BIOMATERIALS, PROSTHETICS, AND BIOMEDICAL DEVICES

1. Introduction

Prosthetics or biomedical devices are objects which serve as body replacement parts for humans and other animals or as tools for implantation of such parts. An implanted prosthetic or biomedical device is fabricated from a biomaterial and surgically inserted into the living body by a physician or other health care provider. Such implants are intended to function in the body for some period of time in order to perform a specific task. Medical devices may replace a damaged part of anatomy, eg, total joint replacement; simulate a missing part, eg, mammary prosthesis; correct a deformity, eg, spinal plates; aid in tissue healing, eg, burn dressings; rectify the mode of operation of a diseased organ, eg, cardiac pacemakers; or aid in diagnosis, eg, insulin electrodes.

Prosthetics and biomedical devices are composed of biocompatible materials, or biomaterials. In the early 1930s the only biomaterials were wood, glass, and metals. These were used mostly in surgical instruments, paracorporeal devices, and disposable products. The advent of synthetic polymers and biocompatible metals in the latter part of the twentieth century has changed the entire character of health care delivery. Polymers, metals, and ceramics originally designed for commercial applications have been adapted for prostheses, opening the way for implantable pacemakers, vascular grafts, diagnostic/therapeutic catheters, and a variety of other orthopedic devices. The term prosthesis encompases both external and internal devices. This article concentrates on implantable prostheses.

2. Biomaterials

A biomaterial is defined as a systemic, pharmacologically inert substance designed for implantation or incorporation within the human body (1). A biomaterial must be mechanically adaptable for its designated function and have the required shear, stress, strain, Young's modulus, compliance, tensile strength, and temperature-related properties for the application. Moreover, biomaterials ideally should be nontoxic, ie, neither teratogenic, carcinogenic, or mutagenic;

nonimmunogenic; biocompatible; biodurable, unless designed as bioresorbable; sterilizable; readily available; and possess characteristics allowing easy fabrication. The traditional areas for biomaterials are plastic and reconstructive surgery, dentistry, and bone and tissue repair. A widening variety of materials are being used in these areas. Artificial organs play an important role in preventive medicine, especially in the early prevention of organ failure.

To be biocompatible is to interact with all tissues and organs of the body in a nontoxic manner, not destroying the cellular constituents of the body fluids with which the material interfaces. In some applications, interaction of an implant with the body is both desirable and necessary, as, for example, when a fibrous capsule forms and prevents implant movement (2).

Polymers, metals, ceramics, and glasses may be utilized as biomaterials. Polymers, an important class of biomaterials, vary greatly in structure and properties. The fundamental structure may be one of a carbon chain, eg, in polyethylene or Teflon, or one having ester, ether, sulfide, or amide bond linkages. Polysilicones, having a –Si–O–Si– backbone, may contain no carbon.

Plastics are found in implants and components for reconstructive surgery, as components in medical instruments, equipment, packaging materials, and in a wide array of medical disposables. Plastics have assumed many of the roles once restricted to metals and ceramics.

Metals are used when mechanical strength or electrical conductivity is required of a device. For example, as of 1995 the femoral component of a hip replacement device was metal, as were the conductors of cardiac pacemaker leads. Titanium and titanium alloys (qv) are well tolerated in the body. This is partly the result of the strongly adhering oxide layer that forms over the metal surface, making the interface between the body and biomaterial effectively a ceramic rather than a metal. Titanium finds wide use as the femoral component of the artificial hip, where it exhibits great strength, comparatively light weight (the density of titanium is 4.5 g/cm^3), and excellent fatigue resistance. Another area in which titanium has replaced all other metals and alloys is as the casing material for cardiac pacemakers, neural stimulators, and implantable defibrillators.

Stainless steel alloys are also useful in orthopedic applications (see STEEL). Stainless steel alloys are used in the manufacture of staples, screws, pins, etc. These alloys are used primarily in applications requiring great tensile strength. Elgiloy, an interesting cobalt-based alloy, was originally developed for the mainspring of mechanical watches. This is used essentially as the conductor of neural stimulator leads, which require excellent flexibility and fatigue resistance. Nitinol, an unusual alloy of nickel and titanium, exhibits shape memory. Its main application has been in dentistry (see DENTAL MATERIALS), where its resilience rather than its shape-memory characteristic is of value.

Ceramics (qv) include a large number of inorganic nonmetallic solids that feature high compressive strength and relative chemical inertness. Low temperature isotropic (LTI) carbon has excellent thromboresistance and has found use in heart valves and percutaneous connectors. LTI carbon, known as LTI, was originally developed for encapsulating nuclear reactor fuel. This material was adapted for biomedical applications in the 1970s. LTI is formed by pyrolysis of hydrocarbons at temperatures between 1000 and 2400°C. Aluminum oxide

[1344-28-1], Al_2O_3, forms the basis of dental implants (see DENTAL MATERIALS). In the polycrystalline form this ceramic is suitable for load-bearing hip prostheses.

Bioglasses are surface-active ceramics that can induce a direct chemical bond between an implant and the surrounding tissue. One example is 45S5 bioglass, which consists of 45% SiO_2, 6% P_2O_5, 24.5% CaO, and 24.5% Na_2O. The various calcium phosphates have excellent compatibility with bone and are remodeled by the body when used for filling osseous defects.

3. Medical Devices

Medical devices are officially classified into one of three classes. Class I devices are general controls that are primarily intended as devices that pose no potential risk to health, and thus can be adequately regulated without imposing standards or the need for premarket review. Manufacturers of these devices must register with the United States Food and Drug Administration (FDA), provide a listing of products, maintain adequate reports, and comply with good manufacturing practices. Examples are stethoscopes, periodontic syringes, nebulizers, vaginal insufflators, etc.

Class II devices have performance standards and are applicable when general controls are not adequate to assure the safety and effectiveness of a device, based on the potential risk to health posed by the device. To classify a device in the Class II category, the FDA must find that enough data are available on which to base adequate performance standards that would control the safety and effectiveness of the device. Examples are diagnostic catheters, electrocardiographs, wound dressings, percutaneous catheters, gastrointestinal irrigation systems, etc.

Class III devices require premarket approval. When a device is critical, ie, life-supporting and/or life-sustaining, unless adequate justification is given for classifying it in another category, it is a Class III device. Class III also contains devices after 1976 that are not sufficiently similar to pre-1976 devices, and devices that were regulated as new drugs before 1976. Examples are bronchial tubes, ventilators, vascular grafts, pacemakers, cardiopulmonary bypass, surgical meshes, etc.

4. Cardiovascular Devices

Treatment of cardiovascular diseases is a vast and growing industry (see CARDIOVASCULAR AGENTS). Cardiovascular disease is a progressive condition which can eventually block the flow of blood through the coronary arteries to the heart muscle, thereby causing heart attacks and other life-threatening situations. The same plaque deposits occur in the peripheral arteries, leading to gangrene, amputations, aneurysms, and strokes. Despite enormous progress in cardiovascular medicine since World War II, challenges and unmet needs abound. Mortality rates have declined significantly, millions of people have been helped to lead normal lives, but the prevalence and incidence of cardiovascular diseases remain high. Open-heart surgery, cardiac pacing, heart transplants, implantable valves,

and coronary angioplasty and clot busters, have been developed, but none of the great advances in cardiovascular medicine is preventive. There has been no "Salk vaccine" to preclude the buildup of fatty deposits or plaque in the arteries.

4.1. Cardiovascular Problems. Despite its durability and resilience, different aspects of the cardiovascular system can malfunction. Some problems are congenital; many are inherited. Diseases can also be caused by infection such as damaged heart valves owing to rheumatic fever. Cardiomyopathy, a diseased heart muscle which may become enlarged, can result from infection or an unknown cause. Other problems may be a function of age. Pacemaker patients often have conduction systems that have simply started to wear out. Lifestyle also plays a role. Although poor diet and smoking cause or contribute to multiple problems such as hypertension and lung disease, when it comes to cardiovascular problems, the main culprit, regardless of its origin, is atherosclerosis. Atherosclerosis is a disease of the arteries resulting from the deposit of fatty plaque on the inner walls.

Plaque. A heart attack, or myocardial infarction, results from insufficient delivery of oxygen to parts of the heart muscle owing to restricted blood flow in the coronary arteries. If heart muscle tissue is deprived of oxygen long enough, it may infarct or die (Fig. 1). The heart attack is often precipitated by a clot, or thrombus, which forms on a severely narrowed portion of a coronary artery. Silent ischemia is somewhat reduced blood supply from narrowing of the arteries. As the name implies, the disease provides no symptomatic warning of an impending problem. When coronary arteries are blocked to the degree that they cannot meet the heart's temporary demand for more oxygenated blood, angina pectoris, or sharp pain, may result. Further progression of the blockage then brings on the myocardial infarction. Atheroma is the medical term used to describe what plaque, the fatty deposits, does to the walls of the arteries. Plaque

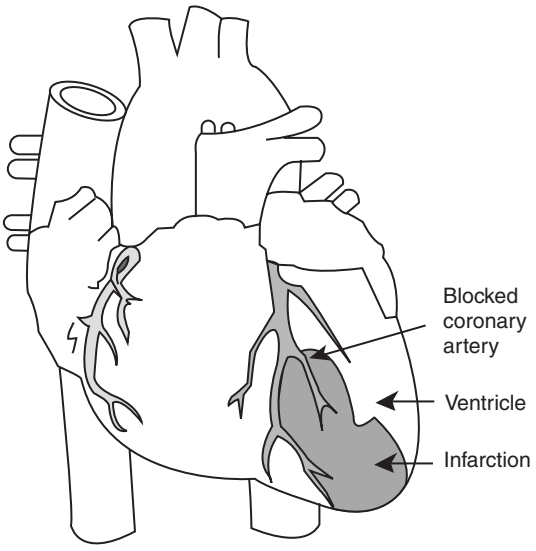


Fig. 1. Myocardial infarction occurs during insufficient delivery of oxygen to a portion of the heart muscle.

also causes other problems such as strokes and aneurysms, as well as complications of peripheral vascular disease.

Lethal Arrhythmias. Arrhythmias are a second significant source of cardiovascular problems. An arrhythmia is an abnormal or irregular heart rhythm. Bradyarrhythmias result in heart rates that are too slow; tachyarrhythmias cause abnormally fast rates. A bradyarrhythmia can be debilitating, causing a person to be short of breath, unable to climb stairs, black out, or even to go into cardiac arrest. Tachyarrhythmias can be unsettling and painful at best, life-threatening at worst.

Arrhythmias are caused by disturbances of the normal electrical conduction patterns synchronizing and controlling heartbeats. The wiring leading to the ventricles might, in effect, break or become frayed, causing a slowdown in the signals getting through, or perhaps result in intermittent electrical impulses. If damage to heart muscle tissue occurs, for example, from a myocardial infarction, this could create new electrical pathways. These in turn set up a separate focus of electrical activity (like another natural pacemaker) generating extra beats which can be highly disruptive. If a tachyrhythmia (tachycardia) occurs in the ventricles, the pumping chambers of the heart, the problem can be severely uncomfortable or even cause death if it deteriorates into ventricular fibrillation. Fibrillation is uncontrolled electrical activity. In this chaotic situation, cells become uncoordinated so that the heart muscle only quivers or twitches and no longer contracts rhythmically. Approximately three-fourths of the more than 500,000 deaths per year in the United States from coronary heart disease are sudden deaths.

There is a close correlation between myocardial infarctions and tachyarrhythmias, illustrated by the presence of complex ventricular arrhythmias among heart attack victims which are estimated to affect one-third of the survivors each year. Frequently, the immediate cause of sudden death is ventricular fibrillation, an extreme arrhythmia that is difficult to detect or treat. In the majority of cases, victims have no prior indication of coronary heart disease.

Valvular Disease. Valve problems severely limit the efficiency of the heart's pumping action bringing forth definitive symptoms. There are two types of conditions, both of which may be present in the same valve. The first is narrowing, or stenosis, of the valve. The second condition is inability of the valve to close completely. Narrowing of the mitral valve, for example, can result in less blood flowing into the left ventricle and subsequently less blood being pumped into the body. If the same valve does not close completely, blood may also back up or regurgitate into the left atrium when the ventricle contracts, preventing even more blood from properly flowing. The backward pressure which results can cause a reduction in the efficiency of the lungs.

Cardiomyopathy. Cardiomyopathy, or diseased heart muscle, may reach a point at which the heart can no longer function. It arises from a combination of factors, including hypertension, arrhythmias, and valve disease. Other problems, such as congestive heart failure, cause the interrelated heart–lung system to break down. Because the heart can no longer adequately pump, fluid builds up in the lungs and other areas.

4.2. Device Solutions. The first big step in cardiovascular devices was the development of a heart–lung machine in 1953. The ability to shut down the

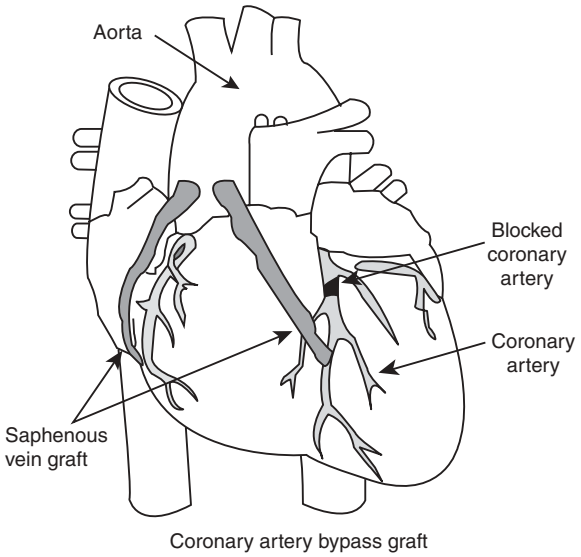


Fig. 2. In coronary bypass, an autologous saphenous vein is used to provide critical blood to the heart muscle, bypassing a blockage in the coronary artery.

operation of the heart and lungs and still maintain circulation of oxygenated blood throughout the body made open-heart surgery possible. Open heart, really a misnomer, actually refers to opening up the chest to expose the heart, not opening up the heart itself. The principal components of the heart–lung machine, the oxygenator and pump, take over the functions of the lungs and heart.

Atherosclerosis. The first solution to the problem of atherosclerosis was the coronary artery bypass graft (CABG) procedure, first performed in 1964. In a coronary bypass procedure, a graft is taken from the patient's own saphenous vein. The graft is attached to the aorta (Fig. 2) where the coronary arteries originate and the opposite end is connected to the artery below the blocked segment. Blood can then bypass the obstructed area and reach the surrounding tissue below. Extensions of this useful surgery are CABG procedures which utilize mammary arteries of the patient instead of saphenous veins.

The second step toward solving cardiovascular disease from atherosclerosis, ie, angioplasty, was preceded by the diagnostic tool of angiocardiography by nearly 20 years. Angiocardiography, or angiography, permits x-ray diagnosis using a fluoroscope. A radiopaque contrast medium is introduced into the arteries through a catheter (see RADIOPAQUES), and angiography allows accurate location of the plaque blockage. Percutaneous transluminal coronary angioplasty (PTCA), a nonsurgical procedure, emerged in the 1980s as a viable method for opening up blocked arteries. A PTCA catheter has a balloon at its tip which is inflated after it is positioned across the blocked segment of the artery. Plaque is then compressed against the arterial walls, permitting blood flow to be restored. The same solutions of bypass surgery and angioplasty have been applied to atherosclerosis in the peripheral arteries.

