Biomedical Inspiration-Concept and applications: Organ system- Circulatory- artificial

blood, artificial heart, pacemaker. Respiratory- artificial lungs. Excretory- Artificial kidney

and skin. Artificial Support and replacement of human organs: artificial liver and pancreas.

Total joint replacements- artificial limbs. Visual prosthesis -artificial eye/ bionic eye

An artificial organ is a man-made device that is implanted or integrated into a human body to

replace a natural organ or restoring a specific function so the patient may return to as normal

a life as possible. They can be used both for functions that are essential to life and also for

purposes that are not related to survival but do improve a person's quality of life. The organs

that can be replaced artificially are quite numerous (including the ears, ovaries, and even the

heart and brain), eg. artificial heart, pacemaker, artificial kidney machine, heart-lung

machine, etc. Perhaps the most common manifestation of an artificial organ is hearing aids

that are used to improve a person's ability to hear and distinguish sounds.

The reasons to construct and install an artificial organ might include:

 Life support to prevent imminent death while awaiting a transplant (e.g. artificial

heart)

 Dramatic improvement of the patient's ability for self care (e.g. artificial limb)

 Improvement of the patient's ability to interact socially (e.g. cochlear implant)

 Cosmetic restoration after cancer surgery or accident

Previously, an artificial organ would be created completely out of synthetic material, such as

plastics or metals. These mechanical organs had some problems, such as difficulty replacing

all the functions of a biological organ and a tendency to only work on a temporary basis. A

significant amount of current research focuses on biological or hybrid bio-mechanical

material and processes.

The main goal is to develop and define technologies that will maintain, improve or even

restore the function of diseased organs. The organ assistance and substitution devices will play a larger role in managing patients with end-stage disease by providing a bridge to recovery or transplantation.

A thorough knowledge of the physical, chemical and flow properties of blood is essential for

understanding and modeling capillary transport phenomena and circulatory system dynamics

in the body. Similarly, in the design and development of extracorporeal devices (i.e., those

external to the body) such as artificial kidneys, blood oxygenators and blood pumps, the same

knowledge is critical. Many of the major practical problems involved in artificial organ

applications result, in fact, from the sensitivity of blood to the unfamiliar shear stresses

imposed by such devices, stress that cause blood cell rupture and clotting problems.

[Man-made devices designed to replace, duplicate, or augment, functionally or cosmetically,

a missing, diseased, or otherwise incompetent part of the body either temporarily or

permanently, and which require a non-biologic material interface with living tissue.].

Design considerations and evaluation process:

Artificial organs can only replace those bodily functions which have been incorporated into

their design. Therefore, in the design of an artificial organ, the first task is to establish the

specification for the device i.e. the function or functions which must be fulfilled by a human-

made construct and the physical constraints that apply because the device must interface with

the human body.

Defining specifications and constraints is the first step in the conceptualization of an artificial

organ. Only when this is done can one think realistically about design alternatives, the

limitations of available materials, and the clinical constraints which will apply, of which the

key ones are connections to the body and duration of expected service.

Once all these considerations have been integrated, the next step is typically the construction

of a prototype. Ideally the device should achieve everything it was expected to do, but usually

it exhibits some level of performance and durability which falls short of design specifications,

either because of some misjudgement in terms of required function or because of some

unanticipated problem arising at the interface between the device and the body.

The following step of development may be called optimization. At this point, new

experiments are needed to establish the reliability and effectiveness of the device in animal

models. This is the stage of validation of the device, which is first conducted in acute

experiments and must later be extended to periods of observation approximating the duration

of intended use in humans.

The final stage of design, for many artificial organs, is individualization, that is, the ability to

fit the needs of diverse individuals. Human come in a wide range of body sizes. In some

cases, the prostheses must fit very strict dimensional criteria, which imply that they must be

fabricated over an extended range of sizes.

