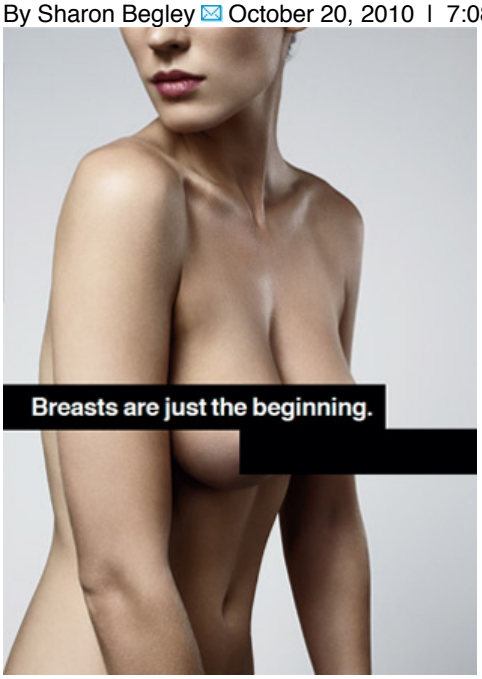
FEATURES
Inside the Business of Selling Human Body Parts
START
Prison Economics: How Fish and Coffee Become Cash
PLAY
Q&A: Photog's Descent Into the Underworld
FEATURES 18.11

All Natural: Why Breasts Are the Key to the Future of Regenerative Medicine

By Sharon Begley ✉ October 20, 2010 | 7:08 pm | Wired November 2010



Who needs implants? How tissue engineering and a new kind of stem cell can help the body rebuild itself.
Photo: David Slijper

To be in the company of Chris Calhoun is to encounter breasts, and encounter the damn things anytime, anywhere—including over a plate of spaghetti in a bustling Manhattan restaurant.

On this spring afternoon, the 44-year-old CEO of San Diego-based biotech company Cytori Therapeutics pulls out his laptop, launches a PowerPoint presentation, and there they are: conical and cantaloupy, As through Ds, beige and pink and taupe and tan, more breasts than you might see in a women's locker room, never mind in the middle of a lunch table.

A passing waiter does a double take at this lively slide show, but Calhoun is oblivious. He's talking excitedly about how these women's bodies led him and his team of scientists to a discovery in tissue engineering, a process that could well be one of the most momentous medical advances of the 21st century: the use of stem cells—specifically stem-cell-enriched adipose (fat) tissue—to enhance, heal, and rebuild injured or damaged organs.

A few taps on his laptop reveal the unsettling "before" images of these seemingly normal breasts. There: a breast with a divot the size of a plum taken out of the bottom from a lumpectomy. There: a chest as flat as a floor mat from a double mastectomy. There: one so misshapen after a partial mastectomy, it's possible to determine what it actually is only because of its healthy companion. "We realized that for these women there was a huge unmet need for a disruptive change in technology," Calhoun says of the work that has consumed his team of researchers and surgeons for the past eight years. "It's the first practical cell therapy." He pauses. "And it's breasts." Which means cancer victims with breasts mutilated by surgery—as well as women who are simply unhappy with their natural assets—can now grow a new and improved pair, with raw materials harvested from their own body fat.

But breast augmentation is just one development (so to speak) in the company's more ambitious plan: to introduce stem cell medicine to the mass market—and not using the ethically fraught kind of stem cells from human embryos. Instead, based on almost a decade of trials that Cytori

and its academic partners have performed on cell cultures, lab rodents, and now humans, they believe their engineered flab cells can treat more organs than you find in a French butcher shop. Chronic heart disease? Check: In human studies released in May, the cells improved patients' aerobic capacity and shrank the size of the infarct (tissue killed by lack of blood). Heart attack? Check: A human clinical trial, also reported in May, found that the cells increased both the blood supply to damaged heart muscle and the volume of blood that the heart pumped. Kidney injury as a result of cancer therapy? Check: In recent rat studies, the cells improved kidney function. Incontinence after prostatectomy? Check: Another recent study reported that, by 12 weeks after injection, the cells had decreased the amount of urine male volunteers were leaking by 89 percent. If Calhoun and his scientists succeed, they won't just create more cleavage. They'll make practical a whole new field, one that medical visionaries have dreamed of for decades: regenerative medicine.

It makes sense to apply Cytori's technology to enhance breasts instead of, say, repair urinary sphincters as a strategic way to move the patented technology out of rats and into people as soon as possible. Hearts, kidneys, and even sphincters have to work in order for us to survive. But we can live just fine without breast tissue, and, outside of feeding offspring, breasts don't have to do much. The fact is, the scientific and regulatory hurdles to getting Cytori's cells into clinical use will be easier to clear for breasts than for other tissue: Breasts simply aren't as necessary as other organs, so the bar for proving to regulators that the technology works will be lower.

It's also a booming market. In 2009, women forked over $964 million to plastic surgeons for breast augmentation, which edges out nose jobs as the most commonly performed plastic surgery in the US.

If Calhoun and his team succeed, they won't just create more cleavage. They'll make possible a whole new field: regenerative medicine.
Photo: Robyn Twomey

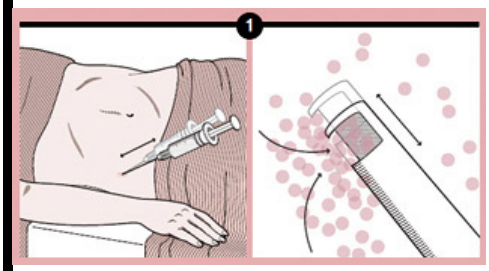
More is driving that trend than just media-hyped views of beauty. Breast cancer is a major factor. Incidence of the disease has risen from 105 per 100,000 women in 1975 to 125 per 100,000 today (though it peaked at 141 per 100,000 in 1999), and the survival rate has increased: 75 percent of women diagnosed in 1975 lived at least five more years, compared with 90 percent today. That means more women will live more years after a lumpectomy or mastectomy. Most of these survivors would just as soon live those years with something that resembles what they had before, thank you very much. Yet only 30 percent of women facing mastectomy are even offered a consultation with a plastic surgeon, notes Michael McGuire, president of the American Society of Plastic Surgeons and an associate professor of surgery at UCLA. And only 25 percent of women who lose a breast to cancer get a new one. (In 2009, there were 86,424 breast reconstructions.)

