DONATE LIFE
EGYPT 2025

Cairo, November 12, 2025

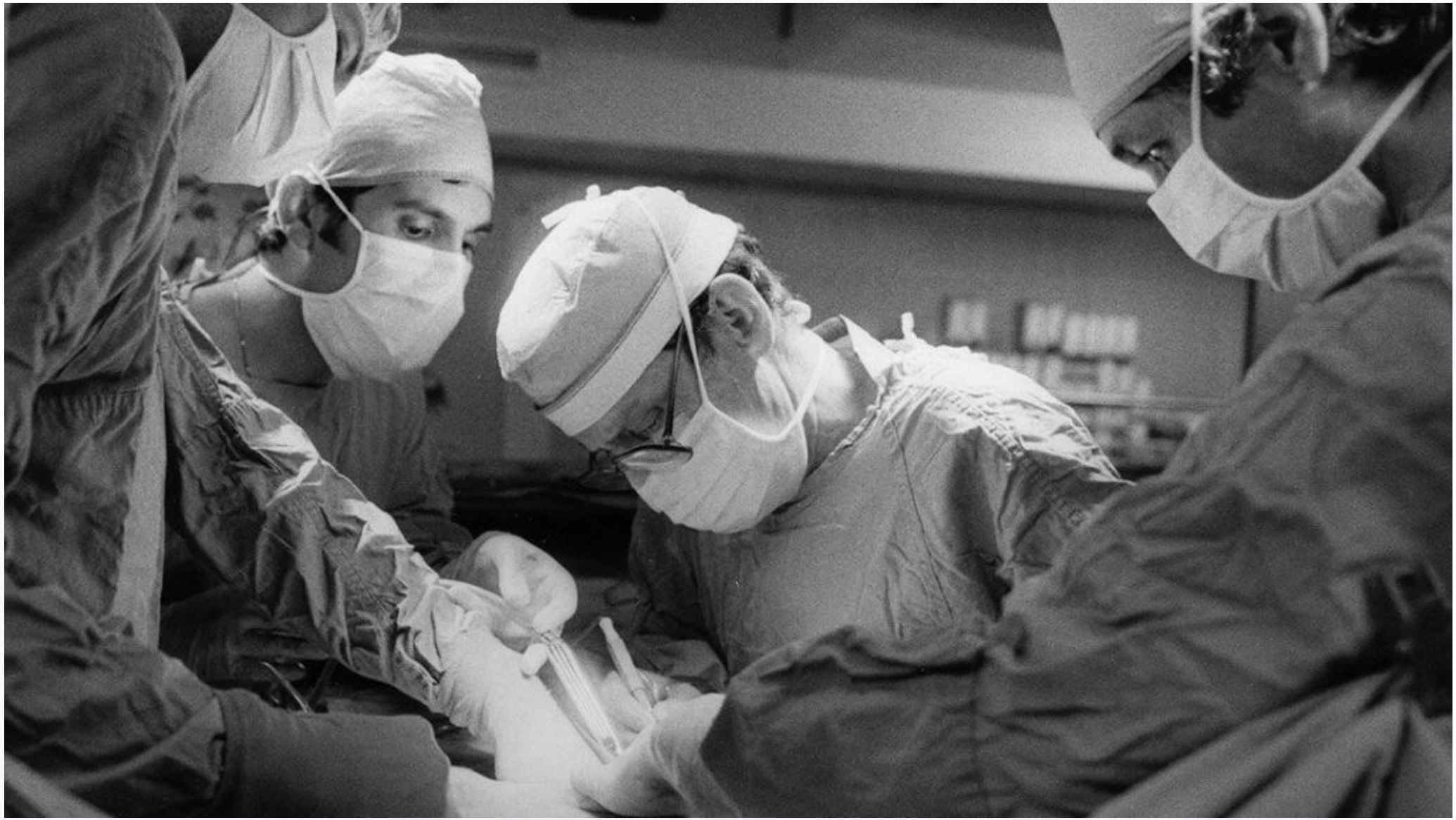
Reflections from a Transplant Pioneer: Ethics, Policy, and the Future of Global Collaboration

Ignazio R. Marino, MD, ScD
Emeritus Professor of Surgery, Thomas Jefferson University, USA

Cairo Charter: One Vision, One Hope, One Heart

The real pioneers

Thomas Starzl performing OLTx with international team



Lasker-DeBakey Clinical Medical Research Award (2012)
Sir Roy Calne and Thomas E. Starzl for the development of liver transplantation, which has restored normal life to thousands of patients with end-stage liver disease

Ethics

1961 Artificial Kidney Center, Seattle, USA: A matter of life or death

A decision-making Committee composed of 7 lay people:

a lawyer, a minister, a housewife, a state government official, a banker, a labor leader, and a surgeon decided who should live and who should die.

(They were called "**THE GOD COMMITTEE**")

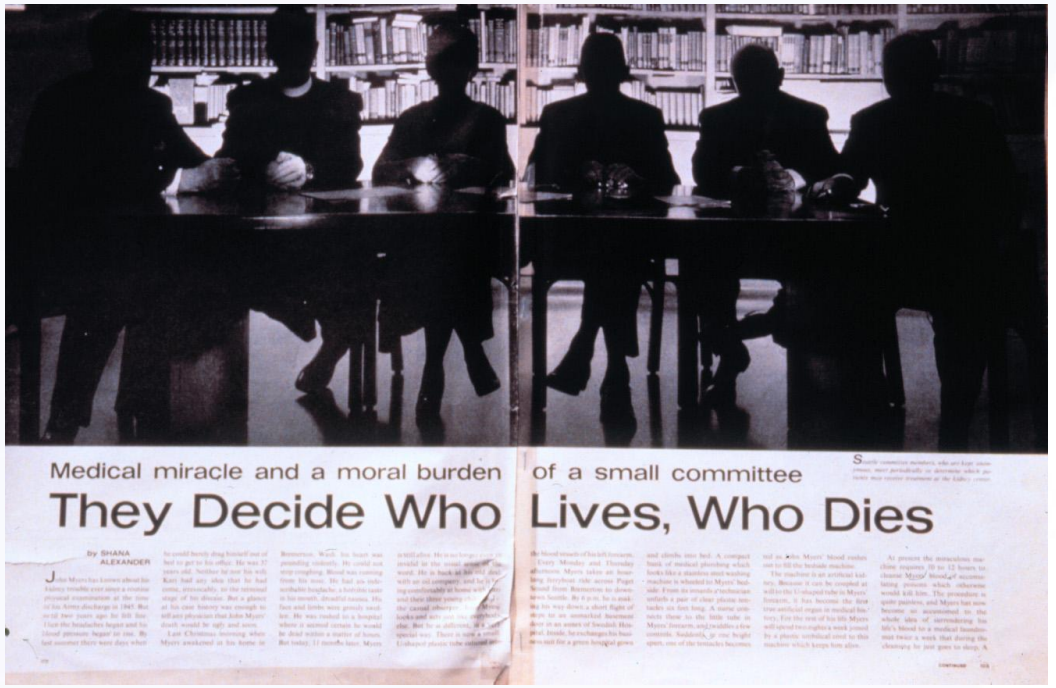
They considered the **patient's marital status**, net worth, nature of occupation, extent of education, **church attendance**, **number of kids** (the more, the better the chance of being chosen), and potential to resume work. They struggled with the ultimate question of **who should be saved: the person who contributes the most to society or the one whose death would impose the greatest burden on society in the form of children left without care or resources**.

God Committee

"*As human beings ourselves*," said one of the members of the Seattle Committee, "*we rejected the idea instinctively, of classifying other human beings in pigeonholes, but we realized we had to narrow the field somehow*."

LIFE Magazine, November 9, 1962

Criteria for acceptance included sex, marital status, and number of dependents, income, net worth, emotional stability, occupation, past performance, and future potential.


Medical miracle and a moral burden of a small committee
They Decide Who Lives, Who Dies

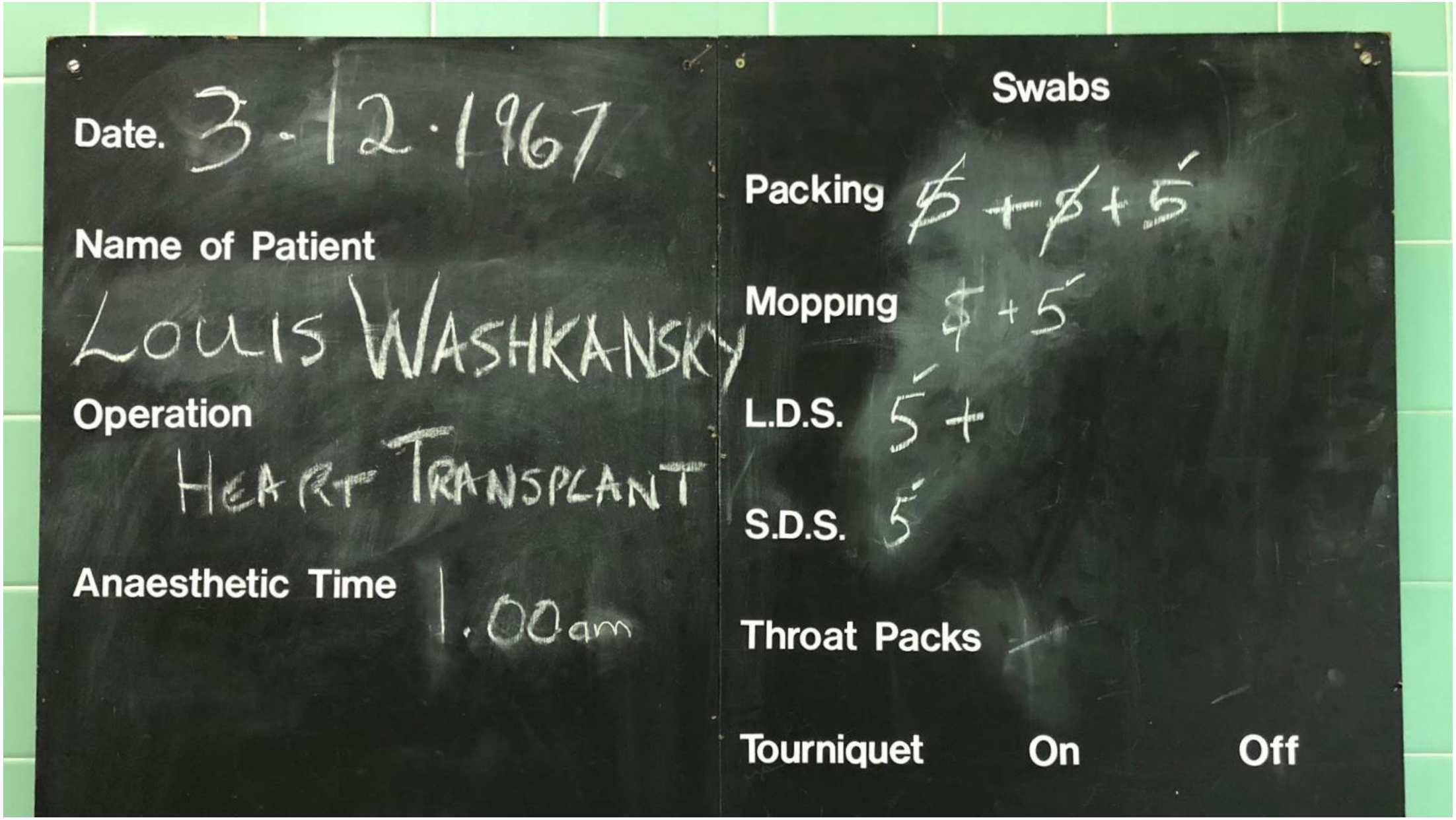
In 1972, President Richard Nixon signed a bill saying the government would pay for dialysis for anyone who needed it.
(Social Security Amendments of 1972)

Coverage (patients)

- **1972 10,000**
- **2016 500,000 1 % of Federal Budget**

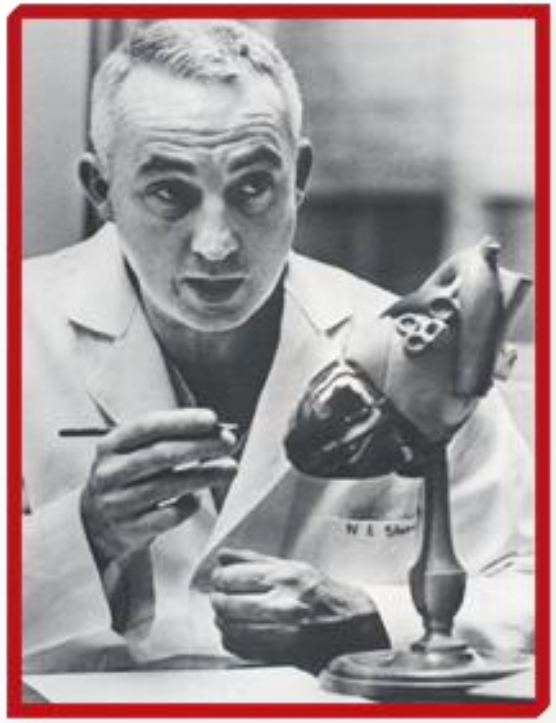
Washington Post, May 15, 2017

"*Essentially* ***we have universal health care in the USA, for one organ*** *in your body* – says John Oliver - *it's like your kidneys, and* ***only your kidneys****, are Canadian*"

