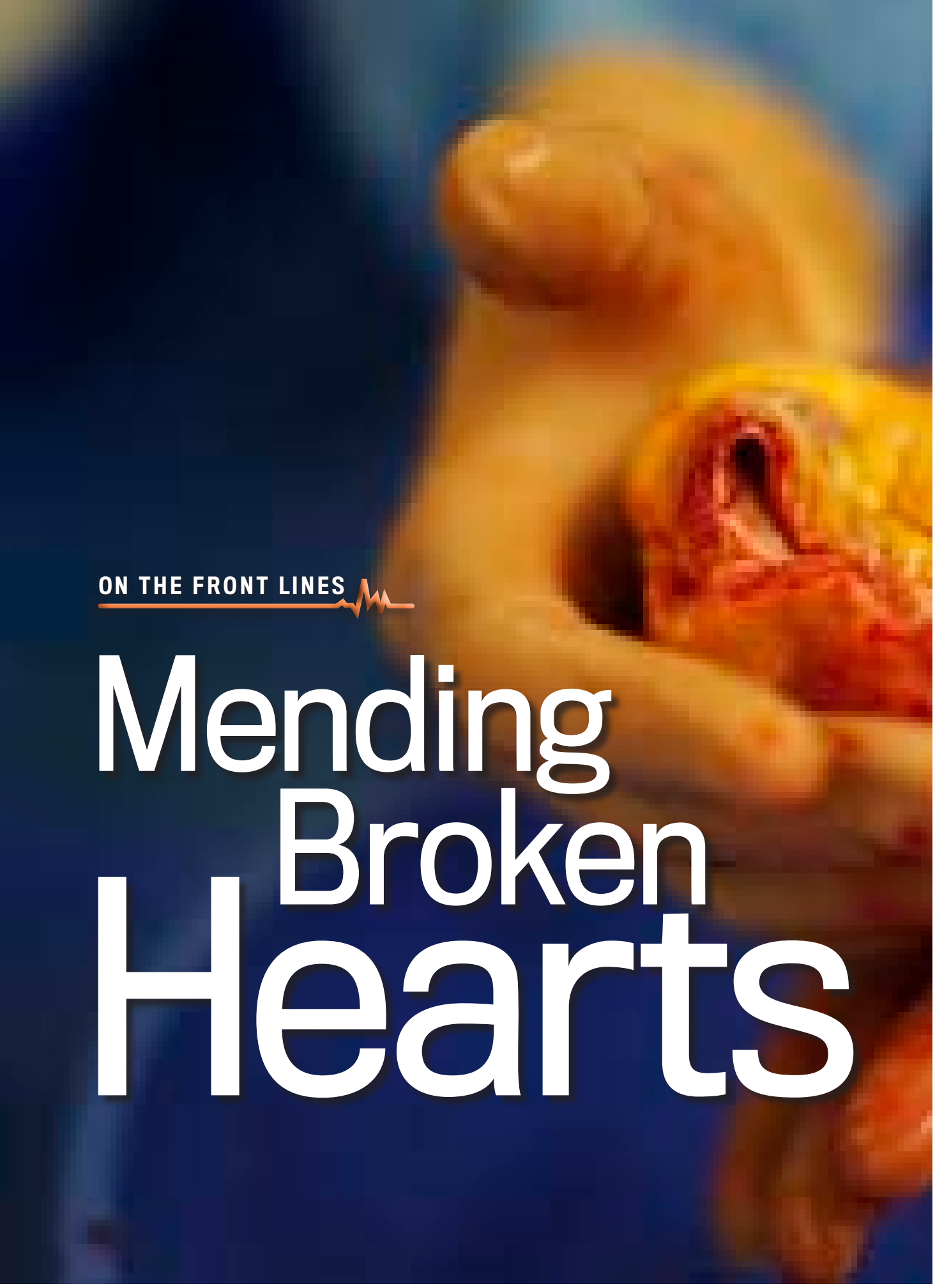

ON THE FRONT LINES

Mending Broken Hearts

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