Evaluation process:

The evaluation process of an artificial organ typically is done in six phase:

1. In vitro bench testing

2. Ex vivo appraisal

3. In vivo studies with health experimental animals

4. In vivo studies with animal models of disease

5. General clinical use.

Artificial heart

An artificial heart is a prosthetic device that is implanted into the body to replace the function

of original biological heart. It is distinct from a cardiac pump, which is an external device

used to provide the functions of both the heart and the lungs. Thus, the cardiac pump need not

be connected to both blood circuits.

A total artificial heart (TAH) is a device that replaces the two lower chambers of the heart.

These chambers are called ventricles. Heart failure is a condition in which

the heart can't pump enough blood to meet the body's needs. "End stage" means the condition

has become so severe that all treatments, except heart transplant, have failed. (A heart

transplant is surgery to remove a person's diseased heart and replace it with a healthy heart

from a deceased donor.).

One of the best known devices is the "Jarvik-7" artificial heart, named for its designer Robert

K. Jarvik, an American physician. Designed to function like the natural heart, the Jarvik-7 has

two pumps (like the ventricles), each with a disk-shaped mechanism that pushes the blood

from the inlet valve to the outlet valve.

The action of the artificial heart is entirely similar to the action of the natural heart. There is,

however, one huge difference: the natural heart is living muscle, while the artificial heart is

plastic, aluminum, and Dacron polyester. As a result, the artificial heart needs some external

source of "life." An external power system energizes and regulates the pump through a

system of compressed air hoses that enter the heart through the chest. Since the system is

cumbersome and open to infection, the use of an artificial heart is meant to be temporary.

Artificial hearts are typically used to bridge the time to heart transplantation, or to

permanently replace the heart in case heart transplantation is impossible.

Engineering design:

Designing is the intellectual attempt to meet certain demands in the best possible way. It is an

engineering activity that impinges on nearly every sphere of human life, relies on the

discoveries and laws of science, and creates the conditions for applying these laws to the

manufacturer of useful products. The engineering design process can be broken down into at

least four stages:

1. Define the problem - clarification of the task.

1.1 Fit of the system – the device must first “fit” the patient. One must consider the

volume and mass of the device, as well as any critical dimension such as the

length, width, or height and the location of any tubes, conduits or connectors. The

device should not project heat in such a way that surface in contact with tissue or

blood are subjected to a temperature rise 50C above core temp. on a chronic basis.

The effect of device movement and vibration should be considered in the design

specification. The acceptable sound levels at various frequencies must be specific.

A device should meet existing standards for electromagnetic interference and

susceptibility.

1.2 Pump performance –pump performance must be specified in terms of cardiac

output range. A heart assist or total artificial heart device must be able to pump a

cardiac output ranging up to 8 litres/min with physiologic inlet and outlet artery

pressure.

1.3 Biocompatibility- the device must not cause excessive damage to the biologic

system. Specifically, the device must be minimally thrombogenic and haemolytic.

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It should have a minimal effect on the immune system. It should not promote

infection, calcification, or tissue necrosis.

1.4 Reliability- the design specification must assign a target reliability for the device.

The design specification must state which components of the system could be

changed if necessary. The reliability issue is very complex and involves moral,

ethical, legal, and scientific issues.

1.5 Quality of life-the design specification must address the quality of life for the

patient.

2. Conceptual design – plan treatment

3. Detailed design – execute the plan

4. Learn and generalize – finally, after the design is complete, the designer should be

able to learn and generalize from the design. This educational process will include

manufacturing of prototypes and testing. General concepts and principles may be

gleaned from the design process that can be applied to further designs.

Circulatory assist devices were initially designed to support patients in hemodynamic

collapse, but are now used for a wide range of clinical conditions ranging from prophylactic

insertion for invasive procedures to cardiogenic shock or cardiopulmonary arrest. There are

three major types of percutaneous devices (as well as surgically-implanted ventricular assist

devices):

 Counterpulsation devices (intraaortic balloon pump [IABP] and noninvasive

counterpulsation)

 Cardiopulmonary assist devices (Cardiopulmonary support or CPS)

 Left ventricular assist devices (eg, Impella)

An intra-aortic balloon pump (IABP) is a mechanical device that is inserted into the aorta,

the body's largest artery. It is a long, thin tube called a catheter with a balloon on the end of it.

