2. Active immunotherapy (vaccines). Cancer vaccines are attractive because they are less toxic than chemotherapy and small-molecule targeted therapies, and they may have a lasting effect. Early results for vaccine effectiveness have been mixed, for several reasons. The U.S. Food and Drug Administration approved the Sipuleucel-T vaccine to treat metastatic prostate cancer. Also, a gp100 vaccine for melanoma and an anti-Id vaccine for follicular lymphoma succeeded in phase III trials, and phase III trials are evaluating others, including the Prostvac vaccine for prostate cancer and Stimuvax and Lucinix for non–small-cell lung cancer. Rosenberg and colleagues have cloned the genes encoding cancer-regression antigens and have used these to develop cancer vaccines to treat patients with metastatic melanoma.

3. Adoptive, or cell transfer, immunotherapy. With this technique, immune cells that can react against cancer are isolated, “grown and educated” to recognize and destroy cancer, and then “adopted” by patients. The aforementioned study using CD8 T cells uses this method.

“Even though it is more labor intensive, adoptive therapy provides a little more control and could prove to be the most effective technique,” said Cassian Yee, M.D., from the Clinical Research Division at the Fred Hutchinson Cancer Research Center in Seattle. In the Aug. 2, 2011, issue of Nature Reviews Clinical Oncology, Rosenberg reported on a pilot trial that found that cancer immunotherapy using the adoptive transfer of autologous tumor-infiltrating lymphocytes resulted in objective cancer regression in 49%–72% of patients with metastatic melanoma.

Rosenberg said one of the greatest appeals of adoptive immunotherapy is that it should lead to truly personalized medicine. “By growing a patient’s own cells for therapy, we end up with a new individualized drug for each patient,” he said. “People like the idea that they can use the body’s own defenses to fight a disease rather than the more debilitating toxic approaches.”

Miller’s laboratory is focused on preclinical and clinical studies to develop effective antitumor immunotherapies. His early studies focused on nonspecific immune stimulation using subcutaneous IL–2. “Strong evidence suggests that this nonspecific therapy alone will be ineffective, and current efforts aim to target effectors specifically to tumor cells.” For natural killer (NK) cells, approaches include combined therapy with monoclonal antibodies and IL–2 to target therapy through antibody–dependent cytotoxicity.

Another major research focus by Miller is NK cell development. Receptors on NK cells have been identified that recognize class I MHC (major histocompatibility complex) molecules. Miller said the hypothesis underlying current research efforts is that “self” MHC molecules influence the NK cell receptor repertoire during development. These NK cell receptors may also play a physiologic role in cancer. “Laboratory evaluation and human clinical trials will test the hypothesis that a mismatch between NK receptor and class I alleles on recipient tumor will result in greater tumor kill,” said Miller. Clinical trials using allogeneic NK cells in acute leukemia and breast cancer are under way.

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Empowering the Body After Breast Surgery

By Kristine Crane

“Alice” no longer has to wear a sports bra. “My breasts don’t move,” said the breast cancer survivor, who had a double mastectomy and reconstructive surgery 2 years ago. Laughing, she explained, “My belly moves, but my breasts are like steel.”

Breasts of steel may be “one of the humorous parts” of an otherwise very emotional process, said Alice. But recreating the depleted muscles around the chest—from the abs to the shoulders—is an often-overlooked challenge for breast cancer patients who undergo surgery. Studies show that surgery patients often experience shoulder morbidity and pain associated with muscle loss.

Alice had been working out regularly with a trainer for a few years before her diagnosis, so she was fit when she had surgery. But afterward, she couldn’t pull weeds from the garden or pick up groceries.

Many breast cancer survivors experience similar frustrations. Although surgery—whether it’s a lumpectomy, mastectomy, or reconstructive surgery—is usually the hardest part, the aftermath often leaves patients with bodies in need of rebuilding. And though a lumpectomy does conserve the breast tissue and surrounding muscle, it may involve removing the axillary nodes in the upper breast and armpit regions, which may affect range of motion and mobility.
**Pilates-Based Program**

A decade ago, Doreen Puglisi, an exercise physiologist in New Jersey, became aware of this problem, because many of her clients were breast cancer survivors. Puglisi was surprised that no formal medical protocol existed to help them rebuild their muscles, so she created the Pink Ribbon Program, a nonprofit focused on rehabilitating patients through muscle alignment and injury prevention. It is based on Pilates, which was created to rehabilitate bedridden soldiers injured in World War I, so it was a natural fit, Puglisi said.

