INTRODUCTION

If I Only Had a ...

"I could stay young and chipper and I'd lock it with a zipper, if I only had a heart," sang the Tin Man to his companions in the 1939 movie *The Wizard of Oz*. There is hope yet for the Tin Man and for the many thousands of patients with diseased hearts, damaged livers, or injured tissues. Spurred on by a severe shortage of donor organs for transplantation, bioengineers, cell biologists, and clinicians are combining their talents to design off-the-shelf replacement parts for the human body. This dream is not new, as our historical timeline on the next two pages reveals.

A daring goal that has captured the public imagination is the implantation of a totally artificial heart into patients with end-stage heart failure (p. 1000), a remarkable achievement despite recent setbacks. Of simpler design, ventricular assist devices, which support the left ventricle until the heart repairs itself, may benefit the majority of patients with heart disease (p. 998). Similarly, a bioartificial liver device, composed of liver cells nurtured in a bioreactor, is undergoing clinical testing as a bridge to support the failing liver until it can regenerate (p. 1005). Meanwhile, despite numerous regulatory hurdles (p. 1003), researchers are developing artificial blood substitutes (p. 1002) for use instead of donor blood during lengthy surgeries or at disaster sites.

From tendons (p. 1011) to bladders, bioengineers are manufacturing "ready-to-wear" designer tissues in the laboratory (p. 1009). They are coaxing cells to assemble into three-dimensional structures on biodegradable scaffolds that can be implanted in patients at sites of tissue injury. Challenges to be addressed before engineered tissues enter the clinic include identifying sources of suitable cells, developing new scaffolding biomaterials (p. 1014), and scaling up production, not to mention discovering ways to preserve the tissue product (p. 1015) and to prevent immune rejection. Animal models of spinal cord injury are being used to test different bioengineering and molecular strategies for their ability to induce the injured spinal cord to regenerate (p. 1029).

Sophisticated microelectronics for signal processing are bringing the dream of merging man and machine closer to reality. A brain-computer interface that enables patients to control artificial limbs through brain neural pathways is under development (p. 1018). The success of cochlear implants, which enable some profoundly deaf patients to hear (p. 1025), has accelerated engineering of the next generation of electrode implants for brainstem auditory centers. Researchers facing the enormous challenge of trying to restore vision to the blind are developing electrode arrays that activate the retina, optic nerve, or even the visual cortex itself (pp. 1022 and 1026).

Designing bionic devices that enhance human capabilities (cybernetics) is raising a host of ethical questions (p. 1020), as is the transplant of xenogeneic tissues from other species into human patients (p. 1008). Even older than the science of replacing body parts is the art of staying young, and antidotes to aging are becoming big business as millions of baby boomers hit their 50s (p. 1032).

The next 38 pages reveal how far we have come in our dream of engineering designer parts for the human body to replace those lost through injury or disease. However, this special section also highlights the many hurdles yet to be overcome before these fascinating technologies enter routine clinical use.

—MARC LAVINE, LESLIE ROBERTS, ORLA SMITH

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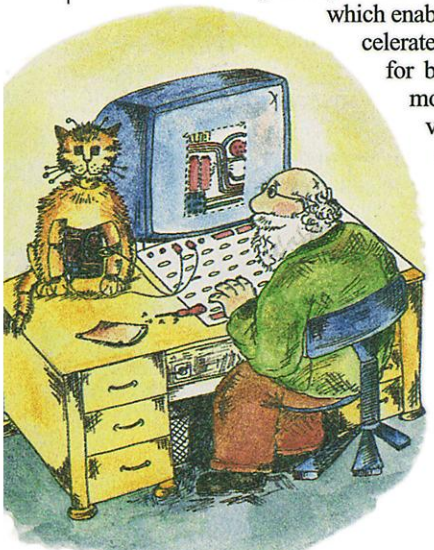
See also Science's STKE, page 923.



Seeking to serve all of *Science*'s readership, we recommend *Boing-Boing the Bionic Cat* to those of our very young readers who are contemplating a future career in bioengineering.

CREDITS: (TOP TO BOTTOM) UNDERWOOD & UNDERWOOD/CORBIS; RUTH DENISE LEAR

Science

Historical Highlights

in Bionics and Related Medicine

Bionics has had a rich and fascinating history. In the development of arm and leg prostheses, progress has come as a slow and gradual process. In other fields, such as organ transplantation, there have been decades between the first attempts at a new procedure and the routine achievement of success. This punctuated progress has frequently been contingent on accumulating new insights from other disciplines, such as the role of the immune system in tissue rejection, or on serendipitous discovery, as was the case for several anti-rejection drugs. Rather than attempting to be comprehensive, we have portrayed in this timeline, highlights from different areas of medical research. Similarly the images, although not always connected to specific dates or events, are intended to portray both interesting artifacts from the past, and today's high-tech advances, which provocatively hint at developments yet to come.