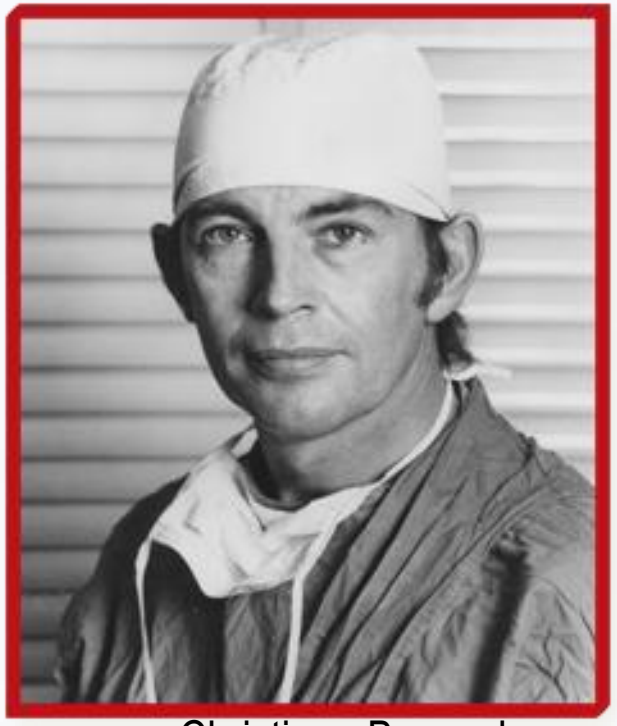

Date. 3-12-1967
Name of Patient
LOUIS WASHKANSKY
Operation
HEART TRANSPLANT
Anaesthetic Time
1.00 am
Swabs
Packing
Mopping
L.D.S.
S.D.S.
Throat Packs
Tourniquet
On
Off

1967

South Africa: *Dr. Christiaan Barnard* in Cape Town, using techniques pioneered at Stanford University by *Drs. Norman Shumway* and *Richard Lower*, performed the first successful heart transplant.

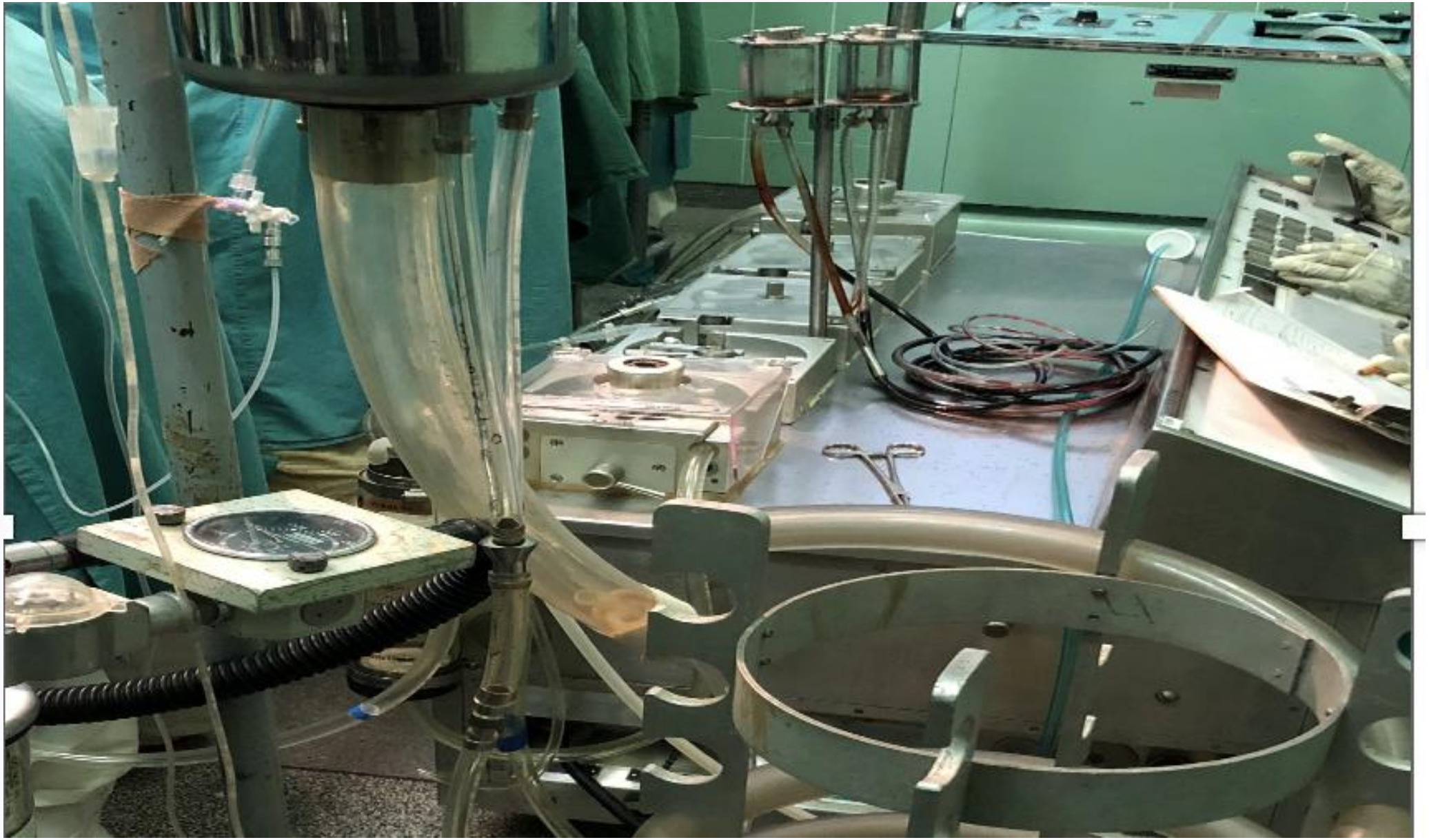


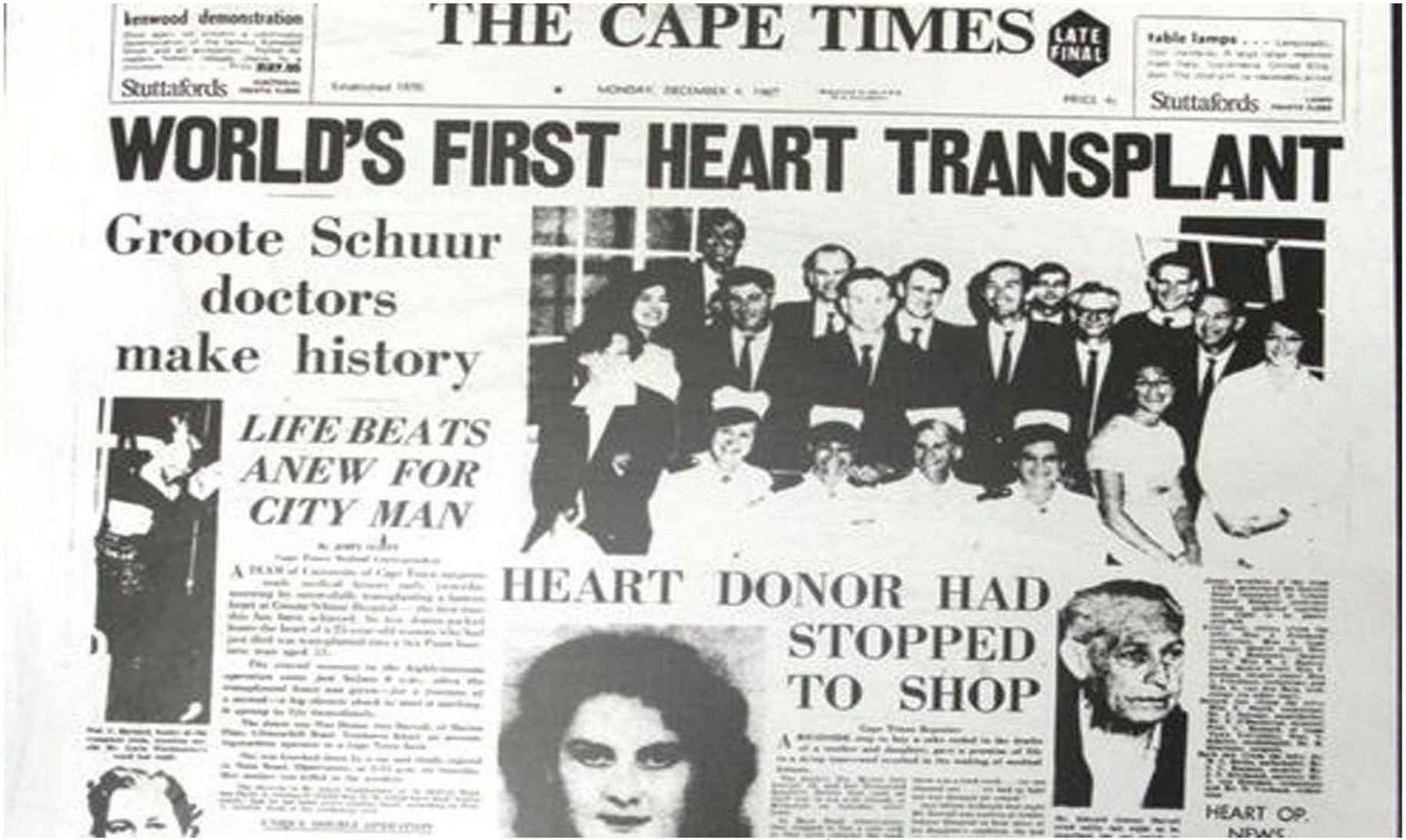
Norman Shumway



Christiaan Barnard

Louis Washkansky





kenwood demonstration

Stuttafords

THE CAPE TIMES

LATE FINAL

MONDAY, DECEMBER 4, 1967

PRICE 4c

table lamps

Stuttafords

WORLD'S FIRST HEART TRANSPLANT

Groote Schuur doctors make history

LIFE BEATS ANEW FOR CITY MAN

HEART DONOR HAD STOPPED TO SHOP

HEART OP. NEWS

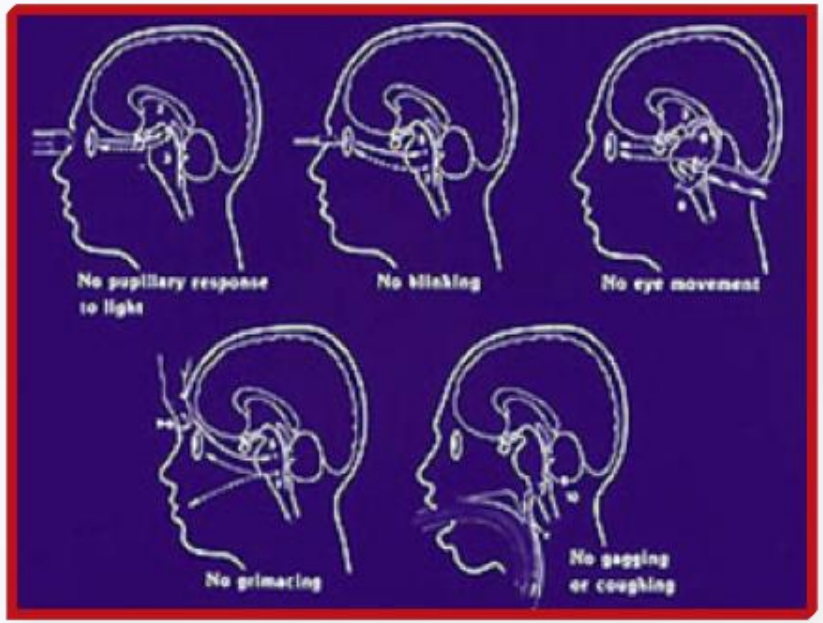
1965

The term "brain-dead" was coined when a renal transplant took place using organs donated from a patient with no recorded brain function

1968

A Definition of Irreversible Coma. Report of the Ad Hoc Committee of the Harvard Medical School to Examine the Definition of Brain Death.