Arrhythmias. The first solution to cardiovascular problems arising from arrhythmias came about as a result of a complication caused by open-heart

surgery. During procedures to correct congenital defects in children's hearts, the electrical conduction system often became impaired, and until it healed, the heart could not contract sufficiently without outside electrical stimulation. A system that plugged into a wall outlet was considered adequate until an electrical storm knocked out power, leading to the development of the first battery-powered external pacemaker.

The first implantable pacemaker, introduced in 1960, provided a permanent solution to a chronic bradyarrhythmia condition. This invention had a profound impact on the future of medical devices. The pacemaker was the first implantable device which became intrinsic to the body, enabling the patient to lead a normal life.

Early pacemakers paced the heart continuously at a fixed rate, were larger than a hockey puck, and had to be replaced frequently owing to power source technology limitations. Advances in electronics, materials, and knowledge have yielded pacemakers about the size of a U.S. 50-cent piece that last five years or more. More importantly, pacemakers restore the heart to functioning in a completely natural way. The pacemaker senses the electrical activity of the heart and kicks in only when something is wrong. If the impulses initiated by the SA node cannot get all the way through to the lower part of the ventricles, the pacemaker takes over completing the electrical process at the same rate indicated by the heart's natural pacemaker. If the SA node is dysfunctional and cannot put out an appropriate signal, sensors (qv) in rate-responsive pacemakers can correlate other data such as sound waves from body activity, body temperature, or the respiratory rate to compute the proper heart rate.

The first automatic implantable cardioverter defibrillator (AICD) was implanted in 1980. As for pacemakers, early generations of AICDs were bulky and cumbersome, did not last very long, and required open-heart surgery. However, these kept people alive by automatically shocking the heart out of its chaotic electric state whenever it went into ventricular fibrillation. Future devices are being designed to provide the full spectrum of arrhythmia control, including pacing, cardioversion, and defibrillation. Techniques are also being developed to map, ie, locate, the source of certain tachyarrhythmias (an ectopic focus or scar tissue) and remove it without open-heart surgery.

External defibrillation was first performed in 1952 and continues as a routine procedure in hospitals and ambulances. The problem of external defibrillation has not been a technological one, but rather a legal one. Only in the 1990s have laws been passed to permit people other than doctors and paramedics to operate semiautomatic defibrillators to provide help when it is needed. New and better defibrillation devices continue to come to market and are easier and safer to use.

Valve Problems. The primary solution to valve problems has been implantable replacement valves. The introduction of these devices necessitates open-heart surgery. There are two types of valves available: tissue (porcine and bovine) and mechanical. The disadvantage of tissue valves is that these have a limited life of about seven years before they calcify, stiffen, and have to be replaced. The mechanical valves can last a lifetime, but require anticoagulant therapy. In some patients, anticoagulants may not be feasible or may be contraindicated. Of the valves which require replacement, 99% are mitral and aortic

valves. The valves on the left side of the heart are under much greater pressure because the left ventricle is pumping blood out to the entire body, instead of only to the lungs. Occasionally, two valves are replaced in the same procedure.

Cardiomyopathy. The best available solution to cardiomyopathy may be one that is less sophisticated than transplant surgery or the artificial heart. The cardiomyoplasty-assist system combines earlier electrical stimulation technology with a new surgical technique of utilizing muscle from another part of the body to assist the heart.

Efforts to develop an artificial heart have resulted in a number of advancements in the assist area. The centrifugal pump for open-heart surgery, the product of such an effort, has frequently been used to support patients after heart surgery (post-cardiotomy), or as a bridge to life prior to transplant. Other efforts have led to the development of ventricular assist devices to support the heart for several months and intra-aortic balloon pumps (IABPs) which are widely used to unload and stabilize the heart.

4.3. Interventional Procedures. The emergence of angioplasty created a specialty called interventional cardiology. Interventional cardiologists not only implant pacemakers and clear arteries using balloon catheters, but they also use balloons to stretch valves (valvuloplasty). In addition, they work with various approaches and technologies to attack plaque, including laser (qv) energy, mechanical cutters and shavers, stents to shore up arterial walls and deliver drugs, and ultrasound to break up plaque or to visualize the inside of the artery.

Typically, procedures have become less invasive as technology evolves. Early pacemaker procedures involved open-heart surgery to attach pacemaker leads (wires) to the outside of the heart. Later, leads could be inserted in veins and pushed through to the interior of the heart, no longer necessitating opening a patient's chest. Using fluoroscopy, the physician can visualize the process, so that the only surgery needed is to create a pocket under the skin for the implantable generator to which the leads are connected.

Clinical evaluation is underway to test transvenous electrodes. Transvenous leads permit pacemakers to be implanted under local anesthesia while the patient is awake, greatly reducing recovery time and risk. As of 1996, the generation of implantable defibrillators requires a thoracotomy, a surgical opening of the chest, in order to attach electrodes to the outside of the heart. Transvenous electrodes would allow cardiologists to perform pacemaker procedures without a hospital or the use of general anesthesia.

Coronary bypass surgery and angioplasty are vastly different procedures, but both procedures seek to revascularize and restore adequate blood flow to coronary arteries. Balloon angioplasty, which looks much like a pacemaker lead except that it has a tiny balloon at the end instead of an electrode, involves positioning a catheter inside a coronary artery under fluoroscopy. The balloon is inflated to compress the offending plaque. Angioplasty is far less invasive than bypass surgery and patients are awake during the procedure. For many patients, angioplasty may not be indicated or appropriate.

Interventional cardiology is but one specialty that has arisen in cardiovascular medicine. Another is interventional radiology for similar procedures in the peripheral arteries, in addition to conventional bypass graft surgery. Competition has been intense among surgeons, cardiologists, and radiologists. Because

coronary artery disease is progressive, many patients who are candidates for peripheral and/or coronary angioplasty may be future candidates for bypass surgery.

Cardiologists may be described in terms of three overlapping specialties: interventional, who perform most angioplasty; invasive, who implant about 70% of the pacemakers in the United States; and diagnostic. A subspecialty of diagnostic cardiology, electrophysiology, has grown in importance because it is critical to the treatment of tachrhythmia patients, especially those who are prone to ventricular fibrillation. The further development of implantable devices in this last area depends on close cooperation between companies and electrophysiologists.

Cardiovascular devices are being employed by a wider diversity of specialists and are thus finding applications in other medical areas. This has been particularly true for devices developed to support open-heart surgery. Oxygenators and centrifugal pumps, which take over the functions of the lungs and heart, are used in applications such as support of angioplasty and placing a trauma or heart attack victim on portable bypass in the emergency room. Some devices are finding utility by improving surgical techniques. For example, cardiac surgeons are working with balloon catheters and laser angioplasty systems as an augmentation to regular bypass surgery.

Other cardiovascular devices developed initially for use in open-heart surgery are used extensively in other parts of the hospital and, in many cases, outside the hospital. Patients have been maintained for prolonged periods of time on portable cardiopulmonary support systems while being transported to another hospital or waiting for a donor heart. Blood pumps and oxygenators may take over the functions of the heart and lungs in the catheterization lab during angioplasty, in extracorporeal membrane oxygenation (ECMO) to support a premature baby with severe respiratory problems, or in the emergency room to assist a heart attack victim. It is possible that future patients could be put on portable bypass at the site of the heart attack or accident. The market for cardiac assist devices and oxygenators plus related products such as specialized cannulae and blood monitoring devices is expected to expand rapidly into these areas.

4.4. Biomaterials for Cardiovascular Devices. Perhaps the most advanced field of biomaterials is that for cardiovascular devices. For several decades bodily parts have been replaced or repaired by direct substitution using natural tissue or selected synthetic materials. The development of implantable-grade synthetic polymers, such as silicones and polyurethanes, has made possible the development of advanced cardiac assist devices (see SILICON COMPOUNDS, SILICONES; URETHANE POLYMERS).

Implantable devices to pace, cardiovert, and defibrillate the heart without the need for open-heart surgery should become widely accepted. Dramatic developments and growth are also taking placein other areas such as the use of laser systems intended to ablate significant amounts of plaque. Laser ablation systems hold considerable promise if restenosis (reblocking of the arteries) rates are reduced. Mechanical or atherectomy devices to cut, shave, or pulverize plaque have been tested extensively in coronary arteries. Some of these have also been approved for peripheral use. The future of angioplasty, beyond the tremendous success of conventional balloon catheters, depends on approaches that can

reduce restenosis rates. For example, if application of a drug to the lesion site turns out to be the solution to restenosis, balloon catheters would be used for both dilating the vessel and delivering the drug. An understanding of what happens to the arterial walls, at the cellular level, when these walls are subjected to the various types of angioplasty may need to come first.

A primary aspect of cardiovascular devices through the twenty-first century is expected to involve the incorporation of diagnostic and visualization capabilities. A separate ultrasound system has been approved for this purpose. Laser angioplasty systems under development include visualization capabilities to distinguish plaque from the arterial wall. Future pacemakers, which already utilize sensors to determine an appropriate heart rate, are expected to incorporate various other sensors for diagnostic purposes. The biggest challenge in averting sudden death is not so much to perfect a life-sustaining device, but to gain the ability to identify the susceptible patient. Appropriate screening and diagnoses for patients having silent ischemia must be developed. If the presence and extent of coronary artery disease can be identified early, intervention could save thousands of people from an untimely death and help others to live a fuller life. Sensors and specific diagnostic devices are expected to play a large role at about the same time as effective implantable defibrillators.

One of the more intriguing cardiovascular developments is cardiomyoplasty where implantable technologies are blended with another part of the body to take over for a diseased heart. One company, Medtronic, in close collaboration with surgeons, has developed a cardiomyoplasty system to accompany a technique of wrapping back muscle around a diseased heart which can no longer adequately pump. A combination pacemaker and neurological device senses the electrical activity of the heart and correspondingly trains and stimulates the dorsal muscle to cause the defective heart to contract and pump blood. Cardiomyoplasty could greatly reduce the overwhelming need for heart transplants. It might also eliminate the need for immunosuppressive drugs. Development of appropriate materials and manufacturing methods are needed to maintain patency without damaging blood in grafts below 4 mm in diameter.

Pacemakers. The implantable cardiac pacemaker (Fig. 3) has been a phenomenal technological and marketing success. In the early 1980s, however, many critics were predicting the demise of these devices and the industry was the subject of congressional investigations over sales practices, alleged overuse, and excessive prices. Critics advocated low priced generic pacemakers, and pacemaker unit volume and prices declined about 10% on average. However, costs have been reduced by curtailing the length of time patients need to stay in the hospital following the implantation procedure and by selection of the correct pacemaker for each patient. Significantly lower cost is attached to a single-chamber device having limited longevity than to the far more expensive dual-chamber device which may be indicated for a young and active patient.

As of the mid-1990s, the market for bradyarrhythmia devices is fully penetrated in Western countries. Some growth is expected to result from an aging population but, by and large, the market is mature. The market for tachyrhythmia devices, in contrast, is only beginning.

Implantable tachyrhythmia devices, available for some years, address far less dangerous atrial tachyarrhythmias and fibrillation. The technical barriers

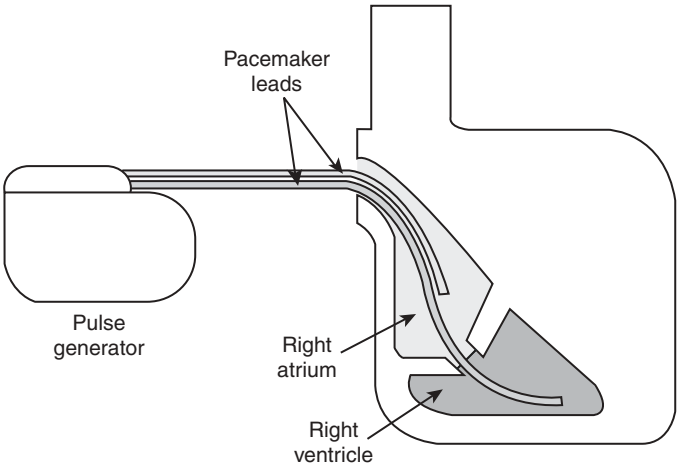


Fig. 3. A pacemaker provides electrical impulses to the heart in an effort to correct potentially fatal arrhythmias.

to counteracting ventricular tachyarrhythmias and fibrillation using massive shocks have been formidable and are compounded by the possibility of causing the very problem the shock is designed to overcome. Newer tachyrhythmia devices are being readied that can safely regulate arrhythmias across the full spectrum.

Surgical Devices. Surgical devices comprise the equipment and disposables to support surgery and to position implantable valves and a variety of vascular grafts. Central to open-heart surgery is the heart–lung machine and a supporting cast of disposable products. Two devices, the oxygenator and the centrifugal pump, amount to significant market segments in their own right. Other disposables include cardiotomy reservoirs, filters, tubing packs, and cardioplegia products to cool the heart. The oxygenator market has been driven more recently by the conversion from bubbler to membrane devices which account for about 80% of the oxygenators used in the United States.

Centrifugal pumps are increasingly being used as a safer and more effective alternative to the traditional roller pump in open-heart surgery and liver transplants. As of the mid-1990s, about 45% of open-heart procedures use a centrifugal pump. In the latter 1980s, that number was less than 10%. Implantable valves, particularly mechanical valves which continue to encroach on tissue valves, are unique. Methods such as valvuloplasty, mitral valve repair, or use of ultrasound are unlikely to reduce the number of valve replacements into the twenty-first century. Valve selection remains in the hands of the surgeon because of the critical nature of the procedure. If anything goes wrong, the result can be catastrophic to the patient.

Vascular grafts are tubular devices implanted throughout the body to replace blood vessels which have become obstructed by plaque, atherosclerosis, or otherwise weakened by an aneurysm. Grafts are used most often in peripheral bypass surgery to restore arterial blood flow in the legs. Grafts are also frequently employed in the upper part of the body to reconstruct damaged portions

of the aorta and carotid arteries. In addition, grafts are used to access the vascular system, such as in hemodialysis to avoid damage of vessels from repeated needle punctures. Most grafts are synthetic and made from materials such as Dacron or Teflon. Less than 5% of grafts utilized are made from biological materials.

Cardiac-Assist Devices. The principal cardiac-assist device, the intra-aortic balloon pump (IABP), is used primarily to support patients before or after open-heart surgery, or patients who go into cardiogenic shock. As of the mid-1990s, the IABP was being used more often to stabilize heart attack victims, especially in community hospitals which do not provide open-heart surgery. The procedure consists of a balloon catheter inserted into the aorta which expands and contracts to assist blood flow into the circulatory system and to reduce the heart's workload by about 20%. The disposable balloon is powered by an external pump console.

Other devices, which can completely take over the heart's pumping function, are the ventricular assist devices (VADs), supporting one or both ventricles. Some patients require this total support for a period of time following surgery (post-cardiotomy); others require the support while being transported from one hospital to another, or while waiting for a donor heart (bridge-to-transplant). Several external and implantable devices are being evaluated for short-term and long-term applications. Considerable interest has emerged in devices providing cardiopulmonary support (CPS), ie, taking over the functions of both the heart and lungs without having to open up the chest. There are several applications for other portable bypass systems or mini-heart–lung machines. Thus far, CPS has been used most frequently in support of anigoplasty prophylactically in difficult cases which could not be otherwise undertaken. The greatest potential is in the emergency room to rest the heart and lungs of heart attack and trauma victims.

Other specialized applications of cardiac arrest devices include extracorporeal membrane oxygenation (ECMO) which occurs when the lungs of a premature infant cannot function properly. The market segments for cardiopulmonary support devices are potentially significant.

