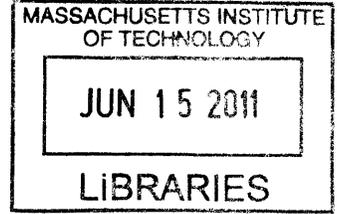


Hallowed Hands

by

Emily Ruppel

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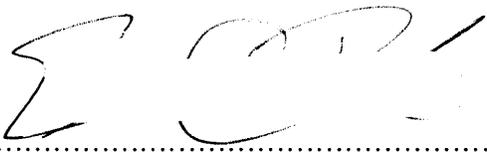
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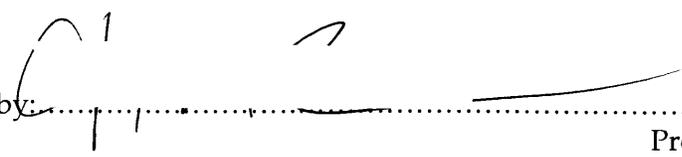
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Signature of Author: 
Graduate Program in Science Writing, June 10, 2010

Certified by:
Professor of Science Writing
Thesis Advisor

Accepted by: 
Professor of Science Writing
Director, Graduate Program in Science Writing

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Emily Ruppel

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ABSTRACT

Human hand transplantation became a medical reality at the turn of the 21st century. Often hailed by media and the general public as miraculous, these life-changing surgeries are also highly controversial. Many doctors, ethicists, and medical professionals feel the benefits of having a hand transplant do not outweigh the risks of the immunosuppressive drugs required to keep the complex foreign tissues alive on the bodies of chronically disabled yet otherwise healthy people. Patients' reactions to having the operation, to the drugs, to the physical therapy, and to the psychological consequences of wearing the hand of a dead person range from grateful acceptance to disgust and requested reamputation.

This thesis explores the struggles and triumphs of human hand transplants through the stories of several patients and doctors. The rise of hand transplantation as a field, including the ongoing controversy surrounding the first successful human hand transplant, is also related as insight into how doctors and patients in innovative medicine make decisions, and where hand transplantation stands as a technology to benefit both medicine and scientific research.

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For their love, faith, and wisdom: Jeromy Edwards, Carol, Fred, Nancy, Eric, and Rachel Ruppel.

i. Prelude

Rich

God, did you need a hand?
Because I lost mine in the fire—
both—like plastic
on oventop melted
to the steering wheel
while the rest of me
climbed out of the truck
inferno.
Nightly before sleep
I see smoke
of the unintended
sacrifice still
making its slow way
heavenward. Imagine Old Test-
ament prophets
growing fat off
my flesh
grinning to the burning
brush where I, wax wick flamed
out fell down unconscious,
down like a log
cinder in
the darkness, voiceless, on
my knees. On my knees.
No hands folded.

Part I. Dead handed

In a small room at Louisville's Jewish Hospital, a chiropractor from Oklahoma clasps a wad of green silly putty with his left hand. Riveting red scars criss-cross both his forearms, and pink flesh bulges up on either side, forming angry-looking gullies in his skin. Country music jangles from a nearby radio, declaring over and over again with power-chord enthusiasm that "Life is a Highway." To the man's right stands a table holding an array of toys: more silly putty, tennis balls, a toddler's shapes-teaching plastic cube, blank paper, and crayons.

Rich Edwards ignores them all, concentrating on the vivid lump between his fingers. His face has none of the placid vacancy of a child rapt in play. Rich is working hard. The furrows between his eyebrows relax and return in cycles of seconds as he tries with all his might to make the slightest impression. The putty, a tool used by hand therapists for tendon and muscle rehabilitation, refuses to yield. Only shallow indentations of Rich's fingertips remain in the shiny dough as a lady in a white lab coat takes notes, then places the Theraputty into his other hand. Rich starts the process all over again, trying to find and pull the piano strings of his mind that---surely, somewhere---still run wires to its keys.

Four months ago, Rich Edwards became the recipient of the nation's third double hand transplant. Almost every day since his surgery, Rich has come to this room and tested his strength. The daily therapy regimen last four hours and includes exercises like flexing and extending each of his fingers, gripping a 1-kilogram weight with the help of an electric muscle stimulator, writing his name, and tossing a ball.

For a hand transplant patient, these tasks are dispiritingly demanding. Rich winces while trying to place one little red cube into its designated socket on a toddler's toy. His squeezed expression reminds me of the faces weightlifters make on the "meathead floor" of my YMCA. Over and over, Rich tells his brain to tell his nerves to send an electric impulse to the muscles they're designed to move, but his fingers flop when they're supposed to tighten, and only with all five gripping at once can he manage to pick up the colorful block. By comparison, the weightlifters have it easy. Rich's hands can't *just do it...*

The exercises may be frustrating, at times disheartening, but if Rich gives up, his secondhands will shrivel into stiff, claw-like features, since the nerves connecting his brain and fingers won't relearn how to operate his muscles. Not because the foreign tissue communicates any differently, but because, like most other amputees, Rich's brain likely boarded up the apartment that once housed its controls for hand function and feeling. Like any logical and efficient landlord, brains won't bother maintaining empty space.

Now Rich is working to coax his neuronal tenants back into two neglected rooms, one on either side of his brain---to re-lease what was once a sense of touch as finely tuned as any in Oklahoma. Still a partner in his busy chiropractic practice near Oklahoma City, Rich dreams of the day he'll have enough strength and feeling to return to his place on the *other* side of the doctor-patient relationship. "I need at least 50 percent of my feeling back. If I can get at least that much control, then I think I could go in there and develop it," Rich said just weeks after surgery.

It could happen. Rich's hopes for his hands' functionality are on the low end of what transplant doctors want their patients to regain. Still, helping future patients will require patience now. Even after hand replantation, (when hands are reattached in the hospital directly following a traumatic injury), recovery takes almost as long as it does following an allotransplant (in which the limb is transferred from a cadaver or braindead donor years later).

Arm replantation was first performed in 1962 by Boston doctor Ronald A. Malt on a 12-year-old little league pitcher whose limb had been sheered off while he was trying to hop a train. Since then, any appendage that's been torn or cut from the body but recovered at the scene of an injury---feet, fingers, scalps, sex organs, noses---have been surgically replanted. Unfortunately, losing a hand in an explosion, crash, fire, or machinery accident often harms the delicate internal structures both in the lost limb and the site of separation. The disembodied hand might also suffer from something like the first stages of frostbite on the way to the hospital, shutting down for lack of blood flow while waiting for care.

Human hand transplants are currently the only biological reconstructive option for long-term amputees, but they aren't a widely available treatment, yet. Many hospitals capable of doing hand replants don't have a staff whose field strength justifies a transplant program, which requires not only good surgeons, but good immunologists, good psychiatrists, and good transplant coordinators. Besides the special difficulty of donor limb procurement (harvesting an external organ requires special permission from the grieving family), hand transplant programs are extremely hard to get into. For those privileged amputees who go through all the physical, financial, and psychological evaluations to get listed, many years may pass before a suitable donor hand is found.

While every hand transplant program's protocol varies slightly, doctors try to match donors for gender, race, age, size, viral status, and blood type, although the latter three are the only mandatory matches. Aesthetic differences, like the skin tone and age of the donor, are made based on the patient's sensitivity to the appearance of the new hand. For instance, some candidates say they wouldn't mind having interracial hands, while others desire a more "normal" appearance.

Since donor hands are carefully selected to match the structural width of the recipient's hand (or hands), hand transplantation is sometimes technically easier than replantation because neither donor nor recipient ends need extensive repair pre-surgery. According to hand surgeons, the mechanics of hand transplantations are fairly straightforward, as surgical techniques for 50 years of hand replantations closely resemble the protocol for transplantation. The additional steps are their mirror opposite---removal of the hand or hands from a dead person's body.

"When finally there is a possible donor," Italian hand transplant surgeon Marco Lanzetta has written, "time is extremely important. No delays in preparing the necessary instruments and materials are acceptable. In our unit, we have a ready backpack containing what we need to face any possible scenario once we reach the intensive care unit where the donor is located." Lanzetta's surgical tackle box includes tools such as marking pens, scalpels, tissue forceps, skin hooks, skin retractors, sutures scissors, dressing scissors, Stevens tenotomy dissecting scissors, five mosquito forceps, a soluble-ended small needle-holder with fine smooth jaws, a Kleinert-Kutz periosteal elevator, two large Kocher clamps, one scalpel with no. 21 blade, one hand saw...

Once scrubbed up at the donor hospital, the hand surgeons begin their work from the outside in, cutting the donor's skin in diagonal lines farther down the arm than the actual amputation. Like sensible tailors, the organ reapers must be sure they'll have enough material to sew onto the receiving stub and to allow for post-op swelling. After pulling back the skin flaps and clamping off the veins and arteries of the donor's arm, the doctors identify, tag for recognition later on, and cut through blood vessels, nerves, muscles and tendons. Last, they sever the bone with an electric saw, bleed dry the cleaved limb (making sure to tie off blood

vessels on the side of the donor's body), and place the anemic hand in a cooled vessel for transportation.

The harvesting doctors' final act is to bandage up the dead person's limb. Not to stave off infection, of course; this gesture is to allow for the attachment of an aesthetic prosthesis so the dead body won't look mutilated during burial.

If you happened to see the white-coated doctors leave the hospital (about an hour after they arrived), there'd be nothing to alert you that the unremarkable styrofoam box they carry contains what some people consider nothing short of a medical miracle, what others deem the stuff of science fiction novels, and still others jeeringly call a "Frankenhand." For better or for worse, the bloodless, expatriated part is about to be reattached, reinnervated, revascularized---remarried, even, to another living human being.