There is also demand from a burgeoning demographic no one would have predicted 15 years ago: young women choosing bilateral prophylactic mastectomy after testing positive for mutations in genes—known as BRCA1 and BRCA2—that increase the risk of breast cancer by a factor of five compared with that for women without the mutations. Others are diagnosed with cancer in one breast, have a mastectomy, and decide to have the healthy breast removed as well. In a 2009 study of women undergoing all forms of surgery for breast cancer, published in *Annals of Surgical Oncology* by researchers led by surgical oncologist Todd Tuttle of the

University of Minnesota, 29 percent opted for this “contralateral prophylactic mastectomy.” Among just mastectomy patients (that is, excluding those who had a lumpectomy or other breast-sparing surgery), the rate of taking out the good with the bad was an astounding 56 percent—even though studies find no survival advantage in removing the healthy breast. Yet Tuttle hears it all the time: *I never want to go through this again*. “Younger and more- educated women are the ones choosing to go this route,” he says. And despite the improvements in silicone implants, they’re still vulnerable to ruptures and may eventually need to be replaced. What’s more, inserting a single implant after cancer surgery can leave a woman asymmetric: It stays put while the surviving breast sags. It’s no wonder, then, that women all over the world are desperate for a better option.

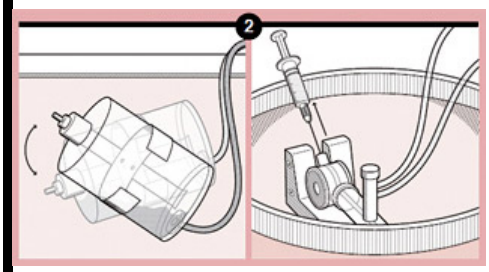
How to Build a New Breast

Cytori’s process for reconstructing or augmenting breasts relies on the recent discovery that human fat contains an amazing concentration of stem cells—cells that can be separated out using a centrifuge. That’s the science part. The artistry comes in when the surgeon makes tiny incisions for depositing the enriched fat cells, building a breast one dot-sized injection at a time like a 3-D pointillist. Here’s how it works.



Step 1 **Liposuction**

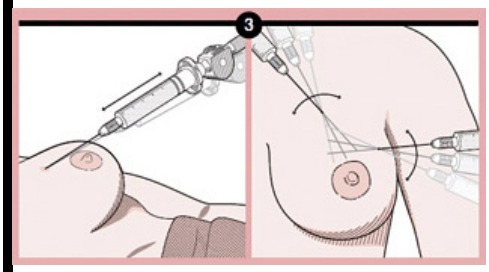
Breast reconstruction usually starts in the abdomen, using liposuction to harvest fat cells. ›› Each liposuction syringe holds about 60 cc (2 fluid ounces) of fat cells and takes five minutes to fill. Repairing the divot caused by an average lumpectomy requires eight to 10 syringes to get about 360 cc of fat tissue. Half the fat is used to create the volume needed to fill the divot and half is processed to isolate stem and regenerative cells. ›› A typical augmentation requires 800 cc (27 ounces) of liposuctioned fat: Volume varies, but in one study 160 cc of injected stem-cell-enriched tissue boosted breast circumference an average of 4 centimeters (1.6 cup sizes).



Step 2 **Centrifugation**

The liposuctioned fat is injected into the Celution System. ›› The fat cells are then “washed” with proprietary enzymes that break down the scaffolding that holds the fat cells together. ›› Next, a centrifuge separates the fat cells from the stem and regenerative cells,

concentrating them into a pellet, which is then extracted. ›› The pellet of cells is added back to some of the liposuctioned fat cells, producing a liquid suspension enriched with stem and regenerative cells and ready for injection.



Step 3 **Injection**

Using a tool called the Celbrush, the surgeon repeatedly deposits the enriched cells in the breast, either at the site of a lumpectomy or throughout the breast for augmentation or repair of a mastectomy. ›› With reconstruction patients, the tip on the brush makes tiny cuts that perforate scarred areas, transforming the bed of damaged tissue into a biological mesh. ›› The Celbrush releases 0.5 cc of cell-enriched tissue each time the surgeon moves its control wheel.The process typically takes a couple of hours, depending on the extent of treatment. ›› The deposited tissue bonds quickly to the existing tissue. Within 48 hours, new capillaries and blood vessels entwine through the new cells, supplying oxygen and nutrients to the now-stable tissue. ›› The injection area isn't painful afterward; patients go home the same day.

Illustrations: Brown Bird Design

Here's the weird thing about breasts: They are a point of obsession, vulnerable to the mercurial whims of mass culture. But one thing remains constant: In every era, a whole lot of women are convinced they have the wrong kind.

For better or for worse (mostly for worse), science, or a rudimentary facsimile thereof, has always been eager to help. European women of the 16th century applied a cumin-seed paste with a cloth soaked in water and vinegar to their breasts to keep them small and firm. In the late 1800s, the Princess Bust Developer consisted of a cream and a nifty device resembling a toilet plunger to increase cup size. Starting in the 1940s pinup era, there were liquid silicone oil injections for breast enlargement (bad idea: leakage, inflammation, granulomas) followed, in 1962, by silicone-filled implants.