JAMA 205: 337, 1968



Policy

LIFE AND DEATH ON THE OPERATING TABLE

Regarding the first liver transplant, performed in 1963 on a pediatric patient, 3-year-old Bennie Solis, who suffered from terminal liver failure and bled to death on the operating table while the surgical staff would desperately try to complete the operation, Dr. Starzl wrote*:

"*[Bennie] was wrapped in a plain white sheet after being washed off by a weeping nurse. They took him away from this place of sanitized hope to the cold and unhygienic morgue.... The surgeons stayed in the operating room for a long time after, sitting on the low stools around the periphery, looking at the ground and saying nothing....* ***It was not the last time I would see this scene, both in my dreams and in reality****. I never heard anyone who was there describe this as 'the Solis case,' or "the first human liver transplantation". If they mentioned it at all, it was always just about Bennie.*"

* Thomas E. Starzl, The Puzzle People, 1992

NEVER FEAR TO FAIL

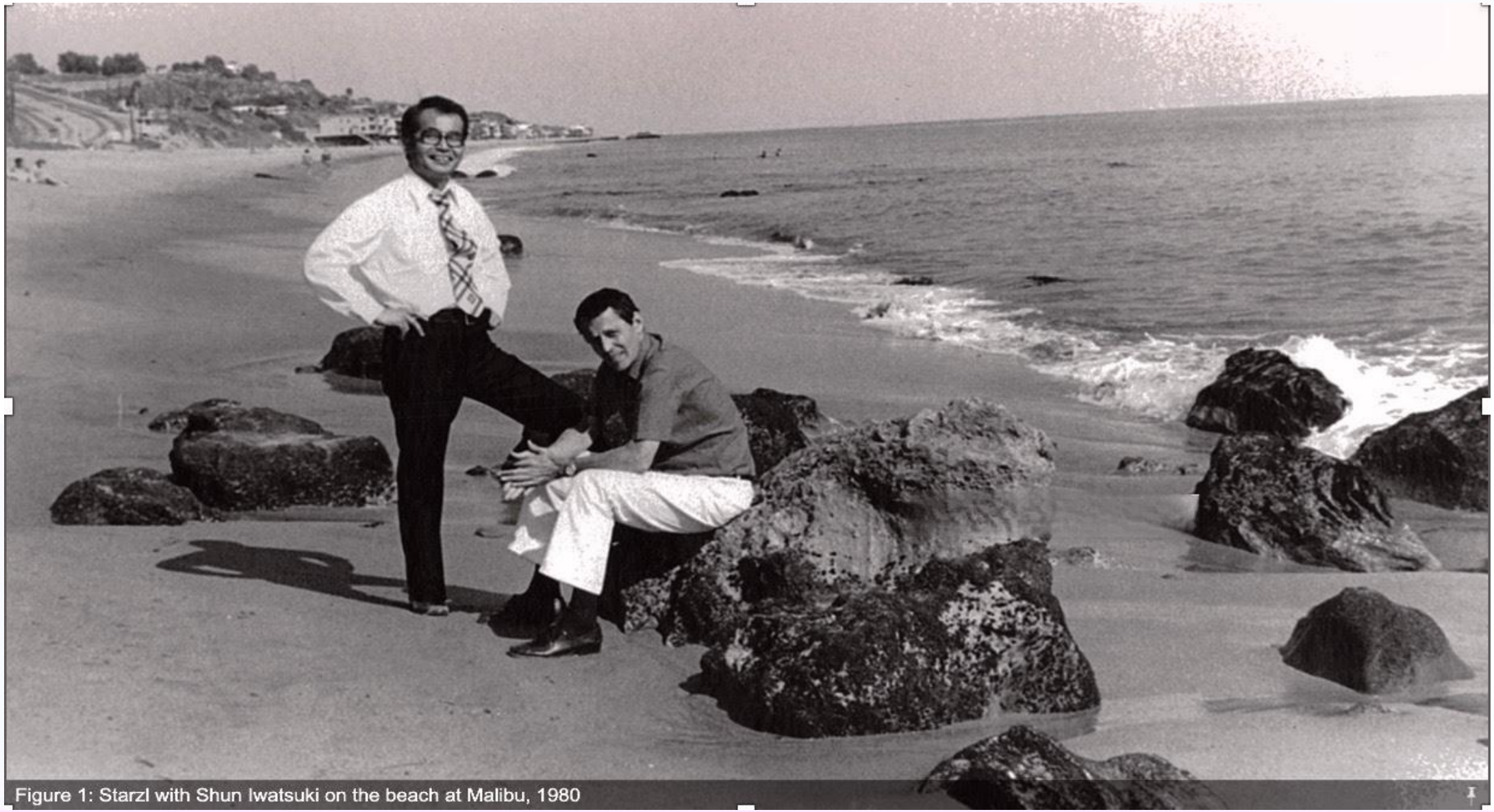
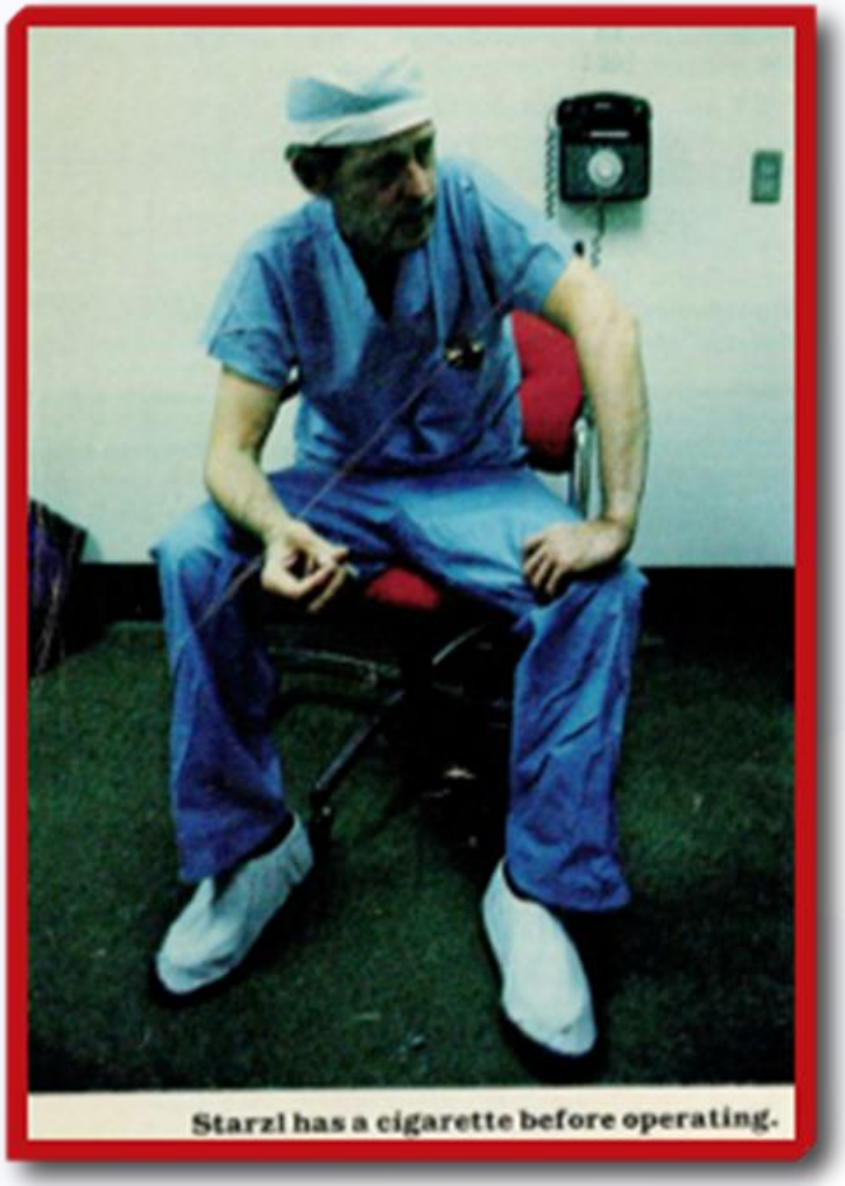


Figure 1: Starzl with Shun Iwatsuki on the beach at Malibu, 1980


LIFE
DUSTIN HOFFMAN
He dons a dress
for his most
surprising role
BASEBALL WIVES
The fascinating
women behind
the boys at bat
September 1982
LIVER
TRANSPLANTS
A breakthrough
in lifesaving
surgery


Starzl has a cigarette before operating.

1983

Liver transplantation is approved as a therapeutic modality by NIH Consensus Conference. It has progressed past "experimental procedure" status into a "clinical service."

National Institutes of Health Consensus Development Conference Statement: Liver Transplantation—June 20–23, 1983

(1) ARE THERE GROUPS OF PATIENTS FOR WHOM TRANSPLANTATION OF THE LIVER SHOULD BE CONSIDERED APPROPRIATE THERAPY?

The Liver Transplant Revolution: Breakthroughs Between 1982 and 1997

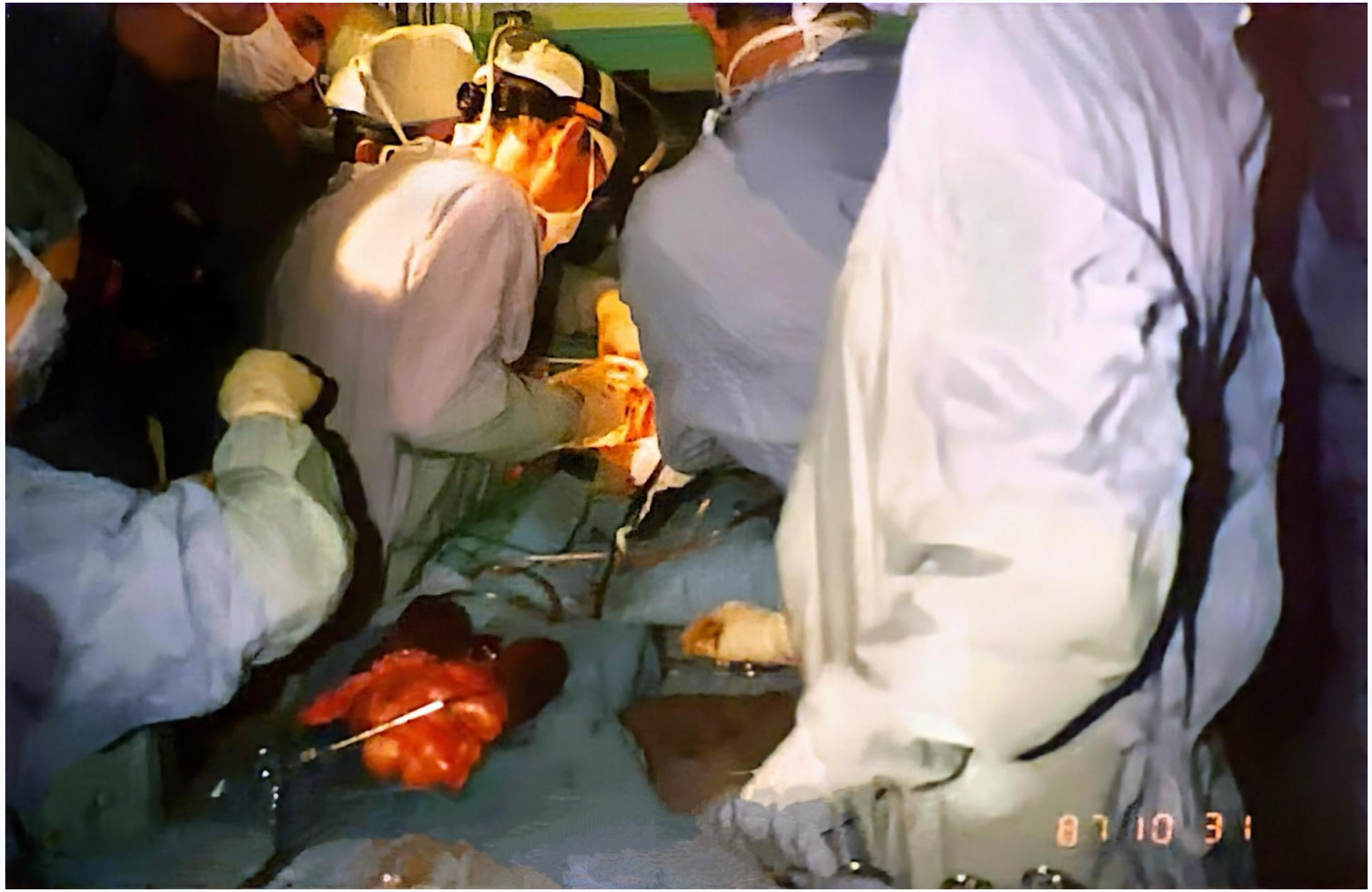
(5 kidneys & 3 livers)

