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HOW TO MAKE A NOSE

ALAN ALDA (NARRATION) It has never been hard to put together body parts -- in the movies.

MAD SCIENTIST It's alive. It's alive. It's alive. It's alive. It's alive.

ALAN ALDA (NARRATION) But Hollywood had better look out, because MIT scientists are getting in on the act.

ALAN ALDA Does he have the nose?

BOB LANGER Yeah, it's coming.

ALAN ALDA You got it? That's the nose?

RESEARCHER It's right in the dish here.

ALAN ALDA (NARRATION) OK now, we are not, repeat not, on a movie set.

ALAN ALDA Wait, what is this?

RESEARCHER This is cartilage. It is a scaffold of...

BOB LANGER You see the nostrils?

ALAN ALDA Yuck! Wait a minute! Look, with nostrils and everything…

BOB LANGER We made a scaffold and there's the little nostrils there -- and that's pure cartilage.

ALAN ALDA You could make it in big blocks and carve whatever shape you want.

RESEARCHER Exactly, exactly, that's the whole idea.

ALAN ALDA Would you mind taking this back? I really don't wanna…I mean it's alive, it's sort of alive.

BOB LANGER Yeah, sort of alive. We just wanted to give you a flavor for it.

ALAN ALDA Unbelievable! You bring in a nose! I can't get over that.

ALAN ALDA (NARRATION) In MIT's Langer lab they're actually figuring out how to make body parts.

RESEARCHER First we make what we call a polymer scaffold, and that's a piece of synthetic material that we can make into the form of a sheet, or other three-dimensional forms.

ALAN ALDA (NARRATION) Now we're making heart muscle, starting with little clumps of synthetic fibers -- the polymer scaffold, as they call it. Then the scaffold is bathed in living heart cells. Bob Langer has pioneered this new field of tissue engineering.

BOB LANGER She's trying to mimic, outside the body, what actually happens inside the body. She's giving it the kind of food it needs, the kind of structure it needs, and even the kind of mixing, you know, that it may get inside the body.

ALAN ALDA (NARRATION) If you get the conditions just right, you can grow pieces of living heart tissue.

ALAN ALDA I'm looking at something that's making heart. Does that sort of strike you, every once it a while, that you're making these things that used to be that if you lost it, that would be the end.

BOB LANGER Well that is what we want to do, you know. It does strike us. What we hope is that some day we'll be able to have a whole series of replacement parts for people so that if they find a problem, we'll be able to help them.

ALAN ALDA It's like an auto part shop, you know.

BOB LANGER That's right.

ALAN ALDA I need a new carburetor and you just go in and you drive out again. I mean, this is... how many years away are we from having a part shop for

bodies, I mean where you can really just get what you need. Is it ten years? Fifty years? A hundred years? Must be hard to guess.

BOB LANGER Right I think it may depend on the part, you know. Some of the easier parts like skin or cartilage, I think you know that's probably five or ten years. Some of the harder parts like heart, that may be many, many years away, fifty or, you know, it's hard to know.

ALAN ALDA (NARRATION) Here, after about two weeks of growth, are the pieces of new heart.

ALAN ALDA They're under a microscope and then you can see it on that monitor?

BOB LANGER That's right, we have a microscope here and then basically they're on the monitor and you can see them beating

ALAN ALDA The dish shaking, those are separate cells beating.

BOB LANGER Right. Say; take a look right down here, for example, or here. And these are individual heart muscle cells, and they're just beating.

ALAN ALDA Is there any way you could make use of that right now, in a heart?

BOB LANGER It's too early to do that now, but some day what I expect is that we could make a sheet of this, you know, and make cardiac muscle. And some day, if we have the right type of cells to actually transplant that onto a patient. You know if they have, er, if some of their heart muscle's damaged.

ALAN ALDA (NARRATION) Right now they're working with animal cells, but Bob Langer's hope is not at all far-fetched. Take a look at one of those pieces of heart as they give it an EKG, like a regular heart checkup you might get from your doctor. The new tissue transmits heartbeats exactly as it should. With tissue engineering advancing rapidly, the search is on for a reliable, and ethical, source of human cells to grow parts from. Three years ago, I visited Michael West at his company, Advanced Cell Technology. He's aiming to make any kind of cell required, starting from the kind of cell we all came from. They're called embryonic stem cells. Embryonic stem cells are the first cells that grow as an embryo develops -- precursors to all body parts. The idea is to grow these stem cells inside unfertilized eggs, which may pose fewer ethical problems than using fertilized embryos.

ALAN ALDA Go straight in?

JOSE CIBELLI Yeah, straight in.

ALAN ALDA (NARRATION) The technique is similar to the one used to clone Dolly the sheep, although I'm actually working with a cow egg here. First I have to pierce it, and suck out the nucleus, containing the cow's genetic material.

JOSE CIBELLI There's a syringe next to your hand now. Turn it.

ALAN ALDA There it is. Here it comes. Watch this, watch this, guys. This is good. This is good. Have I got it?

JOSE CIBELLI Go back a little bit more

ALAN ALDA OK. Got it. Got it.

JOSE CIBELLI Perfect. Right there is perfect.

ALAN ALDA (NARRATION) Next I pick up a human cell -- this one's an adult skin cell. It could be mine, or yours, or anybody's. Then I slide the skin cell into the egg.

ALAN ALDA This is really fascinating to do. But what are you getting out of this? What do you hope to get out of this?