Given this history of far-fetched augmentation schemes, it's not entirely unfathomable that a plastic surgeon would one day realize the secret to enhanced breasts was hidden in a pair of love handles. In 1999, Marc Hedrick, then an assistant professor of surgery at UCLA, was doing yet another liposuction, and not a little suck-out-a-few-ounces-around-my-thighs-please-doctor procedure, either. He vacuumed 8 liters—more than 2 gallons—of fat from his patient. Scientists had long wondered whether fat tissue might contain stem cells. "If it does, then here we are, stupid plastic surgeons, doing the stupidest procedure on the face of the earth," says Hedrick, 48, now sitting in the La Jolla, California, offices of Cytori, which he cofounded in 2002. "I'd just taken 8 liters out of some woman and dumped it in the trash. I asked myself, are there really stem cells in there?"

Meanwhile, a postdoctoral fellow named Min Zhu had become bored with the rheumatology research she was doing and was looking for a new field. She joined Hedrick's lab in spring of 1999, and he set her to the task of finding out once and for all whether there were stem cells in fat. Determining the qualities of a stem cell (versus a regular one) requires proving that it can differentiate into many cells, but Zhu hit a brick wall even before she could attempt that: After she isolated candidate stem cells from fat, the things refused to grow, let alone differentiate.

Her breakthrough came when she figured out that rather than using the standard fibroblasts as feeder cells in her culture, she would use blood. “She just brute-forced it,” Hedrick says. “She was forging her own trail—with a machete.” Using blood to nourish and grow the stem cells, Zhu managed to induce them to differentiate into three lineages: first bone and cartilage, then muscle, and then neuron. She walked into Hedrick’s office and said, “I think I have something.” In April 2001, the scientists published in the journal *Tissue Engineering* their discovery that adipose tissue is chock-full of stem cells.

At the same time that Zhu was making her breakthrough, Cytori’s Calhoun was running a medical device company called MacroPore Biosurgery, and one of his salespeople told him about a plastic surgeon at UCLA named Marc Hedrick, who was doing some interesting tissue work. Curious, Calhoun arranged a sit-down with Hedrick. After some pleasantries, the surgeon dropped his bombshell: We’ve found stem cells in fat tissue. And it’s the mother lode. The cells are in the padding around hips, thighs, abdomen, and flabby upper arms in such quantity that it isn’t even necessary to culture them—get them to grow and proliferate in lab dishes—to harvest an abundant supply. There is roughly one adipose stem cell per 100 fat cells. (By comparison, bone marrow contains one per 250,000 to 400,000 cells.) “Marc said, we can get these cells out, it has nothing to do with embryos, and their potential is enormous,” Calhoun recalls. “I loved him the moment I met him.” That love was worth $1 million, the amount of MacroPore’s money that Calhoun invested in the company Hedrick was starting, called StemSource.

By 2002, Calhoun had persuaded MacroPore’s board to sell a division of the company to Medtronic, the big medical-device maker, for $21 million. Calhoun turned around and used the cash to buy StemSource, inking the deal in October 2002. (MacroPore changed its name to Cytori Therapeutics in July 2005.)

Although StemSource’s original business plan had been to bank stem cells, once it had been acquired by MacroPore, the focus switched to therapeutic uses for those adipose stem cells. Since Hedrick’s surgical practice focused on children with facial defects, he thought the cells could be coaxed to make bone in kids with a cleft palate. But as he and his UCLA team did more studies, Hedrick says, “we realized that although the cells could make bone, what they were really good at was making a new blood supply. We felt like if we could target that, it would be the key to every ischemic disease,” in which tissue dies for want of an adequate blood supply—and therefore oxygen. “That led us to reconfigure the company to investigate using the cells for heart attack patients.”

As he and his team conducted rodent studies for heart disease (at one point, Cytori had hundreds of animals in its labs), Hedrick thought if adipose stem cells could yank heart tissue back from death’s door by restoring blood flow, maybe the cells could keep other tissue alive and healthy. The radiation that women typically undergo after lumpectomy or mastectomy, for instance, damages the surviving tissue and destroys the local blood supply. “The tissue gets hard, and that makes it difficult to reconstruct or put an implant in,” Calhoun says. And thus the idea of using adipose stem cells to reconstruct the breast was born.

After $200 million in R&D, Cytori had its magic box. Called the Celution system, it transforms liposuctioned fat into life-changing stem cells.

By 2003, Hedrick and Calhoun were pushing ahead with research on using their stem cells to repair hearts damaged by heart attack or chronic disease. But at the same time, they were

grappling with the challenge of repairing patients after partial mastectomy and lumpectomy. It's something that's always been a problem for surgeons: Building only part of a breast with conventional methods, it turns out, is more difficult than constructing a whole new one, because it requires what UCLA's McGuire delicately calls "local tissue rearrangement and/or flaps rather than implants." In other words, the doctor squeezes and smooshes and moves tissue to fill in divots and missing quadrants and, with luck, turns what might have been reduced to an A cup during a cancer operation into a match for the B or C on the healthy side. The result, alas, can be "very much less than optimal," McGuire admits. "It's difficult to re-create the shape." And ironically, given how grateful most breast cancer patients are if they can have a lumpectomy rather than a total mastectomy, such breast-sparing surgery can leave a woman with an aesthetically irreparable breast. With tumors smaller than an inch across, lumpectomy leaves a gouge of up to twice that size, says surgeon Jan Vranckx of Leuven University Hospitals in Belgium: "Breast-conserving surgery is good at keeping the cancer from returning only if it is followed by radiotherapy, but that leaves scars and rigid, badly healing tissue. Yet the defects are often regarded as too small to do a full reconstruction."

Calhoun and Hedrick wanted to test their cells on the damaged breasts that other doctors couldn't be bothered with. But Hedrick knew that bringing adipose stem cells into the clinic required more than biology. It also required technology. When Hedrick originally outlined his vision for Calhoun in 2000, he showed him drawings of a device to isolate the stem cells from liposuctioned fat en masse. "We were thinking a box," Hedrick says. "We need some kind of box."

