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The collision of philosophies

S.C. SPANGLER/TRIBUNE-REVIEW

Peering at a smiling self-portrait of her daughter, Kathy Miller questions the death of Katy, 21, who participated in a special trial for liver transplant patients at the University of Pittsburgh Medical Center.

Treat sickest first, or give livers to the less ill?

SPECIAL REPORT BY LUIS FABREGAS AND ANDREW CONTE
TRIBUNE-REVIEW

The father of transplantation felt bewildered.

The transplant center bearing Dr. Thomas E. Starzl's name at the University of Pittsburgh Medical Center now does the very surgeries that doctors there once shunned, even mocked.

Transplantation pioneers at UPMC in the early 1990s criticized colleagues at other hospitals for giving livers to patients who were not critically ill, people who had a better chance of living without surgery until they became sicker.

"It was a moral position," said Starzl, 81. "It was an ethical position, and it was supported by the leadership here from top to bottom.

"Now it has changed ... It's a commercial drive. That's undeniable."

UPMC does more liver transplant surgeries into the least ill patients than almost any center in the country. It has done 102 of them since 2005, second only to Clarian Health in Indianapolis.

The shift in philosophy has been so pervasive that Starzl's bosses at UPMC didn't even want him talking about it. They sent Pitt vice chancellor Randy Juhl to listen in as he talked to the Trib.

"It's humiliating," Starzl said.

Dr. Amadeo Marcos, until last week director of UPMC's transplant institute, later defended the medical center's surgical practices. All patients on the waiting list deserve a crack at a new organ, he said, regardless of how sick they are. UPMC performs surgeries on some of the nation's most critically ill patients.

"We offer transplantation to everybody," Marcos said. "We look at every patient, really try to help them as much as we

can."

Fourteen years ago, UPMC's doctors called the transplant surgeries on the least ill "boutique" cases, as breezily fashionable as a trendy clothing store.

They wrote in the Journal of the American Medical Association that people at the bottom of the liver waiting lists — patients "called in for operation from the 19th hole of the golf course" — have a "higher survival without transplant intervention."

Recent research from the Scientific Registry of Transplant Recipients at the University of Michigan echoes their warnings, showing nearly identical findings. The registry, under contract to the federal government, tracks and analyzes all organ transplantation data.

A changing of guard

When Venezuela-born Marcos arrived in Pittsburgh in 2002, transplant program leaders at UPMC were pushed to boost volume.

The year before had marked a low for UPMC: Only 132 liver transplants were performed. At its peak, in 1990, the center had done 471 cases.

Marcos's predecessor, Dr. John Fung, left UPMC under pressure from top administrators, including CEO Jeffrey Romoff, to do more transplant surgeries.

"There was always that level of emphasis on volume there that, whether consciously or subconsciously, drove how people practiced," said Fung, the transplant center's chief from 1991 to 2004 and now director of surgery at The Cleveland Clinic.

The pressures remain today, Starzl said, who recently announced his retirement. Starzl stopped doing surgeries in 1991 and has been involved in UPMC research involving weaning transplant patients from anti-rejection drugs.

"You set up a program, you depend upon it for a cash flow of an institution and you try to maintain that," he said. "There are certain expectations. … In the change from a crusade to a business, it's just that simple."

UPMC is now a massive medical network with more than $60 million in annual profits.

Marcos, who remains on the faculty of the University of Pittsburgh until June 30, said UPMC's administrators did not pressure him to do more transplants.

Romoff declined to comment. Bill Morris, executive director of UPMC Transplant Services, said in an e-mail that medical center officials would "not discuss financial issues related to transplantation."

The university's Juhl said during the meeting with Starzl that all transplant surgeons have financial pressures and decisions to make.

"It could be worse here because of the lofty height and tradition, and so on," Juhl said.

With Starzl as its guiding star, the place once known as the transplant capital of the world attracted sick patients from as far away as Jordan and Syria.

Today, 127 U.S. programs perform liver transplants, compared to four in 1981, when Starzl arrived in Pittsburgh from the University of Colorado.