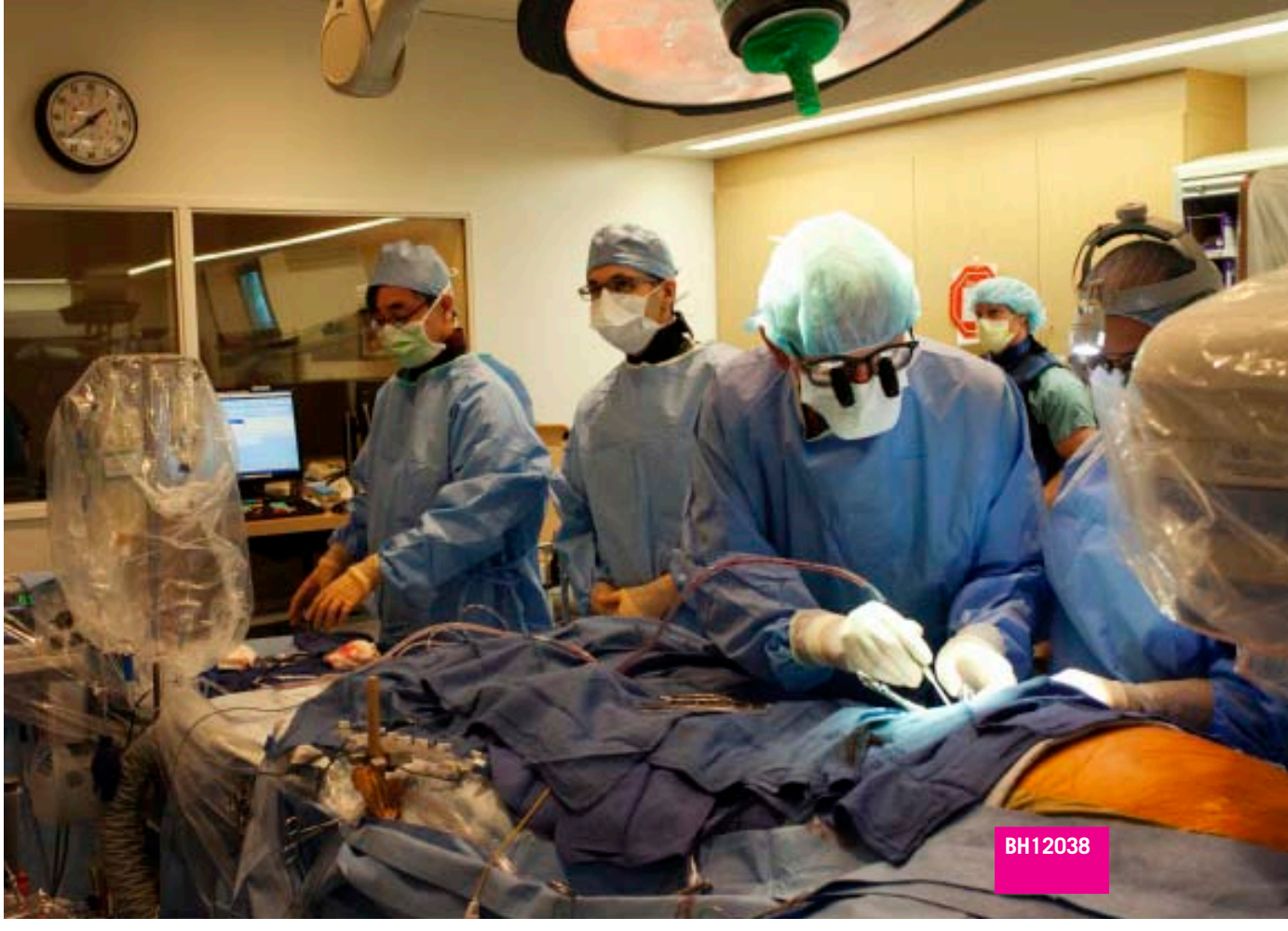
This donor heart is on its way to Cedars-Sinai Heart Institute patient Christine Moore.