MICHAEL WEST Well, the excitement about cloning isn't that we can make a genetic copy of a sheep or a goat. It's that it teaches us some really fundamental biology. That's that every cell in our body has, like the skin cells, has the full genetic potential to recreate life, young life. So our hope is that someday, elderly patients that have heart disease or Parkinson's disease, we could take a little cell from their body that they'd never miss and sort of take the cell back in time and recreate young cells and tissues that can be used for treating disease.

ALAN ALDA (NARRATION) A tiny electric shock will stimulate the adult skin cell to start dividing. Somehow the environment of the egg leads the adult cell to behave like it's young, and begin to make embryonic stem cells. They've tried this with both cow and human eggs, so far with partial success -- the number of divisions the implanted adult cell has made has been limited. But it's a start.

MICHAEL WEST The magic is, it's possible to make this sort of mother of all stem cells, the embryonic stem cell, that's genetically identical to you. So then you could make...

ALAN ALDA So I won't reject it then.

MICHAEL WEST Right

ALAN ALDA If you make me a new organ or make me anything I might need because of the disease I have, I won't reject it. It's not coming from another person or another animal.

MICHAEL WEST Exactly. The big unsolved problem, the reason thousands of people die every day is the lack of transplantable cells and tissues that your body will not reject. And this new technology could be the long sought means of transplanting cells and tissues that your body will not reject.

ALAN ALDA You're working with very tiny...

ALAN ALDA (NARRATION) Back at the Langer Lab, they're working on the assumption that human stem cells of all kinds will eventually be available -- eye cells, for example.

ERIN LAVICK We're trying to create scaffolds that have pore sizes as low as ten microns on the way up to a millimeter.

ALAN ALDA How small are you talking here? A micron is… what relationship is a micron to a human hair, for instance?

ERIN LAVICK Right. So a human hair is about two hundred microns approximately.

ALAN ALDA This is extremely tiny. How do you keep track of what you're doing? How do you actually build things that small?

ALAN ALDA (NARRATION) Erin Lavick is going to teach me how to make a polymer scaffold, like the ones used to build the heart tissue and the nose. But my scaffold is going to have the right, fine pore structure to repair a damaged retina.

ERIN LAVICK This is the polymer dissolved in a solvent.

ALAN ALDA So this is what the scaffolding will be made of?

ERIN LAVICK Right. You're gonna actually squirt it on to the slide.

ALAN ALDA All of it?

ERIN LAVICK M-hmm. And then what you're gonna do, is you're just gonna take that slide and slide it into the water.

ALAN ALDA Oh there's water there?

ERIN LAVICK Yup.

ALAN ALDA Slide it into the water.

ERIN LAVICK Yeah. Just like that. And so what's happening is, when you slide it into the water, all of the solvent starts to come out and go into the water. And that transfer is what's creating the pore structure, in this case.

ALAN ALDA (NARRATION) Erin's made thousands of these scaffolds, gradually refining her methods.

ERIN LAVICK These are some of the scaffolds that we've made using this technique. And these have all been dried. And so what you can see is they're very thin, because you don't want to put something bulky in the back of a retina.

ALAN ALDA This looks like a piece of paper.

ERIN LAVICK M-hmm. But if you look at it under a scanning electron microscope, it actually has pores.

ALAN ALDA (NARRATION) The tiny pores, each about one-twentieth the thickness of a hair, are channels made by the solvent when it flowed out of the polymer. Next, working with Erin's colleague Michael Young, I'm going to seed the scaffold with retinal stem cells.

ALAN ALDA Now I put...

MICHAEL YOUNG Just on…right in the middle of that big polymer.

ALAN ALDA Just a little drop.

MICHAEL YOUNG Yeah. You can use all of that. That should be fine. And that's it.

ALAN ALDA So I've seeded a polymer with stem cells.

MICHAEL YOUNG Yes.

ALAN ALDA (NARRATION) Now we're going to see how the cells like it inside the scaffold. We're working with mouse retinal stem cells, collected from a

newborn animal as the eye was developing, so they're already on track to become part of the eye. Human cells like this aren't yet available.

MICHAEL YOUNG Okay…

ALAN ALDA What are we looking at here?

MICHAEL YOUNG So this is the same type of polymer that we just looked at and seeded except I did it yesterday. You can see the pores in the polymer if I focus. But you can't see any cells, OK? Because they're very small.

ALAN ALDA (NARRATION) But when we shine an ultraviolet light on the cells, they burst into life.

MICHAEL YOUNG Now we can see retinal stem cells.

ALAN ALDA (NARRATION) The cells have been modified to make a fluorescent material as part of their normal life processes, so bright green spots mean healthy cells. This is beginning to look like a living retina. We're going to see what Michael and Erin are doing with the artificial retina, but first take a look at a normal eye. The retina's at the back. It has a thin cover of nerve cells, on top of a thick layer of light-sensitive photoreceptor cells. They react whenever light is focused on them. In one of the first tests, the artificial retina was placed alongside a retina from a special breed of lab animal that has no thick layer of light-sensitive cells.

ALAN ALDA So this layer, these channels, that's that polymer I made in the dish on the slide?

ERIN LAVICK Right.

ALAN ALDA And now you're looking at it sideways and these are the pores that the cells are growing in?

ERIN LAVICK Right. The darker parts are where the polymer actually is and then these lighter parts here are actually the pores themselves.