"Historically, UPMC is the Ford or Mercedes-Benz auto manufacturer of liver transplants," said Dr. Jeffrey Punch, transplant director at the University of Michigan Medical Center. "But now we know there are a few car companies that can make a car at least as good as that company."

Many doctors who trained at UPMC moved on to create programs that now indirectly compete with Pittsburgh, said Dr. Claude Earl Fox, the chief of the U.S. Health Resources and Services Administration from 1997 to 2001.

"You had one factory with a fair amount of raw material," said Fox, director of the Florida Public Health Institute. "Now you've got a lot of factories but you haven't got a lot more raw material, so they're all competing for the raw material, and in this case, the raw material is organs."

In 2006, organ procurement agencies recovered 7,305 livers across the United States. Of those, surgeons transplanted 6,597 and rejected 708.

As those programs made transplantation routine, UPMC sought alternatives to remain at the top. It started using more livers once considered unusable. It began doing surgeries with organs from live donors and stepped up its transplants on patients at the bottom of the waiting list, those not considered critically ill. UPMC also opened a $58 million transplant center in Sicily.

"Now I do want to have the biggest, the busiest and the best transplant program in the world, and that's what we have today," Marcos said in January. "And I want to keep it that way. I want this to be the Mecca as it's always been, the ultimate place for anybody with liver disease to come. And again, we are going to do everything we can to help them."

UPMC transplants livers into less critically ill patients to make the best use of all available livers — not to keep a high number of surgeries, Marcos said.

"This is not to keep volume," Marcos said.

"All centers have moved into the reality of 2008 compared to the reality of the early 1990s," he added. "We don't have the luxury of having every organ we want to transplant those patients."

Transplant novelties

An aggressive workhorse with soap opera star looks and the deep voice of a broadcaster, Marcos brought to Pittsburgh a pair of transplant novelties poised to alter the field.

He began doing transplants using live donors, in which a portion of a healthy donor's liver is cut off and given to an ailing recipient. The surgeries had been his specialty at Strong Memorial Hospital, in Rochester, N.Y., where he worked two years before coming to Pittsburgh in 2002.

Prior to that, UPMC had performed only 18 of those transplants.

In the first year after Marcos arrived, UPMC's annual number of living-donor liver transplants jumped to 25. Last year, there were 36, the most ever.

Marcos also was willing to use livers rejected by other surgeons.

"I did notice that perhaps before I got here they were not willing to truly consider every organ out there," Marcos said.

So-called extended criteria donor livers are generally flagged because they come from deceased donors who don't meet generally accepted quality standards. That can be because of anything from being too old, to too fatty, or too much time inside a cooler as it was transported to the transplant center.

Surgeons say using those livers helps them expand the pool of organs when 17,000 are on a waiting list nationwide and only 6,000 each year get them.

"If there was a surplus of organs available in this country, I really doubt anyone would be using extended-criteria organs," said Dr. Adel Bozorgzadeh, director of solid organ transplantation at Strong Memorial Hospital. "What are you supposed to do? Let the patients die?"

At Strong Memorial, the livers had caused trouble, partly during Marcos' tenure as head of solid organ transplantation.

From 2000 to 2004, the New York Department of Health found 10 violations related to the use of extended-criteria donor livers. Marcos left Strong in 2002.

One patient received a liver so bad, the complications forced a second transplant. Others got risky livers without even knowing about it. State regulators slapped the hospital with a $20,000 fine.

Bozorgzadeh said surgeons at Strong continue to use the livers, with one major difference: Patients now get detailed explanations about the possible background of the livers, and must read and sign lengthy consent forms.

Marcos said extended criteria donor organs are tested thoroughly at UPMC.

All livers undergo a biopsy that can tell doctors, among other things, whether a liver is too fatty, one of the top reasons for rejecting it.

"You can be 20 years old but have a lousy liver biopsy," Marcos said. "We're not using that organ, no matter how young the donor is."

The scientific registry suggests that marginal livers should

THE COLLISION OF PHILOSPHIES

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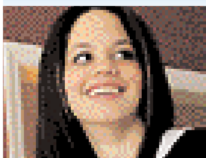
Dr. Claude Earl Fox
Former chief of U.S. Health Resources and Services Administration

"You had one factory with a lot of raw material. Now you've got a lot of factories but you haven't got a lot more raw material, so they're all competing for the raw material."