This next surgery will take about thirteen hours.

Meanwhile, doctors at the transplant team's home hospital have anesthetized their recipient and prepared the limb or limbs for surgery. If performing a bilateral transplant, two teams of skilled microsurgeons will work on each extremity simultaneously. First, they'll amputate the last centimeter of one or both stumps to reveal the internal structures and make for a seamless fitting, likewise clamping, identifying, and tagging their patient's vessels, nerves, and tendons.

To attach the new limb, doctors reverse the process of retrieval, following the well-established process used for replantations. This work they do from the inside out, beginning with bones and ending with skin. Bones are connected by placing two flattened steel rods on either side of their circumference and securing each with five to seven screws. Blood vessels follow bone to reduce the amount of time the donor hand spends without oxygen, and once the veins and arteries have turned a healthy pink, tendons meet matching tendons, muscles are mated, and the shell of the skin zipped up as neatly as possible.

Every element other than bone is tightly woven together with thinner-than-hair sutures and *literally* microscopic stitches. Microsurgery uses light microscopes to help perform the fastidious cuts and needlework needed to fuse, as seamlessly as possible, muscles and tendons back into their complex pulley system, blood vessels and nerves back into functional conduits. Microsurgery is painstaking work, since even the smallest needles, thinnest razors, and most laborious motions might miss their fraction-of-a-millimeter mark or puncture the paper-thin walls of an artery, which is quite the bloody sight.

I watched an aspiring plastic surgeon, J. Rodrigo Diaz-Siso, train for hand transplant surgery at Boston's Brigham and Women's Hospital (an institution renowned for its history of pioneering replants, solid organ transplants, *and* composite tissue transplants) by doing essentially the same procedure on the leg of mouse. The microscope is key---when I looked through the ten-foot-tall whirring machine at my own hand, the magnification made a hangnail I hadn't noticed before look like a cell-decorated diving board off the side of my forefinger. Diaz-Siso was showing me how microsurgeons place their wrists and pinkys on the operating table to maximize the stability of each fine motion.

Diaz-Siso and a hand surgery fellow, Simon Talbot, sat down in backless stools facing each other and bent over their chess-board-size operating table like a couple of old scholars arching over a rare book. After administering mind-numbing drugs to the first mouse, they watched their own movements through a double-sided surgical microscope while shaving, slicing, and finally, snipping through the mouse's string-thin femur with what looked like stainless steel nail scissors. After doing the same to the corresponding leg of the "donor"

mouse, I gripped the edge of the table as they gripped thin steel tweezers to dip a spidersilky suture in and out of the mouse's wound.

In the silences between their moments of greatest concentration, I plied the two surgeons with questions. For instance, if the slightest tremor could botch the whole operation, are microsurgions allowed to drink coffee? "Coffee isn't a sin, but varying the amount of caffeine you usually have on a surgery day is," Diaz-Siso said.

Why don't you reattach the mouse's nerves? Talbot took this one, "Well, first of all this is practice, so the leg doesn't have to be functional; secondly, because the nerves on a mouse are so small that instruments and sutures become an issue. If you compare the relative size of the structures, performing microvascular surgery on a mouse---even with the finest equipment---would be like trying to repair human femur and leg vessels with garden shears."

After the mouse's veins were reined together and the stitches tied off, Diaz-Siso swayed away from the microscope so I could watch its blood course into the new translucent tubing. It was over in a half a second. While it happened I imagined the viscous red fluid in my own body carrying molecules of oxygen and CO₂ to and from my fingertips, my heart compressing approximately 60 times a minute (although in that moment it was drumming co₂) and when I looked away from the microscope, all my arm hairs were standing on end.

One of the doctors on the world's first hand transplant team recounts the experience of releasing that first tourniquet, "This was the most anxious part of the procedure and [Earl Owen, a pioneer of microsurgery] describes the moment he gave the order as defining for him a new concept of the word 'stress.'"

Part II. Second hands

No matter how good a hand surgeon is at stitching everything back together, arm and hand amputees will never again have perfect feeling and function in their once-lost limbs.

Whether replanted just hours after an accident or transplanted from a brain-dead donor twenty years later, full recovery depends on the re-growth of two types of nerves: sensory nerves that carry feelings back and forth from brain to hand, and motor nerves that make muscles move. Unlike blood vessels, which are basically a very complex plumbing system (connect the pipes, turn them on, and the vessels fill), the moment a nerve is reattached, it can't just start working, again. Once severed, nerves die.

Originating in clusters near the brain, nerves under a microscope look like bundled cords composed of fiber-like axons. Axons are like power cords that project from nerve cells, forming the cylindrical paths through which neurotransmitters (the messengers of the nervous system) travel. Neurotransmitters pass signals back and forth from the brain to receptors in muscles and skin throughout a delicate root-like network of off-shoots, called dendrites. If the main power cord of a nerve gets cut: radio silence, and the entire axonal network below the mark dries up. Even if nerves are reattached when a lost limb is replanted, the dead dendrites will be absorbed, like blood inside a bruise, back into the body and replaced by new ones.

If all goes according to plan, the nerves that control the sensation and motor function of Rich's new hands will grow back at a rate of about one millimeter per day. Since gripping muscles are housed in the forearms, he can already hold things with his hands, which move as if they were wearing mittens, and even when he leaves the hospital, Rich will spend hours every day working to isolate control of each finger. Only once axons from their source clusters replace the dying nerves in Rich's new hands will he be able to touch objects around him, like his wife Cindy's hand, and feel her touch in return. That intimate human moment is still two or three years away.

Fortunately, Rich has the rare luck of being an amputee whose nerves and inner tissues weren't damaged by accidental dismemberment. In fact, at the time of his transplant, Rich still "had" his original hands, but they'd been burnt beyond repair when he got trapped in his Suburban and overcome by a brush fire four years ago.

That summer had been hot and dry in Oklahoma, and while no one can say for certain why the fire started, Rich and Cindy think it happened when the truck's catalytic converter sparked a flame in the high grass Rich was driving through. He was in what he calls, "the middle of nowhere, Oklahoma," at midnight on his way to meet friends for a hunting trip when the wheels of his Suburban got stuck in a small ditch, and Rich began pumping the vehicle back and forth to dislodge it. He was still about a mile from camp and couldn't get the truck unstuck when he glanced over his right shoulder and saw a bright flash of orange red. He glanced to his left and saw another.

Fire.

Suddenly, Rich realized he was sitting on the inside of a furnace. He stopped trying to steer the Suburban out of the grass and grabbed his door handle and pulled. At the same moment a loud *Click!* informed him the car's electric system had shut off, with both doors still locked. He tried and tried to pull the manual lock, but the plastic was stuck and wouldn't budge.

The last thing Rich remembers is the windows shattering.

He came to many yards away from the truck, and to this day neither he nor the firefighters who once visited him for chiropractic therapy have any idea why the fire didn't

spread. When Rich arrived at camp---also a mystery---much of his arms, back, and face had been scorched into rippled red surfaces, and the tissues in seven of his fingers were charred through to nothing.

Before getting his hand transplant, all that remained of Rich's once-fine fingertips were a few fused nubs between his left pinky and thumb. For about a year, Rich went through multiple reconstructive surgeries in multiple hospitals, hoping he'd find a surgeon capable of returning any function to his hands. More than five attempts came to no avail. During that time, he couldn't perform chores as simple as getting dressed by himself, taking a shower, or holding a fork to eat food.

His wife was there to help him through the panoply of daily tasks, but as their hope of resuming a normal life sloped down and down, Rich rode the declivity farther and farther from what Cindy calls her husband's "zeal for life."

"I was a busy chiropractor before the accident, and life came to a pure dead stand-still after. We were just fast-tracked, and then: *Boom*. I can't go to the bathroom or practice in my clinic or anything. It was the first time in my life I ever felt depressed. I wouldn't go out of house, just knowing I couldn't do anything. I would think, 'I'm gonna go help in clinic today,' but I'd go in and pick up a paper and drop it. Then there'd be all my patients around saying, 'Doc, how are you doin'? And that's supposed to be *my* job. It would just hit me like a brick," Rich said.

A photo of the man before the fire reveals an uncommonly handsome face beneath the silvering forest of his hair. At the time of the photo, Rich was a popular chiropractor, proud of his ability to help patients that other doctors couldn't. Only the tiniest wrinkles fan out from the corners of water-gray, reflective eyes. The playfully tilted triangle of his smile above the cleanly triangled knot of his tie makes a viewer want to go up and shake his hand. Truly, Rich Edwards looks as though he might, as they say, "have it all."

Those who have much have much to lose, and so it was for Rich and Cindy, who struggled mightily to find meaning and hope in Rich's heartbreaking deformity.

They say their Christian faith helped guide them through.

I asked them if they'd been reading a lot of *Job*.

They answered with laughter and a slow, synchronous nod.

Though both Rich's accident and his hand transplant came about in unlooked-for ways, Rich and Cindy feel neither events were accidental in the grand design, with the latter being as miraculous for them as the first was a disaster. "My accident needed to happen for me to take myself off the throne in my heart. We started reading the Bible every morning together for year. I think it had to happen to change my life," reflected Rich, pausing to scratch his eyebrow with the fingertips of a hand that was otherwise hidden in a white beehive of bandages.

The faithful couple came to Louisville a year and a half after Rich's accident to visit the world-renowned Kleinert and Kutz Hand Center for a reconstructive consultation. But the Kleinert Kutz specialists told them there was nothing more that could be done to fix what Rich called his "deranged hands."