Artificial Hearts. Congestive heart failure (CHF) is a common cause of disability and death. It is estimated that three to four million Americans suffer from this condition. Medical therapy in the form of inotropic agents, diuretics (qv), and vasofilators is commonly used to treat this disorder (see CARDIOVASCULAR AGENTS). Cardiac transplantation has become the treatment of choice for medically intractable CHF. Although the results of heart transplantation are impressive, the number of patients who might benefit far exceeds the number of potential donors. Long-term circulatory support systems may become an alternative to transplantation (3).

In 1980, the National Heart, Lung and Blood Institute of NIH established goals and criteria for developing heart devices and support techniques in an effort to improve the treatment of heart disease. This research culminated in the development of both temporary and permanent left ventricular-assist devices that are tether-free, reliable over two years, and electrically powered. The assist devices support the failing heart and systemic circulation to decrease cardiac work, increase blood flow to vital organs, and increase oxygen supply to the

myocardium. The newer ventricular assists are required to have no external venting, have a five-year operation with 90% reliability, pump blood at a rate of 3–7 L/min into the aorta at a mean arterial pressure of 90 mm Hg (12 kPa) when assisting the human left ventricle, and have a specific gravity of 1.0 for the implantable ventricular assist device.

In contrast, the total artificial heart (TAH) is designed to overtake the function of the diseased natural heart. While the patient is on heart–lung bypass, the natural ventricles are surgically removed. Polyurethane cuffs are then sutured to the remaining atria and to two other blood vessels that connect with the heart.

One successful total artificial heart is ABIOMED's electric TAH. This artificial heart consists of two seamless blood pumps which assume the roles of the natural heart's two ventricles. The pumps and valves are fabricated from a polyurethane, Angioflex. Small enough to fit the majority of the adult population, the heart's principal components are implanted in the cavity left by the removal of the diseased natural heart. A modest sized battery pack carried by the patient supplies power to the drive system. Miniaturized electronics control the artificial heart which runs as smoothly and quietly as the natural heart. Once implanted, the total artificial heart performs the critical function of pumping blood to the entire body (4).

Heart Valves. Since the early 1960s nearly 50 different heart valves have been developed. The most commonly used valves as of the mid-1990s include mechanical prostheses and tissue valves. Caged-ball, caged disk, and tilting-disk heart valves are the types most widely used.

Blood Salvage. In a growing awareness that a patient's own blood is the best to use when blood is needed, newer techniques are reducing the volume of donor blood used in many cardiovascular and orthopedic surgeries. Surgical centers have a device, called the Cell Saver (Haemonetics), that allows blood lost during surgery to be reused within a matter of minutes, instead of being discarded. This device collects blood from the wound, runs it through a filter that catches pieces of tissue and bone, then mixes the blood with a salt solution and an anticoagulant. The device then cleanses the blood of harmful bacteria. Subsequently the blood is reinfused back to the same patient through catheters inserted in a vein in the arm or neck, eliminating the worry of cross-contamination from the HIV or hepatitis viruses (see BLOOD, COAGULANTS AND ANTICOAGULANTS; FRACTIONATION, BLOOD).

Use of intraoperative autotransfusion (IAT) eliminates disease transmission, compatibility testing, and immunosuppression that may result from the use of homologous blood products, reduces net blood loss of the patient, and conserves the blood supply. During vascular surgery, the principal indications for the use of the Cell Saver are ruptured spleen, ruptured liver, aneurysms, and vascular trauma. During orthopedic surgery the principal indications are total hip arthroplasty, spinal fusions, total knee, and any procedure that has wound drains (5).

Blood Access Devices. An investigational device called the Osteoport system allows repeated access to the vascular system via an intraosseous infusion directly into the bone marrow. The port is implanted subcutaneously and secured into a bone, such as the iliac crest. Medications are administered as in

any conventional port, but are taken up by the venous sinusoids in the marrow cavity, and from there enter the peripheral circulation (6).

Blood Oxygenators. The basic construction of an oxygenator involves any one of several types of units employing a bubble-type, membrane film-type, or hollow-fiber-type design. The most important advance in oxygenator development was the introduction of the membrane-type oxygenator. These employ conditions very close to the normal physiological conditions in which gas contacts occur indirectly via a gas-permeable membrane. Blood trauma is minimized by the use of specialized biomaterials such as PTFE, PVC, and cellophane, although lately silicone rubber and cellulose acetate have predominated. A silicone–polycarbonate copolymer, ethylcellulose perfluorobutyrate, and poly-(alkyl sulfone) were introduced in the mid-1980s, and tend to dominate this field.

4.5. Polyurethanes as Biomaterials. Much of the progress in cardiovascular devices can be attributed to advances in preparing biostable polyurethanes. (see URETHANE POLYMERS). Biostable polycarbonate-based polyurethane materials such as Corethane (7) and ChronoFlex (8) offer far-reaching capabilities to cardiovascular products. These and other polyurethane materials offer significant advantages for important long-term products, such as implantable ports, hemodialysis, and peripheral catheters; pacemaker interfaces and leads; and vascular grafts.

Implantable Ports. The safest method of accessing the vascular system is by means of a vascular access device (VAD) or port. Older VAD designs protruded through the skin. The totally implanted ports are designed for convenience, near absence of infection, and ease of implantation. Ports allow drugs and fluids to be delivered directly into the bloodstream without repeated insertion of needles into a vein. The primary recipients of totally implanted ports are patients receiving chemotherapy, bolus infusions of vesicants, parenteral nutrition, antibiotics, analgesics, and acquired immune disease syndrome (AIDS) medications.

Vascular access ports typically consist of a self-sealing silicone septum within a rigid housing which is attached to a radiopaque catheter (see RADIOPAQUES). The catheter must be fabricated from a low modulus elastomeric polymer capable of interfacing with both soft tissue and the cardiovascular environment. A low modulus polyurethane-based elastomer is preferred to ensure minimal trauma to the fragile vein.

Placement of vascular access ports is similar to that of a long-term indwelling arterial catheter. A small incision is made over the selected vein and a second incision is made lower in the anterior chest to create a pocket to house the port. The catheter is tunneled subcutaneously from its entry point into the vein with the tip inside the right atrium. The final position of the catheter is verified by fluoroscopy, secured with sutures, and the subcutaneous pocket is closed. The port septum is easily palpable transcutaneously, and the system may be used immediately. A surgeon typically inserts the vascular access port in an outpatient setting.

To use the port, the overlying skin is prepared using conventional techniques. A local anesthetic is sometimes used to decrease pain of needle insertion, though this is usually not necessary using techniques which utilize small-bore needles. A special point needle is used to puncture the implanted ports as the

point of these needles is deflected so it tears the septum rather than coring it, allowing multiple entries. The septum reseals when the needle is removed.

The primary advantages of implantable ports are no maintenance between uses other than periodic flushing with heparinized saline every 28 days to ensure patency, lower incidence of clotting and thrombosis, no dressing changes, insignificant infection incidence, unobtrusive cosmetic appearance, and no restriction on physical activity.

Pacemaker Interfaces and Leads. Problems of existing pacemaker interfaces and pacemaker lead materials made from silicones and standard polyurethanes are environmental stress cracking, rigidity, insulation properties, and size.

Technical advances in programmable pacemakers that assist both the tachycardia and bradycardia have led to the requirement of implanting a two-lead system. Owing to the ridigity and size of silicones, the only material that fulfills this possibility without significantly impeding blood flow to the heart is polyurethane. The primary needs in this medical area are reduction in making frequent changes and in failure rate, and the ability to have multiple conductors to handle advanced pacemaker technology.

Vascular Grafts. Although the use of vascular grafts in cardiovascular bypass surgery is widely accepted and routine, numerous problems exist in these surgeries for the materials available. Biocompatibility is often a problem for vascular grafts which also tend to leak and lead to scarring of the anastomosis. The materials are not useful for small-bore ($\leq$6 mm) grafts. The primary needs that materials can be developed to address are matching compliance to native vessels, having a lesser diameter for small-bore grafts which would serve as a replacement for the saphenous vein in coronary bypass, thinner walls, biostability, controlled porosity, and greater hemocompatibility for reduced thrombosis.

The advent of newer polyurethane materials is expected to lead to a new generation of cardiovascular devices. The characteristics of polyurethanes, combined with newer manufacturing techniques, should translate into direct medical benefits for the physician, the hospital, and the patient. This field offers exciting growth opportunities.

5. Orthopedic Devices

Bone, or osseous tissue, is composed of osteocytes and osteoclasts embedded in a calcified matrix. Hard tissue consists of about 50% water and 50% solids. The solids are composed of cartilaginous material hardened with inorganic salts, such as calcium carbonate and phosphate of lime.

Bone is formed through a highly complex process that begins with the creation of embryonic mesenchymal cells. These cells, found only in the mesoderm of the embryo, migrate throughout the human body to form all the types of skeletal tissues including bone, cartilage, muscle, tendon, and ligament. Mesenchymal cells differentiate into the various types of progenitor cells: osteoblasts, chondroblasts, fibroblasts, and myoblasts. Bone tissue begins to form when osteoblasts and chondroblasts synthesize cartilage-like tissue by secreting at least one

potent bone cell growth factor (protein hormone), referred to as IGF-II. Bone growth factor is theorized to stimulate an increased expression of IGF-II receptors on the cell walls of other bone cells. This growth factor helps to initiate a cascade of other subcellular activity, leading to the formation of cartilage. The cartilage then hardens into bone when osteoblasts become lodged within the cartilage matrix, and cease to function. These types of mature cells are then known as osteocytes.

A bone is classified according to shape as flat, long, short, or irregular. A living bone consists of three layers: the periosteum, the hard cortical bone, and the bone marrow or cancellous bone. The periosteum is a thin collagenous layer, filled with nerves and blood vessels, that supplies nutrients and removes cell wastes. Because of the extensive nerve supply, normal periosteum is very sensitive. When a bone is broken, the injured nerves send electrochemical neural messages relaying pain to the brain.

Next is a dense, rigid bone tissue, referred to as the hard compact or cortical bone. It is cylindrical in shape and very hard. This dense layer supports the weight of the body and consists mostly of calcium and minerals. Because it is devoid of nerves, it experiences no pain. The innermost layer, known as cancellous bone or spongy bone marrow, is honeycombed with thousands of tiny holes and passageways. Through these passageways run nerves and blood vessels that supply oxygen and nutrients. This material has a texture similar to gelatin. The marrow produces either red blood cells, white blood cells, or platelets.

Rigid bones are needed for kinetic motion, support of internal organs, and muscle strength. The bones that compose the human thigh are pound for pound stronger than steel. Nature meets these needs by separating the skeleton into several bones and bone systems, creating joints where the bones intersect.

Joints are structurally unique. They permit bodily movement and are bound together by fibrous tissues known as ligaments. Most larger joints are encapsulated in a bursa sac and surrounded by synovial fluid which lubricates the joint continuously to reduce friction. The skeleton is constructed of various types of moveable joints. Some joints allow for no movement, such as those connecting the bones of the skull. Other joints permit only limited movement. For example, the joints of the spine allow limited movement in several directions. Most joints have a greater range of motion than the joints of the skull and spine.

The bearing surface of each joint is cushioned by cartilage. This tissue minimizes friction. The cartilage also reduces force on the bone by absorbing shock. The joint area is a narrow space known as an articular cavity which allows freedom of movement.

Ligaments are composed of bands of strong collagenous fibrous connective tissue. This tissue is originally formed by the mesenchymal cells which differentiate into fibroblast cells. These fibroblast cells then further differentiate into specialized cells known as fibrocytes. When fibrocytes mature, they are inactive and compose the ligaments. Ligaments function to tie two bones together at a joint, maintain joints in position preventing dislocations, and restrain the joint's movements. Ligaments may be reattached to bone by the use of an orthopedic anchor.

Tendons are composed of fibrous connective tissue. Tendon tissue is also formed by the fibroblast cells, similar to the way ligaments are formed. These

fibroblast cells then further differentiate into other specialized cells known as fibrocytes. Mature fibrocytes are inactive and compose the cellular portion of tendons. The function of the tendon is to attach muscles to bones and other parts.

The meniscus is skeletal system fibrocartilage-like tissue. It is a type of cartilage found in selected joints, which are subjected to high levels of force. Meniscal tissue originates from mesenchymal cells which differentiate into chondroblast cells. These chondroblast cells then further differentiate into specialized cells known as chondrocytes. When chondrocytes mature, they are inactive and comprise the menisci and other forms of cartilage. The function of the meniscus is to absorb shock by cushioning and distributing forces evenly throughout a joint, and provide a smooth articulating surface for the cartilages of the adjoining bones.

In the knee, the menisci form an interarticular fibrocartilage base for femural and tibial articulation. The menisci form a crescent shape in the knee. The lateral meniscus is located on the outer side of the knee, and the medial meniscus is located on the inside of the knee. If the knee bends and twists the menisci can overstretch and tear. Menisci tears occur frequently and the knee can sustain more than one tear at a time. If not treated appropriately, however, a menisci tear can roughen the cartilage and lead to arthritis. A meniscus tear acts like grit in the ball bearings of a machine. The longer the torn tissue remains affected, the more irritation it causes.

Meniscus surgery can repair or remove the torn cartilage, depending on the nature of the tear. Arthroscopy, a procedure through small skin incisions to visualize and repair the affected joint, is frequently employed. This procedure is sometimes performed on an out-patient basis. If repair of the menisci is not possible the surgeon removes as little of the meniscus as possible.

The body's frame or skeleton is constructed as a set of levers powered or operated by muscle tissue. A typical muscle consists of a central fibrous tissue portion, and tendons at either end. One end of the muscle, known as the head, is attached to tendon tissue, which is attached to bone that is fixed, and known as the point of origin. The other end of the muscle is attached to a tendon. This tendon is attached to bone that is the moving part of the joint. This end of the muscle is known as the insertion end. An example is the bicep muscle which is connected to the humerus bone of the upper arm at its head or origin. The insertion end of the muscle is connected to the radius bone of the forearm, otherwise known as the moving part of the elbow joint.

Muscle tissue is unique in its ability to shorten or contract. The human body has three basic types of muscle tissue histologically classified into smooth, striated, and cardiac muscle tissues. Only the striated muscle tissue is found in all skeletal muscles. The type of cells which compose the muscle tissue are known as contractile cells. They originate from mesenchymal cells which differentiate into myoblasts. Myoblasts are embryonic cells which later differentiate into contractile fiber cells.

The human body has more than 600 muscles. The body's movement is performed by muscle contractions, which are stimulated by the nervous system. This system links muscle tissue to the spinal cord and brain. The network of nerve cells which carries the brain's signals directs the flow of muscular energy.

Most muscular activity occurs beyond the range of the conscious mind. The body, working through the neuromuscular network, manages its own motion.

Typically, in order for motion to occur, several muscle sets must work together to perform even the simplest movements. The bicep is a two-muscle set; the tricep is a three-muscle set. Each set works in tandem. Within each muscle group, muscle fibers obey the all or none principle, ie, all muscle fibers contract or none contract. Therefore, if the muscle fibers of a muscle group are stimulated enough by nerve impulses to contract, they contract to the maximum.

Bones function as levers; joints function as fulcrums; muscle tissue, attached to the bones via tendons, exert force by converting electrochemical energy (nerve impulses) into tension and contraction, thereby facilitating motion. Muscle tissue works only by becoming shorter. It shortens and then rests, ie, a muscle can only pull, it cannot push. Muscles produce large amounts of heat as they perform work. Involuntary contraction of muscle tissue releases chemical energy. This energy produces heat which warms the body, an action known as shivering.