ALAN ALDA (NARRATION) Here you can see the living retinal cells sheltering inside the channels of the artificial retina. This was done just in a dish on the lab bench, but now here's the next step. This is a shot looking into the animal's eye. There at the back you can see the faint shape of the artificial retina, now implanted. Here's the same shot in ultraviolet light, showing that the cells in the implant are alive and healthy. What the researchers think is happening is that the retinal stem cells inside the implant are forming new light-sensitive photoreceptor

cells, which connect to the existing nerve cells in the animal's eye. It's still too early to tell if there's an actual improvement in vision, but it's a big step nonetheless.

ALAN ALDA If you're starting with a retinal stem cell, does that mean it has some properties that already predispose it to becoming a photoreceptor?

MICHAEL YOUNG Exactly. That's what we hope.

ALAN ALDA But it could become some other part of the eye...

MICHAEL YOUNG Yes, yes.

ALAN ALDA ...if it were placed some place else? Or under other conditions? What makes it become a photoreceptor, when you do this procedure?

MICHAEL YOUNG One of the things that we've kind of hit upon is that the host actually instructs the cells at some level. So if we put these cells into an animal who has lost photoreceptors, the majority of these cells actually become photoreceptors. So the injury cue we think is critical.

ALAN ALDA The injury itself somehow creates a cue for the growth of new cells. Now, it's interesting because that sounds like the body is signaling itself and trying to grow new cells...

MICHAEL YOUNG Exactly.

ALAN ALDA ...but it's only when you supply the raw material that the body for some reason is lacking, or is being inhibited from presenting... What's going on here?

MICHAEL YOUNG I think… So if you look at lower animals, frogs, for instance, some fish. They can grow a whole new retina. You take out the retina, they can grow a new one, even in an adult. We've lost that ability. But what we think is still present are some of these injury cues. So maybe these instructions for fixing the retina are actually there, but in higher mammals, for instance, we are simply unable to respond to that. So we are taking advantage, we hope, of these cues that are present. And as you say, adding the raw materials to fix what's wrong.

ALAN ALDA So the cues that are happening could be vestigial mechanisms, vestigial functions that are useless to us because we've evolved away from them. But you can pick up on them and make use of them. What a fascinating…

MICHAEL YOUNG The cells can. We don't actually know what these injury cues are. But we know they're present.

ALAN ALDA (NARRATION) If there's a secret to the new science of bioengineering, this is it. If we just provide the right conditions, stem cells will do their thing -- we don't have to know everything about how complex cellular systems work. So we may be glimpsing a future with almost limitless possibilities for repairing or replacing body parts. In our next story, we'll meet the scientist who wants to put together a whole system of body parts, functioning like a body, on the lab bench.

BODY ON A BENCH

ALAN ALDA How long have you been…

ALAN ALDA (NARRATION) This story is about something called a liver chip.

LINDA GRIFFITH Three years.

ALAN ALDA Three years?

LINDA GRIFFITH Yeah. And we've actually got it there. And it's not just chipped liver.

ALAN ALDA (NARRATION) You know, at MIT you don't expect a lot of jokes.

LINDA GRIFFITH You'll see.

ALAN ALDA Oh, chipped liver. Oh, it's a joke. Oh I get it.

LINDA GRIFFITH A-ha. It's a science joke.

ALAN ALDA It's a science joke. A liver science joke. That's even better. Do you make them in here?

LINDA GRIFFITH Yeah, we make them right over here.

ALAN ALDA (NARRATION) Linda Griffith is a bioengineer who's developing a tiny "bioreactor" that behaves like a liver.

LINDA GRIFFITH So Karel, you got everything all ready to set one up?

ALAN ALDA Hi. How are ya?

KAREL DOMANSKY So we have our miniature bioreactor here…

ALAN ALDA (NARRATION) It's called a liver chip because it uses thin, perforated wafers of silicon -- the same material computer chips are made with. Here they use silicon not for its electrical properties, but because we know a lot about making tiny structures with it. Once the chip is sealed in its case, a broth of about a dozen different nutrients and vitamins is pumped through the perforations. Then comes the final step, that turns a chip into a liver chip.

LINDA GRIFFITH This is the room where we do all of our cell culture. So these are sterile cell culture hoods and incubators for the cells. And Anand is now introducing the cells into the sterile bioreactor.

ALAN ALDA (NARRATION) As with the artificial retina, they seed the chip with stem cells -- young cells on track to develop into liver. As the chip is incubated over the next few days, the cells will take up residence in the chip's perforations. It's like having a colony of livers, living in the lab -- and that's kind of how the researchers feel about it.

ALAN ALDA How do you keep track of these, do you give them little names or…

LINDA GRIFFITH They do give them little names, which I find out when I get the file for a publication or a presentation, it'll have, "Here's the data from Mandy, and Mandy was very good, but Tom was really not."

ALAN ALDA (NARRATION) But now you can work with Tom and Mandy -- you can test drugs, or do experiments that would be out of the question with people.

ALAN ALDA Why did you make a small liver instead of a small heart or a small kidney?