Katy Miller
Received living donor liver from her sister, later died after second transplant



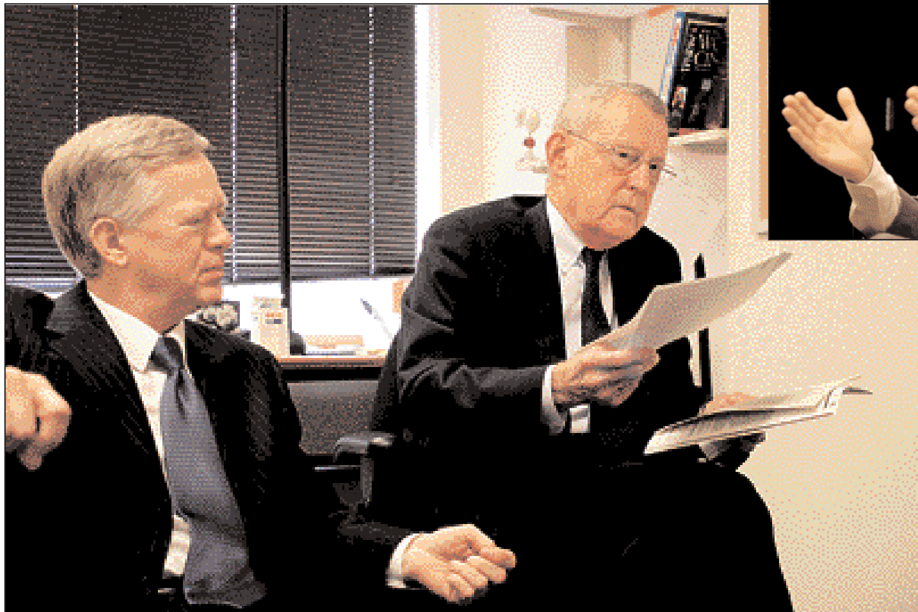
Her death contributed to the rift between Marcos and Starzl.

Dr. Adel Bozorgzadeh
Director of transplantation, Strong Memorial Hospital, Rochester, N.Y.

"If there was a surplus of organs available in this country, I really doubt anyone would be using extended-criteria organs. What are you supposed to do? Let the patients die?"

ANDREW RUSSELL/TRIBUNE-REVIEW

Until last Monday, Dr. Amadeo Marcos was chief of UPMC's transplant institute. He said all patients on the waiting list deserve a chance at a new organ, no matter how sick they are.



JOE APPEL/TRIBUNE-REVIEW

Dr. Thomas E. Starzl (right) is monitored by Randy Juhl, vice chancellor for research conduct and compliance for the University of Pittsburgh during a February interview.

be transplanted into the sickest patients — those about to die without a new organ, even if it's not a perfect one.

Marcos disagreed. "Nobody in his right mind would do a transplant not expecting for it to succeed," he said. "You're not going to take an organ for somebody that's desperate when you know it's going to fail. That doesn't happen."

Before coming to Pittsburgh, Marcos hesitated about taking the job at UPMC because the transplant center had a reputation for not doing many live-donor transplants. It was Starzl, however, who ultimately convinced Marcos to make the move, Marcos said.

The relationship quickly became strained. Starzl said there was never a rift, but merely distance. A "grand canyon," he said.

The thin string that held them together broke with the death of 21-year-old Katy Miller.

Katy's story

The college sophomore had been diagnosed in 2005 with a rare illness called primary sclerosing cholangitis that doctors predicted would destroy her liver. She would eventually need a liver transplant.

But she wasn't sick enough to get a liver from a deceased donor, the most common source of organs for transplantation.

Doctors at UPMC made her an enticing proposition: If she enrolled in a study aimed at weaning patients off anti-rejection drugs, they would do the transplant. The catch: She'd have to find a living donor.

"Our thought was, we'll do this to keep her from getting more sick," said her mother, Kathy Miller of Creekside, Indiana County. "That is why we did it back then. I mean, eventually, she was going to need a transplant. So why not do it when she was healthy?"