After $200 million in R&D, the "box" became the Celution System. It looks like a souped-up photocopier. But instead of taking in originals and spitting out replicas, it turns liposuctioned fat into breast-making gold. The process to fix a lumpectomy divot begins when a surgeon pierces a patient's tummy with a syringe and sucks out about 360 cc (12 fluid ounces) of fat, which is the pink-orange color of a Pacific sunset. Each syringe takes about five minutes to fill; to treat an average divot requires eight to 10 syringes' worth. The fat is squirted into the Celution device. A proprietary mix of enzymes digest the scaffolding that holds the tissue together, freeing the cells; the centrifuge separates the adipose tissue from the stem cells, which form a pellet at the bottom of the tube. Those cells are then combined with some of the remaining liposuctioned fat-tissue cells. The result, now a pale pink suspension containing millions of the stem and regenerative cells, is ready to go. The whole process takes about two hours.

It's worth pausing here to ask just what, exactly, these magic cells are. Cytori calls them adipose-derived stem cells, or adipose-derived stem and regenerative cells, and sometimes adipose-derived progenitor cells. "These things have gone through the ringer in choosing a name," says biomechanical engineer Kent Leach of UC Davis, who has used whatever-they-are to treat bone cysts in racehorses. A stem cell, by definition, is able to differentiate into any of the 200-plus kinds of cells in the human body, just as the cells of a days-old embryo can (and do). Cytori's are unlikely to ever show that range of differentiation. But they can differentiate into fat, bone, and muscle—among other tissues—depending on which signaling molecules they are exposed to. In a petri dish, the scientists provide those "this is what you will be when you grow up" molecules. In nature—that is, an embryo in a womb—biology somehow does.

Now that they had their box, the Cytori team faced one more hurdle: finding suitable subjects. "There aren't good animal models for breast reconstruction after cancer," Hedrick says. "That's why we went to humans so soon."

They found their humans in Japan, where the company had connections to surgeons through their business partners. But Japan made sense for another reason: There, the disfigurement of a mastectomy or lumpectomy is tantamount to social banishment. Much of a traditional woman's social life centers on public baths, and those whose breast cancer has left them deformed seldom go. When Keizo Sugimachi, a surgeon and president of Kyushu Central Hospital in Fukuoka, learned what Cytori was developing, he launched an investigator-initiated (as opposed to Cytori-sponsored) trial, dubbed Restore 1. Over the course of six months in 2006, he treated 20 women who'd had a partial mastectomy two to five years before. It was also the first clinical use of Cytori's Celution System. Hedrick assisted on nearly all of the procedures and helped orchestrate how each would progress. They developed it all on the fly, using a lot of guesswork. How much fat do you extract? How many cells do you add back into the mix? How do you combine the liposuctioned fat with enzymes and growth factors and the other magic potions (all trade secrets) in the Celution machine? Do you overtreat, giving a woman more cell-enhanced tissue than you think is needed in case some of it doesn't take? Where do you make the incision in the breast to inject the cells? How do you deal with scarring from the radiation most mastectomy patients get after surgery? "I think we just guessed right," Hedrick says. "We solved a lot of the problems in the first operation. If it didn't work, it was because we put too much in, or didn't treat the scar, or didn't prepare the tissue bed right."

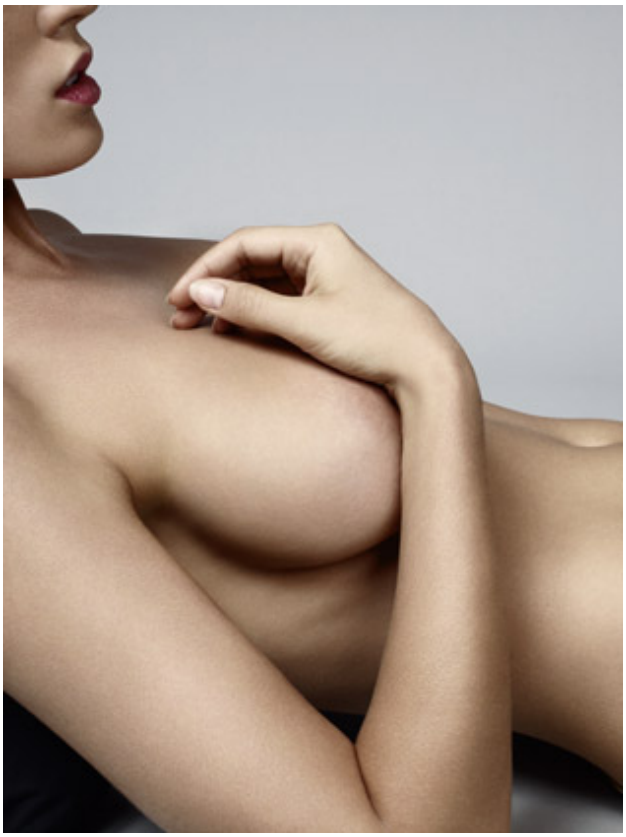


Photo: David Slijper
Makeup: Thorsten Weiss/Community NYC; Hair: Seiji/ The Wall Group; Stylist: Young-Ah Kim

They got better with each case, improving the protocol as they went. In December 2007, Sugimachi told the San Antonio Breast Cancer Symposium that all 20 of the women in Restore 1 tolerated the procedure just fine, none had an immune response, and 79 percent were satisfied with the outcome. There was no significant loss of breast size between one month and the final assessment 12 months later. That was a crucial barometer, given what happens when plastic surgeons inject fat alone, which was a popular cosmetic-surgery technique in the 1980s and 1990s: The injected fat tended to vanish into the surrounding tissue several weeks later like butter into the crannies of a hot English muffin. (Women who opted for this method were encouraged to think of breast enhancement like a dye job—once the effect fades, go back for another session.) But Cytori's adipose stem cells stuck around.