LINDA GRIFFITH Well, partly, just by chance. I happened to join a lab that was interested in liver and I got fascinated by the problems in liver. Liver is your largest organ. It gets almost a third of the blood flow every time your heart pumps. Liver does an amazing number of things. It detoxifies drugs. It keeps track of all the nutrients in your body to make sure the rest of your body gets exposed to almost constant amounts of glucose. It makes almost all the proteins found in your plasma. It synthesizes bile. It does so many things and it's so important, so that when your liver gets sick, you have to replace it with an organ transplant or you die. And so it's such an essential organ, we got very interested in ways that we could… My first interest was in how we could we do replacement livers to implant into people. What we realize now is that gee, if we understood how liver works better and how disease processes go on in liver, we could

develop better drugs and prevent the need for organ transplants in a lot of cases, we hope.

ALAN ALDA Now why do you need this to develop better drugs? Why can't you use cells from a liver in a dish?

LINDA GRIFFITH Well, cells from a liver in a dish will do some of the things the liver does. But it's been really frustrating for years. Hundreds of people, in all kinds of labs and industries have tried to get liver to do things like be infected with hepatitis virus. And when you take liver cells out of the body they just go, "On strike. I'm not doing all those things anymore."

ALAN ALDA (NARRATION) Inside the liver chip the cells are able to behave much more naturally. We moved over to the electron microscope to take a look.

LINDA GRIFFITH ...so that the sample is in the vacuum chamber being bombarded with electrons.

ALAN ALDA (NARRATION) First, here's how nature makes a liver.

ALAN ALDA What's this a picture of?

KATIE WACK This right now is actually a picture of a section of real liver.

ALAN ALDA (NARRATION) Real liver contains thousands of tiny blood vessels like this, bringing in and taking away the many different chemicals which the liver cells, off to the sides, are processing.

KATIE WACK This is a blood vessel that you're looking down into, so it's a cross section of a blood vessel. And they have small holes that sort of act as a filter to the blood. So the blood moves through here and small molecules can go through and come in direct contact with the liver-functioning cells.

ALAN ALDA (NARRATION) Without these tissue structures, of filter holes and blood vessels, it's tough for the liver cells to function correctly. Now let's look at the liver chip.

KATIE WACK So we're looking down on the chip and each of these channels is sort of like a tunnel where the medium can flow through and there's a tissue structure that goes into the channel. So now I'll zoom in closer into one of these channels, so that you can see what the tissue looks like.

ALAN ALDA (NARRATION) The fascinating thing is that the stem cells in the chip grow into structures with many of the key features of real liver. They build

channels -- like blood vessels -- inside each perforation in the chip, and they even make the little filter holes that real liver blood vessels have.

ALAN ALDA What makes it organize itself as though it were in a real liver with these spaces for the blood?

KATIE WACK Well, the environment that the cells are in makes them want to function in the way they do in the body so that they reorganize into structures that are like in the body.

LINDA GRIFFITH It's the Colonel's special recipe that we have in our secret vault at MIT.

ALAN ALDA (NARRATION) And that's not just another of Linda's science jokes. The chip was designed specifically to keep liver cells happy -- the right size channels, the right nutrient flows, and surface coatings they like to stick to. Linda believes we can do this for many body parts.

ALAN ALDA You know when you show me these pictures that are enlarged so much and you were looking at these almost infinitesimally small places in the body, and you say things like, And they open and close depending on various things. Or these little parts of the cells, these cells are in communication with other cells, they're sending out... It sounds like there are so many millions or billions of things going on in the body -- signals being sent, coming back, sending out, going out again -- is there a hope that we'll be able to untangle this puzzle, I mean in anybody's lifetime?

LINDA GRIFFITH Yes. We've started a whole new department actually at MIT to address exactly these kinds of problems -- biological engineering -- and bringing together biologists and engineers and really trying to do systems level biology, starting at the molecular level. So it's just really starting to creep out across universities in America, but I think it'll happen.

ALAN ALDA (NARRATION) Making body parts, like retinas or livers, in the lab depends critically on acquiring the right human stem cells -- not the animal cells they're using here right now.

LINDA GRIFFITH One of the biggest hurdles in this is where we're gonna ultimately get the cells to do it on a large scale. And so part of our project actually is to try to derive stem cell lines that can be cultured and frozen down out of human tissue.

ALAN ALDA Are these stem cells lines that you're talking about creating here, are they outside of the prohibitions placed on stem cell research recently by Washington? Or are they within those protocols?

LINDA GRIFFITH What we are doing is taking cells out of the adult body and trying to derive cell lines, so they're not under the prohibitions. They're much more readily available to the general researcher. We can even get some from you if you sign the consent form.

ALAN ALDA We'll talk later about that.

LINDA GRIFFITH We'll have the memorial cell line.

ALAN ALDA Do you ask most people who come in if they want to give up their stem cells?

LINDA GRIFFITH If we really like them, and we want to have them memorialized in the lab.

ALAN ALDA Gee, you mean I could come some day and visit my cells?

LINDA GRIFFITH You could. Yeah.

ALAN ALDA That would be great. I could maybe have my own chip here.

LINDA GRIFFITH You know you could maybe have your whole body on a chip. If what we're doing really works out, we could take stem cells that circulate in your blood and make a liver, make a heart, make a brain out of those cells. That's our ultimate goal. That's what I want to have done by the time I retire from MIT.

SEARCH FOR THE PERFECT HEART

ALAN ALDA (NARRATION) On July the fourth, 2001, the papers announced a new kind of independence -- for heart patients, available now for the first time. The implantable, self-contained mechanical heart was the culmination of at least 40 years of research. On Frontiers, we've been following progress for almost 10 years. In 1993, we told the story of Mike Dorsey, whose life was saved by a sort of partial artificial heart, called a Heartmate, that assisted his own failing heart.