Rich and Cindy had no choice but to amputate his stiff, misshapen fingers and go the way of prosthetics. Recalling their visit to Louisville, Cindy said, "Rich was just devastated. Sitting there in the office, I saw that he had started to cry, and just when we were about to leave the room, I remembered this thing I heard about a hand transplant. It was just a random conversation and I'd thought it was a rumor. The doctors in Louisville didn't even mention that they could do a hand transplant."

They probably didn't mention it because Louisville's protocol for patient selection requires that all their candidates try at least two prosthetic hands before committing to the procedure, to show that they'd coped with the loss and that no other options would work for them.

But as soon as Cindy brought it up, the hand surgeon spun around and said, "Are you really interested?"

Warren Breidenbach, lead surgeon of the team in Louisville and who arguably performed the world's first successful hand transplant, was intrigued by the opportunity to achieve even better results---since Rich's nerves were never exposed, they'd be completely untouched before their first encounter with the saw, and Breidenbach thought they might regenerate faster and better than the average patient's. Rich passed all the physical and psychological tests, becoming a transplant candidate three years before an acceptable match was made.

There were no, and are still no guarantees that the transplant will take. Unfortunately, while Rich's nerves are creeping down into each fingertip, the muscles inside his new hands are slowly starting to atrophy. Without electrochemical stimulation from the nerves that operate them, muscles can't be strengthened and start to wither. Even with electric muscle contractors, hand therapists can't artificially inspire the tiny nerves inside the hand to help maintain the strength of the muscles they operate, since they're essentially still dead.

Rich's therapy is thus a slow race against time and space: about 12 inches a year. Since not all his severed nerves will grow back perfectly, and some muscle function will be lost in the waiting, Rich and other hand transplant patients can only hope to regain 50-70 percent of an average person's strength and feeling. (Most hand doctors consider 60-80 percent an excellent result). To determine these percentages, hand doctors compare their patients' performance on a series of physical tests to the performance of an average hand. For instance, if the patient can clutch a five pound weight and the normal hand can clutch a twenty pound weight, then their score is 25 percent for that exercise. Doctors also measure their patients' sensitivity to hot and cold, their ability to discern objects (while blindfolded), and their range of flexibility. Then they combine the scores into an average.

Matt Scott, the New Jersey native who at twelve years post-transplant owns the world's longest-surviving hand allograft, said his last rating was at about 65 percent. He finally plateaued about five years after surgery.

In the chapter on "The Louisville Experience" for a collaborative manual on hand transplantation, the team describes Scott's level of dexterity, "He can pick up tiny ball bearings, checkers, poker chips, tie shoe laces, write, and even sign his name. He can also throw and catch a ball. Though he can dress himself, buttoning his clothes is still difficult." Scott reached his twelve-year surgery anniversary just a few days before we spoke on the phone and said he's been able to double the amount of function he had with a top-level prosthetic. All in all, Scott seemed genuinely pleased with the whole experience, stating that the hardest part of the whole thing was the grueling daily therapy post-surgery.

Although it's still unclear what *long* long-term results in hand transplants will be, for the approximately 50 hands that have been transplanted worldwide (on about 30 patients), Scott's level of satisfaction is par for the course. Commenting on the gap between their results and the full capabilities of a normal hand, almost every doctor I interviewed on the Louisville team remarked, *Well, our patients aren't going to be concert pianists, you know...*

Part III: Mind and hand

Twelve years ago, if a disembodied hand couldn't be salvaged at the site of injury---i.e., abandoned during battle, lost inside the belly of a large machine or beast, or simply never found---or if the body part was too badly crushed, burned, or exposed to infection for replantation, an amputee's only reconstructive option was to wear a prosthetic to help perform daily tasks and maintain some semblance of normal appearance.

Unlike artificial hands, modern lower limb prosthetics mostly serve their wearers well and can be virtually indistinguishable from human flesh and bone. Artificial legs are so good, in fact, one notable double leg amputee, Oscar Pistorius, was deemed ineligible to compete in the 2008 Summer Olympics for having an unfair advantage over normally equipped sprinters.

While any amputation, major or minor, can make a person feel unwhole and therefore inferior to people with all their original parts, hands hold more meaning, perform a larger array of functions, and handle more essential and pleasurable sensations than arguably any other part of the human body. Although there are a number of prosthetic replacements for lost upper limbs, many amputees with prosthetic hands only wear them out in public, as a visual courtesy to others. Not that strangers tend to ignore an obviously plastic hand, but the (lack of?) sight of a limb that's been severed is generally more startling to passersby than a fake one. By contrast, prosthetic hands with a more function-restoring focus are often described by their wearers as awkward, heavy, and cumbersome. "Many of our patients have myoelectric [brain-controlled] devices, and most of them keep them in the closet," says Christina Kaufman, an immunologist in Louisville.

That's because even the best prosthetic hands aren't as fast or fully operable as flesh and bone. They only last as long as their batteries, they can break down at inconvenient times, and must be serviced regularly. Perhaps most disconcertingly, all prosthetics have to be put on and taken off frequently---at night, before bed, in the shower, and prior to swimming. Get caught in a downpour, and destroy a couple thousand dollars' worth of equipment.

Since the appearance of the first brain-controlled prosthetics in the 1940's and 50's, scientists have been working on ways to procure viable options for those who suffer the loss of a hand. Smaller and smaller motors, lighter and lighter materials, better and better understanding of the human brain---even the possibility that, someday, sensitive artificial skin could light up the fingertips of mechanical hands---all factor into the vision for the next age of bionics. No matter how close the doyens of human engineering come to replicating these highly specialized organs, one significant function will probably elude the grasp of future technologies: the ability to feel all the textures of the natural world. Hot burner, smooth skin, sharp knife, wet-cold snow, velvet versus sandpaper...

Perhaps one day man and machine will indeed communicate such things. But even in the realization of that optimistic future, and certainly in the meantime, prosthetics pose a problem completely beyond the challenges of manufacturing basic functions.

They aren't *human*.

Before becoming Warren Breidenbach's first hand transplant patient, Matt Scott owned and used an Otto Bock myoelectric prosthetic hand, one of the best brain-controlled devices currently available. Scott described the arc of his relationship with the artificial hand during a long phone interview, "Having a prosthetic just wasn't the same. Don't get me wrong---the prosthetic served me well. It served me *very* well. I was able to become a top paramedic in my field, (with some adjustments), and I got married and fathered two kids. I was successful in the

ways we define success. But mine was a traumatic amputation, you know, and after thirteen years of having a prosthetic, I had grown so dissociated with it that I'd come to detest it."

As Rich Edwards also noted, the suffering of upper-limb loss extends beyond day-to-day absence of ease. Psychiatrists sometimes refer to the loss of a hand as upper limb "castration," which evokes a better sense of the emasculating feelings amputees can have long after they've mourned the lost body part. The coinciding depression can be dangerously potent. During our conversation, Cindy recalled what Rich's years-long wait was like.

"Rich lost his identity as a man. He totally changed. He didn't want to engage in life or conversations. Remember, we were chiropractic, not medical; this was a man who *believed* in the power of the mind... but emotionally and mentally that strong mind he had was gone. No one would have believed Rich went the way that he did."

Cindy raised both her hands, palms up to the fluorescent lights.

The functionality of human hands, of course, is only a fraction of the meaning we attach to them. In some way, hands define us as individuals. We make and do things with our hands, and they're prominently factored into our social lives. On a daily basis, people meet and estimate each other in the amount of a handshake's grace and strength, gesture to traffic, wave hello and goodbye, clap in courtesy or with enthusiasm at the end of a show or speech.

As polymath Jacob Bronowski famously said, "The hand is the cutting edge of the mind." Evolutionary biologists and anthropologists postulate that as a species, our unique brand of cognition, thus the development of the human *being*, is inextricable from the moment the first proto-humans began to use their hands to make tools, to communicate, and eventually, to write things down.

As a direct form of communication, sign language is the most obvious embodiment of hands as speech, but the pantomiming of thoughts is also an integral part of many people's communication patterns, helping to relay meaning where words alone might fail. (I have friends who, losing the gestural use of their hands, might not be conversationally capable of saying anything intelligent again).

What if, every time you brought your hand up to wave away a suggestion of solemnity... it simply wasn't there?

Knowing how little a prosthetic can do to outfit its wearer with function and wholeness, it's no wonder hundreds of amputees volunteered to be the world's first hand transplant patient before even the doctors were convinced that it would work. Though at the time not even the doctors could be *sure* transplanting a limb was possible, the story of human hand transplants revolves around a very clear impossibility. What these programs also use as a kind of mantra was not so long ago a very literal quandary: you just can't replace a human hand.

Part IV. Self-less Cells

It was many years after the nation's first hand transplant in Louisville, my hometown, that I opened the *Courier-Journal* and read an article that kept me rooted to my armchair long after I'd finished my coffee and the cat quitted my company. A California man who'd lost his hand when a gun misfired six years before had just now gotten it back. Like Rich and Cindy, I wasn't even aware that the technology had been developed, but as I pondered the news, it hit me that the patient hadn't actually gotten *his* hand back; he'd been given someone *else's* hand, becoming physically and emotionally linked to a dead person for the rest of his life.

I started to wonder, would the hand transplant patient and his family look down at the alien appendage and get a jarring feeling of *otherness*? How long before the man with a new hand could refer to the hand as "his" (if ever)? If imprisoned for any reason, what would be the consequence of having two different sets of fingerprints? If the donor "had blood on his hands," would it stay there?---if so and the transplant patient found out---would he want it off again?