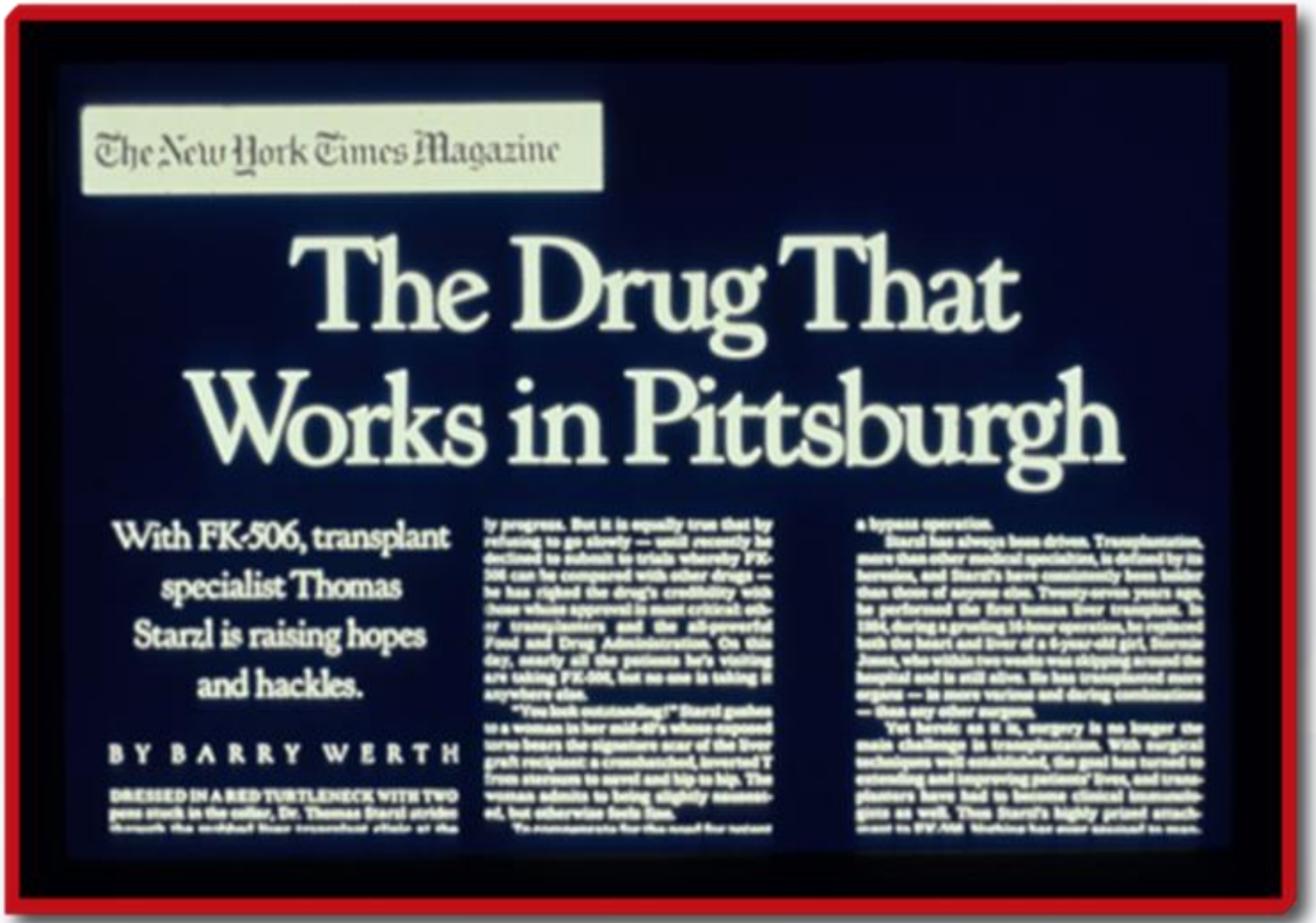
Between 1982 and 1997, the most significant surgical and immunological discoveries in liver transplantation were concentrated into just 15 revolutionary years.

Starzl's Revolutionary Advances

- 1982 - Adding steroids to cyclosporine immunosuppression
- 1983 - Veno-venous bypass
- 1984 - Mouse Anti-Human T-cell antibody OKT3
- 1987 - MVTx
- 1989 - FK506 (Tacrolimus)
- 1990 - OLTx in patients with portal thrombosis
- 1992 - Xenotransplantation
- 1993 - Tolerance induction with bone marrow
- 1994 - Total abdominal exenteration for metastatic cancer
- 1997 - Immunosuppression weaning

October 31, 1987 – Thomas Starzl – 1st MVTx





The New York Times Magazine

The Drug That Works in Pittsburgh

With FK-506, transplant specialist Thomas Starzl is raising hopes and hackles.

BY BARRY WERTH

DRESSED IN A RED TURTLENECK WITH TWO pens stuck in the collar, Dr. Thomas Starzl strides

ly progress. But it is equally true that by refusing to go slowly — until recently he declined to submit to trials whereby FK-506 can be compared with other drugs — he has risked the drug's credibility with those whose approval is most critical: other transplanters and the all-powerful Food and Drug Administration. On this day, nearly all the patients he's visiting are taking FK-506, but no one is taking it anywhere else.

"You look outstanding!" Starzl pushes in a woman in her mid-40's whose exposed torso bears the signature scar of the liver graft recipient: a crosshatched, inverted T from sternum to navel and hip to hip. The woman admits to being slightly nauseated, but otherwise feels fine.

a bypass operation.

Starzl has always been driven. Transplantation, more than other medical specialties, is defined by its heroines, and Starzl's have consistently been bolder than those of anyone else. Twenty-seven years ago, he performed the first human liver transplant. In 1984, during a grueling 16-hour operation, he replaced both the heart and liver of a 6-year-old girl, Stormie Jones, who within two weeks was skipping around the hospital and is still alive. He has transplanted more organs — in more various and daring combinations — than any other surgeon.

Yet heroic as it is, surgery is no longer the main challenge in transplantation. With surgical techniques well established, the goal has turned to extending and improving patients' lives, and transplanters have had to become clinical immunologists as well. Thus Starzl's highly prized attachment to FK-506 [illegible] has ever seemed so much

THE LANCET

Vol 341 Saturday 9 January 1993 No 8837

ARTICLES

Baboon-to-human liver transplantation

T. E. STARZL J. FUNG A. TZAKIS S. TODO A. J. DEMETRIS
I. R. MARINO H. DOYLE A. ZEEVI V. WARTY M. MICHAELS
S. KUSNE W. A. RUDERT M. TRUCCO

Our ability to control both the cellular and humoral components of xenograft rejection in laboratory experiments, together with an organ shortage that has placed limits on clinical transplantation services, prompted us to undertake a liver transplantation from a baboon to a 35-year-old man with B virus-associated chronic active hepatitis and human immunodeficiency virus infection.

Liver replacement was performed according to conventional surgical techniques. Immunosuppression was with the FK 506-prednisone-prostaglandin regimen used routinely for hepatic allotransplantation, to which a daily non-myelotoxic dose of cyclophosphamide was added. During 70 days of survival, there was little evidence of hepatic rejection by biochemical monitoring or histopathological examination. Products of hepatic synthesis, including clotting factors, became those of the baboon liver with no obvious adverse effects. Death followed a cerebral and subarachnoid haemorrhage that was caused by an angioinvasive aspergillus infection. However, the underlying cause of death was widespread biliary sludge that formed in the biliary tree despite a seemingly satisfactory choledochojejunostomy. During life and in necropsy samples, there was evidence of the chimerism that we believe is integral to the acceptance of both xenografts and allografts.

Our experience has shown the feasibility of controlling the rejection of the baboon liver xenograft in a human recipient. The biliary stasis that was the beginning of lethal infectious complications may be correctable by modifications of surgical technique. In further trials, the error of over-immunosuppression should be avoidable.

Lancet 1993; **341**: 65–71.

Introduction

Previous attempts to transplant seven baboon kidneys[1,2] and two hearts[3,4] resulted in graft loss or patient death between 0 and 60 days after transplantation. A common difficulty was uncontrolled cellular rejection, together with antibody-mediated occlusive endotheliolitis of graft microvasculature and parenchymal necrosis.[4,5] Recent laboratory investigations have shown that the presumably humoral component of xenograft rejection could be diminished by a short course of antimetabolite therapy, such as cyclophosphamide, which targeted the B-cell proliferative response.[6,7] By overcoming this antibody barrier, the value of maintenance therapy with T-cell-directed immunosuppressants was unmasked.[6,8]

We now describe a baboon-to-human liver xenotransplantation in which FK 506 and cyclophosphamide were given as immunosuppressants, together with prednisone and prostaglandin, both of which help to mitigate preformed antigraft antibody syndromes and cellular rejection.[9,10]

Patient and methods

Recipient history

A 35-year-old white male had a history of abnormal liver function tests since 1984 with recurrent bleeding from oesophageal varices and haemorrhoids which began 2 years later. Hepatitis B virus (HBV) and human immunodeficiency virus (HIV) had been diagnosed in 1987. When his spleen was ruptured and removed after a motorcycle accident in 1989, his prothrombin time (PT) was

ADDRESSES: **Pittsburgh Transplant Institute and the Departments of Surgery** (T. E. Starzl, MD, J. Fung, MD, A. Tzakis, MD, S. Todo, MD, A. J. Demetris, MD, I. R. Marino, MD, H. Doyle, MD, A. Zeevi, PhD, V. Warty, PhD, S. Kusne, MD), **Pathology** (A. J. Demetris, A. Zeevi, V. Warty, W. A. Rudert, MD, M. Trucco, MD), **Infectious Disease** (M. Michaels, MD, S. Kusne), **and Paediatrics** (W. A. Rudert, M. Trucco), **University of Pittsburgh Health Science Center, Pittsburgh, Pennsylvania 15213, USA.** Correspondence to Dr T. E. Starzl, Department of Surgery, 3601 Fifth Avenue, SC Falk Clinic, University of Pittsburgh, Pittsburgh, PA 15213, USA.

Pittsburgh, 1992. The surgical team with patient Brian (center, seated), the first man who received a baboon liver.

BACKGROUND INFORMATION

JOURNAL OF VIROLOGY, Aug. 1998, p. 6430–6436 Vol. 72, No. 8
0022-538X/98/$04.00+0

Human Immunodeficiency Virus Type 1 Replication Is Modulated by Host Cyclophilin A Expression Levels

LEI YIN,[1] DOUGLAS BRAATEN,[1] AND JEREMY LUBAN[1,2]*

Departments of Microbiology[1] and Medicine,[2] Columbia University, College of Physicians and Surgeons, New York, New York 10032

Proc. Natl. Acad. Sci. USA
Vol. 95, pp. 1758–1763, February 1998
Medical Sciences

Role of cyclophilin A in the uptake of HIV-1 by macrophages and T lymphocytes

BARBARA SHERRY*, GABRIELE ZYBARTH*, MASSIMO ALFANO*, LARISA DUBROVSKY*, ROBERT MITCHELL*, DANIEL RICH†, PETER ULRICH*‡, RICHARD BUCALA*, ANTHONY CERAMI*‡, AND MICHAEL BUKRINSKY*§

*The Picower Institute for Medical Research, Manhasset, NY 11030; and †University of Wisconsin, Madison, WI 53706;

JOURNAL OF VIROLOGY, July 1996, p. 4220–4227 Vol. 70, No. 7
0022-538X/96/$04.00+0

Cyclophilin A Is Required for the Replication of Group M Human Immunodeficiency Virus Type 1 (HIV-1) and Simian Immunodeficiency Virus $SIV_{CPZ}GAB$ but Not Group O HIV-1 or Other Primate Immunodeficiency Viruses

DOUGLAS BRAATEN,[1] ETTALY KARA FRANKE,[2] AND JEREMY LUBAN[1,2]*

Departments of Microbiology[1] and Medicine,[2] Columbia University College of Physicians and Surgeons, New York, New York 10032

JOURNAL OF VIROLOGY, Sept. 1997, p. 7110–7113 Vol. 71, No. 9
0022-538X/97/$04.00+0

Active-Site Residues of Cyclophilin A Are Crucial for Its Incorporation into Human Immunodeficiency Virus Type 1 Virions

TATYANA DORFMAN,[1] ANDREAS WEIMANN,[1] ALESSANDRA BORSETTI,[1] CHRISTOPHER T. WALSH,[2] AND HEINRICH G. GÖTTLINGER[1,3]*

Division of Human Retrovirology, Dana-Farber Cancer Institute,[1] Department of Biological Chemistry and Molecular Pharmacology,[2] and Department of Pathology,[3] Harvard Medical School, Boston, Massachusetts 02115

Proc. Natl. Acad. Sci. USA
Vol. 89, pp. 8351–8355, September 1992
Medical Sciences

Inhibition of human immunodeficiency virus and growth of infected T cells by the immunosuppressive drugs cyclosporin A and FK 506

(antiviral agents/AIDS)