STEP INSIDE THE OPERATING ROOM AT CEDARS-SINAI FOR TWO HEART-VALVE PROCEDURES AND A TRANSPLANT

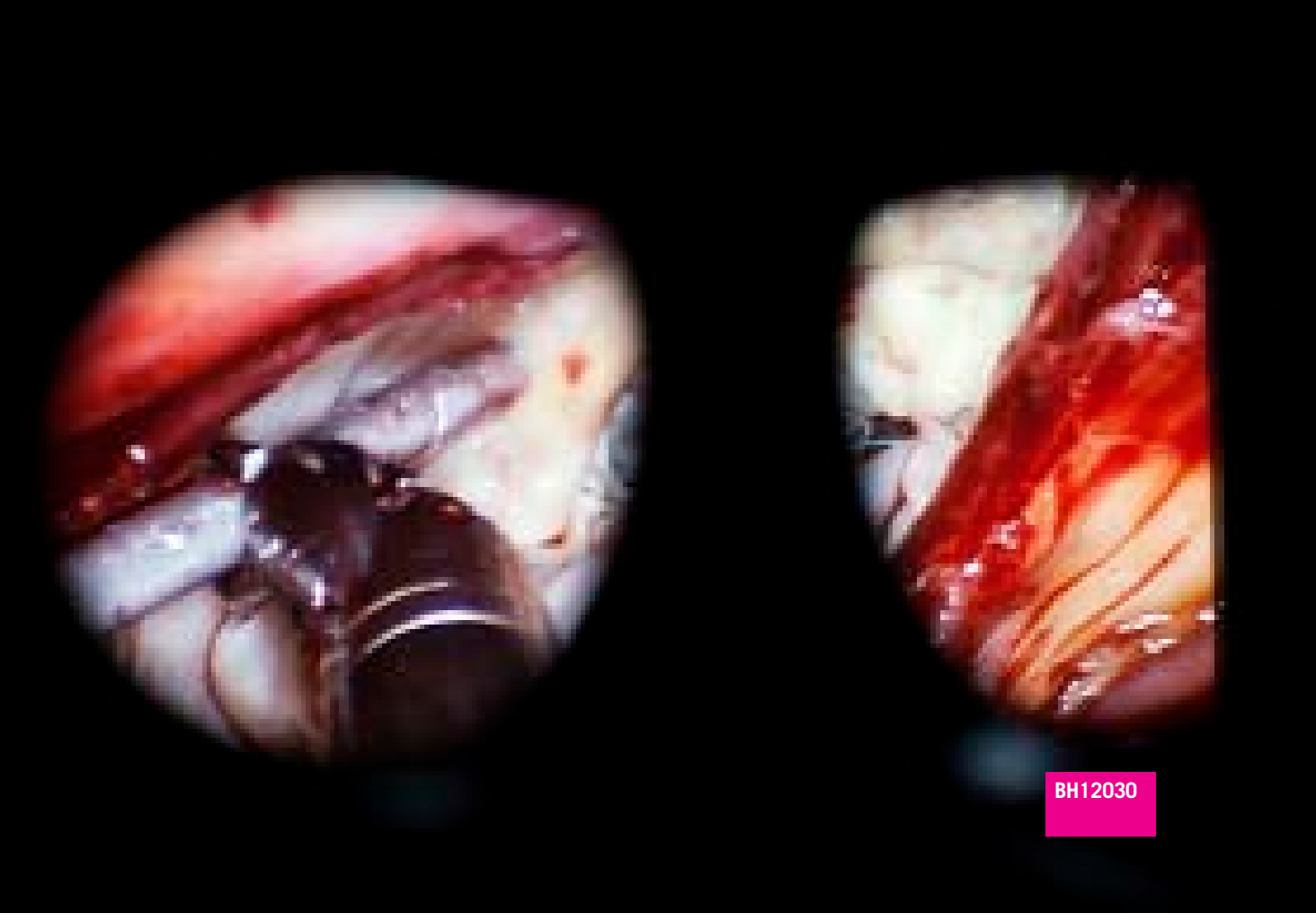
BY KATE GREENE

LOS ANGELES—Michelle Johnson, 40, doesn't have a heart. Or rather, the pump inside her chest is manufactured by SynCardia Systems. For months, the mother of three from San Diego has been tethered to a compact machine that she wheels around while she waits, once again, for the phone call. Diagnosed with congestive heart failure in her late 20s, Johnson received a transplanted heart in 2010; her body rejected it this past January. The Total Artificial Heart and its constant whooshing blurp-blurp should sustain her until another donor heart can be found; until then, she can't drive and has had to stop working as a unit clerk at the University of California San Diego Medical Center. The portable battery lasts two hours ("I can get my nails done, and that's about it"), so she always must bring a backup along as she runs errands and sees her doctor at Cedars-Sinai Medical Center for biweekly checkups. As spring turns to summer, Johnson is again nearing the top of the transplant waitlist. "I'm just ready to get back to normal life," she says.

The art of repairing injured hearts has come a very long way since the first successful cardiac operation took place

QUICK FIX. Two days after a new aortic valve was snaked through his femoral artery to his heart (top), Robert Noonan is cracking jokes and getting set to head home. Open-heart surgery would have meant a hospital stay of over a week.

Photography by Daryl Peveto for *USN&WR*



in 1896, in Frankfurt, Germany. A 22-year-old man, stabbed in the chest, had suffered a wound in the lower heart chamber that pushes blood to the lungs. Surgeon Ludwig Rehn sliced through his ribs, using finger pressure to control bleeding and a needle and silk thread to suture the cardiac muscle. The patient lived. But heart surgery wouldn't truly hit its stride until more than 60 years later, when a safe heart-lung machine arrived to take charge of the pumping while the surgeon worked on a chemically calmed heart through ribs cracked wide. Today's repairs rely on an ever-expanding array of high technology, from ultra-precise imaging and surgical moves executed by robot to man-made heart parts—and hearts. They also depend, of course, on the sensitivity and skill of the physician wielding the scalpel.