5.1. Soft Tissue Injuries. Some of the more common soft tissue injuries are sprains, strains, contusions, tendonitis, bursitis, and stress injuries, caused by damaged tendons, muscles, and ligaments. A sprain is a soft tissue injury to the ligaments. Certain sprains are often associated with small fractures. This type of injury is normally associated with a localized trauma event. The severity of the sprain depends on how much of the ligament is torn and to what extent the ligament is detached from the bone. The areas of the human body that are most vulnerable to sprains are ankles, knees, and wrists. A sprained ankle is the most frequent injury. The recommended treatment for a simple sprain is usually rest, ice, compression, and elevation (RICE). If a ligament is torn, however, surgery may be required to repair the injury.

A strain is the result of an injury to either the muscle or a tendon, usually in the foot or leg. Strain is a soft tissue injury resulting from excessive use, violent contraction, or excessive forcible stretch. The biomechanical description is of material failure resulting from force being applied to an area causing excessive tension, compression, or shear stress loading, leading to structural tissue distortion and the constant release of energy. The strain may be a simple stretch in muscle or tendon tissue, or it may be a partial or complete tear in the muscle and tendon combination. The recommended treatment for a strain is also RICE, usually to be followed by simple exercise to relieve pain and restore mobility. A serious tear may need surgical repair.

A contusion is an injury to soft tissue in which the skin is not penetrated, but swelling of broken blood vessels causes a bruise. The bruise is caused by a blow of excessive force to muscle, tendon, or ligament tissue. A bruise, also known as a hematoma, is caused when blood coagulates around the injury causing swelling and discoloring skin. Most contusions are mild and respond well to rest, ice, compression, and elevation of the injured area.

Tendonitis, an inflammation in the tendon or in the tendon covering, is usually caused by a series of small stresses that repeatedly aggravate the tendon, preventing it from healing properly, rather than from a single injury. Orthopedic surgeons treat tendonitis by prescribing rest to eliminate the biomechanical tissue stress, and possibly by prescribing antiinflammatory medications, such as

steroids (qv). Specially chosen exercises correct muscle imbalances and help to restore flexibility. Continuous stress on an inflamed tendon occasionally causes it to rupture. This usually necessitates casting or even surgery to reattach the ruptured tendon.

A bursa, a sac filled with fluid located around a principal joint, is lined with a synovial membrane and contains synovial fluid. This fluid minimizes friction between the tendon and the bone, or between tendon and ligament. Repeated small stresses and overuse can cause the bursa in the shoulder, hip, knee, or ankle to swell. This swelling and irritation is referred to as bursitis. Some patients experience bursitis in association with tendonitis. Bursitis can usually be relieved by rest and in some cases by using antiinflammatory medications. Some orthopedic surgeons also inject the bursa with additional medication to reduce the inflammation.

5.2. Bone Fractures. A dislocation occurs when sudden pressure or force pulls a bone out of its socket at the joint. This is also known as subluxation. Bone fractures are classified into two categories: simple fractures and compound, complex, or open fractures. In the latter the skin is pierced and the flesh and bone are exposed to infection. A bone fracture begins to heal nearly as soon as it occurs. Therefore, it is important for a bone fracture to be set accurately as soon as possible.

In certain diseases, such as osteomalacia, syphilis, and osteomyelitis, bones break spontaneously and without a trauma. The severity of the fracture usually depends on the force that caused the fracture. If a bone's breaking point was exceeded only slightly, then the bone may crack rather than break all the way through. If the force is extreme, such as in an automobile collision or a gunshot, the bone may shatter. An open or compound fracture is particularly serious because infection is possible in both the wound and the bone. A serious bone infection can result in amputation.

Stress fractures occur when microfractures accumulate because muscle tissue becomes fatigued and no longer protects from shock or impact. These heal, however, if given adequate rest. Without proper rest, unprotected bone beomes fatigued from absorbing the stress which is normally absorbed by muscle. Isolated microfractures become larger and then join together, forming a continuous stress fracture. These are often referred to as fatigue fractures. Stress fractures were first referred to as march fractures.

Stress or fatigue fractures are very painful. Most often symptoms occur after athletic activity or physical exertion. Gradually pain worsens and becomes more constant. Stress fractures do not show up on standard x-rays. A bone scan may be used to confirm the diagnosis. Stress fractures usually occur in the weight-bearing bones of the lower leg and foot. Stress fractures of the tibia account for half of all stress fractures, resulting mostly from athletic activity. These stress fractures are often mistaken for shin splints. In addition to the tibia, the fibula and other small bones of the foot are prone to stress fractures.

5.3. Fracture Treatment. The movement of a broken bone must be controlled because moving a broken or dislocated bone causes additional damage to the bone, nearby blood vessels, and nerves or other tissues surrounding the bone. Indeed, emergency treatment requires splinting or bracing a fracture injury before further medical treatment is given. Typically, x-rays determine whether

there is a fracture, and if so, of what type. If there is a fracture, a doctor reduces it by restoring the parts of the broken bone to their original positions. All treatment forms for fractures follow one basic rule: the broken pieces must be repositioned and prevented from moving out of place until healed. Broken bone ends heal by growing back together, ie, new bone cells form around the edge of the broken pieces. Specific bone fracture treatment depends on the severity of the break and the bone involved, ie, a broken bone in the spine is treated differently from a broken rib or a bone in the arm.

Treatments used for various types of fractures are cast immobilization, traction, and internal fixation. A plaster or fiber glass cast is the most commonly used device for fracture treatment. Most broken bones heal successfully once properly repositioned, ie, fixed in place via a cast. This type of cast or brace is known as an orthosis. It allows limited or controlled movement of nearby joints. This treatment is desirable for certain fractures.

Traction is typically used to align a bone by a gentle, constant pulling action. The pulling force may be transmitted to the bone through skin tapes or a metal pin through a bone. Traction may be used as a preliminary treatment, before other forms of treatment or after cast immobilization.

In internal fixation, an orthopedist performs surgery on the bone. During this procedure, the bone fragments are repositioned (reduced) into their normal alignment and then held together with special screws or by attaching metal plates to the outer surface of the bone. The fragments may also be held together by inserting rods (intramedullary rods) down through the marrow space into the center of the bone. These methods of treatment can reposition the fracture fragments very exactly. A common internal fixation procedure is to surgically fix the femoral neck (broken hip), as shown in Figure 4.

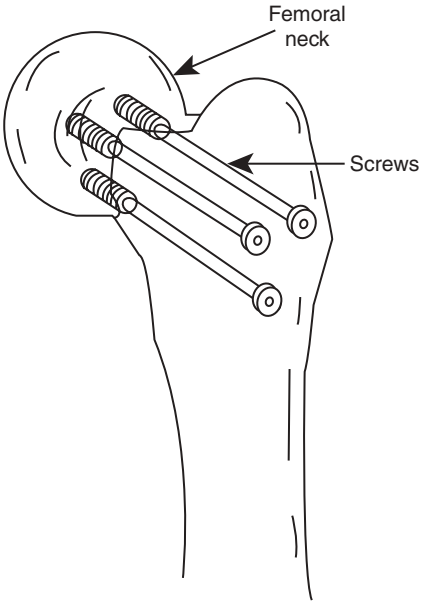


Fig. 4. Internal femur fixation.

5.4. Joint Replacement. The most frequent reason for performing a total joint replacement is to relieve the pain and disability caused by severe arthritis. The surface of the joint may be damaged by osteoarthritis, ie, a wearing away of the cartilage in a joint. The joint may also be damaged by rheumatoid arthritis, an autoimmune disease, in which the synovium produces chemical substances that attack the joint surface and destroy the cartilage. The swelling, heat, and stiffness that occur in an arthritic joint cause inflammation, the body's natural reaction to disease or injury. Inflammation is usually temporary, but in arthritic joints it is long-lasting and causes disability. When arthritis has caused severe damage to a joint, a total joint replacement may allow the person to return to normal everyday activities.

A total joint replacement is a radical surgical procedure performed under general anesthesia, in which the surgeon replaces the damaged parts of the joint with artificial materials. For example, in the knee joint the damaged ends of the bone that meet at the knee are replaced, along with the underside of the kneecap. In the hip joint, the damaged femoral head is replaced by a metal ball having a stem that fits down into the femur. A new plastic socket is implanted into the pelvis to replace the old damaged socket. This is shown schematically in Figure 5. Whereas hips and knees are the joints most frequently replaced, because the scientific understanding of these is best, total joint

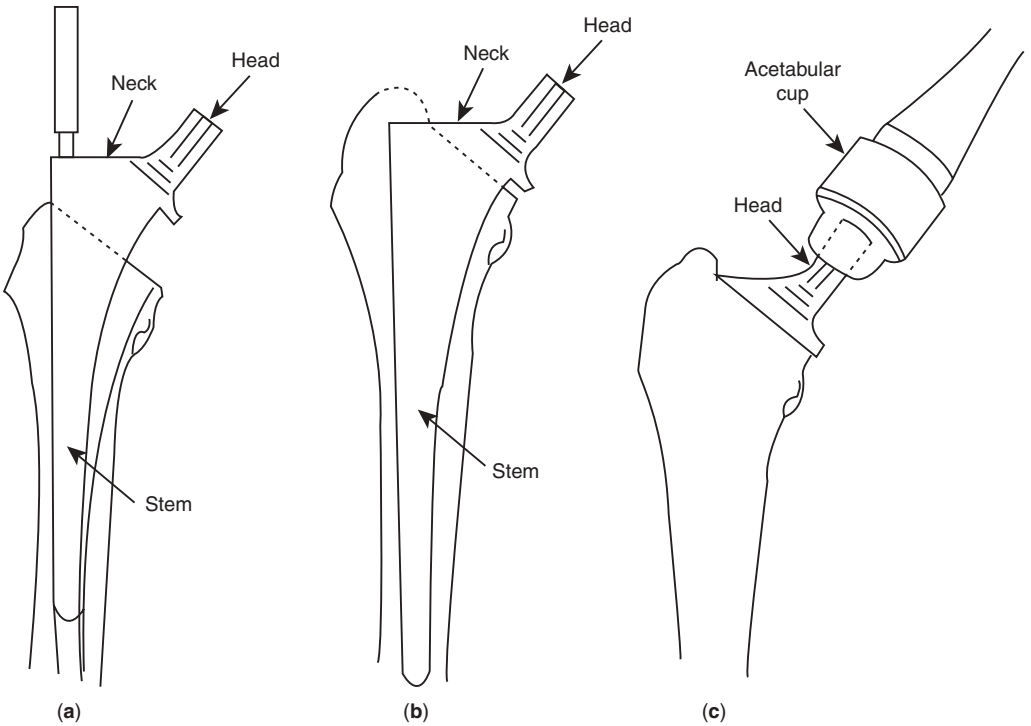


Fig. 5. Three views of a hip implant for joint replacement: (**a**) insertion of the implant into the femur; (**b**) implant in place; and (**c**) femur and implant connected to plastic socket fitted into the pelvis.

replacement can be performed on other joints as well, including the ankle, shoulder, fingers, and elbow.

The materials used in a total joint replacement are designed to enable the joint to function normally. The artificial components are generally composed of a metal piece that fits closely into bone tissue. The metals are varied and include stainless steel or alloys of cobalt, chrome, and titanium. The plastic material used in implants is a polyethylene that is extremely durable and wear-resistant. Also, a bone cement, a methacrylate, is often used to anchor the artificial joint materials into the bone. Cementless joint replacements have more recently been developed. In these replacements, the prosthesis and the bone are made to fit together without the need for bone cement. The implants are press-fit into the bone.

The recovery period following total joint arthropathy depends on both the patient and the affected joint. In general the patient is encouraged to use the joint soon after replacement. In the case of a hip or knee replacement the patient should be standing and beginning to walk within several days. If the shoulder, elbow, or wrist joint is replaced, use of the new joint can begin very soon after surgery, as these are not weight-bearing joints. The patient generally performs appropriate exercises to strengthen and move the joint during the recovery period.

The main benefits to the patient after total joint replacement are pain relief, which often is quite dramatic, and increased muscle power, which was lost because the painful arthritic joint was not used and usually returns with exercise once pain is relieved. Motion of the joint generally improves as well. The extent of movement depends on how stiff the joint was before the joint was replaced. An extremely stiff joint continues to be stiff for some period of time after replacement.

The principal complication for total joint replacement is infection, which may occur just in the area of the incision or more seriously deep around the prosthesis. Infections in the wound area, which may even occur years after the procedure has been performed, are usually treated with antibiotics (qv). Deep infections may require further surgery, prosthesis removal, and replacement.

Loosening of the prosthesis is the most common biomechanical problem occurring after total joint replacement surgery. Loosening causes pain. If loosening is significant, a second or revision total joint replacement may be necessary. Another complication which sometimes occurs after total joint replacement, generally right after the operation, is dislocation, the result of weakened ligaments. In most cases the dislocation can be relocated manually by the orthopedic surgeon. Very rarely is another operation necessary. A brace may be worn after dislocation occurs for a short time. Although some wear can be measured in artificial joints, wear occurs slowly. Whereas wear may contribute to looseness, it is rarely necessary to do corrective surgery because of wear alone.

Breakage of an implanted joint is rare. Breakage occurs when the bone flexes and the metal implant does not flex as much, thereby exceeding its mechanical fatigue point causing the implant to break or crack. A revision joint replacement operation is necessary if breakage occurs.

Nerves are rarely damaged during the total joint replacement surgery. However, nerve damage can occur if considerable joint deformity must be

corrected in order to implant the prosthesis. With time these nerves sometimes return to normal function.

Osteoarthritis, the most common arthritic disorder, affects some 30 million Americans each year. Caused by daily wear and tear on joints or injury, osteoarthritis is painful and restricts daily activity. It can affect the basal joint of the thumb, as well as the knee, hip, and other joints.

Hip Joints. Successful hip joint replacement surgery was introduced in the late 1950s. Since that time design and scientific advances have brought increasingly better clinical results. In excess of 200,000 patients in the United States seek pain relief annually through hip joint replacement. About 18–20% are revision hip systems, ie, second replacement implants. A hip usually becomes painful when the cartilage that lines the hip socket starts to wear out. As total hip systems evolved, designers attempted to eliminate features which led to failure. Modifications were made to each element of the hip system including the femoral stem and acetabular cup. Wear and tear arthritis may be the result of a genetic defect that prevents the body from manufacturing cartilage rugged enough to last a lifetime. Increased life-expectancy, stresses owing to certain occupations, and prior injury that places abnormal stress on cartilage over a long period may also contribute to the development of osteoarthritis. Often arthritic pain can be controlled through the use of antiinflammatory medication. However, if hip pain becomes intolerable, hip replacement surgery may be elected.

In 1974 a prosthesis introduced by Howmedica combined a biomechanically high strength material, Vitallium, with a professionally engineered geometry. This prosthesis marked the first design departure from the diamond-shaped cross-sectional geometry previously used. Sharp corners were eliminated and replaced by broad, rounded medial and lateral borders. The total sectional area was much greater than any of the previous hip joint implant stems. The result of these combined factors was decreased unit stresses on the cement mantle. This system also marked the first time surgeons could choose components from a selection large enough to provide fit for most primary and revision total hip replacement patients.

The next advance in total hip arthroplasty came with the development of various porous surface treatments which allow bone tissue to grow into the metal porous coating on the femoral stem of the hip implant and on the acetabular component of the total joint replacement. These developments arose because of patients who were not able to tolerate cemented implants because of allergies to the cement, methylmethacrylate. More youthful patients are better served by a press-fit implant as well. Figure 6 shows the difference between textured and beaded surface-treated orthopedic prostheses.