It is used to assist the heart to pump more blood around the body and also improves the

delivery of oxygen to the heart.

The IABP is the most commonly used mechanical support device. It has a long clinical record

of success, is simple, is inserted easily and rapidly, is the least expensive of all the devices,

and does not require constant monitoring by technical support personnel.

Cardiac catheterization

Cardiac catheterization (KATH-eh-ter-ih-ZA-shun) is a medical procedure used to diagnose

and treat some heart conditions. Cardiac catheterization involves passing a thin long flexible

tube (catheter) into the right or left side of the heart, usually from the groin or the arm.

Through the catheter, doctor can do diagnostic tests and treatments on heart. The test may last

30 - 60 minutes.

For example, doctor may put a special type of dye in the catheter. The dye will flow through

your bloodstream to heart. Then, doctor will take x-ray pictures of heart. The dye will make

coronary (heart) arteries visible on the pictures. This test is called coronary angiography

. The dye can show whether a waxy substance called plaque (plak) has built

up inside coronary arteries. Plaque can narrow or block the arteries and restrict blood flow to

heart. The build up of plaque in the coronary arteries is called coronary heart disease (CHD)

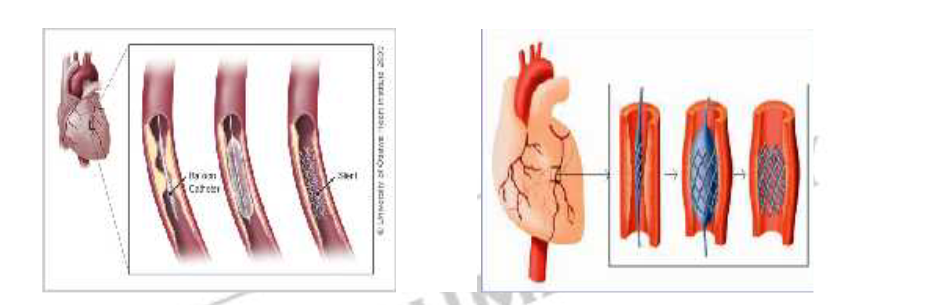
or coronary artery disease.

Stent: A stent is a small mesh tube that's used to treat narrow or weak arteries. Arteries are

blood vessels that carry blood away from heart to other parts of the body. A stent is placed in

an artery as part of a procedure called percutaneous coronary intervention

(PCI), sometimes referred to as coronary angioplasty. PCI restores blood flow through narrow or blocked arteries. A stent helps support the inner wall of the artery in the months or years after PCI.



**Artificial blood:**

Artificial blood can be defined as a liquid that can carry large amounts of oxygen and can

serve as a temporary substitute for blood. Artificial blood also called “blood substitutes” that

are used to fill fluid volume and/or carry oxygen and other gases in the cardiovascular

system.

Blood substitutes can be divided into two categories:

A. Volume expanders: inert and merely increase blood volume. These may be crystalloid-

based (Ringer's lactate, normal saline, D5W (dextrose 5% in water)) or colloid-based

(Haemaccel, Gelofusin).

B. Oxygen therapeutics: mimic human blood's oxygen transport ability. Examples:

Hemopure, Oxygent, PolyHeme.

Artificial blood is supposed to fulfill some functions of biological blood, especially in

humans. The oxygen transport function of blood is most important and it is very difficult to

reproduce. The initial goal of oxygen carrying blood substitutes is merely to mimic blood's

oxygen transport capacity. Artificial blood based on oxygen therapeutics are broken into two

categories: (a) haemoglobin solutions and (b) perfluorocarbon (PFC) emulsions.