MIKE DORSEY I was very sick. I'd walk from here to you, and I'd been out of breath for that time. I couldn't do nothing. It gets a little frustrating when your wife comes and takes things from you, you know, and you can't carry them, you know,

she would take them and carry them in for me. I wanted to do it, but just wasn't able to do it.

ALAN ALDA (NARRATION) The artificial heart first hit the world's headlines in 1982. Barney Clarke's brave struggle to live, and his death after four months, cooled the early enthusiasm for his implant - the Jarvick 7. After a few more unsuccessful attempts, the device was abandoned. But research on mechanical hearts continued. The most promising were pumps that weren't intended to replace the heart, but boost it -- like Mike Dorsey's Heartmate. The designers of the Heartmate took a novel approach to a major problem of the Jarvick 7 - blood clots that would form inside of it, and that could kill when they broke off and traveled to the lungs or brain. The Heartmate's interior was roughened so that a thin layer of blood clots over its entire surface, and sticks there firmly. Mike Dorsey's problem, one that he shares with thousands of others, was a weakening of his heart muscles so that the main pumping chamber - the left ventricle - could no longer pump blood around his body. Installing the Heartmate begins with cutting a hole in the left ventricle and sewing in a short tube. Then the electric pump itself is implanted in the upper abdomen. Blood flows from the heart, through the pump, then back to the patient's aorta. By February 1993, Mike Dorsey's heart was near total failure. His doctors estimated he had just hours to live. Only weeks before, the Heartmate had been approved by the Food and Drug Administration for use at Fairfax Hospital in Virginia to keep a dying patient alive until a heart transplant could be found. The operation began with sewing into Mike's left ventricle the tube that connected with the pump. Then the Heartmate itself was slid into place. The connection was made between the pump and the heart it would assist. Finally, the pump's outflow tube was plumbed into Mike's aorta. The pump was switched on. At this point, no one knew for how long it would need to keep pumping. The Heartmate needed an awkward external, battery-powered air pump, with an air tube penetrating the skin. It was only intended to be a temporary bridge, to keep a patient alive until a transplant heart became available. After seven months Mike was still waiting, confined to the hospital.

MIKE DORSEY It's not really me, I'd rather be moving where I have a destination to go to, instead of standing in one spot, looking at the same old scenery. This is the battery charger here, in order to be more mobile, take two batteries, these, just connect the power source from here.

ALAN ALDA (NARRATION) That's the alarm that went off if there was ever a problem.

MIKE DORSEY If you don't have it right they do not go. You just drop them into the pouch like this, fold the flap down. Now I'm ready for traveling.

ALAN ALDA (NARRATION) Mike got his transplant a few weeks after this, and today he's still going strong. NURSE Hi, Michael.

ALAN ALDA (NARRATION) But now we're much closer to being able to offer patients like Mike a permanently implanted artificial heart. About 125,000 of the 700,000 Americans who die from heart failure each year could benefit from an artificial implant. The Abiomed artificial heart is modeled on the human, with two main pumping chambers and valves to control blood flow.

ALAN ALDA As the blood goes through there it pushes its way through but it can't come back the other way, right?

DAVID LEDERMAN Right.

ALAN ALDA Can that be relied on, after it pumps thousands of times after you pass through, after it flexes thousands of times, to maintain that same resiliency?

DAVID LEDERMAN The answer is yes, and it's not thousands of times. It's approximately one hundred thousand times per day.

ALAN ALDA Oh boy.

DAVID LEDERMAN Which is close to forty million times per year.

ALAN ALDA Forty million times. You can flex this material forty million times…

DAVID LEDERMAN Without it breaking.

ALAN ALDA Not only breaking, but just weakening and softening and fluttering and that kind of thing.

DAVID LEDERMAN Correct.

ALAN ALDA So this is where you test the valves.

DAVID LEDERMAN Yes. This is where we test… We have many valves under test. And we test them under very severe conditions and at an accelerated rate so we can demonstrate twenty years equivalency in one year.

ALAN ALDA (NARRATION) Just like the Heartmate, the Abiomed heart is designed to avoid the danger of blood clots forming inside. But while the Heartmate has a deliberately roughened interior surface, the Abiomed heart aims to be completely smooth and seamless. It also keeps the blood constantly

swirling -- made visible here with fish scales in water -- to minimize stagnant areas where clots might form.

DAVID LEDERMAN That's the outflow.

ALAN ALDA (NARRATION) It's not until I get to hold the heart while it's pumping that I really appreciate how powerful it has to be to substitute for a human heart.

ALAN ALDA I can really feel the beating. Now interestingly, when you see a heart pumping, the outside of the heart is going like that, you see the motion on the outside. Here all the motion is inside this device. I've held onto this heart long enough. Would you mind holding that for a day or two?