ABRAHAM KARPAS*†, MARK LOWDELL‡, S. KIM JACOBSON§, AND FERGAL HILL*

*Department of Haematology, Cambridge University, Hills Road, Cambridge CB2 2QH, United Kingdom; ‡Department of Immunology, The Royal London Hospital, Whitechapel, London E1 1BB, United Kingdom; and §Clinical Microbiology Public Health Laboratory, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ, United Kingdom

Cyclosporin A in combination with HAART in primary HIV-1 infection

Rizzardi GP, Vaccarezza M, Capiluppi B, Tambussi G, Lazzarin A, Pantaleo G.
J Biol Regul Homeost Agents 2000;14:79-81

AGO 2001

il Giornale

da pag.15

CHIRURGIA

Primo trapianto di rene su un paziente sieropositivo

PRO E CONTRO

Perché no:

Girolamo Sirchia, ministro della Salute, già direttore del Nord Italia Transplant, la struttura che coordina i trapianti in Italia

Ho molti dubbi e perplessità. Al Nit ci capitò accidentalmente di effettuare trapianti su soggetti poi rivelatisi sieropositivi; i risultati furono disastrosi e avevamo escluso dal nostro protocollo questo tipo di intervento

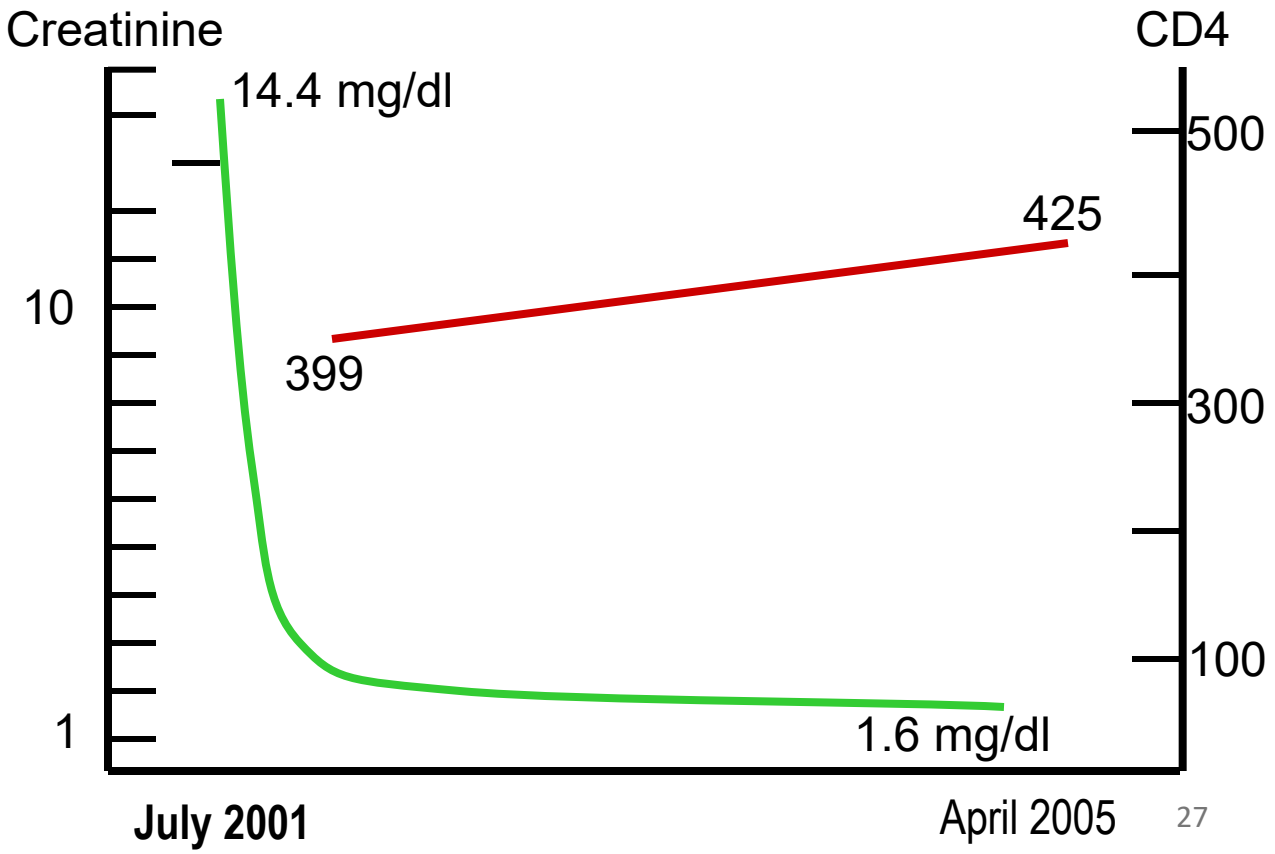
Perché sì:

Fernando Aiuti, immunologo

L'intervento è un grande passo avanti sia dal punto di vista etico sia scientifico. Finora le persone sieropositive, per la cronica mancanza di organi, non venivano incluse nelle liste di attesa prioritarie. Ma oggi, con i farmaci anti-Aids si è allungata la speranza di vita per un sieropositivo, al quale può essere trapiantato un organo

"Three years ago I got transplanted, I am reborn"

La Gazzetta del Sud, September 1,2004



SECA I & SECA II

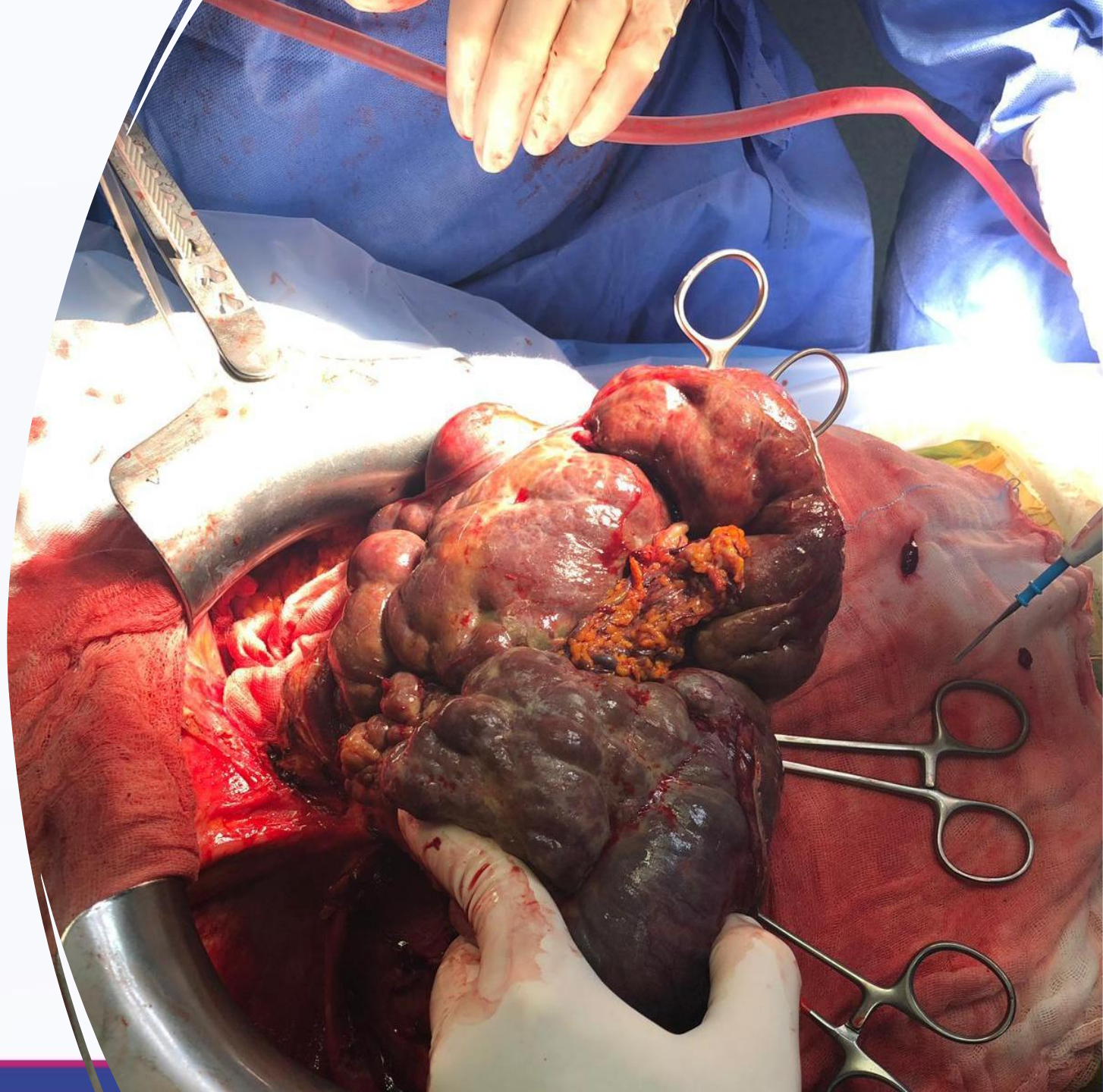
SECA I and SECA II randomized trials investigating the role of OLTx in unresectable liver colorectal metastasis have reported survival rates of 80% at 4 years

Recurrence rates were rather high (60% at 2 years from OLTx), and mainly in the lungs

However, the overall survival was still long, as the disease was controlled by systemic treatment

Successful OLTx for breast cancer metastasis

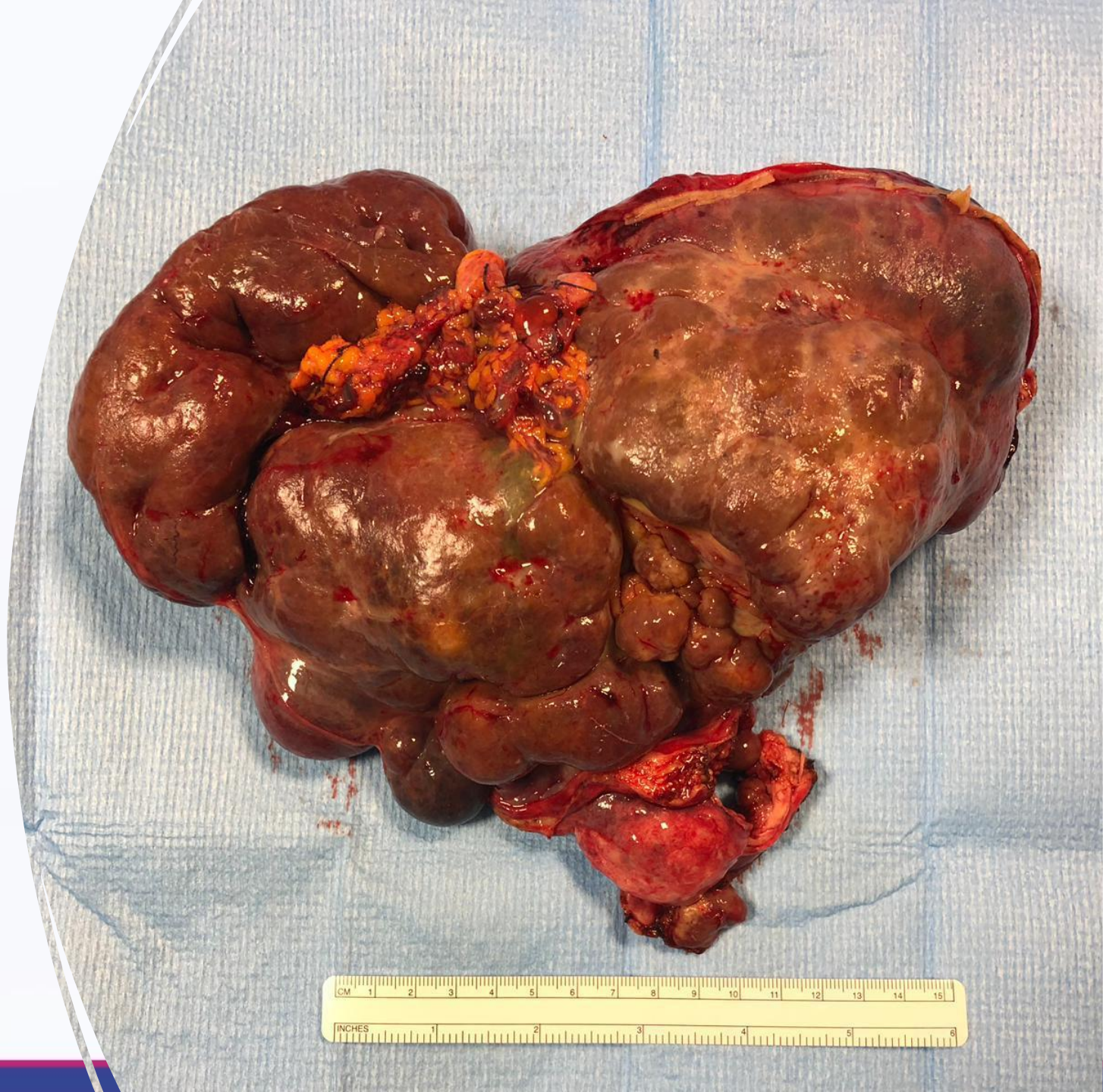
- A 41-year-old female was diagnosed with breast cancer
- She underwent a quadrantectomy and axillary lymphadenectomy in January 2000