Starzl wasn't part of the team that recruited Katy, but agreed with the decision of allowing her to take the chance at having a normal life.

On Nov. 1, 2005, Katy received part of the liver of her eldest sister, Shelly McGinnis.

It wasn't meant to be. Katy died on May 7, 2007, following countless medical setbacks, including a second transplant that wound up infecting her body, shutting down her kidneys and causing internal bleeding.

A picture of Katy on her final birthday shows her skin was jaundiced and that she wore a large shirt to conceal a drain on her belly.

"Now I wish that I had let her run her course," her mother said. "Maybe her own liver wouldn't have deteriorated as fast as it did."

Marcos wouldn't talk about the case, citing privacy laws. As Marcos resigned, UPMC disclosed it had begun a study involving complications in surgeries such as Katy Miller's. Administrators have recruited international experts to conduct the review and have expressed confidence in the program's quality.

Katy's death troubled Starzl, who had collaborated in her care. Although he and Marcos agreed on giving her the transplanted liver, Katy's mother said the doctors disagreed over how to proceed when it failed.

"I've never faced a death that caused so much sorrow," Starzl said.

At 81, Starzl said retirement seems logical. Saying he has "battle fatigue," he will no longer do research and, instead, focus his time on his wife, Joy, their dogs and his love of Mozart.

"These are devastating hits," Starzl said. "In the course of a long and tough life doing difficult cases and being always right at the edge of tertiary care problems, you build up layers of grief, but you can take those if they are thin. When you have a deep rip in the fabric, that's a different matter. And Katy was like that."

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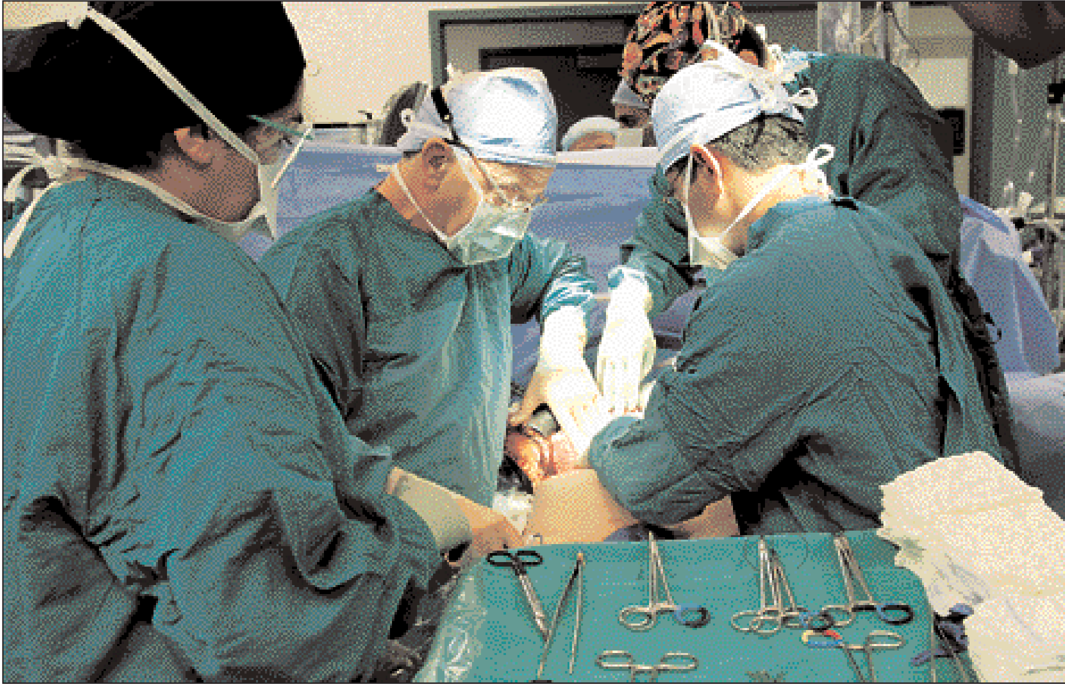


JOE APPEL/ TRIBUNE-REVIEW

Dr. Andreas Tzakis, director of the Miami Transplant Institute, performs a transplant at Jackson Memorial Hospital in Miami. "It's a reward for us," he said, "to help those who need us the most."