This is because Cytori's cells are not becoming breast tissue, as you might assume if you heard that someone was using stem cells for boob jobs. You don't sprinkle the cells in petri dishes and come back in a few weeks to find a crop of breasts. Instead, the fat cells in the Celution mixture provide the volume, filling the divot in the lumpectomy, the missing quadrant in the quadrantectomy, or the empty skin pouch in the mastectomy. Think of them as the big dumb grunts of the battalion. The regenerative cells in the mixture encourage the growth of a blood supply. They're the clever engineers who provide the supply lines that the fat cell grunts need to survive. And that combination is what promises to distinguish the breasts built with—and now let's switch to the more accurate term—adipose regenerative cells from those built with fat injections alone. "If you give the tissue blood, it will survive and not be reabsorbed," Leuven University's Vranckx says. Sensation is about as good as before since the relevant nerves are in the skin and muscle (and, with lumpectomies, the nipple remains intact).

It's the cells' ability to induce the formation of blood vessels, however, that also makes them attractive as therapy for ischemic heart disease. Although some researchers have claimed that adipose regenerative cells can differentiate into epithelial cells, which can form capillaries and other blood vessels, the evidence is pointing to something more modest but no less useful: The cells churn out proteins, among them vascular endothelial growth factor, that induce surrounding cells to form blood vessels. As a result, cells that had been starved for blood and therefore oxygen are suddenly awash in both.

If the science part of this was figuring out how to process the fat in the box, the art comes in doing the injections. You don't take a big syringe full of the stuff from the Celution machine and cram it into the breast as if you were filling a cannoli. You meticulously inject hundreds of tiny dollops, like a pè2tissier making little rosettes with a piping tube on a fancy cake. To accomplish that, Cytori created the Celbrush. It has a blunt tip to make tiny cuts that break the scar tissue, transforming it into a biological mesh. As the Celbrush is moved, the surgeon turns a wheel,

which releases the tissue half a cc at a time. “You do that hundreds of times and you create a lattice with stem cells,” Hedrick says. Adds Calhoun, “It’s really as close to sculpture as anything done in plastic surgery today.” The injection area is not painful afterward, while the liposuction site is only slightly sore. Patients go home that day.

A clinical trial in Europe in 2008 and 2009, called Restore 2, used the next generation of the Celution machines, also with tantalizing results. It studied women who’d had a partial mastectomy, including Irene MacKenzie, 51, who works for the national health service in Scotland. She was diagnosed with breast cancer six years ago, and after a partial mastectomy was told by her surgeons that reconstruction wasn’t necessary, let alone possible.

MacKenzie had heard about a surgeon, Eva Weiler-Mithoff of the Glasgow Royal Infirmary, who might be able to help. MacKenzie sought her out and in the spring of 2008, Weiler-Mithoff called and told her about the Restore 2 trial, for which she was a lead investigator. MacKenzie signed on. She liked the results but in January 2009 returned to Weiler-Mithoff for another go. “She told me maybe we should have put more cells in, so I went back,” says MacKenzie, who now pronounces herself delighted with her new breast. In December 2009, Weiler-Mithoff told the San Antonio Breast Cancer Symposium that the procedure improved breast deformity in most of the 31 patients who were assessed, with the new breasts holding up for the six to 12 months that the women had been followed. How the new breast felt and moved on the chest wall kept improving. “One of the most striking aspects of the trial was how happy the patients were” with their new breast, says Weiler-Mithoff, who compares the injections to putting in “little pearl strings of fat.” The women, she says, “felt whole again.” MacKenzie’s need for a touch-up, however, shows that not everyone gets the desired results the first time. In fact, all but one of Vranckx’s post-mastectomy patients needed at least two procedures. The Celbrush, after all, is the instrument of an artist. “So far, we’ve been able to repair defects that we couldn’t before,” Vranckx says. “But it can take eight hours to do two breasts—eight hours bringing one droplet after another to the breast. It’s sculpting, and not everyone can be a sculptor.”

Restore 1 showed that Cytori’s cells could rebuild breasts lost to cancer. The next logical step was trying it out for breast augmentation. Perhaps not surprisingly, once again this happened in Japan. The country has a strong and entrenched cultural prejudice against putting anything foreign into one’s body; organ transplants were slow to be adopted in Japan and still remain rare. But if that ick factor is the immovable object, the Western-inspired desire for bigger breasts is the irresistible force.

In late 2007, cosmetic surgeon Tatsuro Kamakura of Cosmetic Surgery Seishin in Japan began a study of the Celution System for breast augmentation, eventually enrolling 20 women. In 2008 he told the Congress of the Japan Society of Aesthetic Surgery that the first three patients kept their new volume and that the tissue remained soft and natural. He had injected an average of 160 cc of stem-cell-loaded fat droplets, boosting breast circumference an average of 4 centimeters (1.6 cup sizes). In commercial use, a new breast could run about $2,000 to $2,800, depending on physician charges. “It’s probably a $1 billion market,” Calhoun says. “You can buy an appliance with a 30 to 40 percent unpleasant rate or you can use your own cells. Which would you choose?”

But the possibilities aren’t boundless. “It’s not a substitute for implants for women who want to look, um, unnaturally large,” Hedrick says. “You can’t take a flat-chested woman and make her look like a dancer at a strip club. We’re not targeting that market. If they don’t care about looking natural, let them do silicone. The goal of this is a natural, soft-tissue feeling. Plus, there is a whole new market of women who would love another 100 to 200 cc but would never have an implant. I think that’s bigger than the current breast implant market”—a sea of women who wouldn’t consider a silicone implant but who would be intrigued by the opportunity to have their breasts plumped with cells from their own bodies while reducing the fat in their hips and abdomen to boot.