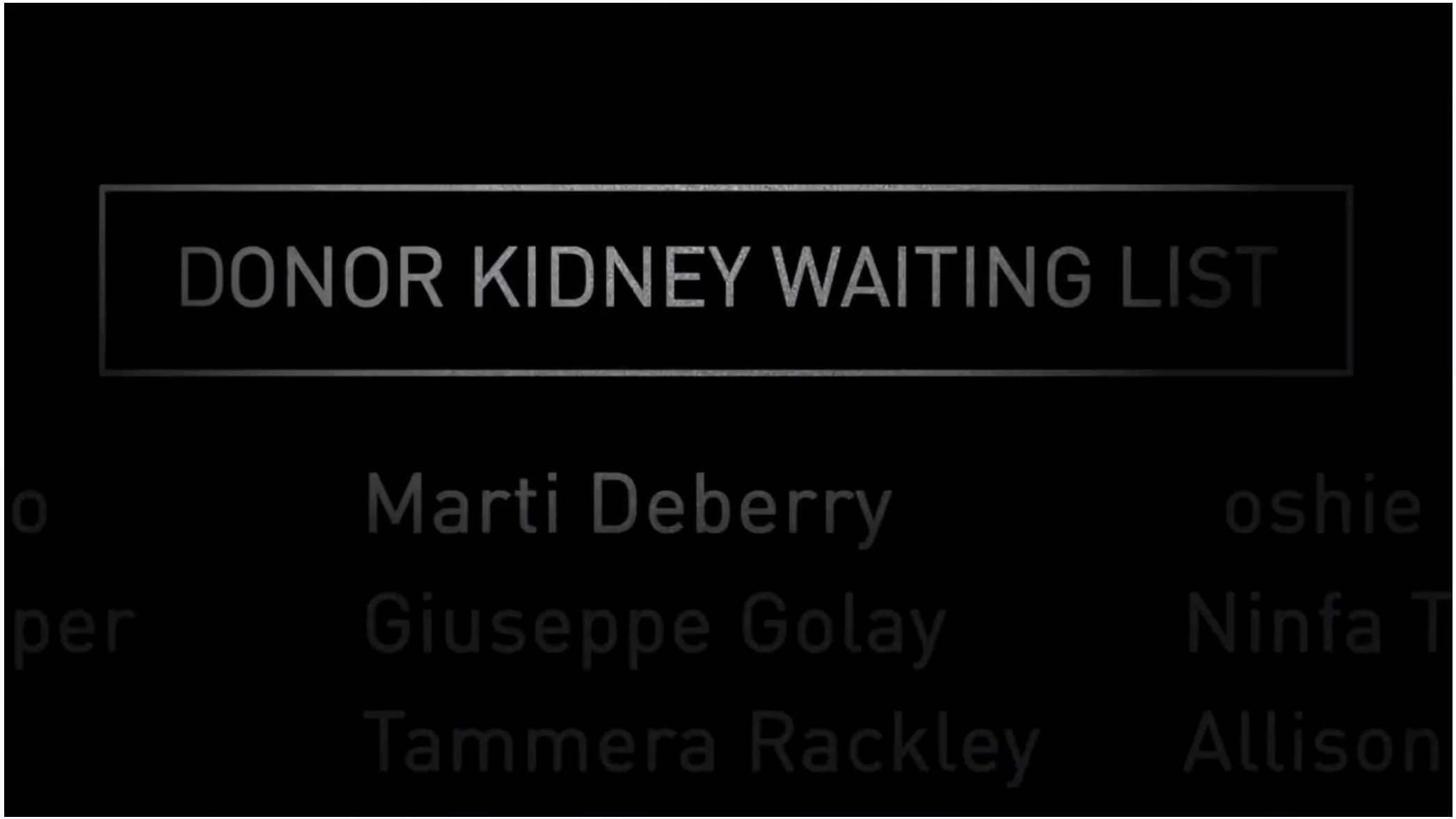
Successful OLTx for breast cancer metastasis

THE PATIENT UNDERWENT OLTx IN JULY 2019 (ALIVE AND WELL IN 2025)

BUT the Italian POLICY allows indication for liver failure, and not the oncological disease itself: as a consequence only 1 patient has been transplanted



Global collaboration


DONOR KIDNEY WAITING LIST
Marti Deberry
Giuseppe Golay
Tammera Rackley

Kidney Exchange: Some History

Felix Rapaport The case for a living emotionally related international kidney donor exchange registry,*Transplant Proc.* **1986**

1991 Korea: Kwak JY , Kwon OJ , Lee KS , et al. ”Exchange-donor program in renal transplantation: a single-center experience,” *Transplant Proc* , 1999

1999 Basel: Thiel G, Vogelbach P, Gurke L, et al. ”Crossover renal transplantation: hurdles to be cleared!”, *Transplant Proc* , 2001

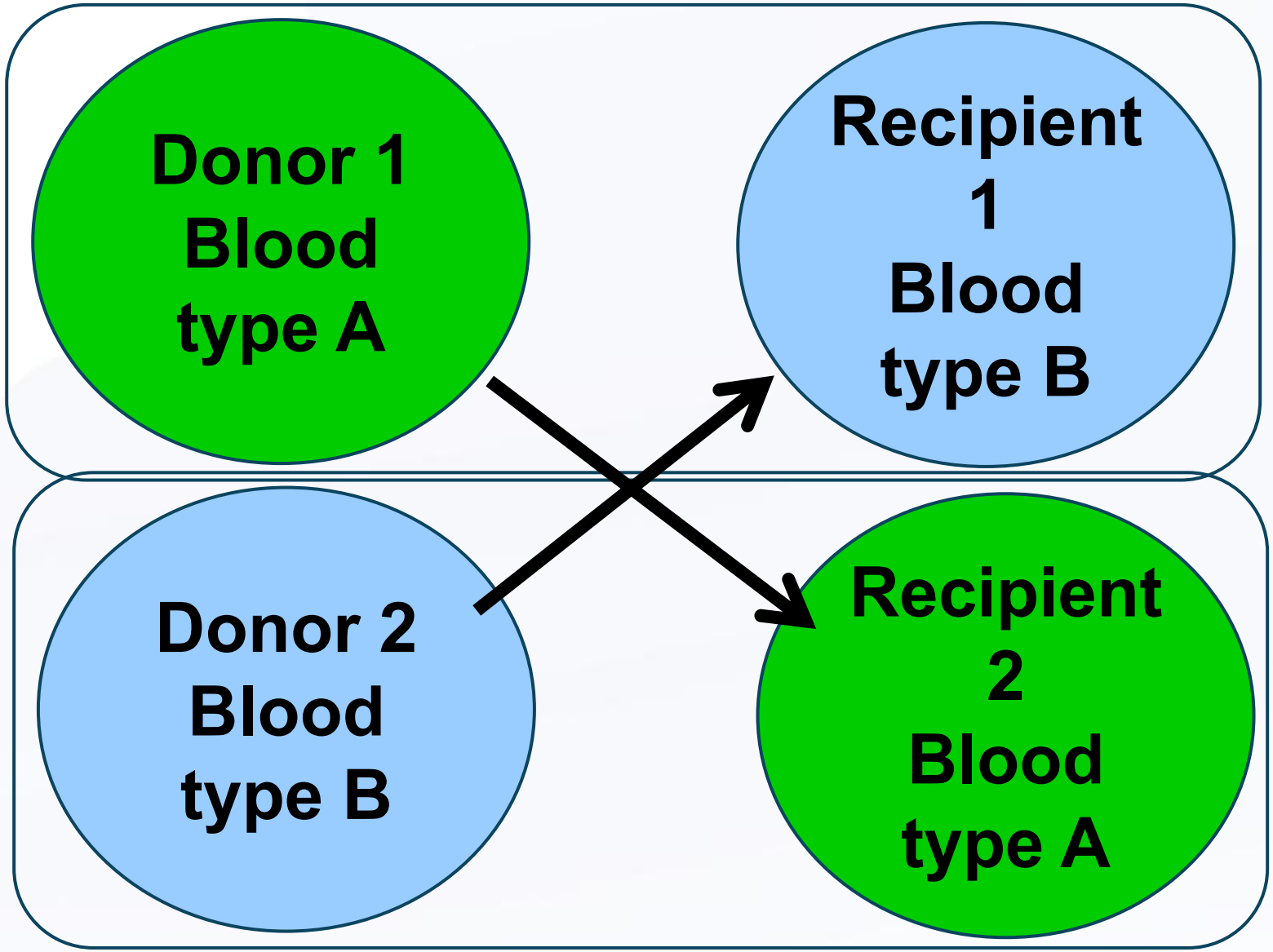
Netherlands: de Klerk M, Keizer KM, Claas FH, et al. ”The Dutch national living donor kidney exchange program” *Am J Transplant* , 2005

2000 USA: Anthony P Monaco and Paul E Morrissey, Rhode Island Hosp
Delmonico FL, Morrissey PE, Lipkowitz GS, et al. “Donor kidney exchanges”, *Am J Transplant* , 2004

Roth AE, Sonmez T, Unver MU “Kidney Exchange,” *Quart J Econ*, 2004

Roth, AE, Sönmez, T. Ünver MU, Delmonico FL, and Saidman SL, Utilizing List Exchange and Undirected Good Samaritan Donation through “Chain” Paired Kidney Donations,” *Am J Transplant*, 2006

Simple two-pair kidney exchange



The NEW ENGLAND JOURNAL of MEDICINE

VOL. 360 NO. 11

ESTABLISHED IN 1812 MARCH 12, 2009 NEJM.ORG

A Nonsimultaneous, Extended, Altruistic-Donor Chain

Michael A. Rees, M.D., Ph.D., Jonathan E. Kopke, B.S., Ronald P. Pelletier, M.D., Dorry L. Segev, M.D., Matthew E. Rutter, M.D., Alfredo J. Fabrega, M.D., Jeffrey Rogers, M.D., Oleh G. Pankewycz, M.D., Janet Hiller, M.S.N., Alvin E. Roth, Ph.D., Tuomas Sandholm, Ph.D., M. Utku Ünver, Ph.D., and Robert A. Montgomery, M.D., D.Phil.

SUMMARY

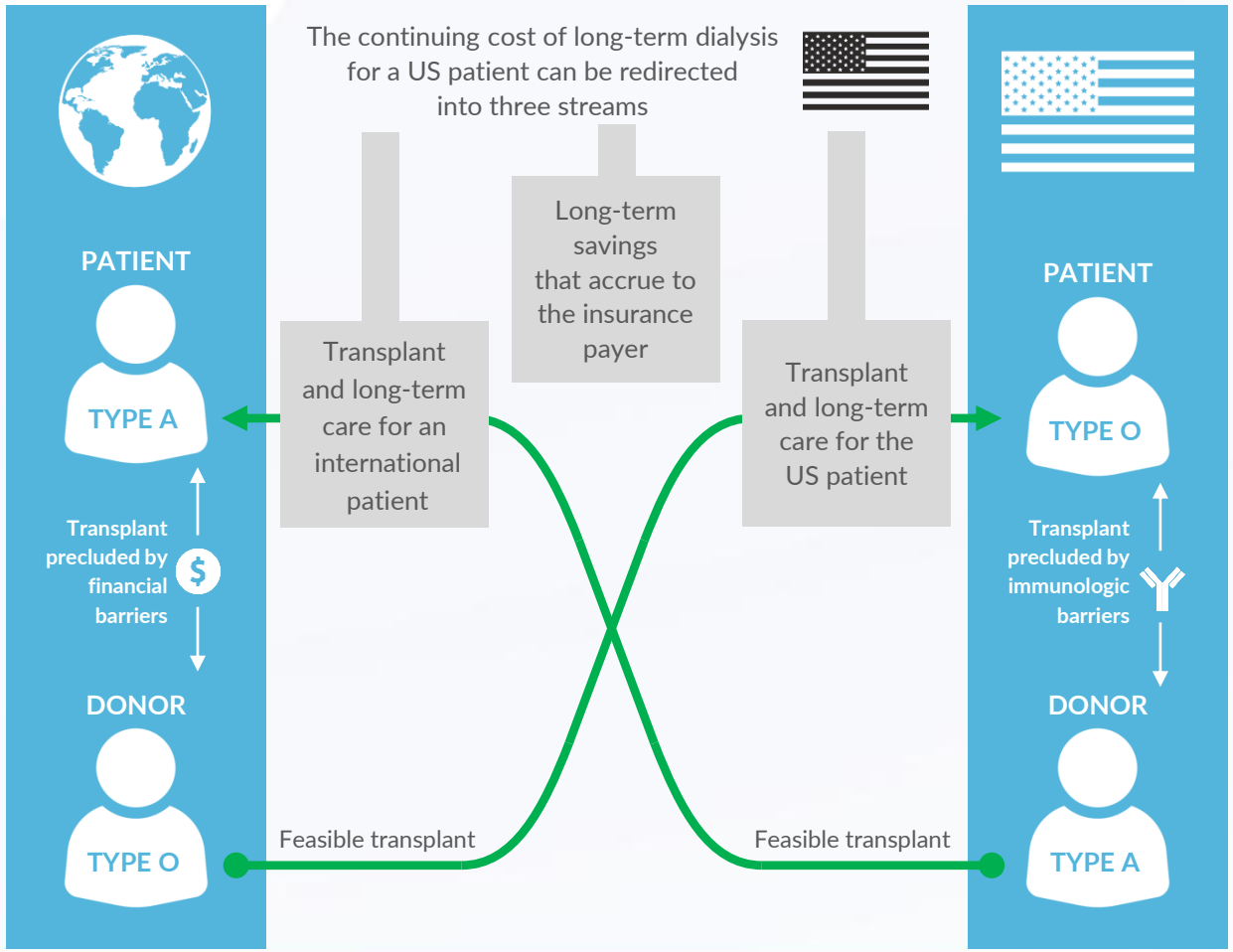
We report a chain of 10 kidney transplantations, initiated in July 2007 by a single altruistic donor (i.e., a donor without a designated recipient) and coordinated over a period of 8 months by two large paired-donation registries. These transplantations involved six transplantation centers in five states. In the case of five of the transplantations, the donors and their coregistered recipients underwent surgery simultaneously. In the other five cases, "bridge donors" continued the chain as many as 5 months after the coregistered recipients in their own pairs had received transplants. This report of a chain of paired kidney donations, in which the transplantations were not necessarily performed simultaneously, illustrates the potential of this strategy.