Reconstructive surgery may involve taking muscles from other parts of the body—such as the abs or the glutes—to re-create the breasts. Because the body may naturally compensate for the loss of those muscles in a harmful way, Puglisi’s program aims to rebuild them safely under the guidance of certified instructors. Certified Pink Ribbon Program instructors—most of them Pilates instructors—go through training that involves meeting survivors, learning about the medical procedures and treatments they’ve undergone, and creating a safe exercise protocol.

Alice’s trainer, Ulrick Rosemond, said hearing the survivors’ testimonials was mind-opening. “I got schooled in survivorship,” he said, adding that many women talked about experiencing a loss of confidence in their femininity and strength, along with a sense of isolation and abandonment by the medical community. He felt like he was fulfilling a real need when he went back to train with Alice; he was also more caring and less demanding with her. She couldn’t use heavy weights because of the risk of lymphedema, but gradually she improved her upper-body strength and posture.

Within just a few months, Alice regained her normal fitness level—and confidence in her body, said Rosemond. “It was nice to see she was back on her game. That’s the true sign of a survivor.”

**Hands-On Approach**

Two years after creating the program, Puglisi herself was diagnosed with breast cancer. “I used [the program] to rehab myself,” she said, adding that her experience was the catalyst for making the program national. In the U.S., she has trained more than 700 Pilates instructors, as well as physical and occupational therapists and oncology nurses, to be Pink Ribbon instructors. She also trained 150 instructors in Spain, Italy, Denmark, and the UK.

Alyiah Hardy, a certified instructor, has worked with about a dozen breast cancer survivors in Rockville, Md. Each client receives a 30-minute private session to assess range of motion in the shoulder, tightness in the chest and shoulders, and core strength and movement. Some continue to have one-on-one sessions; others opt for group workouts. “They come in frazzled, with the weight of the world on their shoulders,” said Hardy. “A lot of them feel really good and energized when they leave.”

Patty Borja knows that feeling. “I look forward to it because I know I’ll feel better when I leave,” she said. The 61-year-old breast cancer survivor has been coming to Hardy’s studio since shortly after her double mastectomy 4 years ago. Borja had been a physical education and swimming instructor for 30 years, so she found it frustrating that after surgery, she couldn’t even walk her dog. Now she has resumed all her normal activities, and her body doesn’t ache as much as it used to.

**Finding Support**

At the St. Joseph Medical Center breast center in Kansas City, Mo., the Pink Ribbon Program has become something of a support group. “The group setting is really wonderful for them . . . they really feel like they’re getting their life back. They learn from each other, encourage each other. If anything, that’s a big part of it,” said Jane Metsker, a nurse navigator with the program who is also a breast cancer survivor. Metsker made the Pink Ribbon Program a part of the clinic’s WELL (“women embracing and loving life”) program, which includes nutritional guidance and Zumba classes. In the 2 years since the program started, about 75 women have gone through it, and many continue the exercises on their own, said Metsker.

Many Pink Ribbon Program participants found out about it on their own—by word of mouth or through ads in magazines or newspaper articles. Puglisi’s goal is to get the program into more hospitals and clinics so that it’s more readily available for patients. Currently, about a dozen U.S. medical centers make it available. Part of the challenge is in making it more widespread is that only a few studies have addressed exercise rehabilitation programs for cancer survivors. One, published in the European Journal of Physical and Rehabilitation Medicine in 2010, showed that patients doing Pilates made more substantial improvements in functional capacity and flexibility, as well as fatigue, depression, and quality of life, than those who did not. The study concluded, “Pilates exercises are effective and safe in female breast cancer patients. There is a need for further studies so that its effect can be confirmed.”

Puglisi said the program is gaining more recognition, with quality of life becoming a more important measure in studies. She continues to hear testimony that the program works: Cancer free for 7 years, Puglisi recently started rock climbing. “I was thrilled—more than physically, psychologically, and emotionally—because to me it says I’m capable of doing anything.”

For more information on the Pink Ribbon Program, visit [http://www.pinkribbonprogram.com/](http://www.pinkribbonprogram.com/).