U.S. News spent several days in May at Cedars-Sinai, watching several of the Heart Institute's eight surgeons at work. The center, No. 16 in cardiology and heart surgery in the 2012-13 *U.S. News* Best Hospitals rankings, has been first in the number of adult heart transplants performed in each of the past two years (87 in 2011, plus two heart-lung transplants). One morning brought the minimally invasive replacement of an aortic valve, which controls blood flow away from the heart. Traditionally an open-heart surgery, here at Cedars-Sinai a synthetic valve is snaked up into the patient's heart through the circulatory plumbing by pushing it through the femoral artery from an incision at his groin. The repair of another patient's mitral valve, between her heart chambers, involved an incision between her ribs and surgical tools wielded with exceptional dexterity by a precision robot. Finally, word came that there would be a heart transplant, the hospital's 40th of 2012.

A few months before this Monday morning, Robert Noonan, a retired paper salesman from Thousand Oaks, Calif., found he was struggling to catch his breath. "The internist said I had a tight valve, and if I didn't fix it I'd die," says Noonan, 79. Specifically, he had aortic stenosis, in which the three-leaved flap between his left ventricle and the aorta, the large artery carrying blood away from the heart, was broken, unable to open completely and restricting blood flow. Noonan had no intention of dying, he says. So he talked to doctors at Cedars-Sinai and joined a clinical trial to fix his valve in a way unavailable to him a couple of years ago. The procedure should "add years to his life and life to his years," says Raj Makkar, director of interventional cardiology and the cardiac catheterization lab.

At 7:30 a.m., Noonan is prepped and wheeled to the "cath lab" for a procedure in which a series of wires and tubes are inserted into the femoral artery in his right leg. Just as a network of underground caves can take miners to a cache of gold without the need to blast in from above, the femoral artery

ROBOT ASSIST. **Surgeon Alfredo Trento controls the robotic da Vinci Surgical System (above), peering through the viewer to see what the camera sees as he remotely repairs** Betty Trusel's **mitral valve and maneuvers a wand (upper left) to freeze heart cells and correct her irregular heartbeat. Below, Trusel gets a post-surgery workout.**

leads the surgeon straight to the aortic valve. A compressed artificial replacement will be snaked up to Noonan's heart by a special delivery catheter guided by X-ray.