The questions lingered after I'd entered a graduate program at MIT; once again, an article from down the road brought hand transplants to the front of my thoughts. A team at Boston's Brigham and Women's Hospital had just announced their intention to perform them. When I first read about the BWH program, I was perusing an online health blog and came across the following comment:

This whole idea is absolutely insane and represents a triumph of technique over common sense. In an era when we cannot afford basic health care it is incomprehensible that we would be considering expanding use of what is essentially an extraordinarily expensive cosmetic procedure. These types of transplants end up being a living prosthetic with little true functional capacity while being obliged to a lifetime of expensive and morbid immunosuppression. The costs in surgery, medication, and rehab are staggering for this and there is no way anyone can justify the cost-benefit with a straight face.

The commenter claimed to be a practicing plastic surgeon by the name of Dr. Robert Oliver Jr., who was a resident in at the University of Louisville when the Jewish Hospital team performed Matt Scott's hand transplant. He wrote that he saw Matt Scott on a follow-up visit "a number of years ago" and that the man was still essentially living without a hand.

My questions and their intensity increased.

The fact is, every one of these life-changing surgeries, which newspapers often blithely call medical *miracles*, demand a marriage-like commitment and, like a marriage, practically advertise the gravity of their drawbacks. Intensive physical therapy, a strict regimen of toxic, immune-system-impairing drugs, possible graft rejection (in which the new limb can swell to twice its normal size, turn black and have to be re-amputated), heightened susceptibility to diabetes and cancer, possible mental trauma (imagine stroking your spouse's body with someone *else's* hand), and possible early death loom close behind the needle and saw.

Miracles aren't supposed to come with a catch.

The catch lies within all potential transplant patients, where something their immune system sees as an invader---the donor hand---gets attacked by the body it was put there to

improve. The biggest obstacle blocking widespread application of hand transplants is this: immune systems are good at what they do. Responsible for protecting us from anything that crosses the borders of the body but isn't supposed to be there, the immune system's list of potential targets includes viruses, harmful bacteria, malignant cancer cells, and unfortunately, the hearts, livers, kidneys, and hands of strangers.

The largest and most active component of the immune system is its panoply of white blood cells, called leukocytes, which act like independent one-celled organisms within the body, recognizing, trapping, and removing foreign invader cells. T-cells, (also known as T-lymphocytes) make up 60-80 percent of the white blood cells in your body and are the smartest of the leukocytes. They're also its biggest bullies. T-cells spend all day and night patrolling around your body and submitting all its cells to persistent chemical questioning.

T-cells are shaped like microscopic Medusas, if Medusa's head were completely covered with cropped, snake-like hair. The aggressive, tubey structures on the outside of T-cells "listen in" on what other cells are saying, but they only speak one language---yours. If a T-cell attaches one of its hairlike filaments to a normal skin cell, and that cell is sending out the same chemical signal as the one the T-cell already knows, then absolutely nothing happens, as the cell is understood to be "self."

But if any foreign molecule with its own DNA code, like a virus, wriggles inside one of your cells, it presents a signal on the outside of that cell that's different from the signal made by your cell's own DNA.

Once an alien signal is detected by the hairs of a T-lymphocyte, you can guess what happens next. The T-cell mounts a xenophobic response that rivals the most obnoxious patriot you've ever met. T-cells aren't interested in getting to know the body's interlopers; they either kill them directly, or mark them for destruction by other white blood cells, which surround the offensive hosting cells and eliminate them.

These all-important search-and-destroy missions are carried out automatically, by everyone's body, every day. The brain doesn't have to reach down and play Lady Justice, as all substances in the body are judged on a scale of "self" to "not self." 1 or 0. Usually, the quiet wars within us are unnoticed, even unnoticeable, routine engagements. Most people don't even think about their immune system until their T-cells can't respond to an invading toxin or bacteria with enough force to stop its campaign in the body, and they get sick.

But transplant patients think about the immune system all the time. With approximately ten pills a day, they are basically giving themselves the pharmaceutical equivalent of the AIDS virus. A bittersweet nostrum, immunosuppressants impair the ability of T-cells to do their job, which is the only reason why transplanted organs composed of cells that *don't* try to mimic the patient's own DNA (like some viruses) aren't immediately killed off by the body.

Immunosuppressive drugs. The words have a halting rhythm, internal syllabic ups and downs. Which is fitting; the development of immunosuppressive drugs has been a kind medicinal paradox, since damaging the immune system is obviously not a health-promoting activity---but they are also what led to the world's first whole organ transplants, which eventually saved lives, and then to composite tissue allotransplants (CTA's), beginning with the hand.

The history of transplantation basically begins with the plight of several severely burned fighter pilots in World War II. The extent of the soldiers' wounds inspired the Glasgow Royal Infirmary to form a special burns unit. Plastic surgeon Thomas Gibson collaborated with a young Brazilian zoologist, Peter Medawar, to conduct skin graft experiments to care for the

injured soldiers, and they noted that patients who'd been given grafts from another person experienced more rejection following a second one.

Medawar was the one to postulate, and later prove, that rejection of the skin grafts was caused by cells in the recipient's immune system. Doctors then started looking for ways to manipulate the immune system enough to allow for transplantations. The 1950's and 60's saw the rise of the first immunosuppressive drugs, thus the dawn of transplantation as a solution to chronic infirmity.

As Boston doctor Joseph Murray noted, "Medawar said it best, 'This whole period was a golden age of immunology, an age abounding in synthetic discoveries all over the world, a time we all thought it was good to be alive. We, who were working on these problems, all knew each other and met as often as we could to exchange ideas and hot news from the laboratory.'" In the 1950's, Murray had been researching skin and kidney transplants in dogs, and he and his colleagues noticed that the closer the genetic makeup from the donor to the recipient, the better the rate of survival for the graft. These studies led him to perform the world's first kidney transplant between two adult identical twin brothers in 1954, using no immunosuppression. (In the rare case of a donor with perfectly matched DNA, T-cells have no cause to retaliate against the graft).

Transplants between strangers were first performed in the 1960's, although the first available immunosuppressants were far from perfect. Patients often died from the effects of the drugs or the failure of the needed organ, itself. Heart transplants were abysmal. Even when the immunosuppressive therapy improved and started to prolong the survival of transplant patients, ethical questions persisted, concerning everything from the "right" one had to own another's heart to the spiritual implications of living with it (which in some ways is harder than having and holding a transplanted hand, since hearts are never seen and can seem more mysterious, less *endowable*...).

It was around this time that a little-league pitcher in Boston lost and regained his severed arm, and soon after that, doctors in Guayaquil, Ecuador attempted to transplant a hand onto an ex-sailor. The graft may have been technically effective; however, with the immunosuppressants available at the time, now considered "primitive," the hand rejected within three weeks... just long enough to frighten the world away from performing another one for over 30 years.

The drug that revolutionized transplantation, cyclosporine, was introduced in 1982. Researchers in Britain extracted the drug from a fungus, hoping to find a new penicillin, but the substance had no effect on bacteria. It did, however, suppress the immune system, with far fewer side effects than previous drugs. According to a BBC documentary on the history of surgery, "Cyclosporine was the breakthrough that transplant surgery had been waiting for. Finally, the immune system could be controlled, and transplant surgeons could start saving lives, instead of ending them."

Cyclosporine greatly increased the number and efficacy of solid organ transplants, and also showed improvements for animal limb transplants, but not enough to lead to extensive trials. Hands and other organs made up of many tissues were thought to be impossible to transplant, due to the high antigenicity (rate of rejection) of skin. By the mid-1990's, a combination of new drugs, (the "cocktail" transplant doctors often refer to in the news), were able to reduce the toxic side effects of transplantation, and with these drugs, experimental trials in limb transplantation were conducted on small animals, many of whose grafts survived for many months (equivalent to years in humans). Large animal studies were still needed to

confirm the possibility of hand transplants, but in every experiment performed on primates, the animals either lost their new limbs within months or days, or died in one of two ways.

In the first way, drug dosages got so high and the animal's immune system so weakened that they died from complications that would barely effect an otherwise healthy body. In the second way, the primates died from a malady with an aptly ominous acronym--GVHD, or Graft Versus Host Disease. When a transplant patient has an abnormally weak immune system and their graft includes healthy, smart immune cells, a curiously horrible thing can occur. The protector cells of the foreign tissues actually mount an attack *against* their host organism. Immunologist Christina Kaufman describes the phenomenon, "When that happens, your whole gut basically sloughs off your body, and you die. It is *not* a pretty way to go..."

This is where the field of hand transplantation stood when Warren Breidenbach and his team in Louisville decided to go exploring through its stark and unpromising landscape. The scenery: a bunch of dead rats, a few dead monkeys, and one dead human hand.

Part V. Hand Ball

Sitting at the formidably large oval conference table across from Dr. Breidenbach, I was becoming nervous. I had a lot of questions, some of which only he could answer, but for five minutes the hand doctor's attention had been traveling down what seemed an intractable tangent. Meanwhile, the rising sun of mid-morning started making its way through the slats in the long blinds as if on purpose, intensifying the light and dark stripes of the large windows, casting shadows across Breidenbach's right cheek. In an effort to rebridle the conversation, I interjected the most obvious question I could think of--how he'd made history.

So tell me, what first inspired you to go into hand transplants?

Breidenbach folded his hands and placed them on the table. "I didn't. I ran from it. I refused to be a part of it."

Whatever I'd expected him to say, that wasn't it.

He went on to explain that hand surgery in the 90's had, "like most innovative fields, kind of flattened out--and the research I was doing in hand surgery was boring me." Around that same time, Jewish Hospital approached the Kleinert and Kutz hand doctors to form a think tank group for determining the next big advance in their field, saying they'd supply the funding to pursue whatever project the group identified. (The two institutions have had a 50-plus year partnership and had already performed a number of firsts in hand and microsurgery).