'The sicker they are ... you see a miracle'

These two hospitals do transplants only on the critically ill

MIAMI — Dr. Andreas Tzakis cuts open the woman's belly to reveal her sick liver.

Its surface is bumpy and dark pink.

"It's supposed to be smooth and light pink," Tzakis said, his mouth covered with a green surgical mask.

In the next three hours, Tzakis and his surgical team at Jackson Memorial Hospital will disconnect the sick liver and replace it with a new one. It is a surgery he's done thousands of times and it gratifies him.

"It's a reward for us," he said. "To help those who need us the most. The sicker they are and the better they do … you see a miracle."

Such philosophy emanated from Tzakis' mentor at the University of Pittsburgh, Dr. Thomas E. Starzl. The father of transplantation taught Tzakis and hundreds of other students to always transplant the sickest.

"My upbringing was to try to help the people who need me the most," said Tzakis, 56, who completed a two-year fellowship under Starzl and moved on to head one of the most successful transplant programs in the country. "I like to do the high-MELD patients because it's where I get more satisfaction."

At Jackson Memorial, the third largest public hospital in the nation, the vast majority of its 200 liver transplants every year — 95 percent — are done on critically ill patients, those who are MELD 15 or above and thus favored on the waiting list.

Tzakis, who by his own count has performed more than 3,000 transplants, said he is following the rules established by the United Network for Organ Research. The agency has implemented rules to ensure the first available livers go to patients with MELD scores above 15.

"Since we always have patients who have a high-MELD score and since we have a limited number of organs, we use it on the high-MELD score," Tzakis said.

Like Tzakis, many of Starzl's disciples practice under the same philosophy.

Dr. John Fung worked for 13 years as UPMC's chief of transplantation and collaborated with Tzakis in 1992 on the world's first human transplant using a baboon liver. He said the lowest-risk patients shouldn't be transplanted.

His argument: Even with a perfect liver, transplant recipients already have a 10 percent chance of dying in the first year — exceeding the risk of just waiting to get sicker.

"There is a point where, and we've argued this for years, the lowest-risk patients shouldn't be transplanted because they don't need it," said Fung, who in 2004 left Pittsburgh to become chairman of surgery at The Cleveland Clinic. "Their risk of dying on the waiting list is low, and they are better off just waiting."

With rare exceptions, that's the philosophy at Cleveland, where only 3 percent of transplants in the past two years were performed on patients with MELDs lower than 15.

The practice of transplanting into the less ill emanates from internal hospital pressures, Tzakis said.

"The futility factor comes into play," he said. "When is it too late to transplant someone? Sicker patients require a lot more resources."

That includes more doctor time, additional drugs and longer stays in intensive care units, which are notoriously costly and often scarce at a time when more chronically ill patients require hospitalization.

"The hospital doesn't like it, the insurance company doesn't like it, the doctors don't like it because it requires a lot of work," he said. "If you put all those things together, there's a lot of pressure to do patients with low-MELD scores."

The patients with low-MELD scores wind up getting organs that have been rejected by surgeons across the country, but Tzakis doesn't mind using those organs on sicker patients with higher scores.

"If it's a good enough liver, you can place it in anybody on the list," Tzakis said.

PITTSBURGH TRIBUNE-REVIEW

Glossary

Model for End-Stage Liver Disease (MELD)
Based on three blood tests — for bilirubin, creatinine and INR — the scoring system is a predictor of patient mortality and determines the allocation of livers among adults. It ranges from 6 for the least ill patients to 40 for those who are critically ill.

United Network for Organ Sharing (UNOS)
A private nonprofit based in Richmond, Va., that coordinates the national transplant system through a contract with the U.S. Health Resources & Services Administration.

Scientific Registry of Transplant Recipients
A research agency, based at the University of Michigan, in Ann Arbor, that tracks and analyzes clinical data about organ donors, transplant candidates and recipients, as well as patient and graft survival rates. Operates under contract with HRSA.