The so-called transcatheter aortic valve replacement uses a valve that got a Food and Drug Administration nod last year for people too sick for the standard open-heart version of the procedure. But it may hold great promise for other people with aortic stenosis, too, experts say. "Eventually, everybody would like to do this procedure on even ideal candidates for [open-heart] surgery, because it's much less invasive," says Makkar. But it's not without risk, and more data are needed on how well catheterization serves people who could undergo a full-fledged operation with only moderate risk, like Noonan, or with low risk.

Since Noonan has had surgery affecting his right femoral artery before, a vascular surgeon gets the ball rolling, to ensure the artery is hearty enough to stand up to an inserted catheter. It is. Within two hours, Makkar has easily slipped the new valve into place, and expanded it to fit the opening of the aorta, pressing the leaves of Noonan's faulty valve to the vessel walls. The catheters come out, and Noonan is taken to intensive care to recover. He is walking and cracking jokes within a day, and by Wednesday, he is well enough to go home. With open-heart surgery, his hospital stay would have lasted more than a week.

Tuesday's valve repair requires more working room than the sliver of space provided by a catheter. So surgeons turn to the da Vinci Surgical System, a robotic innovation whose slender

PRE-OP VISIT. Cardiologist Jon Kobashigawa (second from left) checks in on Christine Moore before her transplant.

tools and 360-degree action can outmaneuver even the most adept human hands. The da Vinci has found its way into more than 1,700 hospitals worldwide since 2000, when the FDA gave it a green light. Cedars-Sinai surgeons have been using the system since 2004, controlling the cutting and suturing from a console at one side of the OR while robotic arms follow their commands, without so much as a tremor, at the table.

Today's problem: Betty Trusel's mitral valve, whose job is to regulate the flow of oxygen-rich blood from the left atrium down to the left ventricle, where it is then pumped out to the rest of the body. Her valve doesn't close completely, allowing blood to leak back into the atrium. Trusel, 85, has known about her valve problem for years, but found it didn't interfere much with her life at home in Los Angeles, where she worked until March with individual clients as a hair and makeup artist after a long career at MGM Studios. But lately it has become increasingly difficult to breathe.

Again, a mitral valve repair usually would be an open-heart surgery. But Alfredo Trento, director of cardiothoracic surgery, has thought it best to avoid the trauma, given Trusel's age. In the OR, a 2-inch-long incision is cut into the right side of Trusel's chest, the opening stretched wide. Through her ribs, the doctors insert instruments and a camera aimed toward the heart. Trusel's heart must be completely still while it's worked on, so the surgical team plugs the heart-lung machine into the vessels coming and going, temporarily diverting the blood flow. They inject her with a potassium solution that stops her heart for 30 minutes at a time.