"At the time we began our research nobody else in the world was talking about doing hand transplants," says Gordon Tobin, chair of the plastic surgery department at nearby University of Louisville and one of the original members of the project. "It was a dead topic--so at first, hand transplantation was *not* the main objective of the think tank." Many of the surgeons in the group, Breidenbach included, wished to put their energies into establishing better tools for evaluating hand function, since current models aren't very comprehensive--but at some point Breidenbach became convinced that hand transplants were the way to go.

According to Breidenbach, that moment came in '93 or '94, when he went to a conference for the American Plastic Surgery Research Council in Houston. At one of the meetings, Spanish doctor Raymond Llull stood up in the audience to talk about how a recent paper on limb transplantation in a rat model showed the feasibility of human hand transplants. "Llull said, 'It's time to do this. We're ready.' I was shocked, but I pulled up his paper and read it," he said. Breidenbach threw the idea out onto the table back in Louisville, and Jewish Hospital decided to proceed with funding the attempt. Breidenbach was becoming animated, "You see, by the time we started this project, all the evidence supporting hand transplantation was already there. Dr. Llull was trying to articulate that, and although he was *saying* it, there was no *logic* as to why the operation should succeed. I never believed it was possible that from '93 to '99 we would have solved the riddle."

What was the riddle?

"The riddle was: *how* do you get a hand onto a patient when the literature at that time seemed to show it couldn't be done?" I asked him how he'd solved it, and again to my surprise, Breidenbach answered, "I didn't. I just listened. I'll never forget--in one of the early meetings, Jon Jones, Lead Transplant Surgeon at the University of Louisville, said, 'Well I can keep the

hand *on*, but I don't think it'll *work*.' And I said 'Well I guarantee you it will *work*, but I don't think you can keep it on!'

"So it was clear there was a reasonable chance the tissue would stay alive, but was there scientific evidence to support it? A few people said, 'Well let's just do it,' and I said, 'Well you don't understand the political issue---we put a hand on someone and it fails, although in the transplant world that might seem okay, in the hand surgery world they'd go after me.'"

Breidenbach paused to remind me that trying to do a hand transplant without having wealth of evidence proving it should work would have ended in catastrophe if the transplant failed, for those involved and for the dream, itself. Breidenbach suggested the group focus on accomplishing three things before proceeding with the attempt. First, they needed to perform successful large animal experiments; second, they needed to review the literature and come up with the unifying logic that Lull's paper lacked; and third, they needed to show that hand transplants would be ethically sound. The think tank group, which had started out as a handful of people meeting weekly in a conference room and grown to over twenty interested doctors from multiple fields, broke up into three teams.

The research team, led by Tobin, worked in labs at the University of Louisville, which also has a long-standing relationship with Jewish Hospital. According to Tobin, "At first, the whole experimental phase was very discouraging. I mean, there *had* been some success with mice, but their immune systems are so different from ours that few people would take those results and think they'd be transferrable in humans. And monkeys, well... It was Jon Jones who suggested we use pigs. Although primates are generally thought to be closest to us on the evolutionary chain, in some ways they're more like us and in some ways they're not."

One major anxiety hindering human hand transplants was the idea that skin would require higher levels of immunosuppression than internal organs and the effects of the drugs on a "healthy" body would be too detrimental to justify a non-life-saving transplant (see: dead monkey). So when the U of L team tried three different drug combinations and applications on their pigs, to one group of subjects the team gave the same amount of immunosuppression routinely prescribed for solid organ transfers, not really thinking it would work.

The "skin" of the pigs stayed on. As it turns out, pigs may metabolize immunosuppressants more like human beings than primates do. Tobin continued, "Those of us who thought we wouldn't see success for another ten years were very surprised. If we'd continued using primates, this whole thing might have never gotten off the ground."

The literature review was guided by Breidenbach, who has a background in biochemistry and enjoyed reading about high-level immunology. The papers were scattered from topic to topic, and the variables of all the experiments differed from lab to lab. "I couldn't make any sense of it. Someone would do an experiment with drug A and B, someone else B and C... The first person might do it for 60 days and stop, the next maybe 30 days. It was hard to synthesize a consistent theme." But in the end...

"It was shocking. By time we finished literature review, it was completely clear that every tissue in the human hand had already been successfully transplanted with normal doses of immunosuppression. Many of the articles had flown below the radar even though they shouldn't have."

Finally, the moral and philosophical issues in non-life-saving organ transplants had to be openly addressed. To that end, the Louisville ethics group systematically called into question everything the team had been working for. They consulted Chicago ethicist Martin Siegler, a doctor famous for his work in helping develop the standard ethical guidelines for kidney transplants. With Siegler's counsel they developed a protocol that included publicly

announcing their intention to perform a hand transplant. As Tobin explains, "In innovative medicine, being demonstrative and clear allows the public and other professionals to weigh in with their critiques and suggestions long before you put a patient on the table. It also protects investigators from doing something for their own glory rather than for the good of the patient."

The team held debates at conferences and published their experimental results and editorials in the academic journals of both fields---hand surgery and transplantation. At its most basic, the issue was one of cost versus benefit. Critics asked, why hand transplants, and why now?

Neil F. Jones, Director of the U. C. Irvine Hand Center in California, critiqued the weak statistics backing hand transplants even two years later, "only approximately 60 rat limbs and two primate limb transplants have survived for longer than 200 days and only eight of 19 pig [CTA's] showed no signs of rejection at 90 days. It seems unlikely that human hand transplant survival will be any better than the survival of a kidney transplant, which has a half-life of approximately 7.5 to 9.5 years... [furthermore,] chronic immunosuppression may predispose a hand transplant patient to an 80 percent chance of developing postransplant diabetes, and a four percent to 18 percent potential risk of developing a malignancy."

That's not including the less serious effects of the drugs, which on Louisville's website read like a late night infomercial---side effects may include but are not limited to: hypertension (high blood pressure), acne, tremor of the hands, gastrointestinal discomfort, increased risk of infection, increased hair growth, weight gain...

"The crux of the matter is how much immunosuppression can be justified for a non-life-saving procedure? ... Since limb transplantation will not prolong life but will improve its quality, the risk-to-benefit evaluation becomes far more delicate, subjective, and hence, controversial," states a 2005 paper in the *Lancet* by prominent transplantologists.

Of course, the discussion of *how much* cost versus benefit would be moot if what worked on a pig or a rat simply didn't translate to human beings. Tobin reflects, "Of course, there was lots of criticism---and there really should be, since anytime you make that leap from animal to human beings, there are unknown risks that can't be born out in the laboratory."

Plenty of people, including Louisville team member Christina Kaufman, still admittedly, "thought the hand would turn black and fall off."

Supporters argued that all innovative medical procedures *could* wait and wait for the most perfect moment to finally move into the clinical arena (and who is to decide what that perfect moment is?), but if doctors could be helping their patients now, and the patients are willing to accept the risks, then why shouldn't they be allowed to try?

Debates raged in the media and in the conference room. It was possible. It was impossible. And, of course, from both sides: *you just can't replace a human hand.*

In November 1997, the First International Symposium on Composite Tissue Allotransplantation met at Jewish Hospital in Louisville. For three days the scientific, clinical, and ethical barriers to CTA were debated by local and international experts in surgery, psychology, immunology, medical history, and ethics, with the pronouncement that the world was ready and the surgery could proceed.

The following lead appeared in *Time* magazine in August of the next year, "Pioneering surgeons used to wait until after the operation before claiming their fifteen minutes of fame. Not anymore. In Louisville last week a team of doctors announced their intention to perform 'the world's first successful hand transplant'---using a limb from a fresh cadaver---before lifting a scalpel or even picking a patient."

The lattermost task was and is one of the most difficult, enigmatic, and crucial aspects of transplanting a human hand. From the close of the conference in November 1997, when surgeons were encouraged to find suitable patients, it was a year before the Louisville team decided Matt Scott would be the right person to receive that rare privilege (or curse).

First, they tested the hell out of him.

Physical tests included X-rays, precise measurements of his (missing) hand (i.e. bone girth, muscle remnants, stump circumference, skin tone), and extensive bloodwork. The team contacted Scott's insurance company and made sure they would help cover *all* the post-transplant drugs and therapy. Scott was told the operation had every chance of failing, and to mitigate any irrational hopes that might undermine his understanding those odds, Scott's mental and emotional health was scrutinized by a specialist in transplant psychology, Martin Klapheke.

Over the phone, Klapheke related the extent of the team's precautionary measures, "We really went the long mile on this, doing hours and hours of psychological testing in addition to interviews. We tried to do the opposite of artificially instilling confidence. We almost played Devil's Advocate, saying, 'Here's what might go wrong...' In no way did we want to nudge anyone towards it. We said, 'These are the ups and downs,' then we did it all over again."

They even made Matt designate a patient advocate---that is, an outside observer who would have nothing to gain or lose from Matt's groundbreaking surgery and who'd cross-examine him on all of Klapheke's questions to see if his resolve would buckle.

Tobin explains their apparent obsessiveness, "These days it's easier because we have a good measure of success, but when we were first working on this, there was none of that. To Dr. Breidenbach's credit, he was very very honest with the candidates. He said, I give it about a fifty-fifty chance of falling off within a year, and you might not have any function at all, and you could die. I thought that was very straightforward of him not to overrepresent the results."

Twelve years down the road, Matt Scott is the first person in the world to have helped doctors prove the theoretical benefits of human hand transplants might hold up in reality---that for the right patient at the right time, the rewards of accepting the bittersweet remedy really do outweigh its risks.

Scott *isn't*, however, the first amputee in history to have believed a hand transplant possible before anyone had effectively performed one, nor to have pondered, acknowledged, and legally consented to all of the above risks, nor to have lain down on an operating table with another man's cold, bloodless hand beside him. Ten years ago, Matt Scott was not the Neil Armstrong of human hand transplants. He might be, today---but that all depends on your definition of "first success."