ALAN ALDA (NARRATION) The Abiomed heart is run by rechargeable batteries that receive their power through the skin. Both Mike Dorsey's Heartmate, and Barney Clark's Jarvick 7, had unhygienic and vulnerable tubes penetrating the skin. Over about three years, the entire Abiomed system -- surgical procedures, implanted heart and power supply -- was tested about a hundred times in calves, animals about the same size as human patients would be. By the middle of 2001, five surgical teams around the country were ready to conduct the first human trials. Bob Tools, a 59-year-old with severe heart failure, was the pioneer. His doctors estimated he had about 30 days to live. The FDA had approved five implants, but only for patients as sick as Bob Tools. He had already been judged to be too sick to receive a heart transplant. In a seven-hour operation, Bob Tools' failing natural heart was removed, and replaced by the artificial system. This is the computer control, with the battery that will be recharged through the skin. The control and battery will rest directly below the heart, in the abdomen. Now the heart itself. It's attached using cloth collars, sewn to the arteries. After the implant, Bob Tools began to make a remarkable recovery. He'd been bedridden before, barely able to raise his head, and here he was on his feet. He was even beginning to gain a little weight. The equipment cart here is just to monitor the heart's operation. It doesn't have to be attached. Bob Tools made steady progress, mostly confined to the hospital, but with the occasional excursion for the benefit of the press. Bob told reporters he liked to hear the implant pumping away in his chest. "As long as I can hear the sounds," he said, "I know I'm here." Over the next four months, four more equally sick patients received implants. Then, four and a half months after his surgery, Bob Tools suffered a major stroke. He died three weeks later, but he'd lived five times longer than was expected before the implant. To date, two patients are still alive, but there's been one other fatal stroke. Abiomed believes blood clots may have formed around these plastic struts on the heart's attachment collars. They're removing the struts, and ten more implants have been approved. So we'll soon

see if this system has the potential for the widespread impact that it's inventor thinks it can achieve.

ALAN ALDA Are you going to be extending a lot of people's lives because now they'll be able to have an artificial heart?

DAVID LEDERMAN We hope yes. The fact is that two thousand years ago the average life span was 30 years, and a hundred years ago the average life span was 47 years and today the average life time is 75 years. And there are a large number of people who reach 75 and beyond who are neurologically intact, who are very productive, and the only thing that is wrong is a hip, which we replace today, or a muscle like the heart, which we should be able to replace. And there is no reason why the end of life should come prematurely.

NERVES OF STEEL

ALAN ALDA (NARRATION) Don Crago is paralyzed from the waist down. But using artificial electrical muscle stimulation, he can walk. Dr. Byron Marsolais started this project.

DR. BYRON MARSOLAIS He has absolutely no control of his legs at all. He is totally and completely paralyzed, and every bit of motion that happens is coming through the electrical stim.

ALAN ALDA Don, do you get all your balance from holding on to this walker? DON CRAGO Yes, I do. Yes, I do. And…

ALAN ALDA Does that put a lot of pressure on your arms? DON CRAGO No, not really. Most of the pressure's on my legs. Actually, I prefer to let my legs do the work, 'cause if I did it with my arms, I would be tired out.

ALAN ALDA Yeah. How tiring is it to take it every step? DON CRAGO Not too bad. It's comfortable, you know? But after the end of the walk, I will breathe heavy.

ALAN ALDA Standing takes a lot of energy because you have to stimulate the muscles for a prolonged period?

DR. BYRON MARSOLAIS Right. He is standing by stimulating the flexors and the extensors --the antagonistic muscles -- all at the same time. So he's stiff as a board.

ALAN ALDA And that charge just has to be constant...

DR. BYRON MARSOLAIS It's constant...

ALAN ALDA If you let up on it, he's liable to tip one way or another.

DR. BYRON MARSOLAIS Oh, he would, for sure. And so he looks good standing tall and stiff...

ALAN ALDA But you feel the strain?

DR. BYRON MARSOLAIS But he's got strain. DON CRAGO Yeah, I feel a strain.

ALAN ALDA (NARRATION) My introduction to the Functional Electrical Stimulation, or FES, program, was 10 years ago.

DR. BYRON MARSOLAIS Now what I'm trying to get to is his gluteus maximus muscle, the big seat muscle.

ALAN ALDA (NARRATION) Dr. Marsolais showed me how he implants wire electrodes.

ALAN ALDA What you're inserting into the muscle, that's not the electrode itself.

DR. BYRON MARSOLAIS No, no, this is just a little probe, a very tiny probe.

ALAN ALDA And the reason you're doing this is to see if you can get the muscle to react, to give its greatest response?

DR. BYRON MARSOLAIS Exactly. And I want just the right muscle. That's the muscle that we want, it goes right down here into the femur, which is the big leg bone. And you see how it's beginning to jump there? It's starting to do what we want. I think I can do better. And in order to do better I have to get it right beside the nerve.

ALAN ALDA (NARRATION) Dan Kemp, paralyzed in a car accident is on the table.

ALAN ALDA Now I think Dr. Marsolais looks like he's found the spot here.

DR. BYRON MARSOLAIS That looks pretty good here, yup. That's getting a pretty good, tight...

ALAN ALDA I can see it.

DR. BYRON MARSOLAIS See how that jerks thing together there.

ALAN ALDA It looks like about an inch-and-a-half from where you were first searching for it.

DR. BYRON MARSOLAIS Yes, that's right, although we're angled a bit down. We started about here and now we're about here, so we were a good inch away.

ALAN ALDA (NARRATION) Once he's found the best stimulation point for the muscle, a hair-thin permanent wire implant is slid into place. Dan was one of many experimental subjects who volunteered for the program. In his case he received 8 electrodes in each leg.

DR. BYRON MARSOLAIS Now we just bring this down to exactly the position that we were before.

ALAN ALDA (NARRATION) The patients, and Dr. Marsolais, were literally stepping into the unknown.