1504 Iron prosthetic hand with flexible finger joints.

1597 Reconstruction of the nose by tissue grafting.

1628 Early theory on the circulatory system developed.

1666 Blood transfusion between two dogs.

1667 Blood transfusion between sheep and human.

1682 Repair of human skull with dog skull bone.

1807 Development of an endoscope for minimally invasive surgery.

1822 First successful fresh skin autograft.

1842–1847 Anesthetic properties of a number of compounds first discovered and demonstrated.

1847 Introduction of silver amalgam for dental fillings.

1858 Publication of the first edition of *Gray's Anatomy*.

1863 Introduction of antiseptic surgical techniques.

1881 First temporary skin graft.

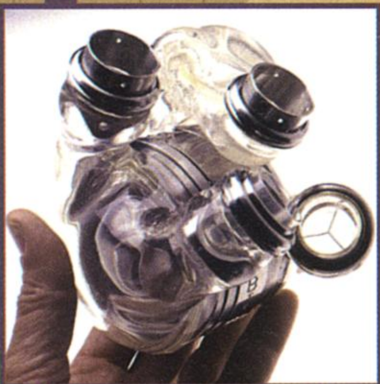
1883 Development of Ringer's solution for keeping tissues alive outside the body.

1888 First reports on use of contact lenses to correct vision.

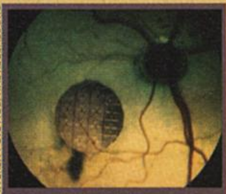
1901 Identification of different blood groups.

1905 & 1906 First reports of corneal transplants.

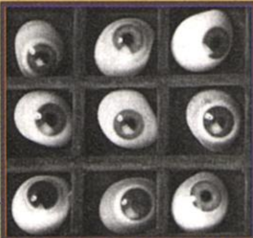
1905 Discovery of technique for growing tissue cells in vitro.


ABIOMED, INC.

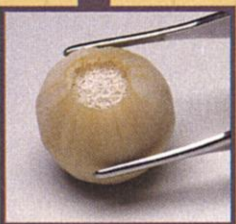
AbioCor self-contained, replacement heart


DR. H. SACHS, UNIVERSITY EYE HOSPITAL REGENSBURG

Subretinal chip in a cat eye


JON VAN ALLEN, UIHC MEDICAL MUSEUM

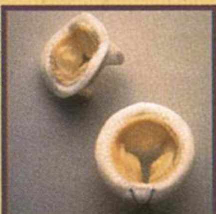
Glass eye prostheses c. 1900


BIOVASCULAR, INC.

Ocu-Guard orbital implant wrap


LIFECELL CORPORATION

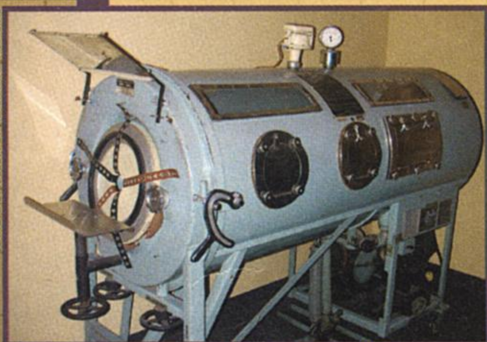
AlloDerm® processed human dermis


MEDTRONIC, INC.

Bioprosthetic Mosaic aortic valve


MEDTRONIC INC.

Mechanical Medtronic Hall aortic valve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Emerson respirator (iron lung), c. 1950


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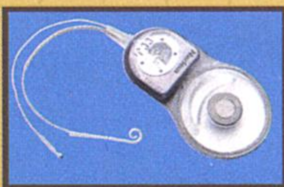
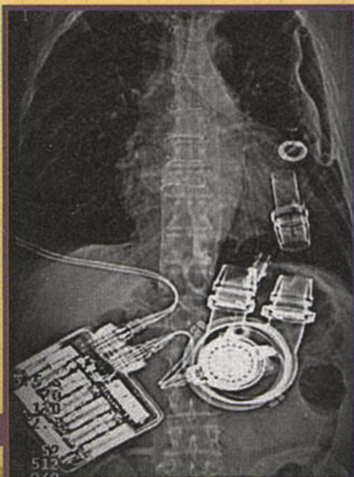
Debakey left ventricular assist device, c. 1966


COCHLEAR LTD.