Typically, experimental medical treatments go through years of testing in animals before they reach people, but as women in Japan were being treated with Cytori’s cells, the company was still conducting studies on animals to assess the safety of the procedure. As recently as 2007, Cytori’s principal scientist, John Fraser, was performing key experiments on mice. The problem is that the reason adipose regenerative cells work—inducing the formation of blood vessels—is also the reason they might be dangerous, especially to cancer survivors. Such angiogenesis, after all, is what allows metastatic tumors to thrive. But Fraser’s experiment showed that in mice, the adipose regenerative cells did not trigger the formation of breast tumors, promote their growth, or cause them to metastasize to the lungs. The human trials have not followed the women for very long, so it is still possible that a dangerous side effect like cancer—much worse than needing a touch-up, as Irene MacKenzie did—will emerge.

“People do challenge me: ‘Why are we moving so fast?’” Fraser says, standing in a corridor adorned with posters of scientific results he and his colleagues have presented at conferences. Hedrick jumps in: “It’s because we think like doctors taking care of patients. We have a lot of doctors working here. When we felt there was clear sailing, we hit the gas pedal. Where we felt there were obstacles, we slowed down.” Adds Fraser, “We’re not cowboys.”

They might find themselves in an industry shoot-out, however, as the allure of adipose-derived stem cells has drawn other companies to the field. The most flamboyant is AdiStem, based in Hong Kong. Its process, like Cytori's, begins with liposuction. The fat is mixed with enzymes and centrifuged, then the precipitated cells are centrifuged again. That, however, is where the similarity ends. AdiStem next mixes its cells with plasma and exposes them to laser light, the company claims, to photoactivate stem cell functionality. CEO Vasilis Paspaliaris says the resulting cells can then potentially be used to treat autism, idiopathic pulmonary fibrosis, osteoarthritis of the knee and hip, type 2 diabetes, acne scarring, and hair loss, as well as in post-lumpectomy cosmetic reconstruction. Although Paspaliaris says all the results seem promising, he believes "the most convincing" are those for the face. Some Los Angeles cosmetic surgeons are already using the AdiStem process with face-lifts.

These claims have raised eyebrows. It hasn't helped that AdiStem posts videos of its autism "treatments" on YouTube or that there are no peer-reviewed scientific papers on use of photoactivation to increase stem cell functionality. AdiStem "is one of many small opportunists who are jumping on the adipose-derived stem cell bandwagon," Calhoun says. "At the right time, we will protect our markets and enforce our patents, but at present it seems to be a potential waste of capital, resources, and energy." Cytori's bigger concern is that although these companies may pose no competitive threat, they are a PR disaster waiting to happen.

Although regulators in Europe and Japan were satisfied with the animal and human studies Cytori submitted for approval of the Celution machine, the US Food and Drug Administration has yet to weigh in. Vranckx, who met with FDA officials, says that despite Fraser's mouse experiment, the agency is worried about injecting blood-vessel-promoting cells into patients who have had breast cancer. But although Cytori can't market its Celution System without FDA approval, doctors can purchase it, just as they can prescribe a drug approved for one use for a completely unrelated purpose but can't advertise it for that use. In fact, the FDA takes the position that as long as cells are removed and returned to the same person in one procedure, a physician does not need approval to do it. Still, without FDA approval, Cytori can't promote its device; without promotion, it is unlikely to be widely adopted. Cytori is currently in discussions with the FDA for permission to conduct a clinical trial of its device. If the trial is a success—in particular, if there are no adverse effects from the cell injections—the next step would be to seek FDA approval for the entire process or conduct a second trial. Although a lot could still go wrong—surprises in clinical trials have killed many an experimental drug and device—Calhoun hopes positive results will launch his billion-dollar vision of regenerative medicine.

There is one other key feature that the next-generation Celution machine shares with a photocopier, as Calhoun demonstrates. Just as the latter has a touchscreen control panel that displays options (paper size, number of copies, magnification), so does the Celution, only here, the options are organs. "See? There's a picture of a breast, a heart, a disc in the back," he says. "You push that and the machine loads different software, which adds the right drugs," reagents, and other biochemicals to the liposuctioned fat cells. He envisions an iPhone-like business model, with individual doctors devising apps to repair different organs with the perfect slurry of adipose regenerative cells. If it works, the breasts on his laptop will have plenty of company.

Sharon Begley (sbegle@aol.com) *is science editor and a science columnist at* Newsweek.

Pages: Previous 1 2 3 4 5 | Full Page | Next

Tags: breast, Chris Calhoun, regenerative medicine, stem cell
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Comments (48)

Posted by: BongoJoe | 10/21/10 | 10:36 am |

This is the best article I've ever read. Have this boob-stem-cell company contact me with an IPO

so that I can invest.
Just think of it… first, they make sure all women can have great boobs, then they cure all sorts of diseases and injuries.

Posted by: MobileUser | 10/21/10 | 10:38 am |

The article mentions creating fat, bone, or muscle from these stem cells. Could an athlete have their fat re-injected to create bigger muscles? Bigger pecs, bigger, biceps, bigger calves?

Posted by: CityZen | 10/21/10 | 10:48 am |

This is a great example of where I think more medical research should head towards: using the body's own ability to heal itself, rather than implanting foreign materials into the body. It's nothing short of fantastic!

Posted by: FriedZombie | 10/21/10 | 11:02 am |

@BongoJoe I'm right there with you, I can guarantee that Warren Buffet is jumping on this bandwagon once they get approved by the FDA, and so am I

Posted by: braino | 10/21/10 | 11:09 am |

Too much text, too little photos. I'm utterly disappointed Just joking Great research.

Posted by: delahaya | 10/21/10 | 11:29 am |

"Breasts simply aren't as necessary as other organs".