ALAN ALDA How do you feel when you are going through this? Do you feel a little like a guinea pig? DAN KEMP Yeah I do, but it's well worth it. You know, down the road, people will be able to look back and say if it wasn't for people like me that they wouldn't have gotten as far as they've got in the new procedures. So you know it goes down the line. Everybody helps everybody else, whether they realize it or not.

ALAN ALDA (NARRATION) Eric Bellamy, paralyzed in a motorbike accident, agreed with Dan that it was worth being a guinea pig. He saw simple, basic ambitions for himself, and for the program.

ERIC BELLAMY I see being in a chair always, but I see being able to go up steps and knock on a friend's door and say, Hey, I'm down here. Instead of running around the house and screaming, Hey I'm here, I'm here. I see being in a convenience store -- one step, you know. Being able to get up and go through a narrow door to go get into the bathroom -- just for them answers. And if they can come up with that right there. Your life's in a chair, but being able to overcome difficulties would be a tremendous step. And that's what we're working on right now.

ALAN ALDA (NARRATION) Eric was one of 5 volunteers who received the most complex of the experimental systems, with a total of 40 implanted, and 8 external electrodes. The computerized control box could handle 48 electrodes simultaneously, with connections made through the skin on his thigh. One big

goal was to establish how many muscles need to be stimulated for effective standing and walking. Working out how to sequence the firing of the electrodes was another challenge.

PAUL MILLER OK, go ahead and stand up.

ALAN ALDA (NARRATION) In this trial, 20 muscles per leg were being stimulated, compared to the 50 per side that are involved in natural walking. Eric was able to walk relatively smoothly, although he still needed to use his arms to balance. Developing an artificial balance mechanism is still one of the goals, but they have been able to reduce the number of muscles needed for walking to only 8 per side - as in the latest system we saw Don Crago using earlier. But Eric's muscles also had to work constantly at full blast.

PAUL MILLER They're using tremendous amounts of muscle mass. Their quadriceps are on 100%. Their gluteus muscles are on 100%; their hamstring muscles are on 100%. Their back muscles, everything's just blasted.

ERIC BELLAMY Whenever they do something, their using 100% of all their strength. Whether it's one step, two steps, they're using everything they got. Letting me stand, everything goes right into it. 100%, bam!

PAUL MILLER OK?

ALAN ALDA (NARRATION) With tough, motivated subjects like Eric, they were eventually able to work out how to reduce the high levels of muscle stimulation, and they also figured out the best design philosophy. It's that simpler is better -- they realized that even the most complex systems were going to get tripped up by the real world sometimes. Better instead to go for simpler, standard systems that can bring basic benefits to the largest number of people, quickly. Many of the pioneers in FES research have now dropped out. Eric got a bad infection. Dan couldn't keep up the long commutes to the hospital. But today, many people with spinal cord injuries have good reason to be thankful for the pioneers' efforts.

JEN PENKO This is an easy introduction to the real world, I guess you could say.

ALAN ALDA (NARRATION) Jen Penko, who was made paraplegic in a snowboarding accident, is one of the beneficiaries. She's showing me a rehab area at Cleveland Metro Medical Center - the first of 3 centers around the country to be working with the simplified, standard systems.

JEN PENKO For instance there's curb cuts and those types of things.

ALAN ALDA It takes a little extra energy to get up that, doesn't it?

JEN PENKO A little bit, but you'll get curbs in the real world that are a lot more difficult than that.

ALAN ALDA Yeah.

JEN PENKO You can just set it right there, because I'll get myself set up.

ALAN ALDA (NARRATION) Jen has a simplified system that just does one thing - allows her to stand.

JEN PENKO So the light by the "stand" means that it's ready to stand and all I need to do is press this button to go, and it'll stand. Ready?

ALAN ALDA Yeah.

JEN PENKO Are you sure you're ready?

ALAN ALDA Yeah, yeah. I'm ready, I'm ready.

ALAN ALDA (NARRATION) Jen's system has only 4 implanted electrodes per side, but that allows her to stand and get around just enough to really make a difference.

JEN PENKO So here I can reach up, grab window cleaner and hand it over to you.

ALAN ALDA How long can you stand before you start to feel stressed out or you're breathing heavily?

JEN PENKO We did a test on that. 33 minutes and 8 seconds was my time figure right now. And that was a few weeks ago, so. Usually when you're in a grocery store, one of the tough things, when you're in a wheelchair, is you can't really see within these big bins. So that way you can reach over, pick up some Weight Watchers, good lord knows I need it. And you can start to see things from a standing level that you really can't see from a sitting level. Whereas if I was at a sitting level I'd be lucky if I'd be able to see what was actually in there.

ALAN ALDA Do you want to go to walking? Is that something you have in mind?

JEN PENKO Absolutely. Absolutely. To be able to ambulate is fantastic. I mean, just to be able to stand. We're focusing on the functional things, but there's

a lot of health benefits to standing as well. I mean, people that are in wheelchairs that don't stand, you have problems with the shortening of muscles, with osteoporosis, with circulation,

ALAN ALDA So you have to be able to get into pretty much any kind of a seat…

ALAN ALDA (NARRATION) Simply transferring from one seat to another is a big benefit.

ALAN ALDA ...automobile seat, and a booth like this which is different from a chair. One, two three. Those are three slow seconds.

JEN PENKO They are. And considering I'm from the Boston area, I've had to learn how to count a lot slower than out here. So it took me a long time to learn how to count.

ALAN ALDA They count slower in Cleveland?