Hydroxyapatite (HA) coating on the surface of the hip stem and the acetabular cup is the most recent advancement in artificial hip joint implant technology. This substance is a form of calcium phosphate, which is sprayed onto the hip implant. It is a material found in combination with calcium carbonate in bone tissue, and bones can easily adapt to it. When bone tissue does grow into HA, the tissue then fixes the hip joint implant permanently in position. These HA coatings are only used in press-fit, noncemented implants.

The acetabular component is as integral to successful total hip arthroplasty as is the femoral hip stem component. The life of the acetabular component

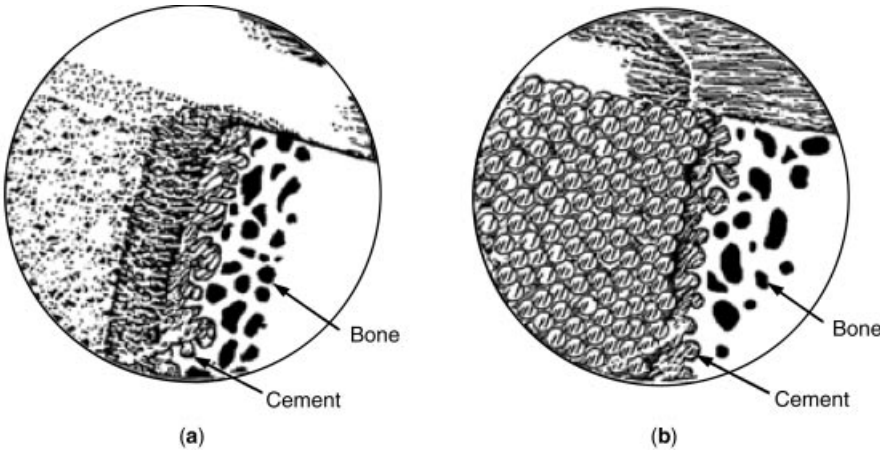


Fig. 6. Surface treatments: (**a**) textured and (**b**) beaded.

depends on proper placement and bone preparation in the acetabular region of the hip girdle, proper use of bone cement, and superior component design.

The history of the development of the acetabular component parallels that of the femoral component. In 1951 an acetabular prosthesis based on a chromium–cobalt alloy having screw-in sockets was successfully introduced. Beginning in 1955, methylmethacrylate was used as a cementing agent, and work was undertaken to find suitable materials for use as an articulation surface in the acetabular. Teflon appeared to provide a good lubricating, articulating surface. However, over time Teflon exhibited poor wear conditions when it contacted the metal femoral head, and as the body developed systemic reaction to Teflon particles, failures occurred. Since then ultrahigh density polyethylene has proven successful as acetabular cups.

In 1971 a metal-backed polyethylene acetabular cup was introduced. This cup provided an eccentric socket which was replaceable, leaving the metal and replacing only the polyethylene. Because of the success of this component, metal-backed high density polyethylene (HDPE) liner is standard for prosthetic acetabular components. Research confirms that metal-backing reduces the peak stresses in the bone cement, and that HDPE forms a successful articulating surface for the prosthetic joint.

Over time a large variety of materials have been used, including ivory, stainless steel, chromium–cobalt, and ceramics for the acetabular component. None proved sufficient. The implant material composition must provide a smooth surface for joint articulation, withstand hip joint stresses from normal loads, and the substance must disperse stress evenly to the cement and surrounding bone.

The material in use as of the mid-1990s in these components is HDPE, a linear polymer which is tough, resilient, ductile, wear resistant, and has low friction (see OLEFIN POLYMERS, POLYETHYLENE). Polymers are prone to both creep and fatigue (stress) cracking. Moreover, HDPE has a modulus of elasticity that is only one-tenth that of the bone, thus it increases the level of stress transmitted to the cement, thereby increasing the potential for cement mantle failure. When

the acetabular HDPE cup is backed by metal, it stiffens the HDPE cup. This results in function similar to that of natural subchondral bone. Metal backing has become standard on acetabular cups.

The femoral component is composed of the head, neck, collar, and stem (see Fig. 5). The head, or ball, is the surface component which articulates with the acetabular cup of the total hip implant. This is an important element in the implant design because this surface absorbs the greatest stress and has the most force applied to it. Consequently the head gets the greatest wear. The diameter of the femoral head affects the distribution of forces in both the femoral and acetabular components. This variable also influences the range of motion that the implant permits, therefore affecting the stability of the ball-in-socket prosthetic joint. The most common head diameters range from 22 to 32 mm. Each size offers advantages and disadvantages. No general consensus exists as to which size is better. As a result, many manufacturers offer more than one head diameter to suit surgeon preference and patient requirements.

The 22-mm diameter is preferred by some doctors who believe that a small-diameter head encourages mechanical fixation of the socket without cement fixation. Other benefits associated with the 22-mm head size include its suitability for use in a patient having a small acetabulum, and the fact that it allows for a thicker acetabular component, which permits more wear and absorbs more energy than do thinner walled components. The larger (32-mm) head diameter range is recommended by other surgeons and has been incorporated into most hip systems. Using this large diameter the surface of the head has a greater area, resulting in decreased stress per unit area. Other advantages include less chance of subluxation (joint dislocation) at the extremes of motion and therefore improved prosthetic joint stability. However, some doctors express concern that the increased articulating surface contact area promotes increased frictional torque.

The stem/neck length and cross-sectional geometry of the neck affects the forces acting on both the neck and the stem. The neck must be large enough to prevent failure, but not so large as to limit range of motion. Further, the neck length should be consistent with the anatomy of the patient.

The most important design consideration in the neck of the femoral component is that it support body weight without breaking. This requires that the head/neck ratio be appropriate. Neck length is measured from the center of the femoral head to the collar of the stem. Variations to neck length, combined with offset neck/stem angle, and head diameter, permit surgeons to adjust leg length of the total hip implant leg to be consistent with that of the opposite leg. It was for this reason that surgeons introduced the concept of providing different neck lengths.

The stem/neck offset, ie, distance from the center of the head to the center of the stem, changes upon a change in the neck length. Increased neck length, and therefore increased offset, raises the bending moment of the stem, thereby increasing the chances for prosthetic failure. The various neck geometries used by designers of prostheses represent attempts to find a satisfactory combination of shape, bulk, and material which can withstand cyclic loading and joint forces without breaking. Most neck/stem angles are neutral (135°) in order to estimate average human anatomy and equalize the moment arms.

An important issue of stem design is length. Increased stem length means more stem area for improved stress distribution. Another benefit to a longer implant stem is engagement of the isthmus, the most narrow portion of the femur. Expanding the stem into this area of contact increases prosthetic stability, helps prevent the stem from shifting position, decreases the amount of micromotion, and achieves better alignment along the neutral axis of the femur. Stems are available in varied lengths to match human anatomy and improve isthmic engagement. The most advanced hip implants on the market are totally modular, so that they are nearly custom made to fit into the femur and the acetabulum of the pelvic girdle.

Starting from the bottom of the hip implant, a modular implant begins with a press-fit, distal, high density, ultrahigh molecular weight, polyethylene (HDPE) plug tip, at the bottom of the femur stem. Then a machined and polished titanium, chromium–cobalt–molybdenum, or vanadium–aluminum metallic alloy diaphyseal–endosteal grooved stem segment is added, followed by a machined, polished, and hydroxyapatite-coated metaphyseal metallic alloy stem segment, the upper portion of the hip implant stem. A custom-fit metallic alloy collar plate, which rests upon the resected (cut-away) head of the femur, comes next, followed by a sized modular metallic alloy neck upon which a chromium–cobalt–molybdenum or zirconium ceramic head, ie, ball that sets upon the hip stem neck, rests. The head then articulates with the acetabular cup liner (see Fig. 5).

The head of the femoral component then articulates with an ion-bombarded, HDPE, high walled, acetabular liner which fits into a screwed in, machined, titanium, chromium–cobalt–molybdenum or vanadium–aluminum metallic alloy hydroxyapatite-coated acetabular shell/cup. Each of the separate parts of the modular system for total hip arthroplasty is manufactured in several different sizes.

Total hip implants of the nature described have hospital list prices in the range of $5000–$8000. Fully custom-made implants cost approximately $10,000. The low end basic total hip implant is forged or cast stainless steel, cemented in place, one size fits all, and costs $1000.

Prosthesis Design. The challenge in prosthesis design is to create an implant that mimics the material characteristics and the exact anatomical functions of the joint. Stress and loading forces on the hip joint and femur are extraordinary. Stresses on the hip joint exceed 8.3 MPa (1200 psi). Standing on one leg produces a loading force on the hip joint of 250% of the total body weight. Running increases these forces to five times the total body weight. The hip joint is surrounded by the most powerful muscle structure in the body enabling movement while supporting sufficient structural force and loads. Proper surgical technique is as critical to the success of an implant procedure as is the design of the device itself. Therefore, matching surgeon skill, an appropriate implant design for the patient, and the correct tools generally forms the best solution for a successful procedure.

A significant aspect of hip joint biomechanics is that the structural components are not normally subjected to constant loads. Rather, this joint is subject to unique compressive, torsion, tensile, and shear stress, sometimes simultaneously. Maximum loading occurs when the heel strikes down and the toe pushes off in walking. When an implant is in place its ability to withstand this repetitive

loading is called its fatigue strength. If an implant is placed properly, its load is shared in an anatomically correct fashion with the bone.

Design variables introduced on various prostheses represent efforts to share the stresses and normal loading characteristics of human locomotion. The size, shape, and tissue structure of bone are most commonly affected in the healing of fractures. Bone remodeling was first described in 1892 by the German physician Julius Wolff in *The Law of Bone Transformation*. In terms of force loading and stresses, Wolff's law states that bone responds to mechanical demends by changing its size, shape, and structure.

Resorption of bone tissue occurs in total hip joint replacement patients if sufficient stresses are not adequately transmitted to the remaining bone in exactly the same way that the bone transmitted those stresses originally. Therefore, the design and proper placement of the neck collar and hip stem must be effective in recreating anatomical structure.

Bone remodeling is the ability of bone to change its size, shape, and structure by adapting to mechanical demands that are placed on it. Bone grows where it is needed, and resorbs where it is not needed. The type of bone tissue that grows depends on the stress level it sustains. Someone who performs strenuous exercise undergoes cortical bone changes resulting in bigger, denser bones. On the other hand, someone who performs minimal physical activity loses bone density through resorption. This is a problem for those who must stay in bed for prolonged periods. The problem of bone density loss owing to minimal physical stress has also been a unique concern for NASA astronauts. Special exercises have been designed for the astronauts to counteract the effects of weightlessness and to slow down bone resorption during long orbital flights.

The process of aging reduces bone size and strength. Thinning and resorption occur in the cancellous bone. Also, cortical bone resorbs and bone shrinks in diameter and thickness. The older the person, the more fragile the bone.

Research based on Wolff's law of bone transformation has resulted in some other important observations. Fluctuating loads, such as those that occur in walking, are better for bone than consistently applied loads, such as weight gain. However, if the effective applied load becomes extreme, pressure necrosis, ie, bone death, occurs. Pressure necrosis is a significant concern in hip arthroplasty. Necrosis means the localized death of living tissue. Undue pressure on living cells causes death. Some total hip replacement failures are the direct result of pressure necrosis.

Some of the early design hip prostheses, created without a complete understanding of stress forces and anatomical loading characteristics of normal activity, had sharp points at the distal end and along the medial and lateral sides of the stem. Improperly seated, or merely subjected to normal forces, these stems directed concentrated stresses into the interfacing cement. This point loading resulted in cement fracturing into fragments and bone tissue suffering pressure necrosis, resulting in implant failure. More rounded prosthetic designs, and the tools and instrumentation to properly seat them, distribute the load over the widest area. This distribution mimics that of natural bone and prevents pressure necrosis.

Biomaterials. Just as stem designs have evolved in an effort to develop an optimal combination of specifications, so have the types of metals and alloys

employed in the construction of total joint implants. Pure metals are usually too soft to be used in prosthesis. Therefore, alloys which exhibit improved characteristics of fatigue strength, tensile strength, ductility, modulus of elasticity, hardness, resistance to corrosion, and biocompatibility are used.

Titanium alloy, composed of titanium, aluminum, and vanadium, is preferred by some orthopedic surgeons primarily for its low modulus of elasticity, which allows for transfer of more stress to the proximal femur. This alloy also exhibits good mechanical strength and biocompatibility (9). The stem flexibility optimizes the transfer of stress directly to the bone, and offers adequate calcar loading to minimize femoral resorption.

Vitallium FHS alloy is a cobalt–chromium–molybdenum alloy having a high modulus of elasticity. This alloy is also a preferred material. When combined with a properly designed stem, the properties of this alloy provide protection for the cement mantle by decreasing proximal cement stress. This alloy also exhibits high yields and tensile strength, is corrosion resistant, and biocompatible. Composites used in orthopedics include carbon–carbon, carbon–epoxy, hydroxyapatite, ceramics, etc.

Tools and Procedures. Arthroscopy is a surgical procedure used to visualize, diagnose, and treat injuries within joints. The term arthroscopy literally means to look inside the joint. During this procedure the orthopedic surgeon makes an incision into the patients skin and inserts a pencil-shaped arthroscope. An arthroscope is a miniature lens and lighting systems that magnifies and illuminates the structures inside the joint. A television screen which is attached to the arthroscope displays the image of the joint on screen.

This is a minimally invasive procedure (MIP) resulting in a shorter hospital stay, faster recovery, and less evident scar in comparison to other types of surgery. Arthroscopic surgery gives the surgeon a precise, direct view of the affected bones and soft tissues. This procedure allows the surgeon to see areas of the joint that are difficult to see on x-rays and more of the joint than is possible even after making a large incision during open surgery. Arthroscopy can be performed under local, general, or spinal anesthesia. The area surrounding the joint is sterilized, and then the joint is expanded to make room for the arthroscope by injecting a sterile solution into the joint. The surgeon makes a small incision into the skin through which the arthroscope is inserted. A surgical instrument probes various parts of the joints to determine the injury. Surgical repair, if needed, is performed using specially designed surgical instruments which are inserted into the joint through the small incisions. This surgery can be viewed on a television screen. The small incisions that were made during surgery are closed usually using only one or two sutures.

Patients' immediate post-operative pain is lower compared to a standard operation and healing and rehabilitation more rapid. Patients can resume near-normal activities in just days. In some cases athletes, who are in prime physical condition, can return to challenging athletic activities within a few weeks. Complications are rare, but do occur on occasion. Most complications associated with this surgery are infection, phlebitis, excessive swelling or bleeding, blood clots, or damage to blood vessels or nerves.

6. Bioresorbable Polymers

Biomaterials scientists have worked diligently to synthesize polymeric structures which exhibit biocompatibility and long-term biostability. Devices made from these polymers are intended to be implanted in the body for years, and in some cases decades.

The concept of using biodegradable materials for implants which serve a temporary function is a relatively new one. This concept has gained acceptance as it has been realized that an implanted material does not have to be inert, but can be degraded and/or metabolized *in vivo* once its function has been accomplished (10). Resorbable polymers have been utilized successfully in the manufacture of sutures, small bone fixation devices (11), and drug delivery systems (qv) (12).

Several groups have experimented with bioresorbable polymers that have a predictable degree of bioresorbability when exposed to the physiological environment. By the judicious choice of bioresorbability rate it is hoped that as the polymer is resorbed it will leave surface voids where natural tissue would grow, resulting in autologous organ regeneration. The temporary nature of the device will impart initial mechanical functionality to the implant, but after time will be resorbed as the natural tissue regenerates. This concept has been experimentally applied to the regeneration of tissue such as in the liver (13), skeletal tissue (14), cartilage (15), and the vascular wall (16).

