare interview. "It's difficult, because I always realize I haven't chosen it. I was never given the chance—or circumstances never allowed me—to say, 'Stop, I want to get out of this; this is not what I wanted.'" ■

Peter Evans is an award-winning British journalist and author.