February 2012, NKR: a NDD chain of length 60 (30 transplants)

5-7 million people die every year worldwide due to the inability to pay for either dialysis or kidney transplantation. This figure is double the number of yearly deaths due to tuberculosis, malaria, and AIDS.

Liyanage T, Ninomiya T, Jha V, et al. Worldwide access to treatment for end-stage kidney disease: a systematic review. Lancet 2015;385:1975-82.

GLOBAL KIDNEY EXCHANGE



Global Kidney Exchange

The GKE proposal is “self-financing”:

- cost of hemodialysis (USA) ≈ $ 90,000 per year
- average time under dialysis ≈ 5 years
- cost of transplant ≈ $ 120,000
- saving in 10 years per patient ≈ $ 600,000

THE MADRID RESOLUTION ON ORGAN DONATION AND TRANSPLANTATION

In response to the global disparities in access to transplantation, a growing demand for organs, and the self-evident harms of transplant tourism, a meeting of 140 representatives of international scientific and medical bodies, government officials and ethicists was held in Madrid from the 23rd to the 25th of March, 2010. … **The purpose of the meeting was to call for a global goal of national responsibility in satisfying organ donation and transplantation needs, with sufficiency based on resources obtained within a country for that country and via regulated and ethical regional or international cooperation, when needed.**

Opposition to Irresponsible Global Kidney Exchange

Francis L. Delmonico ✉, Nancy L. Ascher

Accepted manuscript online: 21 August 2017 Full publication history

We are writing in opposition to the proposed Global Kidney Exchange that would solicit living donors from economically underdeveloped countries such as Mexico, the Philippines, Kenya, India and Ethiopia (1). The experience of representatives from **countries such as India and Mexico** reported at the Vatican Pontifical Academy of Sciences Summit on the topic of organ trafficking in February 2017 was very clear—these locations **are sites of organ trafficking** (2-6). The capacity of this project to assure that targeted donors in underdeveloped countries will be emotionally – related, free of coercion, and fully informed of risk, **is not feasible when the culture is so experienced with organ sales.**

“the plan is really not about the international recipient (nor…about the international donor), but only about getting organs for US citizens. So it is exploitative."

Organ Trafficking

Private audience on organ trafficking

Private audience on organ trafficking

Vatican City, September 19, 2014

Workshop on “Modern Slavery and Climate Change: the Commitment of the Cities” Vatican City, July 2015

Parolin:
Creo que sería bueno tratar sobre trata de personas y esclavitud moderna.
La trata de órganos puede tratarse en conexión con la trata de personas.
Muchas gracias
Francisco

From the Declaration signed by Pope Francis and the Mayors

Vatican City, 21 JULY 2015

…As mayors we commit ourselves to building, in our cities and urban settlements, the resilience of the poor and those in vulnerable situations and reducing their exposure to … economic, social and environmental shocks and disasters, which foster human trafficking and dangerous forced migration.

At the same time, we commit ourselves to ending abuse, exploitation, trafficking and all forms of modern slavery, which are crimes against humanity, including forced labor and prostitution, **organ trafficking**, and domestic servitude...

Black markets have to be taken seriously

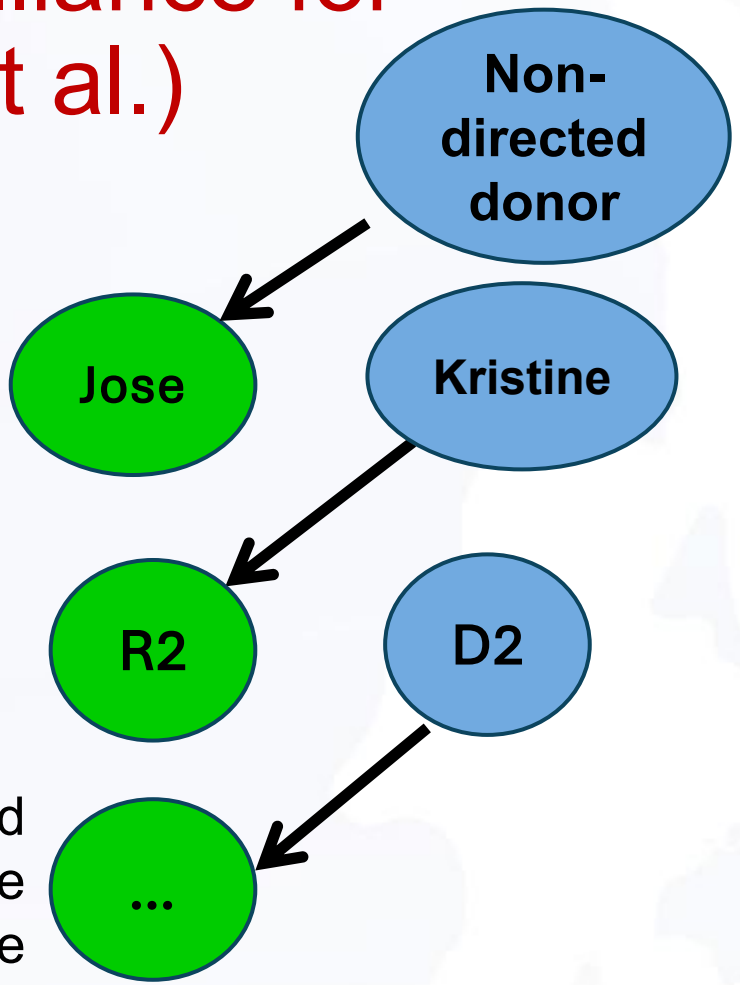
- That's why the first GKE pair was started in the **Philippines** with a **husband and wife**. The second GKE pair from **Mexico** were **first-grade cousins** cared for by a world-renowned nephrologist.

- We think the right course of action is to proceed carefully, slowly at first, and with constant monitoring.

Global Kidney Exchange
Results to Date

- All of the non-US patients **were matched in less than one year** of waiting in the APD United States-based system, and **the high PRA patients had been waiting more than 5 years**
- International **recipients have 100% 5-year patient/graft survival**
- **All international donors are alive with normal creatinine and blood pressure**.

Global kidney exchange, with a pair from the Philippines—January 2015, Alliance for Paired Donation (Rees et al.)



Jose Mamaril received a kidney from a non-directed American donor in Georgia. His wife**, Kristine**, donated one of her kidneys to an American recipient in Minnesota, whose donor continued the chain by donating to a patient in Seattle. *THE BLADE/JETTA FRASER*

GKE in Mexico: A Bridge of Life

"Just as US President Donald Trump is seeking to build a wall of thousands of miles on the border with Mexico, a tireless surgeon and a renowned economist join forces to exchange organs between citizens of both countries."

Why is GKE Special?

Kidney exchange exists in rich countries with lots of highly sensitized patients, which allows us to help some poor patients at no cost.

Transplant International

INVITED COMMENTARY

Global kidney exchange should expand wisely

Alvin E. Roth[1], Ignazio R. Marino[2], Obi Ekwenna[3], Ty B. Dunn[4], Siegfredo R. Paloyo[5,6], Miguel Tan[7], Ricardo Correa-Rotter[8], Christian S. Kuhr[9], Christopher L. Marsh[10], Jorge Ortiz[3], Giuliano Testa[11], Puneet Sindhwani[3], Dorry L. Segev[12], Jeffrey Rogers[13], Jeffrey D. Punch[14], Rachel C. Forbes[15], Michael A. Zimmerman[16], Matthew J. Ellis[17], Aparna Rege[17], Laura Basagoitia[18], Kimberly D. Krawiec[19] & Michael A. Rees[3,20]

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11 Baylor University Medical Center, Dallas, TX, USA
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13 Wake Forest Baptist Medical Center, Winston-Salem, NC, USA
14 University of Michigan, Ann Arbor, MI, USA
15 Vanderbilt University Medical Center, Nashville, TN, USA
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Introduction

We read with great interest and appreciation the careful consideration and analysis by Ambagtsheer *et al.* of the most critical ethical objections to Global Kidney Exchange (GKE). Ambagtsheer *et al.* [1] conclude that implementation of GKE is a means to increase access to transplantation ethically and effectively [2]. These conclusions by their European Society of Transplantation (ESOT) committee on Ethical, Legal, and Psychological Aspects of Transplantation (ELPAT) represent a step forward toward a greater understanding and an open, honest debate about GKE. Taken together with the strong endorsement of GKE by Minerva *et al.* [3] in Lancet and the positive position statement of the American Society of Transplant Surgeons (ASTS) [4], Ambagtsheer *et al.* successfully dispel previously raised doubts [5–13] to which we have previously responded [2,14–17].

One previous argument against GKE that Ambagtsheer et al (and Minerva *et al.* [3]) reject is that the general populations of some involved countries are not in support of this construct [18,19]. We have recently published new data to refute this argument as well. In surveys in Germany, Spain, United States (U.S.), and Philippines asking whether GKE should be legal,

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Letter to the Editor

National Trends in Machine Perfusion and Living Donor Liver Transplantation: Complement or Competition?

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To the Editor:

The landscape of liver transplantation in the United States is shifting rapidly with the rise of machine perfusion (MP) technologies and normothermic regional perfusion (NRP). Following Food and Drug Administration approval in 2021,[1] MP—particularly normothermic MP—has seen growing adoption, enabling ex vivo graft assessment under physiologic conditions. Hypothermic MP, in contrast, supports graft metabolism at low temperatures and mitigates ischemia-reperfusion injury. Both modalities, along with NRP, have shown promise in improving outcomes in extended criteria donors, especially for donation after circulatory death (DCD) livers, reducing primary nonfunction, and ischemic cholangiopathy.[2-4] Distinctions between perfusion types—normothermic versus hypothermic, portable versus back-to-base, with or without NRP—have clinical and logistical implications.[5] As both extended criteria donor and living donor liver transplantation (LDLT) are often targeted to low Model for End-stage Liver Disease (MELD) recipients,[6] we analyzed their use across centers to assess potential overlap or shifts in practice. Using Organ Procurement and Transplantation Network data from January 2016 to December 2024, we identified US transplant centers performing both LDLT and deceased donor liver transplants (donation after brain death and DCD) with documented MP use. Yearly trends were analyzed using simple linear regression. This study was Institutional Review Board-approved (HP-00114199).

Among 59 centers, 53 617 transplants were performed. MP usage rose from 0.4% to 28.8%, with DCD use increasing from 5.8% to 31.8% (Figure 1A). Most MP cases (90.7%) employed normothermic protocols. LDLT rates remained relatively stable: 5.8% in 2016 versus 6.3% in 2024. Median waitlist time dropped from 106 to 34 d (Figure 1B), consistent with recent data showing that waitlist removals are now outpacing additions.[7] Median lab-MELD scores were stable: 15 for LDLT, 19 for DCD, 20 for MP, and 25 for donation after brain death. Four centers showed declining LDLT volumes ($P < 0.05$), while 3 of those showed a concurrent rise in MP cases ($P < 0.03$). Confounding variables—such as COVID-19, changing exception-points criteria (hepatocellular carcinoma, cholangiocarcinoma, colorectal liver metastases), improved acute on chronic liver failure care, and expanded hepatitis C virus treatment—also influenced transplant activity during this period.