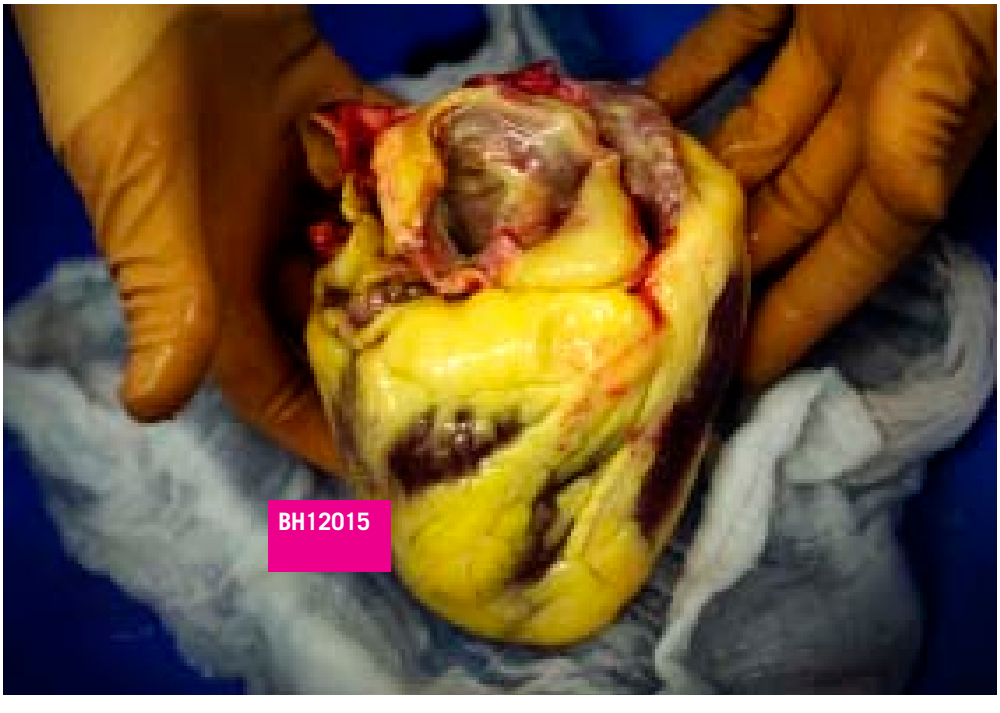
Trento sits at the da Vinci console about 10 feet away, grabs the machine's controls, and looks into binocular eyepieces to access the inserted camera and see the heart in 3-D. He knows from Trusel's echocardiogram that her mitral valve is floppy, but when he sees it on the screen, he is troubled by its large size. "Let me see what I can do," he says, moving the controllers as robot-held scissors and clamps cut and remove the extra mitral valve tissue, snipping heart strings known as chordae tendineae that connect the valve to the heart ventricle wall.

Before he tightens the remaining valve tissue with permanent sutures, Trento addresses another problem, Trusel's irregular heartbeat. To do this, he applies a frosty wand containing liquid nitrous oxide at minus 75 degrees Celsius to her heart tissue. The extreme freeze kills off cardiac cells in a complex pattern, forcing beat-inducing electrical signals to move in an orderly fashion rather than the chaotic paths that cause the irregularity.

Two days after her surgery, Trusel is wearing makeup and walking around the intensive care unit with her nurse for exercise, clearly no longer troubled by a lack of oxygen. In fact, she takes her laps so quickly the nurse repeatedly urges her to slow down.

It was 3 o'clock Wednesday morning when Christine Moore of Orange, Calif., 62, got her summons. She packed her bag and headed with her husband to the hospital. "There was no traffic," says Moore, a part-time receptionist at the Orange Senior Center. "We made it in an hour."

First diagnosed with an irregular heartbeat in 1980s, Moore had a stroke in 1996 and about 10 years ago began experiencing edema, the swelling characteristic of a failing heart caused by excess fluid trapped in the tissues. She con-



RENEWED HOPE. **Procurement technician Jacqueline Anderson (above) wheels in** Christine Moore's **new heart, at left. Surgeon Alfredo Trento has opened Moore's chest in preparation (right) and finishes Cedars-Sinai's 40th transplant of 2012 a mere two hours after putting the heart in place. Donor hearts travel no longer than four hours and are inserted within minutes of arrival.**

trolled the swelling using diuretics well enough until last year, when Jon Kobashigawa, her cardiologist, suggested she might be ready for a heart transplant. Moore's condition, known as restrictive cardiomyopathy, isn't completely understood, but it means that her heart just doesn't stretch properly. The situation became dire in April, after Moore gained 27 pounds of fluid weight and had trouble breathing. She was moved to the top of the list for patients with type B blood in need of a transplant.

As Wednesday dawns, Moore settles in with her husband for a long day of waiting, with no food or drink. "I'm very thirsty and my mouth is bored," she observes. Her new heart will be coming from another state, and the retrieval must be coordinated with the surgical teams for the other people receiving organs from the donor. Surgeon Danny Ramzy must fly to the donor's hospital, remove the heart, and fly it back to Cedars-Sinai.