One Wednesday morning in the fall of 1998, a couple weeks after the publication of the international conference proceedings, Warren Breidenbach was cleaning up from a routine surgery when he got some very surprising news.

September 22nd, 1998.

A 41-year-old Frenchman has a terrible motorbike accident. In the crash, he suffers a cracked skull and massive bleeding on the brain. Fortunately and unfortunately, he does not survive the event.

Just hours after the man's total brain death is pronounced, French statesman and doctor Jean-Michel Dubernard is sitting in a taxi in Paris when he receives a long-awaited phone call. He argues spiritedly with the cab driver, and after stopping at a bank to prove he can pay for the trip, Dubernard convinces the stranger *not* to drive him back to his Paris apartment, but four hours to the southeast. Nothing must get between himself and the braindead man.

The French countryside, and time, flies by while Dubernard makes phone calls. One to London, to tell transplant doctor Nadey Hakim to find a flight to France, one to Italian surgeon Marco Lanzetta, who then gets in his car in Milan and drives over the Alps, and one to Australian Earl Owen, who, staying at a hotel in Lyon, gathers himself and his patient and goes straight to Edouard Herriot Hospital.

The moment had finally come to prepare for surgery.

Jean-Michel Dubernard had no connection with the ill-fated motorist until he received that longed-for call. He and a special collection of anesthetists, surgeons, immunologists, and psychiatrists had convened in France three weeks before, waiting with an ambivalent, macabre hope. They needed a hand from some afflicted family's deceased son or daughter. One that matched the skin, bones, and blood of Clint Hallam, their eager patient. They had waited days, then weeks, for just such a sacrifice.

They'd waited years for the opportunity.

Dubernard first dreamed of performing a hand transplant long before the field opened up experimentally. His involvement in the history of hand transplants arose in part from his friendship with Earl Owen, a well-known Australian microsurgeon whom Dubernard invited to help lead a microsurgery workshop in Lyon almost 30 years ago. It was Owen who familiarized him with the technical challenges of hand replantation, fueling what Dubernard, in his animated, lilting French accent calls, "Ze dream..."

For years after meeting Owen, Dubernard kept abreast of the literature for experimental limb transplants, but like Breidenbach, he says he found it a rather mixed bag and difficult to analyze. Since the papers on primates were not encouraging, he came to realization that the best bet might be to tackle hand transplants directly in humans. On the phone, Dubernard spoke fast and excitedly of the moment that set the wheels of so many spinning towards Lyon that September day. In 1996, Owen had come to visit Dubernard in Lyon. While the two doctors watched the parade of the first Lyon dance festival in Bellecour square, Dubernard shared his intuition about hand transplants. After some discussion and fired by Owen's drive and enthusiasm for the project, they decided to take the plunge and look for suitable patients.

Owen found "Clint H.," a patient of his in Australia who'd lost his hand in 1984 after an accident with a circular saw. Hallam had previously volunteered for the hand transplant program in Louisville but was denied candidacy due to his location in Australia. Perceiving his earnest desire to have the procedure, the French team listed Hallam after, "a thorough physical examination and psychological assessment," while Dubernard was making the final arrangements to perform the hand transplant in Lyon.

But doubt still nagged the French physician. Dubernard writes of his uncertainties at the time, "Can one see and use the hands of a dead person, every day and all day? Can one own another person's hand? I contacted Jean Cournut, President of the Parisian Psychoanalysis Society, and himself a psychiatrist and a Freudian psychoanalyst, and told him about Clint H. We went through all the psychological aspects of hand transplantation over and over again."

On the phone, Dubernard laughs when recalling how he spent so much time in the psychiatrist's office that his wife thought he'd secretly been seeking mental counseling.

Eventually he became convinced that a hand transplant would truly be therapeutic, and likewise convinced the head of the organ procurement agency in France and the ethics committee of Lyon University. Owen and Dubernard consulted lawyers and drew up detailed consent forms. They picked a team and a time to convene. In early September 1998, their chosen cadre of doctors trickled into Lyon from around the world.

The final test of readiness was administered by Gabriel Burloux, a reputed French specialist in body image issues and the official psychiatrist of the team. "Earl and Clint arrived in Lyon in early September. They stayed at the Reine Astrid Hotel where Gabriel Burloux joined us and immediately disappeared into Clint's room. Earl and I waited patiently in the lobby but with growing anxiety as nearly two hours passed. When Gabriel finally emerged, he gave us the green light," writes Dubernard.

Accounts differ as to how long the Europeans waited for a donor in Lyon before dispersing, but the Australians, who couldn't make it back in time if a donor was found, stayed on for three more weeks. As Owen and Hallam drained their pockets on living expenses and hotel bills, Hallam was becoming agitated.

In the long hours, the doctors learned why.

Hallam lied about the contents of a suitcase supposedly lost on the flight from New Zealand. This suitcase was supposed to contain money that Hallam had ensured doctors would pay for the expensive hotel and hospital bills. (The doctors were donating their time). When the suitcase didn't turn up, Owen and Clint moved to a more affordable hotel. Dubernard writes, "Clint admitted he could not muster the funds. He was virtually penniless. We forgave him for lying on the grounds that he was so determined to have the transplant, but doubts about his behavior nevertheless persisted. I had a brainwave."

Dubernard's idea was to go to Paris to ask his friend and generous research sponsor Charles Merieux for the funds to cover the necessary costs. Although the French team had come to their conclusions about hand transplants independently of the Louisville team, their case now had the added boon of support from the '97 international symposium---the conference publication had just come out, with the unmistakably positive pronouncement, "Just do it." Merieux agreed.

As Dubernard was leaving Paris, relieved and excited by the news, a call with even better news came through. They had a donor. The next day, the skilled international team completed what was immediately deemed the world's first successful hand transplant. Clint Hallam's immediate reaction after rising from the anesthesia was to praise the doctors who gave him back "his" hand, calling it a miracle.

The media went wild. Precious few people had been privileged to know about the team's intentions, and several accounts (including the English transplant doctor Nadey Hakim's own version) tell of the "quiet assembly" of the team and furtive meetings behind closed doors. Dubernard writes that he and Owen decided not to consult the national ethics committee in France, knowing that that review board would draw out the philosophical debates so long as to be impractical. They say they didn't contact news networks because they had no desire to announce their success before they had a success to announce.

To add to the fervor surrounding the surprise of the crowning moment, on the same day Hallam was transplanted in Lyon, the first lady of France, Bernadette Chirac, had come to Edouard Herriot hospital for a scheduled visit and was able to watch part of the surgery. From that point on, the doctors had no need to inform journalists of their revolutionary operation--- Chirac had unwittingly brought the journalists to them. Dubernard, who describes himself as a

naturally shy man, writes, "I cannot recount the pestering we were submitted to from that moment onwards. We were forced to prepare a press release and hold a press conference."

Two days later, medical reporter Roger Dobson noted in the *Guardian*, "The biggest shock was no doubt felt by a rival transplant team in Louisville who had---perhaps naively, some say foolishly---announced their intention to carry out just such an operation by the end of this year. But the hand of fate, as the world now knows, favoured the multi-national Lyon team who had kept their endeavour so secret. ... in the new world of super surgeons and pioneering physicians, being first is all important: to Lyon the laurels, to Louisville the professional abyss."

But there were also shocks for the team in Lyon. Two days after Hallam was transplanted, Australian newspapers revealed that their patient had been less than honest about the moment he lost his limb in circular saw, among other things. An article in the *Weekend Australian* reports, "He neglected to say 'while in prison.' ... [but] Hallam's criminal record was the least of the information he failed to tell his doctor. Hallam is facing fraud charges in Perth, a warrant for his arrest stands in New Zealand and he is connected to a string of frauds involving more than \$1 million and spanning three countries."

Owen responded to the news to say it didn't matter who Hallam *had* been---doctors take a Hippocratic Oath to help everybody. In the months that followed, the team was pleasantly surprised to see Hallam's nerve connectivity daily improving, and that the fingernails on his donor hand were growing at a faster pace than his own, showing early signs of success.

Hallam left the surgeons' care just after Christmas, ostensibly bound for Australia to confront his outstanding charges, but ending up, at various intervals, all over the world. "We knew that he was in the United States as he was regularly appearing on TV and in the newspapers," writes Dubernard. Eventually, "Clint came back. He was doing his rehabilitation exercises alone. Clint had always shown streaks of brilliance but his behavior was difficult to understand."

In a BBC documentary on the history of surgery, Hallam talks of how, throughout the next two years, he started to detest the limb for its mismatched appearance and poor functionality. He never regained much feeling in his hands, he said, and had such limited motion and strength that he could barely grip his toothbrush. "One of the hard things to accept for me is that I'm almost more handicapped with my new hand than I was with one and a half [prosthetic] hands," he claimed.

There were other hardships. The side effects of the drugs Hallam had to take became too much for him once he'd begun to resent the hand. "First, I have diabetes," he said, "the second side effect is more physical in that my body has gone from 'chest' to 'breasts,' and that's a *little* bit difficult to deal with."

So Hallam made what he may have thought was a *little* modification, and stopped taking all of his meds.

Pictures of Hallam's dying right hand are enough to make most viewers' stomachs twist and tighten. The skin of the alien appendage is red, swollen, and peeling off in large flakes. One can almost imagine the dull, throbbing pain inside the slightly curled, puffy digits, on top of which five fingernails float like ridged gray oyster shells atop a bed of ice.