JEN PENKO I guess they do.

ALAN ALDA (NARRATION) Another part of the design philosophy is modularity. If Jen and her doctors decide everything is working well, she can get another 8 electrode implants, which will allow her to walk. JEN Now I'll sit.

ALAN ALDA So you have the same three seconds before it puts you in the seated position?

JEN PENKO Uhuh. Same audio that it goes through as well. Same beeping cycle.

ALAN ALDA Yeah.

JEN PENKO So it's just like a habit. Training me like a mouse. There you go -- beep. Three seconds later -- beep. And I'm standing up.

ALAN ALDA What do you call the thing that's implanted? What is that? JEN It's my receiver.

ALAN ALDA How big is it?

JEN PENKO Um, it's about that big. It's not very big at all. In fact...

ALAN ALDA (NARRATION) A big change with the standard systems is that, like with the Abiomed artificial heart, no wires pass through the skin.

JEN PENKO So this is the box that hold the batteries, that holds the software and circuit boards.

ALAN ALDA (NARRATION) Instead there's a transmitting coil with an implanted receiver.

JEN PENKO I have it taped onto the skin so it won't move. So I have this coil that sends the radio waves to the receiver that's right here, and you see the little bump in the skin right there? That's the receiver.

ALAN ALDA (NARRATION) There are now nearly 200 standard systems in use, but research is continuing. Jim Jatich received the very first implanted electrodes, in 1986, to allow his left hand to grip.

JIM JATICH Since I had this implant, once it's put on me in the morning, I'm on my own and I can write for myself, feed myself, answer the phone, take messages, work on a computer. I do engineering drawings on the computer; I'm trying to start my own business doing that.

ALAN ALDA That would have been out of the question, I mean without a tremendous amount of help.

ALAN ALDA (NARRATION) When we met Jim in 1993, he'd already been an FES research subject for fifteen years, helping to try out new systems. Back then, for example, they were perfecting a joy stick controller for the 8 electrodes that give him his handgrip. The joystick was attached to his right shoulder. So a quick shrug of the shoulder activates the grip. And then a double shrug relaxes it. Jim was also one of the first to try an implanted receiver, so no wires penetrate the skin. Today Jim is trying another experimental control system.

JIM JATICH What we have is like a joystick implanted in the bones of my wrist. There's a magnet and a sensor, and as the wrist bones pass each other that sends a signal to the implant, and depending at what angle I'm at, whatever is programmed into the computer on the back of my wheel chair, that's how much strength and how fast my hand closes.

ALAN ALDA So the magnet and the sensor, depending on how far apart they are, as you move your hand back, that regulates everything that's gonna happen.

JIM JATICH Right

ALAN ALDA (NARRATION) Jim and the researchers have been working with the implanted magnet control for a couple of years.

ALAN ALDA Now if that were full of coffee and heavy…

JIM JATICH You can see how strong I'm holding it.

ALAN ALDA Yeah, you have a really good grip on that.

JIM JATICH Yeah.

ALAN ALDA Yeah. You're a good actor, too. Looked like you had something in there.

JIM JATICH Oh, it's hot!

ALAN ALDA (NARRATION) With the magnets controlling his left hand, Jim's joystick can now control a new implant system in his right hand, so he'll be working with the researchers on tasks that need two hands simultaneously. Jim's essentially a member of the research team, but one perhaps with a special perspective on the benefits the FES program.

JIM JATICH You know I've talked to friends of mine that are paralyzed. They won't go into restaurants when we have meetings, you know like a support group meeting, because they can't feed themselves. They don't want to see anyone feeding them so whenever we have meetings in a hospital or something they show up, but when we have it in a restaurant they won't go, because someone has to feed them, you know.

ALAN ALDA So there's a series of things that don't get done, because of a simple thing like not being able to pick up a fork. I mean, you get less social.

JIM JATICH That's right. An example is a girl that came into this project to get an implant. When she first came in, her face was down, she wouldn't talk to anyone, no eye contact. After she got the implant she's feeding herself, going out to restaurants, she enrolled back in school. Now she's an advocate, talking to everyone about it. She started a support group. And I mean, you know it just changes people's lives. And that's the kick I get out of it, to see how people change.

ALAN ALDA (NARRATION) You'll recognize the radiant young bride walking down the aisle. Well, not quite walking -- let's say progressing. It's Jen Penko, and that's her Dad by her side. A year after we filmed her in Cleveland, Jen married her long time sweetheart, Tim. Jen made it to the altar standing tall,

under her own steam -- thanks to her basic, standing FES implant. She doesn't yet have her walking system. PASTOR We have gathered in the presence of God to witness the joining together of Jennifer Penco and Tim French, and in the celebration of God's greatest gift, the gift of love -- a love that abides and grows through difficulty and trial. This, you see, has been Tim and Jennifer's experience over the past three years, of facing injury, months of painful therapy, healing, and renewal, and has led to the miracle of Jennifer walking down the aisle this day.

ALAN ALDA (NARRATION) "For those moments, I totally forgot that I was wheelchair bound," Jen told us later. It was "...a moment in our lives that we would never forget, of accomplishment for achieving something that we had worked toward for so long. For that time, I wasn't disabled. All the negative sides of disability disappeared, to be replaced with the gifts of abilities," she said. It would be hard to imagine a more vivid demonstration of the benefits of another kind of marriage -- the new marriage of biology and engineering that this program has been about.

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