Extended-criteria donor livers
These organs do not meet all generally accepted quality standards. Doctors disagree about what makes a liver unusable. The ideal organ is a whole liver from a donor who is 18 to 40 years old who suffered brain death from trauma. Here are some deceased donor characteristics that have been linked to an increased chance of the organ not working right: medical history of systemic illness or cancer, exposure to transmissible infectious disease, post-recovery biopsy results, age.

A full glossary is available at: www.unos.org

Medical ethics issue focuses on 'doing no harm' to patients

With a limited supply of organs, liver transplant surgeons must worker harder to maintain the guiding principle of doing no harm, medical ethicists said.

Give a liver to a patient too soon, and the doctor could cut short the person's life or unnecessarily burden them with having to deal with the complications of organ rejection medicines. Wait too long and the patient could become too sick to truly benefit from transplantation — or the organ might not be available.

"Risk versus benefit has to be weighed together," said Dr. Eugene Boisaubin, clinical ethicist at the University of Texas Medical School in Houston. "If the total risk of the transplant potentially exceeds the chance of a person's continued health or survival otherwise, that's got to be seriously considered."

Unlike other medical fields where parts like knees or hips come off the shelf, transplantation is complicated by the limited supply of organs. Money makes decisions even more complex because the surgeries mean big business for medical centers.

Transplant programs have financial incentives to perform surgeries on patients who are not as critically ill because they cost less and heal faster. Those patients, however, face a greater risk of dying if they undergo a liver transplant than if they keep waiting.

"You want to never be in a position where, in order to get transplants done or bring business to a program, you're putting patients at more risk than they have to face," said Arthur L. Caplan, director of the Center for Bioethics at the University of Pennsylvania in Philadelphia.

Federal allocation rules further complicate the question of giving livers to patients at the bottom of the waiting list. Those people only can get organs that have been rejected for every sicker patient in that region of the country. Surgeons who use the rejected livers wonder why others pass on them; those who do not use them question why anyone would.

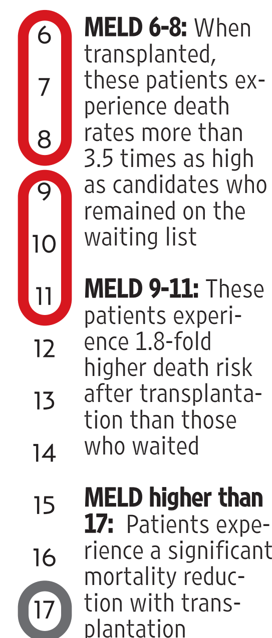
"When you have an ethical perspective, you would not allocate an organ that is going to come to you after it has been turned down by virtually the whole region," said Dr. Cosme Manzarbeitia, UNOS regional director for Pennsylvania, Delaware, Maryland, New Jersey, West Virginia and Washington, D.C. "If I give that organ to someone who has less mortality waiting than with the transplant, I think that's unethical."

While few people want to talk about money and transplantation, they go together, Caplan said. That's why there are 127 centers doing adult liver transplants, including three in Pittsburgh — University of Pittsburgh Medical Center, Allegheny General Hospital and the VA Pittsburgh Healthcare System.

"It's an altruistic system: People are doing it to save lives," Caplan said. "All that said, money plays a role. It's a lucrative area of medicine." Success rates drive doctors in their decisions, too. A place that treats more of the sickest patients will appear to have worse results because those patients do not have the best odds. Yet some patients will not be sophisticated enough to realize that, Boisaubin said.

Risky organs

Patients at the bottom of waiting lists, those with MELD scores below 15, often get livers with a so-called high donor risk index (DRI). The DRI is a scale that measures how well a liver is going to work. Livers with a DRI of 1.7 or higher have greater odds of not working.



SOURCE: "THE SURVIVAL BENEFIT OF DECEASED DONOR LIVER TRANSPLANTATION AS A FUNCTION OF CANDIDATE DISEASE SEVERITY AND DONOR QUALITY," AMERICAN JOURNAL OF TRANSPLANTATION 2008; 8: 419-425

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STARZL INSTITUTE: NOBODY HAS A UNIT LIKE THIS

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Starzl institute: 'Nobody has a unit like this'

A third of liver patients fall into 'less sick' category

On a recent clinic day at UPMC Montefiore, dozens of liver and kidney transplant patients clogged the seventh-floor waiting room.