Two years and four months post transplant, after touring the world with it, after hundreds of headlines and thousands of pills, Hallam demanded that the new hand be sawed off again. No one would do it. Initially, the French team refused to perform the amputation, instead urging Hallam to resume his medications.

According to Dubernard's account, "When Clint discovered that Denis C., [the man who received the world's first bilateral hand transplant, also led by Dubernard] had had an audience

with Pope John-Paul II, Clint also went to Rome but he failed to meet the Pope. He was very disappointed. Was this why he discontinued treatment in September 2000? Palmira Petruzzo, an Italian vascular surgeon and member of our team, took great pains to persuade him to resume the drugs but to no avail. One month after discontinuation, the signs of rejection were still only moderate. They disappeared rapidly on treatment but so did the patient."

Years later, Gordon Tobin related his own observations via phone from Louisville, "Hallam was going all around, traveling a lot, selling pictures of the hand and his story---and once he stopped taking his medication and his hand was rejecting, he even called us and offered to be a 'guinea pig' for our immunologists---if we would pay him. He went to a few places to get his hand amputated, but as he wanted the BBC to film the amputation, they all refused."

Hallam finally turned up in California, where he'd convinced a center to amputate the hand. The center reportedly balked at the last minute, instead offering to pay Hallam's airfare to London. The world's debatably successful first hand transplant was amputated by a member of the original transplant team, Nadey Hakim, in a London hospital on February 2nd, 2001. This, too, was carried out in secrecy.

In an article for the *New York Times*, physician and reporter Lawrence K. Altman describes in detail the final days of Clint's time as the world's first successful hand transplant patient:

To avoid news media attention, Dr. Hakim scheduled Mr. Hallam under a false name for a leg amputation at the Harley Street Clinic [in London]. Dr. Hakim agreed to pick up Mr. Hallam at his hotel at 3 p.m. for a 6 p.m. operation. But Mr. Hallam did not appear.

At 6, Dr. Hakim said, Mr. Hallam called to say that he had received 5,000 British pounds from news organizations for an interview and pictures of his arm and was now ready for the amputation. At 8 p.m., Mr. Hallam was on the operating table. Surprised nurses scurried to bring in the correct instruments for a hand, not leg, amputation. By 9:30 the amputation was over. A few days later, Mr. Hallam paid a reduced hospital bill of \$4,000, Dr. Hakim said.

Mr. Hakim expressed mixed feelings about Mr. Hallam's case. He was relieved because his patient had escaped healthy and without complications. But, Dr. Hakim said, "We gave him a chance, and he destroyed it by stopping the drugs."

Clint Hallam may or may not be the world's first successful hand transplant patient, but as an article in the UK paper the *Observer* notes, he certainly can claim to be the keeper of a surgical novelty. Hallam is now the first man in history to lose his right hand three times---first in a buzz saw accident while in jail for fraud, second in a failed replant, and finally after the amputation of a dead Frenchman's transplanted hand.

VI. Sense vs. Sensibility

Four months after the French team's surprising announcement and 4,000 miles away, doctors in Louisville, Kentucky, played the tortoise.

Unlike history's first two hand transplants, Matt Scott's surgery was a picturebook fulfillment of the fairytale phrase, "Third time's a charm." His graft survived past two weeks, past two years, even past ten years, with relatively good function, feeling, and appearance.

If this *were* a fairy tale, however, the Brothers Grimm would have written it. Every bit as gruesome as the original Black Forest legends, (most fairy tales are far less benign in their original versions than their modern Disney-fuddled retellings), Scott's transplant didn't just make headlines once. Whatever the Louisville doctors most feared about harvesting a dead man's hand would soon play out in the life story of their first painstakingly selected patient.

"Already last week the story took a macabre twist," an article in *Newsweek* reports, "Though the donor hand was supposed to be anonymous, tabloid snooping pressed the man's family to reveal his identity: Glenn William Johnson, a convicted murderer who took his own life the day prior to the operation." And the *Sunday Mirror* expands on the chilling details, "Johnson had ended up killing himself after blasting his girlfriend and ex-wife with a gun."

The not-yet-fairy-tale quickly turned into, "A circus." Jerry Wright, director of the Kentucky Organ Donor Affiliates, seemed wearied by the thought, even on the phone. "We still don't know how that information got out--some think the donor family said something--but KODA keeps things like that *strictly* confidential." Scott's ending turned out to be a happy one(so far), but no one could have known that at the time.

Looking back through history and comparing the two first patients' experiences, the story of human hand transplants might resemble a fable even more than it does a fairy tale. In this next simplified bedside version, the perhaps-too-clever-for-his-own-good fox character, Clint Hallam, becomes the recipient of a rare endowment: a new hand. Unfortunately, the gift is lost to the character's unsinkable desire for fame and fortune.

By contrast, Matt Scott (the faithful-protagonist-beset-by-unsavory-circumstances character), waits patiently for a promised change, wanting no extra attention or money---nothing but the wholeness a new hand might bring him. What he gets for his trouble is the severed limb of a convicted murderer. Fingers that had been fingerprinted, and thus---quite literally---would still be wearing their own sordid past. But Matt Scott powers through, and does what he promised to do, making the less-than-perfect hand his own. No matter what. (A worthy moral).

Years after his transplant, Scott met his donor family to thank them for the gift. To this day, Scott says he feels nothing but gratitude for the experience, stating that, "If it fell off tomorrow, I'd do it again. I feel like I've been healed in a way that would make another amputation far easier than the first one."

Like most fables, this one's moral extends beyond its yin-yang main characters. The French doctors who gave Hallam his rejected hand bore far more public scrutiny for that surgery *ex post facto* than Louisville ever did before (or after) performing their first transplant.

Dr. Bohdan Pomahac, who heads up the CTA program at Brigham and Women's Hospital, says, "I think that there are a lot of politics and little stories behind the story---Max Dubernard who did it first was really in competition with Warren Breidenbach, and there's no question that they selected a patient that was not the right candidate---but they got the victory and no one knows that Warren was number two. Even though Warren's patient did way better, because he was properly cared for and selected. I think that Warren did the right thing, which

is to do everything that you feel is best. It's never going to be perfect; you never have all the questions answered or the doubts completely eliminated, but you make it as perfect or close to perfect as you can, and you go for it."

According to Breidenbach and others on the Louisville team, there are no hard feelings. They say they knew that by publishing about the prospects of human hand transplants, there was an additional prospect that they'd get "scooped," as it were. Being first was not the point. In some ways, the French team's groundbreaking exploit was a relief.

Says Breidenbach, "You have to give Dr. Dubernard credit---he's a mover, a pusher, and in a different position than me. In France he's the equivalent of a senator; he's a well-known, famous transplant surgeon and the head of a university department. All in all, he's far less touchable than me. Quite frankly, Dubernard's a guy I like. He's very charismatic and smart---you know, the kind of guy I'd like to go to dinner with." (Although it's doubtful they'd have had much to say to each other the day the French team announced their success...)

In addition to their questionable choice of a patient, Dubernard and Owen have been censured for their secrecy in the planning and execution of their first hand transplant. Dubernard explained his reasoning over the phone, "There is no sense in saying you are going to do something if you don't *do* it---do you like football? It is like saying to the other team, 'I am going to put a goal in,' but then you don't, because you never know what's going to happen. I think that if you're going to do something, if you have the dream and you can help someone, then you should just *do* it---as they finally said during the 1997 conference in Louisville at their last meeting."

In a recent paper, the Louisville team published what seems to be their official opinion on the matter of Clint Hallam and the world's first successful hand transplant, "It is the Louisville team's view that failure could have been prevented by careful screening and a thorough psychosocial and psychiatric evaluation of this candidate."

So if failure *could* have been prevented with more thoughtful scrutiny of Hallam's financial and moral deficiencies, should the laurels of "first success" continue to be conferred?

It's difficult to know. It's also debateable whether first or seconds or thirds should matter at all in the medical field, since all doctors *should* be trying to do is change their patients' lives for the better. But as many reporters pointed out in September of '98, few people know the name of the guys who walked second and third on the moon, whether or not they deserve as much credit as Neil Armstrong.

If the French team did rush in their assessment of the situation and their patient---if they had conveniently ignored signs that Hallam might not be the best choice (how, after all, was a "penniless" man going to pay for all those drugs?)---and *if* the situation had been like it was in the 1960's and the world had just waited to see what would happen... what would Clint Hallam's epic failure as a patient have done to the field of composite tissue transplants?

In a paper called, "Lessons from Hand Transplants," London plastic surgeon Shehan Hettiaratchy reasons, "In the aftermath of the failure of the first hand transplant, surgeons and patient have traded accusations. He did not comply with therapy, allege the surgeons; my body had taken enough, counters the patient. Essentially they are both illustrating the same point; immunosuppression for a non-vital, highly antigenic transplant is verging on the edge of what is acceptable. Limb transplantation has come out of Pandora's box and putting it back will be difficult. These operations have extended the boundaries of reconstructive surgery and provided hope to many patients. However, the transplants already done must be regarded as true experiments and critically evaluated."

Much of that evaluation takes place in the “soft” science of psychology. It is obvious that hand transplants are technically doable, but even when all the appropriate steps are taken to ensure a good match and a willing participant, unrealistic expectations can preclude success for anyone who’s desperate for a result that isn’t really possible. Even with a good psychologist on their team, doctors can’t ensure that their patient has truly given “informed consent” if the individual wants the procedure badly enough to lie to get it.

As Dubernard points out, it’s sometimes difficult to know what “lying” even means, especially in the doctor/patient relationship. On his decision to overlook his Hallam’s dishonesty, Dubernard said via phone, “I would not change anything in retrospect. You *have* to dream. This is where the individual imagination meets the collective imagination...” then continued, I thought somewhat wistfully, “It is clear that I am a good surgeon and I had the chance to have the best possible technical team. I read all the literature and checked my honesty with myself over hours with a psychiatrist. We did the technical experiments and the testing necessary to determine whether Clint Hallam was ready and aware of the risks and commitment. I still think Clint *could* have been a very good patient.”