I have to disagree with that. Breast are beautiful and utterly necessary. They are the perfect stress relief for your hands, they bounce and sway, they nourish babies – I could go on and on…

Posted by: Techimo | 10/21/10 | 11:38 am |

It's about time we found a good use for stem cells. Hmmm… what else needs to be bigger… rounder… more full…?

Posted by: CityZen | 10/21/10 | 11:42 am |

"Hmmm… what else needs to be bigger… rounder… more full…?"
.
Brains?

Posted by: jgood42990 | 10/21/10 | 2:43 pm |

Company is already public. Symbol is CYTX.

Buy now if you're smart!

Posted by: elgrau | 10/21/10 | 3:01 pm |

agree…the REAL billions to made here would have to be this tech applied to peni (plural??)! My guess is ~75% of all males would want to try it…that's a HUGE market..lol!

Posted by: elgrau | 10/21/10 | 3:07 pm |

That's what she said…

Posted by: kibbles | 10/21/10 | 3:21 pm |

hey i just came here to read the article…

Posted by: Rick4 | 10/21/10 | 5:47 pm |

Dudes! Warn me before you send beautiful almost exposed naked breasts to my office! Luckily

my clerk is the pre-sexual harassment litigious type. Can't wait to read it after I remove it from my locked desk drawer!

Posted by: Soldier_Cynic | 10/21/10 | 6:17 pm |

Nobel Prize for Medicine

Posted by: pacificfurn | 10/21/10 | 6:45 pm |

I like this fact; "and not using the ethically fraught kind of stem cells from human embryos". No babies were sacrificed to create these cures and no federal tax dollars went towards their murder.

Posted by: 8x10 | 10/21/10 | 7:25 pm |

And glad to see the model in the photo does NOT have implants!

Posted by: meathamper | 10/21/10 | 7:35 pm |

I love that URL. …ff_futureofbreasts/

Posted by: tehb2 | 10/21/10 | 9:52 pm |

I like everything about this article!

Posted by: lbuckler | 10/24/10 | 2:05 pm |

The regenerative medicine industry is enjoying double-digit growth. I saw a press release last week which commenting on a career spike in regenerative medicine jobs. I think it was from http://www.regenerativemedicinejobs.com

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Posted by: lbuckler | 10/24/10 | 3:14 pm |

Here's the link to that article from RedOrbit:
http://www.redorbit.com/news/science/1933448/a_career_spike_in_regenerative_medicine_jobs_demands_innovative_business/index.html

Here's a quote: "Most life science companies have now begun investing in regenerative medicine strategies and the trend has even leaked outside of life science to companies such as Google Ventures which has informally identified regenerative medicine as one of their primary areas of interest when looking at companies in which to invest."

In fact GV recently made its first investment in regenerative medicine in a company called Ipierian.

Posted by: tek1 | 10/24/10 | 5:20 pm |

http://www.ketdesing.com

Posted by: blehtastic | 10/24/10 | 8:52 pm |

Finally!
.
This is the best news in medicine that I've heard in a very long time.
.
Soon they'll be able to take the fat from my beer gut to grow me the new liver I'll desperately need.

Posted by: puxnstx | 10/24/10 | 10:32 pm |

It was a very interesting article. I will most definitely follow future research and development in this area of medical procedures. However, I have to say shame on WIRED for the magazine cover. Did they have to stoop that low. I have to tear the cover off to read the rest of the magazine at work.

Posted by: mobileuser22 | 10/25/10 | 10:49 pm |

Great article – but even my 8 year said 'here mom – this isn't appropriate for us' At least mail it with a plain brown cover! Very disappointing.

Posted by: James59 | 11/2/10 | 5:57 pm |

An interesting idea, but I hope this technology can be applied to restoring the male foreskin as well without the cultural taboos getting in the way. There are plenty of men circumcised as infants that don't like it, or wish they'd been left as is. I'm one of them. This should be an option for us.

Posted by: eforblue | 11/2/10 | 11:57 pm |

I bought this issue of Wired because of the cover. Definitely the best cover of the year, take that Maxim!

Posted by: strictmachines | 11/5/10 | 2:52 am |

Interesting article. Does anyone know who modeled for these photos for the cover story?

Posted by: jojo99 | 11/5/10 | 3:42 am |

"CEO Vasilis Paspaliaris says the resulting cells can then potentially be used to treat autism, idiopathic pulmonary fibrosis, osteoarthritis of the knee and hip, type 2 diabetes, acne scarring, and hair loss,…"
—-
OK, so when do we the follow-up story on male hair replacement using this technology? I want details and prices!

Posted by: darkguardian1314 | 11/6/10 | 12:41 am |

Great article but the photos were too revealing for work and on the front cover no less.

Posted by: Weks327 | 11/7/10 | 2:25 pm |

My immature middle-school friends freaked out when they say the cover. They were like, " Dude! why do you have a magazine with boobs on the cover!?" And I had to explain to them what it was really about, and they still freaked out. Here's to an awesome magazine!

Posted by: carrietastic | 11/8/10 | 12:57 am |

http://i4.photobucket.com/albums/y144/Catrolynn/derpd.png
I know someone's probably already done it…but I had to.

Posted by: carrietastic | 11/8/10 | 12:58 am |

agggh crap. Wrong link the first time. Sorry WIRED!
http://i4.photobucket.com/albums/y144/Catrolynn/ujelly.png

Posted by: eforblue | 11/8/10 | 7:07 pm |

Today I took this issue of Wired magazine out of my bag while I was sitting on the subway. The person sitting next to me started to stare in despite. I turned to her and said, "This is your future."

Posted by: williamrandymiller | 11/9/10 | 12:20 am |

Great article. Interesting ideas. Several questions were left unanswered, though. I hope someone actually reads these comments….

Did anyone test the numbers/percentages of stem cells in the fat cells of young and old people? I'm wondering if the body naturally uses those stem cells to make repairs as we age. If so then the ladies who have had these procedures will die young.