A man with jaundiced skin wrapped his fingers around a Styrofoam coffee cup. A woman, not older than 30, watched a portable DVD player. Yet another man in a wheelchair stared into space.

"*Nobody* has a unit like this," said Dr. Amadeo Marcos, showing off the 21-room clinic. "*Nobody* has a clinic entirely devoted to transplantation."

After all, it's the Starzl Transplantation Institute, named after the now semi-retired transplant great who finished his career in these very same hallways.

It took 30 minutes for Marcos, the center's director of transplantation until he resigned last week, to explain why the Starzl institute has performed more liver surgeries — 4,930 since 1988 — than any other center in the country.

The institute's infrastructure makes it a city of sorts, and includes the types of services typically shared by an entire hospital: its own blood bank, pharmacy and radiology suite. Asked how many operating rooms are available, Marcos responded: "As many as we need."

That confidence has been a part of Marco's often-charming personality. Wearing a dark brown suit and loafers, with brown hair, Marcos, 46, walked the hallways with an impish grin as he is greeted by virtually everyone who sees him.

"It's so good to see you," said a patient in an elevator.

Marcos, 46, came to Pittsburgh in 2002 with an impressive resume. By the time he left the University of Rochester Medical Center in New York, he had performed 56 liver transplants using live donors, a then-emerging field that Pittsburgh was just starting to delve into.

Marcos also arrived with a reputation of being an aggressive surgeon willing to take risks that few others would. He was convinced that the nation's organ shortage could be addressed by making use of more organs from dead donors.

That means using organs from donors often considered questionable. Although there is no agreement over what constitutes a marginal liver, those organs can come from older donors, or people who've died from cardiac arrest.

At the Starzl institute, as in other transplant centers, those organs go to patients who are less sick.

Marcos disputed scientific data that show those patients are better off waiting for a transplant until they become sicker.

"Organs that are questionable don't do well on higher-MELD patients," he said. "The common knowledge is that we can't use them in sicker patients."

At the Starzl institute, nearly one of every three liver transplants is done on patients with a low-MELD score, a highly debated practice.

"It's pretty much impossible to show patients with low-MELD scores benefit from transplants," said Dr. Jeffrey Punch, a UNOS regional councilor and director of the transplant center at University of Michigan Medical Center. "The burden of proof is on the people transplanting patients with low-MELD to prove they're doing a benefit."

Marcos defended the practice, saying UPMC practices responsible medicine.

"Don't get this impression that we have all these livers and don't turn anything away," he said. "We responsibly look at every offer out there."

Of about 1,300 livers offered to UPMC every year, only about 600 are evaluated through a biopsy, said Bill Morris, executive director of transplant services at UPMC. The other 700 are either passed upon, or rejected as being unfit.

Marcos said his motivation is to save patients and he accepts that some of his colleagues will think otherwise.

"You can't expect all transplant surgeons to have the same philosophy," he said.

It isn't known what role, if any, Marcos' philosophy played in his sudden resignation. UPMC officials will not say why he left, even though a key program overseen by Marcos — the live-donor liver transplants — is under review by a panel of experts.

"The program grew while I was there," Marcos said this past week. "I did a great job."

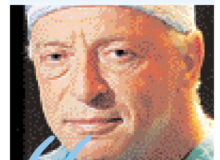
Dr. John Fung
Chief of surgery, The Cleveland Clinic

"There is a point where, and we've argued this for years, the lowest-risk patients shouldn't be transplanted because they don't need it."

Dr. Jeffrey Punch
Transplant director, University of Michigan Medical Center

"It's pretty much impossible to show patients with low MELD scores benefit from transplants. The burden of proof is on the people transplanting patients with low-MELD to prove they're doing a benefit."

Dr. Andreas Tzakis
Director, Miami Transplant Institute



"The hospital doesn't like (transplanting sicker patients), the insurance company doesn't like it, the doctors don't like it because it requires a lot of work. If you put all those things together, there's a lot of pressure to do patients with low-MELD scores."