Nucleus 24 Contour cochlear electrode array


ARROW INTERNATIONAL

LionHeart left ventricular assist device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Prosthetic arm, c. 1920's


JARVIK HEART INC.

Jarvik-7 heart, 1986


OTTOBOCK ORTHOPEDIC INDUSTRY, INC.

Responsive prosthetic SensorHand

1905 Successful direct blood transfusion between humans.

1905 Early attempt at an artificial hip replacement.

1908 Early attempt at knee replacement surgery (using a cadaver for the replacement part).

1911 Paraffin injection to treat vocal fold paralysis.

1914 Citrate identified as a blood anti-coagulant, allowing for blood storage.

1928 Iron lung developed for treatment of polio victims.

1939 Hard (plastic) contact lenses introduced.

1943 Kidney dialysis machine developed.

1949 Role of immune system in tissue rejection identified.

1951 First artificial heart valve implanted.

1953 Development of the heart-lung machine.

1953 Demonstration of acquired immune tolerance to foreign grafts.

1954 Kidney transplant between identical twins.

1956 First successful bone marrow transplant.

1957 First cochlear implant developed.

1958 Early attempts at developing an implantable pacemaker.

1958 Identification of the importance of the histocompatibility system for tissue matching.

1963 First liver transplant.

1966 First successful pancreas transplant.

1967 First successful heart transplant. Patient survived 18 days.

1969 First biocompatible ceramic that could bond to collagen and bone developed.

1969 Total artificial heart implanted in a human as a temporary measure.

1972 Testing of modern design steel/polymer hip joint.

1973 Successful unrelated bone marrow transplant.

1978 The immunosuppressant cyclosporine is introduced.

1979 First auditory brainstem implant.

1980 First successful single-channel cochlear implant in a child.

1981 A peripheral nerve bridge is implanted into the injured spinal cord of an adult rat.

1982 Genetically engineered insulin becomes commercially available (the first genetically engineered drug).

1982 Implantation of the Jarvik-7, a permanent total artificial heart.

1983 First successful single lung transplant.

1984 Baby Fae receives heart from baboon and survives 20 days.

1986 First successful double lung transplant.

1987 First clinical use of a bioartificial liver device.

1990 FK506 immunosuppressant becomes available.

1990 First living donor lung transplant.

1993 FDA approval of left ventricular assist device as a bridge to heart transplantation.

1995 Jeff Getty receives a baboon bone marrow transplant.

1997 Transplant of pig neurons in patients with Parkinson's disease.

1998 Human hand transplant.

1998 Total larynx transplant.

2000 Implantation of a prototype artificial pancreas.

2001 Implantation of the AbioCor, a permanent self contained total heart replacement.

A. ATALA, HARVARD

An engineered human bladder

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Artificial leg, c. 1937

NATIONAL MUSEUM OF HEALTH AND MEDICINE

Biomet hip implant, late 20th century

OTTOBOCK ORTHOPEDIC INDUSTRY, INC.

C-Leg System, leg prosthesis

NATIONAL MUSEUM OF HEALTH AND MEDICINE

Porcelain denture, c. 1850

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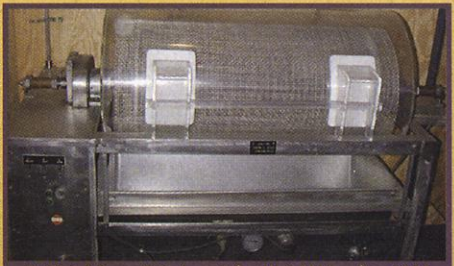

Kolff-Brigham dialysis unit (artificial kidney), c. 1950

NICK ROMANENKO, RUTGERS PHOTO SERVICES

Tendon-controlled artificial hand

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Howmedica Spherocentric knee implant c. 1970's

OTTOBOCK ORTHOPEDIC INDUSTRY, INC.

Mechanical knee joint

NATIONAL MUSEUM OF HEALTH AND MEDICINE

Silver dentures with ivory teeth, c.1800

Main sources:

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W. B. Murphy, *Spare Parts: From Peg Legs to Gene Splices* (Twenty-First Century Books, Brookfield, CT, 2001).

International Encyclopedia of Science and Technology (Oxford University Press, Oxford, UK, 1999).

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