Have they tested to see if the stem cells are replenished? I'm assuming they are not. If this is correct then each person has a limited number of these stem cells that can be used. Some day soon it will be possible to grow new hearts, livers, etc. I would hate to be the doctor who had to

inform the poor lady that she could not have a new liver because she used too many of these stem cells in her breasts.

It would seem to me that the ultimate step in this line of research would be to learn how to multiply the magic stem cells. The goal would be to harvest a few of these stem cells, and then multiply them in the lab to get useful quantities, before converting them into blood cells, liver cells, brain cells, or whatever. If you can multiply the stem cells then you have unlimited potential. Are they working on that?

Posted by: Sam10 | 11/10/10 | 1:38 pm |

Great Article but I thought there was way too much fluff around the meat. He could have reduced this article down to 2-3 pages with just the facts about the research and left out all the other information that does not directly relate to the scientific aspects of the study.

Posted by: JonPerlmanMD | 11/11/10 | 2:14 pm |

It is such an exciting time to see the evolution of medicine and plastic surgery. Early data suggests the safety of fat injection supplemented by stem cells in the breast. For years the safety of fat injection to the breast has been questioned (for good reason I feel). If studies confirm safety, both breast enhancement and other organ regeneration will be dynamically improved. This really represents an impending paradigm shift.

Posted by: Redjester | 11/12/10 | 12:02 am |

HI! I was recently on a trip to Denver, CO. On the trip back I stopped at a bookshop located in Dallas Airport. Guess, my dear Wired friends, what I saw?

http://www.flickr.com/photos/josephy/5168775062/

ONLY THE BEST IN TEXAS HAHAHA!

Posted by: mfuenzalida | 11/12/10 | 6:00 am |

I just received my copy of Wired (I live in South America) and having a cover with boobs on it makes it kind of ackward to carry it in public places. I keep explaining people it's not a "gentlemen's magazine"

Posted by: CindyLu | 11/14/10 | 2:23 pm |

I read this article with great interest. Using extraneous fat cells to create new cells is genious! I only have one question…

Where do I donate?

Posted by: crazykitties | 11/15/10 | 8:25 pm |

I call bullshit on this. First the idea of breast cells are being pushed as the next big stem cells, meant for healing. Yet the article clearly implies that women undergoing breast augmentation could do better with this procedure, which does not involve stem cells as much as it involves the transfer of plain old fat cells. To add insult to injury, the article claims that a whopping 25% of breast cancer patients don't have reconstruction, and the assumption is that they don't know it is available! Are you kidding me? Every breast cancer patient I know under the age of 60 has been given the name of a plastic surgeon prior to treatment. This arbitrary number most likely reflects the fact that most breast cancers occur in women over the age of 60! Many of those women would not want to risk their lives with complications of infections and would rather put their efforts into healing.
Shame on you for presenting such lies, that women don't currently have good reconstruction choices after breast cancer! Not one woman I know is willing to risk a recurrence in exchange for more socially acceptable breasts! By the way, I had both of mine removed for breast cancer, and my reconstruction with silicone implants has been no big deal.
If it were, I am certain that I, like many women, could find a reason to live without my breasts. This article insults breast cancer patients.

Posted by: ugbechie | 11/19/10 | 6:59 am |

thank for the best

Posted by: RBC | 11/19/10 | 2:47 pm |

It's too bad that you had to stooped to having a cover like this, because I tossed the magazine without reading it. Is your editorial staff still in Junior High? Certainly you can write an interesting article on a new development in medicine without having to draw attention with soft porn.

Posted by: magnatronic | 11/19/10 | 3:26 pm |

RBC, you threw out the magazine without reading it just because of the cover? Isn't that a little extreme? I don't understand why breasts are so offensive; not just to you RBC but also to all the other readers who have such a strong reaction. I liked the cover and even more, I liked the article. I hope all of these prudes don't keep Wired from going out on a limb with future covers.

Posted by: stkcarm5 | 11/19/10 | 5:38 pm |

Just like the regenerative science used for breasts regenerative science is being turned to restoring the prepuce or foreskin, ridged band, frenulum, and nerve endings lost to circumcision by foregen at foregen.org

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Posted by: lnpierce | 11/20/10 | 8:57 am |

This is by far one of the most amazing articles I've read. Wired, the only magazine I subscribe to. The only magazine I read cover to cover. I hear Wired.

Posted by: slinkymoon | 11/20/10 | 5:33 pm |

"Breasts simply aren't as necessary as other organs".

I also disagree. Having the ability to feed offspring is tremendously important. Breast feeding is healthier for the immune system of both the mother and the child. And in times of intimacy? It is known that breasts play an important role in a woman's ability to enjoy sex. Boys, unless you're content to have her fake her orgasms, you must pay special attention to her breasts at the outset. A woman's sensuality is just as important as your need to get off. Aren't I stating the obvious here on both counts?

Posted by: tulayim | 11/20/10 | 8:47 pm |

travesti

Posted by: amaya | 01/6/11 | 10:14 pm |

Am I the ONLY ONE who found something wrong with BongoJoe's comment? You REALLY think it's better to give women better breasts FIRST, and THEN save people's lives? How could you put physical looks above life itself? That is such an awful, shallow thing to say. I really hope your spouse (if you have one that is) does not get breast cancer; going by what you're saying it sounds like you would be more concerned with scheduling reconstructive surgery for them than chemotherapy and other appointments that they actually need. You know, so they could LIVE?

Not to mention, you say that they should "make sure ALL women can have great boobs". Are we living under a dictatorship? I'm sure there are women out there who are fine with their breasts and don't want any enhancements done to them. I know I'm one of them. So stop acting like we're going to live in a fantastic utopia where every woman will have DD-cup sized breasts.