One area in which predictable biodegradation is used is the area of degradable surgical sutures. An incision wound, when held together with sutures, heals to about 80% of initial strength within four weeks. Surgical suture is one of the earliest clinical implants in recorded history. Catgut suture, obtained from ovine or bovine intestinal submucosa, was known in 150 AD in the time of Galen, who built his reputation by treating wounded gladiators (17).

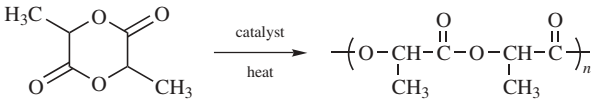
Catgut is infection-resistant. The biodegradation of catgut results in elimination of foreign material that otherwise could serve as a nidus for infection or, in the urinary tract, calcification. As a result, chromic catgut, which uses chromic acid as a cross-linking agent, is still preferred in some procedures. Chromic catgut is considered by some to be the most suitable suture material for vaginal hysterectomy owing to its extensibility and rapid absorption. Treatment of natural catgut with synthetic polymers exemplifies the merging of old and new technology. Coating catgut with a polyurethane resin allows catgut to retain its initial tensile strength longer (18).

The first synthetic polyglycolic acid suture was introduced in 1970 with great success (19). This is because synthetic polymers are preferable to natural polymers since greater control over uniformity and mechanical properties are obtainable. The foreign body response to synthetic polymer absorption generally is quite predictable whereas catgut absorption is variable and usually produces a more intense inflammatory reaction (20). This greater tissue compatibility is crucial when the implant must serve as an inert, mechanical device prior to bioresorption.

6.1. Polylactic Acid. Polylactic acid (PLA) was introduced in 1966 for degradable surgical implants. Hydrolysis yields lactic acid, a normal intermediate of

carbohydrate metabolism (21). Polyglycolic acid sutures have a predictable degradation rate which coincides with the healing sequence of natural tissues.

Polylactic acid, also known as polylactide, is prepared from the cyclic diester of lactic acid (lactide) by ring-opening addition polymerization, as shown below:

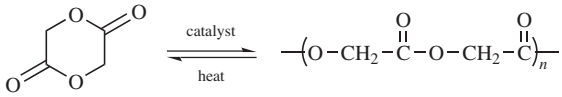


Lactic acid is an asymmetric compound existing as two optical isomers or enantiomers. The L-enantiomer occurs in nature; an optically inactive racemic mixture of D- and L-enantiomers results during synthesis of lactic acid. Using these two types of lactic acid, the corresponding L-lactide (mp 96°C) and DL-lactide (mp 126°C) have been used for polymer synthesis. Fibers spun from poly-L-lactide (mp 170°C) have high crystallinity when drawn, whereas poly-DL-lactide (mp 60°C) fibers display molecular alignment on drawing but remain amorphous. The crystalline poly-L-lactide is more resistant to hydrolytic degradation than the amorphous DL form of the same homopolymer. Therefore, pure DL-lactide displays greater bioresorbability, whereas pure poly-L-lactide is more hydrolytically resistant.

The actual time required for poly-L-lactide implants to be completely absorbed is relatively long, and depends on polymer purity, processing conditions, implant site, and physical dimensions of the implant. For instance, 50–90 mg samples of radiolabeled poly-DL-lactide implanted in the abdominal walls of rats had an absorption time of 1.5 years with metabolism resulting primarily from respiratory excretion (22). In contrast, pure poly-L-lactide bone plates attached to sheep femora showed mechanical deterioration, but little evidence of significant mass loss even after four years (23).

Improved techniques for polylactide synthesis have resulted in preparation of exceptionally high molecular weight polymer. Fiber processing research has resulted in fiber samples having tensile breaking strength approaching 1.2 GPa (174,000 psi). This strength value was obtained by hot-drawing filaments spun from good solvents (24).

6.2. Polyglycolic Acid. Polyglycolic acid (PGA), also known as polyglycolide, was first reported in 1893, but it wasn't until 1967 that the first commercially successful patent was granted for sutures (25). Like polylactide, polyglycolide is synthesized from the cyclic diester as shown below:



An important difference between polylactide and polyglycolide, is that polyglycolide (mp 220°C) is higher melting than poly-L-lactide (mp 170°C). Although the polymerization reaction in both cases is reversible at high temperature, melt processing of polyglycolide is more difficult because the melting temperature is close to its decomposition temperature.

Unlike poly-L-lactide which is absorbed slowly, polyglycolide is absorbed within a few months post-implantation owing to greater hydrolytic susceptibility. *In vitro* experiments have shown the effect on degradation by enzymes (26), pH, annealing treatments (27), and gamma irradiation (28). Braided polyglycolide sutures undergo surprisingly rapid hydrolysis *in vivo* owing to cellular enzymes released during the acute inflammatory response following implantation (29).

Low humidity ethylene oxide gas sterilization procedures and moisture-proof packaging for polyglycolic acid products are necessary because of the susceptibility to degradation resulting from exposure to moisture and gamma sterilization.

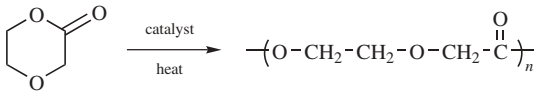
6.3. Poly(lactide-*co*-glycolide). Mixtures of lactide and glycolide monomers have been copolymerized in an effort to extend the range of polymer properties and rates of *in vivo* absorption. Poly(lactide-*co*-glycolide) polymers undergo a simple hydrolysis degradation mechanism, which is sensitive to both pH and the presence of enzymes (30).

A 90% glycolide, 10% L-lactide copolymer was the first successful clinical material of this type. Braided absorbable suture made from this copolymer is similar to pure polyglycolide suture. Both were absorbed between 90 and 120 days post-implantation but the copolymer retained strength slightly longer and was absorbed sooner than polyglycolide (31). These differences in absorption rate result from differences in polymer morphology. The amorphous regions of poly (lactide-*co*-glycolide) are more susceptible to hydrolytic attack than the crystalline regions (32).

Similar to pure polyglycolic acid and pure polylactic acid, the 90:10 glycolide: lactide copolymer is also weakened by gamma irradiation. The normal *in vivo* absorption time of about 70 days for fibrous material can be decreased to less than about 28 days by simple exposure to gamma radiation in excess of 50 kGy (5 Mrads) (33).

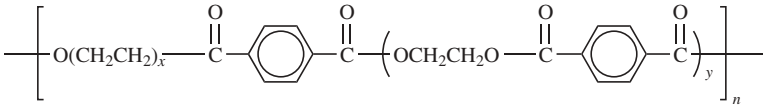
The crystallinity of poly(lactide-*co*-glycolide) samples has been studied (34). These copolymers are amorphous between the compositional range of 25–70 mol % glycolide. Pure polyglycolide was found to be about 50% crystalline whereas pure poly-L-lactide was about 37% crystalline. An amorphous poly(L-lactide-*co*-glycolide) copolymer is used in surgical clips and staples (35). The preferred composition chosen for manufacture of clips and staples is the 70/30 L-lactide/glycolide copolymer.

6.4. Polydioxanone. Fibers made from polymers containing a high percentage of polyglycolide are considered too stiff for monofilament suture and thus are available only in braided form above the microsuture size range. The first clinically tested monofilament synthetic absorbable suture was made from polydioxanone (36). This polymer is another example of a ring-opening polymerization reaction. The monomer, *p*-dioxanone, is analogous to glycolide but yields a poly(ether–ester) as shown below:



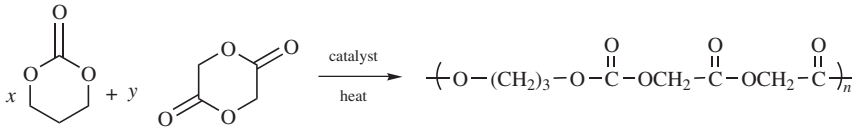
Polydioxanone (PDS) is completely eliminated from the body upon absorption. The mechanism of polydioxanone degradation is similar to that observed for other synthetic bioabsorbable polymers. Polydioxanone degradation *in vitro* was affected by gamma irradiation dosage but not substantially by the presence of enzymes (37). The strength loss and absorption of braided PDS, but not monofilament PDS, implanted in infected wounds, however, was significantly greater than in noninfected wounds.

6.5. Poly(ethylene oxide)–Poly(ethylene terephthalate) Copolymers. The poly(ethylene oxide)–poly(ethylene terephthalate) (PEO/PET) copolymers were first described in 1954 (38). This group of polymers was developed in an attempt to simultaneously reduce the crystallinity of PET, and increase its hydrophilicity to improve dyeability. PEO/PET copolymers with increased PEO contents produce surfaces that approach zero interfacial energy between the implant and the adjacent biological tissue. The collagenous capsule formed around the implant is thinner as the PEO contents increase. The structure of a PEO/PET copolymer is shown below:



A family of PEO/PET copolymers has been synthesized and the characterized structures found to be close to those expected in theory (39). A wide degradation envelope has been achieved by adjusting the PEO-to-PET ratio. Mechanical properties prove useful for medical applications, and the 60/40 PEO/PET composition is reported as optimal.

6.6. Poly(glycolide-*co*-trimethylene carbonate). Another successful approach to obtaining an absorbable polymer capable of producing flexible monofilaments has involved finding a new type of monomer for copolymerization with glycolide (40). Trimethylene carbonate polymerized with glycolide is shown below:

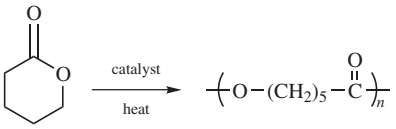


In order to achieve the desired fiber properties, the two monomers were copolymerized so the final product was a block copolymer of the ABA type, where A was pure polyglycolide and B, a random copolymer of mostly poly(trimethylene carbonate). The selected composition was about 30–40% poly(trimethylene carbonate). This suture reportedly has excellent flexibility and superior *in vivo* tensile strength retention compared to polyglycolide. It has been absorbed without adverse reaction in about seven months (41). Metabolism studies show that the route of excretion for the trimethylene carbonate moiety is somewhat different from the glycolate moiety. Most of the glycolate is excreted by urine whereas most of the carbonate is excreted by expired CO_2 and urine.

6.7. Poly(ethylene carbonate). Like polyesters, polycarbonates (qv) are bioabsorbable only if the hydrolyzable linkages are accessible to enzymes

and/or water molecules. Thus pellets of poly(ethylene carbonate), $+OCOOCH_2CH_2+_n$ weighing 200 mg implanted in the peritoneal cavity of rats, were bioabsorbed in only two weeks, whereas similar pellets of poly(propylene carbonate), $+OCOOCH(CH_3)CH_2+_n$ showed no evidence of bioabsorption after two months (42). Because poly(ethylene carbonate) hydrolyzes more rapidly *in vivo* than *in vitro*, enzyme-catalyzed hydrolysis is postulated as a contributing factor in polymer absorption. Copolymers of polyethylene and polypropylene carbonate have been developed as an approach to achieving the desired physical and pharmacological properties of microsphere drug delivery systems.

6.8. Polycaprolactone. Polycaprolactone is synthesized from epsilon-caprolactone as shown below:

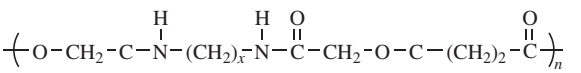


This semicrystalline polymer is absorbed very slowly *in vivo*, releasing ε-hydroxycaproic acid as the sole metabolite. Degradation occurs in two phases: nonenzymatic bulk hydrolysis of ester linkages followed by fragmentation, and release of oligomeric species. Polycaprolactone fragments ultimately are degraded in the phagosomes of macrophages and giant cells, a process that involves lysosome-derived enzymes (43). *In vitro*, polycaprolactone degradation is enhanced by microbial and enzymatic activity. Predictably, amorphous regions of the polymer are degraded prior to breakdown of the crystalline regions (44).

Copolymers of ε-caprolactone and L-lactide are elastomeric when prepared from 25% ε-caprolactone and 75% L-lactide, and rigid when prepared from 10% ε-caprolactone and 90% L-lactide (45). Blends of poly-DL-lactide and polycaprolactone polymers are another way to achieve unique elastomeric properties. Copolymers of ε-caprolactone and glycolide have been evaluated in fiber form as potential absorbable sutures. Strong, flexible monofilaments have been produced which maintain 11–37% of initial tensile strength after two weeks *in vivo* (46).

6.9. Poly(ester–amides). Another approach to obtaining improvements in the properties of synthetic absorbable polymers is the synthesis of polymers containing both ester and amide linkages. The rationale for designing poly(ester–amide) materials is to combine the absorbability of polyesters (qv) with the high performance of polyamides (qv). Two types have been reported. Both involve the polyesterification of diols that contain preformed amide linkages. Poly(ester–amides) obtained from bis-oxamidodiols have been reported to be absorbable only when oxalic acid is used to form the ester linkages (47). Poly(ester–amides) obtained from bis-hydroxyacetamides are absorbable regardless of the diacid employed, although succinic acid is preferred (48).

The absorption rate has been examined *in vivo* for a series of poly(ester–amides) having the following formula:

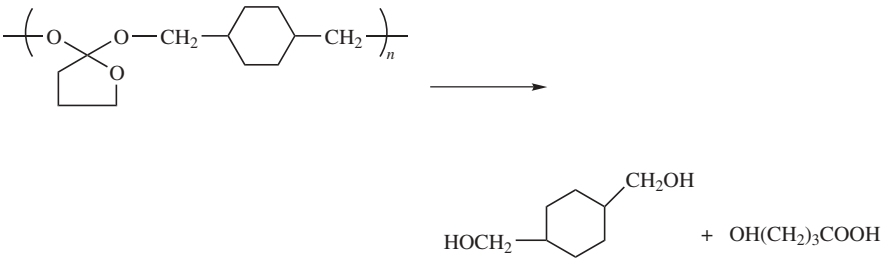


Polymers, where $x = 6$, 8, and 10, are absorbed within six months; the polymer where $x = 12$ requires over 19 months for complete absorption. Absorption correlates with the water solubility of the starting amidediol monomers. All are at least sparingly soluble except for the $x = 12$ amidediol which is virtually insoluble. *In vivo* strength retention of poly(ester–amides) in fiber form is greatest for the $x = 12$ polymer. This material loses very little strength for four weeks then slowly decreases to 50% strength at 8–10 weeks depending on molecular weight and fiber processing conditions.

The metabolic rate of poly(ester–amide) where $x = 6$ has been studied in rats using carbon-14 labeled polymer. This study indicates that polymer degradation occurs as a result of hydrolysis of the ester linkages whereas the amide linkages remain relatively stable *in vivo*. Most of the radioactivity is excreted by urine in the form of unchanged amidediol monomer, the polymer hydrolysis product (49).

6.10. Poly(orthoesters). The degradation of a bioresorbable polymer occurs in four stages: hydration, loss of strength, loss of integrity, and loss of mass. This typical behavior limits most of the previously mentioned polymers for use as matrices for slow release drug delivery implants because incorporated drugs that are water soluble have been found simply to leach out at a first-order rate. Thus bioabsorbable polymers which are extremely hydrophobic have been developed to prevent hydration yet still possess hydrolytically unstable linkages. This results in degradation of polymer on the exposed surfaces only thereby releasing the drug content at a more uniform rate. Such polymers have been termed bioerodible.

Poly(orthoesters) represent the first class of bioerodible polymers designed specifically for drug delivery applications (50). *In vivo* degradation of the polyorthoester shown, known as the Alzamer degradation, yields 1,4-cyclohexanedimethanol and 4-hydroxybutyric acid as hydrolysis products (51).