As Dubernard spoke, I, too, felt the weight of a sigh---*C’est la vie...*

Not long after that conversation, I came across an essay by author William Kennedy, who writes, “Deceit as a way of life is ubiquitous. Animals hide, mimic, change color, play dead to avoid predators; people disguise themselves, hallucinate, dream, forget and lie to avoid reality, but unlike animals they also lie to themselves.”

Just like the doctor who regretfully turns away a potential patient, Kennedy’s commentary made me consider why I haven’t tried to find and contact Clint Hallam for his side of the story. I simply couldn’t consider Hallam a reliable resource, no matter how convincing he was, and no matter how much I’d like to believe him.

It’s always a balancing act for hand transplant doctors (and all doctors who have the dream and drive to practice innovative medicine) to find candidates that are enthusiastic about a new technique or technology---but not *over*-enthusiastic. Psychologically, the ideal hand transplant candidate must be heartily dissatisfied with his or her situation but not clinically depressed with long-term issues concerning self-image. A 2001 paper by doctors in Louisville states, “[In explaining how people make difficult decisions], there is research showing a large preference for a risky alternative that has a chance of erasing a loss and returning to the previous status quo. This is just the situation we have in hand transplantation. Thus, the patient would be more willing to accept risk than would the physician.”

While even the basic qualities of the “perfect patient” for hand transplantation have yet to be determined, the list of reasonable indications (those conditions that *indicate* doctors have a responsibility to intervene) is in constant evolution. For instance, congenital defects are currently a counter-indication for hand transplants, because doctors worry a brain that never once communicated with a hand would not know how to respond to it if one suddenly appeared in later years.

But critics of hand transplants at the turn of the century said essentially the same thing about traumatic amputees. In fact, some of the patient selection criticism borne by Dubernard’s team had nothing to do with Hallam’s personality or past. It had to do with how long (over ten years) he’d been without a hand. Some doctors assumed that the human brain wasn’t plastic enough to take command and control the sudden reappearance of the lost limb. Similar concerns arose when Breidenbach transplanted David Savage in 2006, who had mangled his hand in a metal press over 30 years prior to his surgery. Savage, however, has also done just fine---he still has and daily uses his hand. In fact, the afternoon I spoke to Savage on the phone,

the thumb on his transplant hand was aching because he'd smacked it with a hammer while fixing his garage.

Thankfully, the neuroscientific naysayers were wrong. When successful, risky cases like Savage's clear the road for similar amputees, while also shedding light on how the human body and brain adapt to hand transplants and the drugs that keep them alive. Each surgery performed (even those that aren't done experimentally) raises the level of medical knowledge about these procedures, which raises doctors' ability to ensure better outcomes in the future. But only by reaching beyond the protocol and procedures that are most likely to be successful can hand transplant doctors more fully understand the indications for an operation, both when screening out and screening *in* their future patients.

As new teams form all over the world, each one's experience will help the others know not only who should have a hand transplant, but whether, in the long run, hand transplants are really worth the uncountable hours of effort and thousands of dollars they require to be effective treatments. According to Pomahac, "If you objectively look, you could say hand transplants are a mix of failure and success. We still don't quite have enough data to support unequivocally---especially unilateral hands---that this is really worth doing. I think part of it is that we just don't know enough."

Skeptics abound. A 2009 survey of North American hand surgeons' attitudes towards hand transplantation showed just a quarter in favor, almost half against, and the rest undecided on their opinion of the operations (at least until the drugs improve). On the other hand, *can* those doctors who haven't spent time researching the outcomes of these procedures, or talking extensively with the amputees who are desperate for a normal life, really give an informed opinion on the matter?

"To me its all about relieving pain and suffering," says Martin Klapheke, "You know, when they first asked me to do this program, I was a little hesitant because in my mind I was like, 'Well, I dunno if this is really necessary...'. It was only after talking to all these amputees that I overcame my ignorance about this sense that they had of feeling incomplete, damaged, not whole. I mean they just *longed* for that sense of wholeness again. This quality of life issue was so important that it clearly made sense."

As hand transplant programs are created, patients listed, and the number of amputees with transplanted appendages swells, the question remains---should human beings, as a "soulful" species, be allowing this at all? Are hand transplants eventually going to be more harmful than they are helpful? Prominent ethicists are still scratching their heads over a question people ask every day: *Do you need a hand?*

During a 2008 panel on transplantation innovation, Dr. James Young, chair of the Academic Department of Medicine at the Cleveland Clinic, said, "Putting a new hand or face on someone is astounding. It changes the morphology of the brain, which can be observed with functional magnetic resonance imaging. It changes the soul, if that is what you want to think of when talking about the brain."

If we can take an organ with so much meaning, so much gravitas, and so much visibility off of one person and put it on another, what could we conceivably *not* transplant? Human kidney transplants opened the way for human heart (and liver and lung) transplants; those life-saving operations opened the way for the life-changing CTA's of the hand, (and now the face) for the chronically disabled and disfigured. What will be transplantology's next major "world's first?" Is there a boundary limiting the possibilities composite tissue transplants have now opened up? I29f there is a line that medical science just can't cross... will that border be one of practicality or morality?

“CTA has now made theoretically all parts of the body transplantable,” said Dr. Breidenbach at the end of our conversation. “But let me make this clear---in *theory*, not reality...”

In some ways, hand transplants still *are* as much theory as reality. In theory, all the hand transplant patients that still have their grafts are still experimental subjects. No one knows what the long-term results of hand transplants will be. If these patients’ immunosuppressive regimen chronically fails, and their hands stop functioning, or worse, the heavy drugs abrupt their lifespan to a great degree, hand transplants might turn out to be no more than a briefly inspiring (or ridiculous) large-scale experiment. Depending on how you look at it, and where you’re coming from.

“Somehow future abandonment is irrelevant. It will never negate the value of these early hand transplants. We’re just going to learn so much. And they’ll probly have positive benefits that you can’t know now. Even in those early kidney transplants, people weren’t able to *see* that it would lead to transplanted hearts, lungs ... It’s a win/win situation. Most of our patients actually, literally said, ‘I realize it may not work for me, but I also realize what you learn from doing this might help people on down the road,’” says Klapheke.

That’s certainly true for Rich and Cindy. Whether or not Rich’s hands will ever be capable of easing others’ pain in the chiropractic sense, simply having them is, in its own way, something he’s doing to help others. For Rich and others like him, hand transplantation may be a solution to chronic infirmity whose struggles are, themselves, a kind of rehabilitation.

As Rich works to strengthen his new hands, he and Cindy are thankful that they had the choice to participate in something that so many call miraculous---whether or not the visible scars abide.

I imagine the couple saying so, every morning back home in Oklahoma. Kneeling together, both hands folded.

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Interviews

(In order interviews were conducted).

Dr. Warren Breidenbach III
Formerly: Lead Hand Surgeon
Kleinert, Kutz, and Associates Hand Care Center
Louisville, Kentucky
Currently: Chief, Division of Reconstructive and Plastic Surgery
University of Arizona
Tucson, Arizona

Brenda Blair, RN, MSN
Research Manager
Christine M. Kleinert Institute

Dr. Michael Marvin
Director of Transplantation at Jewish Hospital
Associate Professor of Surgery at the University of Louisville
Louisville, Kentucky

Dr. Richard Edwards

Former Chiropractor
US third double hand transplant recipient
Edmonton, Oklahoma

Edwards, Cindy
Wife of double hand transplant patient Dr. Richard Edwards

David Savage
Louisville program hand transplant patient
Bay City, Michigan

Dr. Bohdan Pomahac
Director, Plastic Surgery Transplantation
Medical Director, BWH Burn Center
Assistant Professor, Harvard Medical School
Boston, Massachusetts

J. Rodrigo Diaz-Siso
Research Fellow
Division of Plastic Surgery
Brigham and Women's Hospital
Harvard Medical School
Boston, Massachusetts

Matt Scott
Paramedic Associate Director
Camden College, New Jersey
US first hand transplant recipient

Dr. David Kaiser
Associate Professor
Program in Science, Technology, and Society
And Lecturer, Department of Physics
Massachusetts Institute of Technology
Cambridge, Massachusetts

Dr. David Jones
Associate Professor
Program in Science, Technology, and Society
Massachusetts Institute of Technology
Cambridge, Massachusetts

Dr. Jean-Michel Dubernard
Transplant Surgeon and Former Deputy, French National Assembly
Edouard Herriot Hospital
Lyon, France

Dr. Christina Kaufman
Executive Director, Christine M. Kleinert Institute
Louisville, Kentucky

Dr. Martin Klapheke
Formerly: Director of Transplant Psychiatry at Jewish Hospital
Louisville, Kentucky
Currently: Professor of Psychiatry
UCF College of Medicine
Orlando, Florida

Dr. Simon Talbot
Hand/Microsurgery Fellow
Brigham and Women's Hospital
Boston, Massachusetts

Jerry Wright
Director, Kentucky Organ Donor Affiliates
Louisville, Kentucky

Dr. Gerald Brandacher
Visiting Associate Professor of Surgery
Scientific Director, Composite Tissue Allotransplantation (CTA) Program
Department of Plastic and Reconstructive Surgery
Johns Hopkins University School of Medicine
Baltimore, Maryland

Dr. Gordon Tobin
Professor of Surgery and Chief of Plastic and Reconstructive Surgery
University of Louisville
Louisville, KY