Finally, at 6:30 p.m., Moore is asleep on the table and Trento has made his first incision. Her sternum is cut with a saw, her rib cage pulled open, and her blood is soon circulating through the heart-lung machine. Ramzy is expected to return just before 7:30, and, right on time, he delivers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STILL WAITING. When she arrives for a checkup, her artificial heart powered by a portable battery, Michelle Johnson **learns she's back on the transplant list.**

the donor heart on ice in a red cooler. At 7:35, Trento frees Moore's own sick heart and puts the new one in its place. He attaches the five major channels that bring blood into and out of the heart: the left atrium, the inferior vena cava, the pulmonary artery, the aorta, and the superior vena cava.

Trento, 61, has been performing heart transplants almost half his life, beginning 15 years after Christiaan Barnard pioneered the procedure in 1967 in Cape Town, South Africa. That patient, a man in his mid-50s, lived for 18 days before dying of pneumonia contracted while on immune suppressant drugs to keep his body from rejecting the heart. By 9:30, Trento has completed one of his fastest transplants ever. In eight to nine days, he says, Moore should be able to leave the hospital. Her full recovery will take about two months.

To make her immune system as hospitable as possible to the new heart, Moore will at first take a relatively new mix of anti-rejection drugs that includes tacrolimus, mycophenolate, and prednisone, and after six months just tacrolimus and mycophenolate at reduced doses. A 2006 study led by Kobashigawa, director of Cedars-Sinai's heart transplant program, found that this combination significantly lowered the odds of rejection compared to standard treatment with cyclosporine. Cedars-Sinai claims one of the lowest first-year rejection rates in the country at 5 percent.

At the moment, about 3,200 people in the United States are on the waiting list for a heart transplant. Here in Region 5 (California, Utah, Nevada, New Mexico, and Arizona), the median time on hold is 108 days. Various factors push people higher on the list: They are in the hospital, or taking high doses of medication, or require mechanical pumping help from a ventricular assist device or a full artificial heart. Each week on Friday, the Cedars-Sinai transplant team gathers to present new candidates and discuss the condition of the people already on the list. It's at these meetings that people who have recently faced health setbacks get promoted closer to the lifesaving operation.

While some people are born with heart defects that lead to a transplant, like Moore, others require a new heart because of the damage done by small and large heart attacks over a lifetime. In the not-too-distant future, predicts Eduardo Marbán, director of the Cedars-Sinai Heart Institute, an infusion of stem cells may provide a better answer for these patients. "We hope to create a viable alternative to transplants for patients with advanced heart disease," says Marbán, who, with colleagues, developed the new procedure. "We have a glimmer of hope with our early work."

That work was described in a head-turning *Lancet* paper in February. Stem cells in the heart naturally replace about 1 to 2 percent of heart cells a year, just to keep up with the wear and tear of daily life. But in a heart attack, says Marbán, a person can lose 40 percent of heart muscle overnight. By taking biopsies of heart muscle from patients after their heart attacks, growing stem cells outside the body, and injecting them back in, his group theorized, they could speed up the natural regenerative process. Indeed, Marbán's team found that patients given a dose of cardiac stem cells derived from their own hearts saw their scar tissue shrink by half over the next year whereas people who didn't get the treatment saw no shrinkage. And the patients treated with their own heart cells actually grew some new heart muscle.

Other researchers have tried using stem cells derived from bone marrow to treat heart damage, without appreciable results. The new technique, says Marbán, appears to be the first that "can reverse an injury thought to be permanent."

Although researchers haven't confirmed it, a person who has been partially healed by stem cells might logically be at lower risk of developing heart failure, and of eventually needing a transplant. Marbán's next steps are to look at the possibility of preparing cardiac stem cells from donor hearts that couldn't be used for transplants either because they were too small or the wrong blood type. If successful, doctors could have a ready supply of cells and skip the biopsy and culturing. Eventually, Marbán hopes, the best medicine for a failing heart will be a simple quick shot.

Meanwhile, Michelle Johnson waits for her new one. ●