6.11. Poly(anhydrides). Poly(anhydrides) are another class of synthetic polymers used for bioerodible matrix, drug delivery implant experiments. An example is poly(bis(*p*-carboxyphenoxy)propane) (PCPP) which has been prepared as a copolymer with various levels of sebacic anhydride (SA). Injection molded samples of poly(anhydride)/drug mixtures display zero-order kinetics in both polymer erosion and drug release. Degradation of these polymers simply releases the dicarboxylic acid monomers (52). Preliminary toxicological evaluations showed that the polymers and degradation products had acceptable biocompatibility and did not exhibit cytotoxicity or mutagenicity (53).

7. Shape Memory Alloys

TiNi shape memory alloy (SMA) has attracted much attention for biomedical applications such as implants (bone plate and marrow needle) and for surgical and dental instruments, devices and fixtures, such as orthodontic fixtures and biopsy forceps (see Shape Memory Alloys). This is due to its excellent biocompatibility and mechanical characteristics. Research on biomedical applications of SMA was started in the 1970s with animal experiments initially, followed by clinical tests. The first example of successful biomedical and dental applications of SMA are available and many new applications are being developed.

SMAs' properties which led to their wide acceptance in biomedical applications include biocompatibility, superelasticity, shape memory effect, hysteresis, and fatigue resistance (54). Studies show that TiNi has superior corrosion resistance, due to the formation of a passive titanium-oxide layer (TiO_2) similar to that found on Ti alloys. This oxide layer increases the stability of the surface layers by protecting the bulk material from corrosion and creates a physical and chemical barrier against Ni oxidation.

7.1. Shape Memory Effect. Pre-deformed SMAs have the ability to remember their original shape before deformation and are able to recover the shape when heated if the plastic deformation takes place in the martensite phase (55,56). The shape recovery is the result of transformation from the low-temperature martensite phase to the high-temperature austenite phase when it is heated. The shape memory effect makes it easy to deploy an SMA appliance in the body and makes it possible to create a pre-stress after deployment when necessary. That is, the SMA appliances are first packed up in a compact state during deployment and then restored to its expanded shape by means of heating. If the phase transformation temperature of an SMA is below the body temperature, the heat of the body can easily induce shape recovery. In the case where the phase transformation temperature is higher than body temperature, the SMA appliances are usually heated by warm salt water or a high frequency magnetic field.

The shape memory effect has been utilized also for actuator functions in medical applications as a urethral valve and artificial sphincter.

7.2. Superelasticity. SMAs exhibit superelasticity when they are in the austenite phase (54,56). Figure 7 shows the typical superelastic stress–strain curve (solid line) compared with the stress–strain curve of stainless steel (dashed line). An important feature of superelastic materials is that they exhibit constant loading and unloading stesses over a wide range of strain.

As shown in Figure 7, the effective strain range Σ_{eff}(TN) of TiNi corresponding to an optimal force zone is much larger than Σ_{eff}(SS) of stainless steel. Hence, a superelastic device can provide a constant pressing force even if the pressed part recedes by a limited amount during the installed period. On the contrary, the pressing force of the appliance made from stainless steel will drop drastically if the pressed part deforms, so that the performance will deteriorate. An orthodontic arch wire was the first product to take advantage of this property. This characteristic is put into use in superelastic eyeglass frames (57). These eyeglass frames have become very popular in the United States, Europe and Japan, and are available in almost every optician's store. These frames can be twisted a full

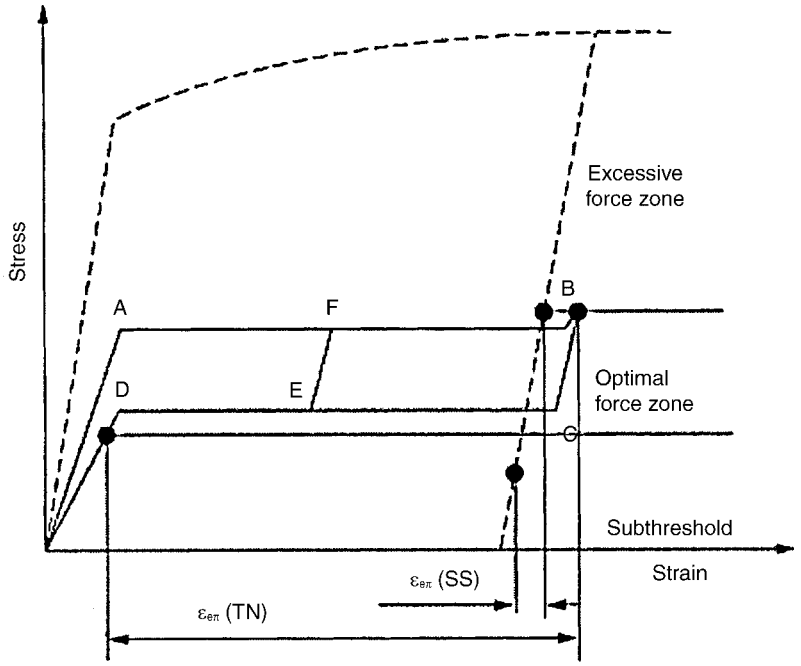


Fig. 7. Typical stress–strain curve of superelastic materials and stainless steel. The superelastic materials exhibit constant unloading stress over a wide range of strain.

180°, but more importantly the frames press against the head with a constant and comfortable stress not only is "fit" less important, but small bends and twists that may develop do not cause discomfort to the wearer.

The superelasticity of SMAs makes it easy to depoly SMA stents. Stents made from stainless steel are expanded against the vessel wall by plastic deformation caused by the inflation of a balloon placed inside the stent. TiNi stents, on the other hand, are self-expanding.

7.3. Hysteresis of SMA. Superelastic SMA demonstrates a hysteretic stress–strain relationship (see Fig. 7), that is, the stress from A to B in the loading phase and the stress from C to D in the unloading are different. Hysteresis is usually regarded as a drawback for traditional engineering application, but it is a useful characteristic for biomedical applications. If the SMA is set at some stress–strain state, for example E, upon unloading during deployment, it should provide a light and constant chronic force against the organ wall even with a certian amount of further strain release (eg, from E to D). On the other hand, it would generate a large resistive force to crushing if it is compressed in the opposite direction, since it takes the loading path from E to F. Hence, the SMA material exhibits a biased stiffness at point E, which is very important in the design of the SMA stent. Since the stress at the loading phase from A to B and the stress in the unloading phase from C to D depends on the material composition of the SMA, the desirable stress–strain curve can be obtained optimizing material composition.

7.4. Anti-kinking Properties. The stress of stainless steel remains nearly constant in the plastic region (see Fig. 7). This means that a small increase of stress in the plastic region could lead to a drasticincrease of strain or the failure of the medical appliance made from stainless steel (54). On the other hand, the stiffness of superelastic TiNi increases drastically after point B at the end of the loading plateau. The increase in stiffness would prevent the local strain in the high strain areas from further increasing and cause the strain to be partitioned in the areas of lower strain. Hence, strain localization is prevented by creating a more uniform strain than could not be realized with a conventional material.

7.5. Applications. *Orthopedic Marrow Needles.* Figures 8 and 9 show two types of marrow needles, which are used in the repair of a broken thighbone (55,57–59). When the Kunster marrow needle of stainless steel is used, the blood flow inside the bone can be blocked and recovery can be delayed. It also has the drawback of low torsional strength. On the other hand, a Kunster marrow needle of SMA can be inserted into the bone in its initial straight shape and turned to curved shape by heating as shown in Figure 8. The Kunster marrow needle shown in Figure 9 has a complicated shape for the purpose of reinforcement, which makes it difficult to insert the needle in the broken bone. Using the shape memory effect, insertion can be greatly improved as shown in the figure, without loosing the reinforcing function, because the needles can be inserted in a

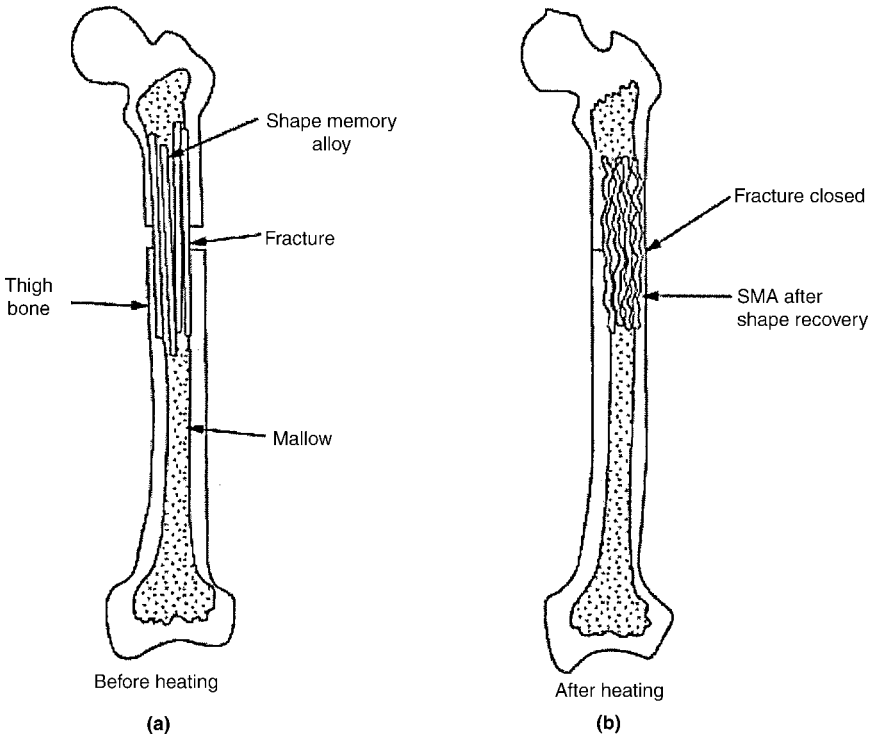


Fig. 8. Kunster marrow needle (57).

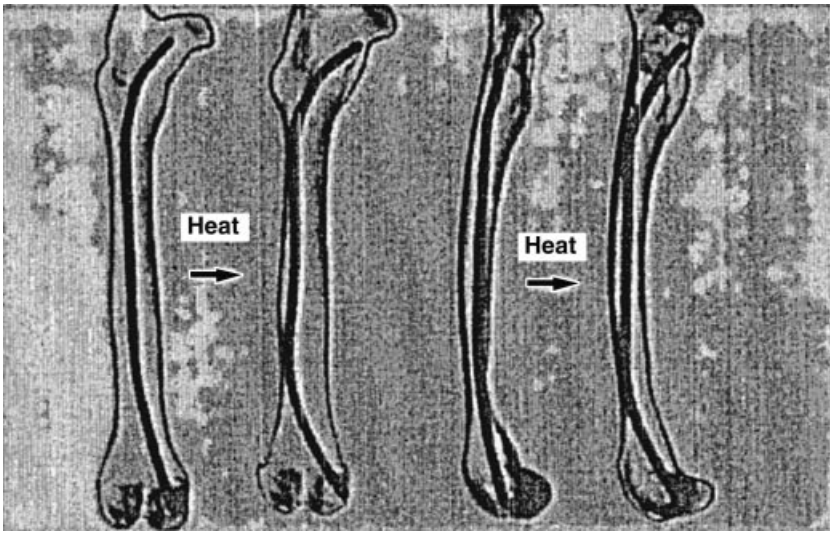


Fig. 9. Marrow needles before and after heating (56,59).

simpler shape and the necessary size and shape are recovered by heating the needle in the marrow.

Currently available joint prostheses are made of bone cement to be fixed in the bone. Stress acting on the joint prosthesis is quite intense and severe; three to six times the body weight of the patient under nominal action and under such stress being cycled up to 10^6 times. Conventional bone cement causes several inconveniences: gradual loosening after implantation and resultant infection and other complications. The prosthetic joint made of TiNi SMA was developed to avoid such problems. High wear resistance is also another advantage of the TiNi prosthetic joint.

Bone Staple and Bone Plate. Bone staple and bone plate are used to fix broken bones (55–57). A bone staple (Fig. 10) made of SMA can be inserted at low temperature in holes opened in the bone and then heated by the body temperature to recover its original shape to provide a compressive force in the surfaces of the broken bone. Bone plates are attached with screws for fixing broken bones. Bone plates made of TiNi SMA (Fig. 11) are more effective in connecting the

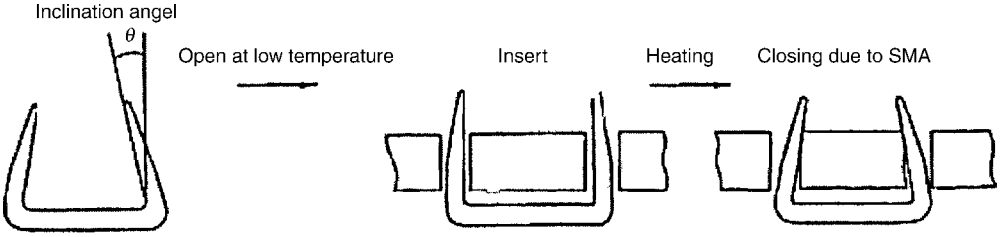


Fig. 10. Bone staple used to fix broken bones (55,57)

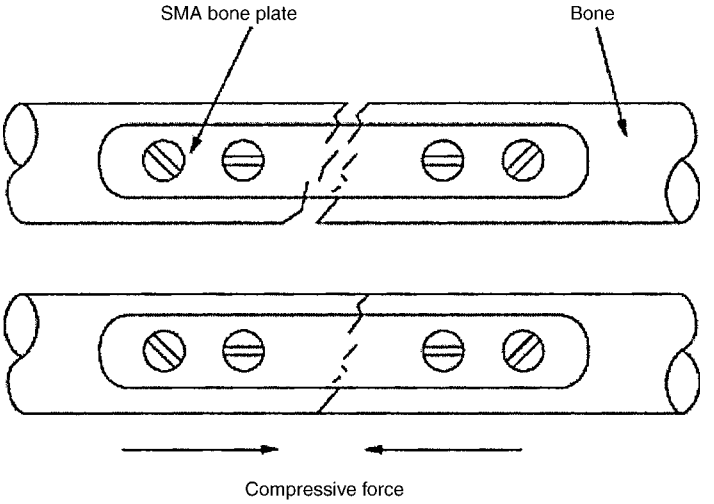


Fig. 11. Bone plate used to fix broken bones (55–57).

broken bones than the bone plates made of conventional material because the SMA bone plates can provide compressive force on the fracture surface of the broken bones as well as a repair as shown in Figure 11. Healing proceeds faster under uniform compressive force.

Dental Applications. Owing to its superelasticity, TiNi has found many applications in dentistry. It is obvious that superelasticity presents the orthodontists with better mechanical characteristics as compared to the conventional elastic materials such as stainless (56,60). When fixtures made of conventional elastic material such as stainless steel are used, the reforming force drops and the fixture loosens with the movement of the teeth. Hence, the fixture must be replaced several times before the treatment is finished. When SMA fixture is used, it can maintain a constant reforming force in a wide range of teeth movement owing its superelasticity so that no future replacement is required after the initial installation. Clinical results show also a faster movement of the teeth and a shorter chair time as compared with stainless steel wire.

Among the methods for restoring the mastication funtion of patients missing more than one tooth, a teeth-root prosthesis is considered to be the method that creates the most natural mastication function. Blade-type implants made of TiNi SMA have been used of Japan (56,57). The open angle of the blade is used to ensure a tight initial fixation and to avoid accidental sinking on mastication. But to make the insertion operation easy, a flat shape teeth-root prosthesis is implanted in the jaw-bone and then the opened shape is changed by heating.