Like LDLT, MP may enhance access to deceased donor grafts for low MELD patients.[1,6] The 2 strategies appear complementary. LDLT remains vital, especially in pediatric and oncology settings, as seen in countries where MP has been standard of care for a longer period,[8] and requires continued institutional and policy support. Equity concerns persist as MP is costly and logistically complex, favoring well-resourced centers. Similarly, sustaining LDLT programs demands long-term investment and surgical expertise. A balanced policy approach is needed to maintain access to both modalities and ensure system-wide equity. Finally, the growing use of NRP in US DCD transplants—sometimes followed by MP—adds further complexity and potential benefit. Sequential perfusion strategies may improve DCD outcomes, but their impact on LDLT volume remains to be clarified.[9]

In conclusion, MP is transforming access to marginal deceased donor livers in the United States, yet its effect on LDLT varies by center and context. While our findings do not support a broad displacement of LDLT by MP, isolated center-level shifts suggest a nuanced relationship. In this context, MP and LDLT appear more complementary than competitive. However, this letter format lacks the granularity necessary to establish causality. Future work should include multivariate analysis and center-level granularity to guide policies that support innovation without compromising equity.

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This study used data from the Scientific Registry of Transplant Recipients (SRTR), which are available upon request through the SRTR data access process. No new data were generated by the authors.

Visual abstract is available online at doi.org/10.1097/TP.0000000000005509.

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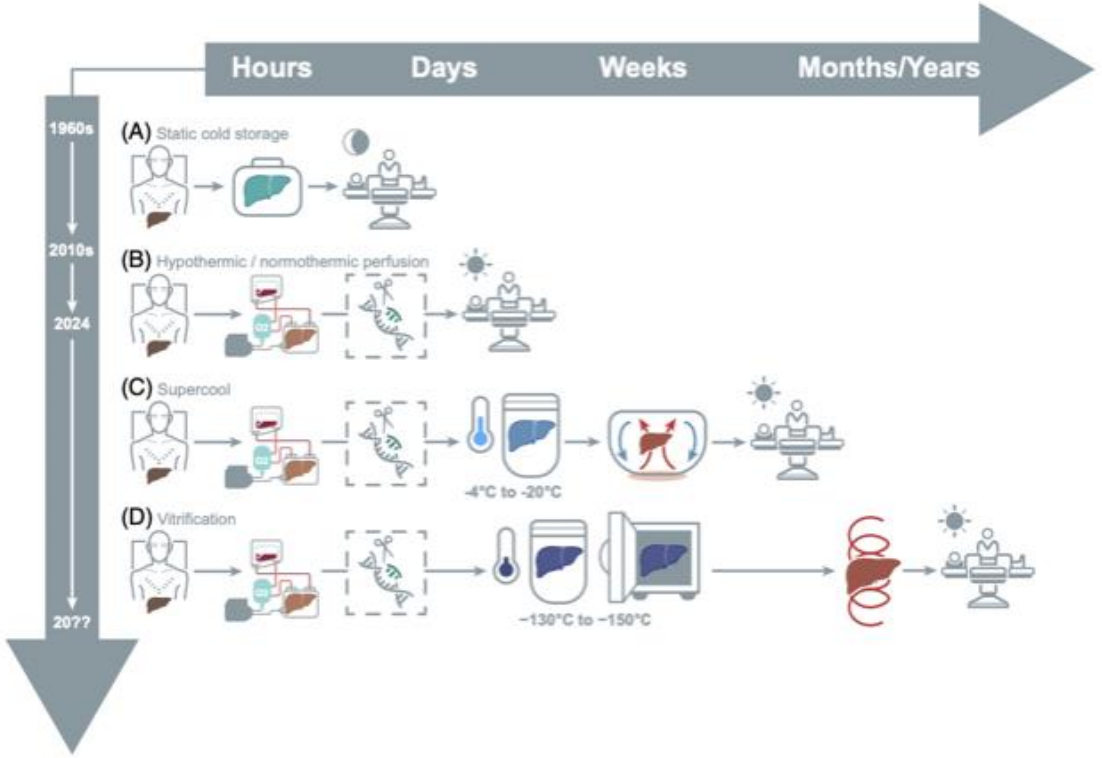
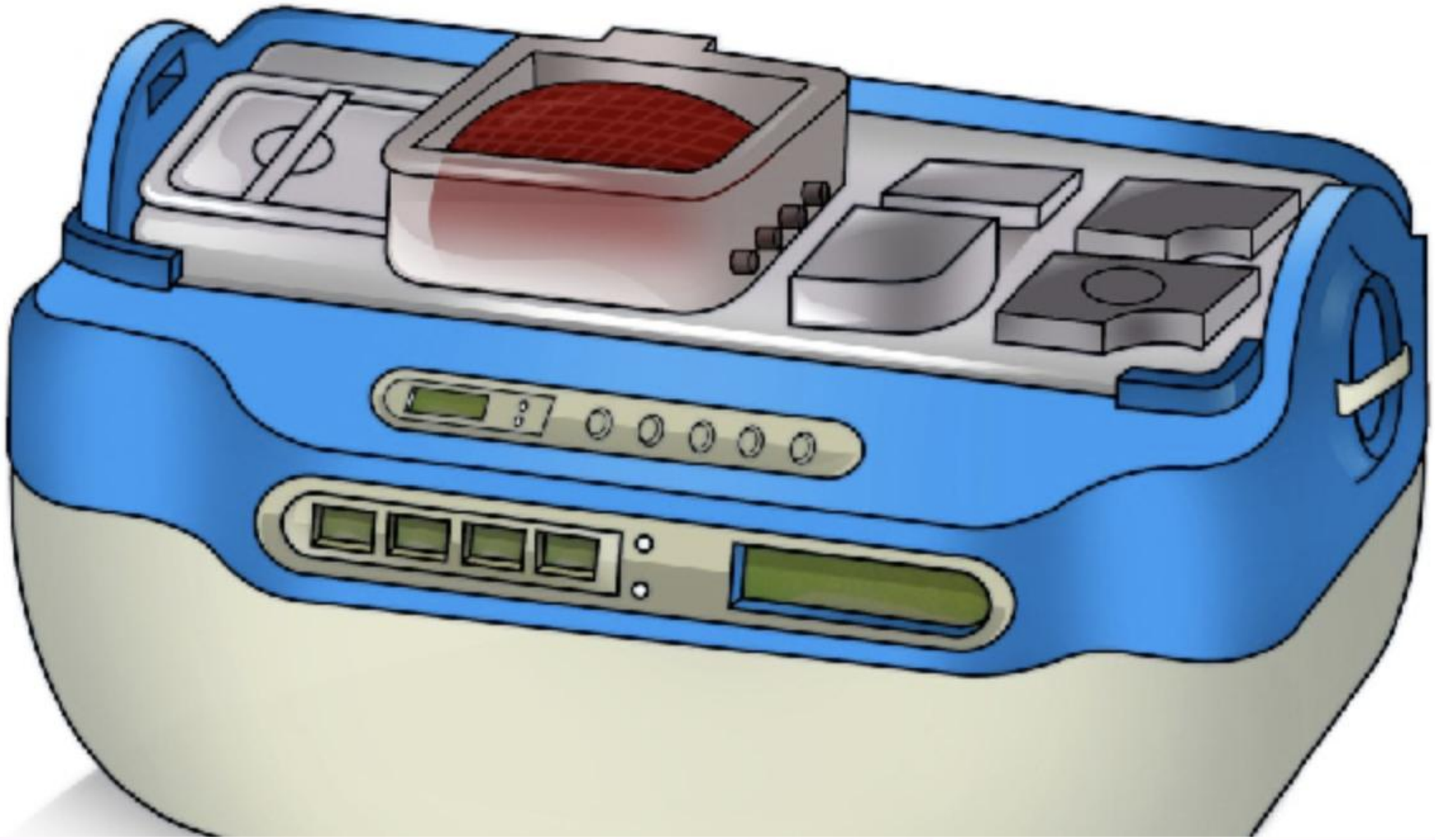


FIGURE 4 From liver preservation (±intervention) to liver banking. (A) Static cold storage. Starting from the earliest days of liver transplantation in the 1960s, deceased donor livers have been preserved with static cold storage, severely limiting preservation time often necessitating transplantation in the middle of the night. (B) Hypothermic/normothermic perfusion. The emergence of hypothermic and normothermic perfusion modalities has extended preservation times, facilitating daytime transplantation. The physiological conditions of normothermic perfusion are spurring intense explorations of novel interventions to alter and/or improve the allograft. (C, D) Supercooling and vitrification. Cryopreservation through either supercooling or vitrification achieves a dramatic reduction of cellular metabolism and energy demands that may translate into similarly dramatic increases in preservation times, perhaps even extending to years. Liver preservation may transform into liver banking which would open up a completely new landscape for transplantation through the accommodation of optimal donor-recipient matching, recipient preparation, and peritransplant logistics.



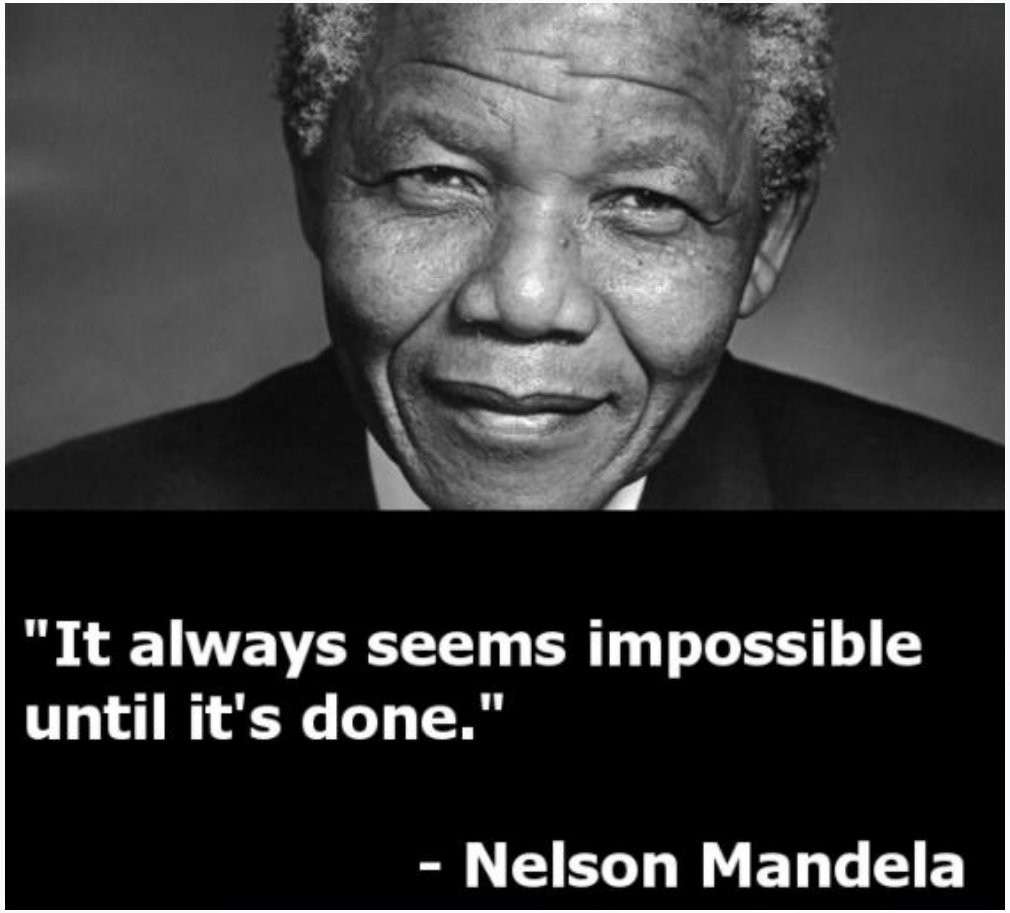
Global Kidney Exchange
Results to Date

- In the United States, shipping kidneys is legally or logistically not possible across national borders, **requiring 12 non-US donors to travel to the US and two US donors to travel outside the US**.

- For **UAE and Israel, transnational shipping of living donor kidneys was allowed**.

BELIEVE IN THE POWER OF HYPOTHESIS TO CHANGE THE WORLD

The courage to fail. Be persistent even in the sorrow of failure, until you succeed in proving the hypothesis was right



DONATE LIFE
EGYPT 2025

Thank You

Cairo Charter: One Vision,
One Hope, One Heart