The key to partial denture is the development of an attachment used for connecting the partial denture with the retained teeth for which clasps have been conventionally used. One of the drawbacks of clasps made of conventional elastic materials is loosening during use; this can be improved by replacing the elastic materials with a superelastic. TiNi alloy (56,61). Another drawback of clasps is of esthetic nature, since they are visible with the teeth alignment. In order to overcome this problem the size of the attachment must be smaller

than the width of the teeth so that it can be embedded in the teeth completely. A precision attachment using a small screw has recently become available, but they have to be designed and fabricated very precisely so that they lack the flexibility to follow the change in the setting condition due to the shape change of the jawbone during long-term use. Because of its flexibility, using an attachment made of SMA can solve this problem. The SMA attachment consists of two parts: the fixed part, which is made of a conventional dental porcelain-fusible cast alloy and attached to the full cast crown on the anchor teeth, and the movable part, which is made of TiNi SMA and fixed on the side of the partial denture.

Surgical Instruments. Since superelastic tubing became available in the early to mid 1990s, a variety of catheter products and other endovascular devices using TiNi have appeared on the market. Early applications of TiNi are retrieval baskets with TiNi kink-resistant shafts, as well as a superelastic basket to retrieve stones from kidneys, bladders, bile ducts, etc. An interesting example is the interaortic balloon pump (IABP) used in cardiac assist procedures. The use of NiTi has allowed reduction in the size of the device compared with the polymer tube based designs, and increased the flexibility and kink resistance compared with stainless steel tube designs (54).

Biopsy forceps made from stainless steel are very delicate instruments that can be destroyed by even very slight mishandling. TiNi instruments, on the other hand, can handle considerable bending without buckling, kinking or permanent deformation. For example, a 1.5 mm biopsy forcep that consists of a thin wall TiNi tubing together with a TiNi actuator wire inside are able to be bent around a radius of less than 3 cm without kinking, and still allow for the opening and closing of the distal grasper jaws without increased resistance. The instrument continues to operate smoothly even while bent around tortuous paths.

Stent. The term stent is used for devices that are used to scaffold or brace the inside circumference of tubular passages or lumens, such as the esophagus bilary duct, and most importantly, a host of blood vessels including coronary, carotid, iliac, arota and femoral arteries (54). Stenting in the cardiovascular system is most often used as a follow-up to balloon angioplasty, a procedure in which a balloon is placed in the diseased vessel and expanded in order to reopen a clogged lumen. Ballooning provides immediate improvement in blood flow, but 30% of the patients have restenosed within a year and need further treatment. The placement of a stent immediately after angioplasty has been shown to significantly decrease the propensity for restenosis. Stents are also used to support grafts, eg, in the treatment of aneurysms.

Most stents today are stainless steel and are expanded against a vessel wall by plastic deformation caused by the inflation of a balloon placed inside the stent. TiNi stents, on the other hand, are self-expanding. They are shape-set to the open configuration, compressed into a catheter, then pushed out of the catheter and allowed to expand against a vessel wall. Typically, the manufactured stent outer diameter is about 10% greater than the vessel in order to assure that the stent anchors firmly in place. The flexibility of TiNi is about 10–20 times greater than the stainless steel and can bear as high as 10% reversible strain. The NiTi stenta are made of knitted or welded wire, laser cut or photoetched sheet, and laser cut tubing. The preferred devices are laser cut tubing avoiding overlaps and welds.

7.6. Applications Under Development. *Artificial Urethral Valve.* Urinary incontinence is the involuntary discharge of urine caused by the weakness of the urinary canal sphincter muscles due to aging and the expansion of the prostate gland. An artificial urethral valve system driven by an SMA actuator is a potential solution to the problem (62).

The artificial urethral valve should be compact, should have no protrusions so it could be easily implanted in the lower abdominal and attached onto the urethra. A compact cylindrical such valve of stainless steel shells and a circular-arc nitinol plate is currently being considered (Fig. 12). The valve can be opened by the actuation of a SMA element, which is cylindrical at body temperature and goes flat with increased heat. The valve is closed by the force of the bias spring in the normal state and opened to release the choked urethra and allow urinary flow. To heat the SMA, a nicrome wire , insulated with a polyimide membrane, is placed on the surface of the nitinol plate.

The energy to drive an in-dwelled valve is supplied from outside the body by a transcutaneous energy transformer system (63,64)

Artificial Sphincter. Similar to the urethral value, the development of an artificial sphincter is required for medical treatment of patients with fecal incontinence due to a colostomy, congenitally anorectal malformation or surgical operations for anorectal diseases. The lack of anal sphincter is the main reason

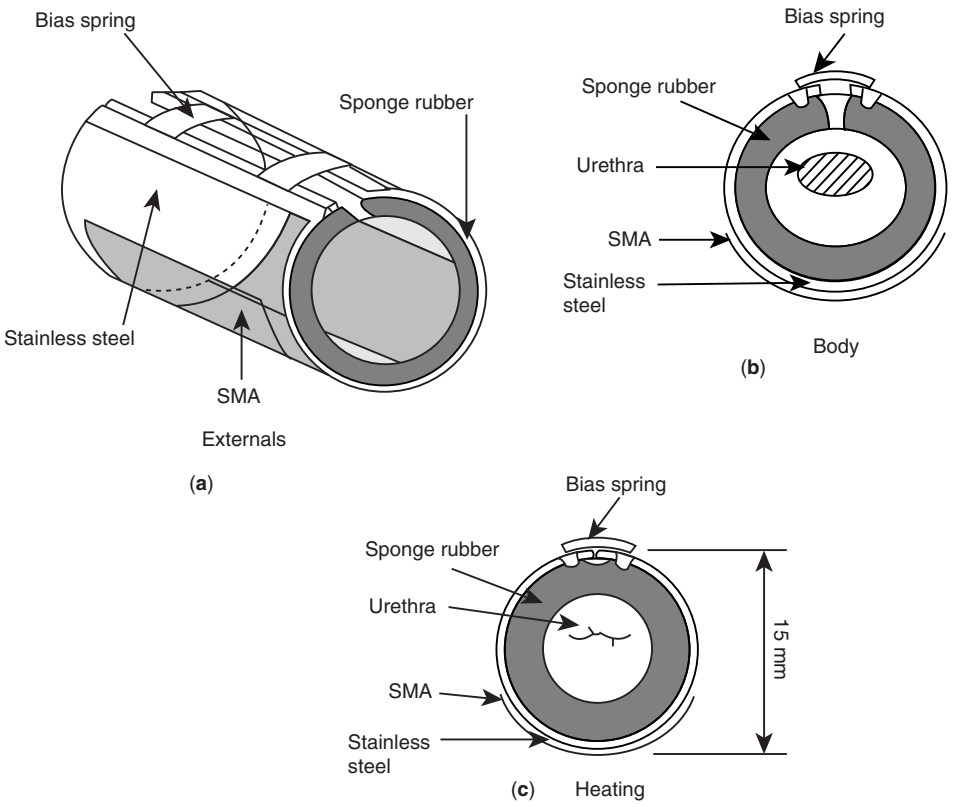


Fig. 12. Geometry of urethral valve: (**a**) externals; (**b**) body; (**c**) heating.

for the problem. An artificial sphincter using SMA actuator is one of the solutions to this condition (65).

A proposed such actuator consists of two SMA plates joined by two hinges and heating coils attached to the SMA plates. The material used for the SMA plates, Ti51at % Ni, is known to exhibit an all-round shape memory effect (ARSME), ie, shows a shape change reverse to the "memorized" one in its martensitic phase. Since the highest temperature for the complete reverse transformation might reach 55°C, thermal insulated materials; cork sheets and sponge rubber sheets are covered at the outer and inner sides of the SMA plates respectively. When electric power is applied to the coils for heating, the reverse transformation occurs in the SMA plates, accompanied by a shape changes from a flat shape to an arc, ie, the restrained shape during annealing. The shape change results in a gap between two SMA plates for opening the intestines. After switching off the electric power, the shape of the SMA plates is recovered by natural cooling, and the intestines will be closed again.

7.7. Piezoelectric Materials and Sample Applications. Piezoelectrical material can convert a mechanical signal to an electric signal (See SMART MATERIALS). Electrical voltage generated by mechinical stress in piezoelectric materials decays very fast due to the charge dissipation. The voltage signal takes the form of a very brief potential wave at the onset of the applied force, and a similar brief wave at termination. It increases with an applied force but drops to zero when the force remains constant. There is no response during the stationary plateau of the applied stimulus. Voltage drops to a negative peak as the pressure is removed and subsequently decays to zero (66). The response is quite similar to the response of the Pacinian corpusclein the human skin (67), one of the sensory receptors in the dermis. In addition PVDF[poly(vinylidence fluoride)] piezofilm is suitable for uses in the biomedical field, since it is very flexible and sensitive to the fast variation of the stress or strain. This section reviews several recent studies on medical applications of PVDF film.

Active Palpation Sensor for Detecting Prostatic Cancer and Hypertrophy. Prostatic carcinoma and hypertrophy are examined in general by the rectal palpation using the doctor's index finger as a probe together with ultrasonic tomography. The morphological features of the two lesions typical to these conditions are key in their diagnosis. The prostatic hypertrophy is a symmetric enlargement of the prostate glands with the stiffness varying from soft to hard. Prostatic cancer, on the other hand, assumes a hard asymmetrical uneven tumor. The palpation depends on the tectile perception of the forefinger, which is said to be ambiguous, subjective, and much affected by the physician's experiences. The development of a palpation sensor for detecting the prostatic cancer and hypertrophy is, hence, important.

The tip probe of the active palpation sensor is mounted on a linear z-translation aluminum bar, which fits into acylindrical outer aluminum shell by a DC micro motor and crank mechanism (Fig. 13). The mechanism for driving is essentially the same as that of an electric toothbrush. The oscillating probe is positioned with its face to the prostate gland.

The probe is an assembly of layered media. The base is a thin aluminum circular plate of 10 mm diameter, on which a cylindrical sponge rubber, a PVDF piezopolymer film of 6 mm across and 28 μm thick as the sensory receptor,

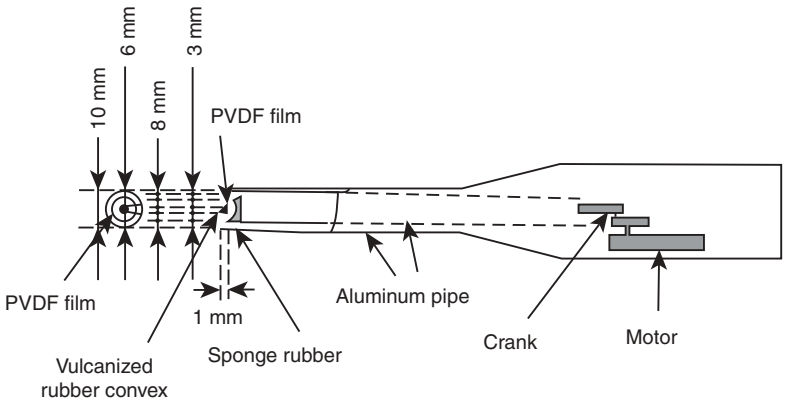


Fig. 13. Active palpation sensor that has a recessed sensor head.

and a thin acetate film as the protective agent of piezopolymer film are stacked in sequence (68). The sensor head is pressed sinusoidally against the object and the output signal from the piezopolymer film is collected and sent to a digital storageoscilloscope and further forwarded to a personal computer for processing.

The output voltage from the piezopolymer film is proportional to the rate of the straininduced in the film, which means that the maximum amplitude of the signal from the sensor is rather superposed by noises from the measuring system. Data analysis can be then performed by using the absolute output signal of the sensor integrated over the period of data collection.

Haptic Sensor for Monitoring Skin Conditions. Skin health and its appearance are related to its morphological features such as rashes, chaps or wrinkles. Assessment of the pharmacological action of liniments on skin disease is a matter of importance, which has drawn much attention to the development of objective techniques for measuring morphologic features of skin (69). The evaluation of cosmetic efficacy of toiletries is another use of objective measuring techniques. Noninvasive technology has made great progress in the studies of dermatology during the last decade. Several methods have been developed to measure the mechanical properties of the dermis including the measurement of transepidermal water loss using evaporimeter (70) and the image processing of an egative replica of dermis (71). Those methods, however, fall under the category of indirect measuring techniques of dermis. In this section the development of haptic tribosensors for monitoring skin conditions and distinguishing atophic and normal healthy skins directly are introduced.

Tribo-sensor. A tactile sensor for the measurement of skin surface conditions is a layered medium, the construction of which is analogous to the human finger (Fig. 14). It is composed of an aluminum shell as the phalanx, a sponge rubber as the digital pulp, a PVDF piezopolymer film of 28 μm thick and 12 mm across as the sensory receptor, an acetate film as the protective agent of piezofilm, and a gauze on the surface as the fingerprint that enhances the tactile sensitivity of the sensor. The sensor is attached onto the tip of an acrylic elastic beam and a strain gauge is mounted on the surface of the beam to monitor the applied force to the skin from the sensor.

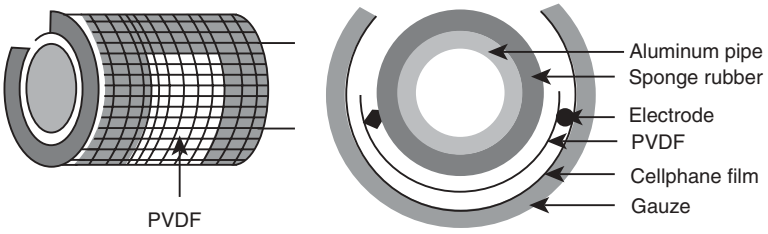


Fig. 14. Schematic of PVDF piezofilm sensor.

The sensor in the tribosensor measurement system is moved by hand over a skin sample, attempting to maintain a constant speed and force (Fig. 15). The voltage signal from the PVDF sensory film is sent to a digital storage oscilloscope and then transmitted to a personal computer for signal processing. It is necessary to reduce the potential difference between the surface of the skin and the sensor to minimize the overlap of noises on the sensor signal during measurement. To achieve this, the subject and the sensor are grounded and a band-pass filter is inserted after the sensor to remove noises from the power sources. During skin identification and signal processing, an area of infected skin of a subject is compared with the skin of healthy subjects. A method of identifying skin samples employing signal processing and neural network-based training is then introduced.

The material in this section on shape memory alloys has been adapted from the longer article that appears in Ref. 72.

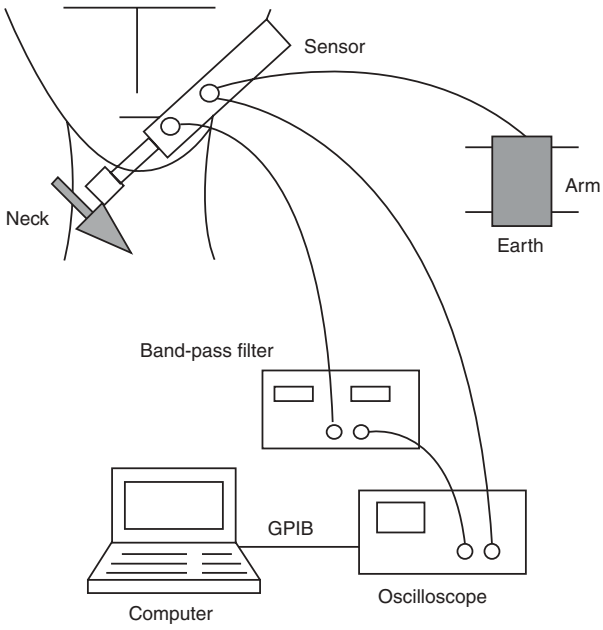


Fig. 15. Setup of measuring instruments.

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