**Haemoglobin solutions:**

Hb derived from humans, animals or artificially via recombinant technology. Different types

of haemoglobin solutions: (i) purified Hb solution & (ii) modified Hb solutions : (a)

polymerized Hb, (b) polymer conjugated Hb (P-L-P conjugated polymerized Hb), (c) intra-

molecular cross-linked Hb (DCL Hb- diaspirin cross-linked Hb), (d) recombinant Hb ( a few

parts of an amino acid sequence of human Hb are replaced to prevent the dissociation into

dimmers and to maintain adequate oxygen affinity –γHb 1:1) & (e) Hb vesicles (purified Hb

& lipid – phospholipids encapsulated Hb, eg. PEH, LEH-liposome encapsulated Hb).

Substances called perfluorochemicals (PFC) have the ability to carry oxygen and carbon

dioxide.

**Perfluorocarbons :**

PFC are chemically inert compounds consisting of fluorine-substituted hydrocarbons. It

increases oxygen solubility in plasma and facilitates effortless transport of oxygen in

circulation. Perfluorochemicals will not mix with blood; therefore emulsions must be made

by dispersing small drops of PFC in water. This liquid is then mixed with antibiotics,

vitamins, nutrients, and salts, producing a mixture that contains about 80 different

components, and performs many of the vital functions of natural blood. PFC particles are

about 40 times smaller than the diameter of a red blood cells (RBC). This small size can

enable PFC particles to traverse capillaries through which no RBCs are flowing. In theory

this can benefit damaged, blood-starved tissues, which conventional red cells cannot reach.

PFC solutions can carry oxygen so well that mammals and humans can survive breathing

liquid PFC solution, called liquid breathing.

1st generation PFCs : Perfluorodecalin (PFD, perfluorotrypropylamine (FTPA)

2nd generation PFCs : Perfluorooxtyl bromide (PFOB), Bis (perfluorobutyl) ethylene.

**Liver Support System / Liver Assist Devices (LAD) / Bio-artificial LAD**

Artificial extracorporeal liver support is a detoxification treatment for liver failure patients

and is based / worked on the same principles of hemodialysis. The main aim is to mimic the

primary functions of liver, such as detoxification, synthesis and regulation. The liver support

system is design in such a way that it can able to remove the lipophilic, albumin-bound

substances such as bilirubin, bile acids, metabolites of aromatic amino acids, medium chain

fatty acids and cytokines.

The liver function includes the breakdown, synthesis, modification, storage and regulated

release of carbohydrates, lipids, amino acids, proteins and nucleic acids. It produces bile and

delivers to the intestine for digestion and excretion of wastes.

Bio-artificial liver assist devices apply mechanical principles to the biologically active

models for the “global” replacement of primary liver functions. Among various

configurations, hollow-fiber bioreactors have been actually used in human patient. Hollow-

fiber bioreactors, similar to hemodialysis devices, contain numerous numbers of hollow

fibers of a semipermeable material. Cultured or seed hepatocytes (liver cells / porcine

hepatocytes) are filled in the extracapillary space (ECS) of hollow-fiber bioreactor. These

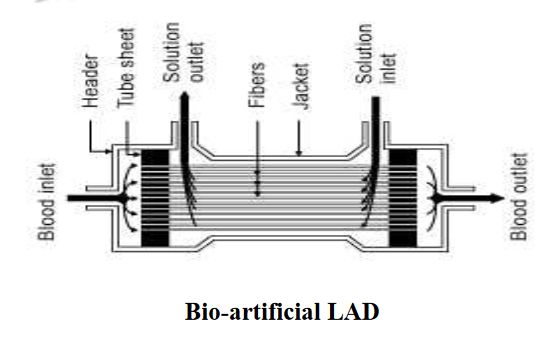
hepatocytes secrete bile that perfuse through the membrane and mixed with patient’s blood or

plasma in the intracapillary space (ICS). A membrane oxygenator and heater are included in

the artificial liver assist devices. The heater keeps the patient’s blood / plasma at body

temperature. The membrane oxygenator provides the house hepatocytes with the oxygen they

require for proper function. A complete operation last for 6 - 8 hours.



Artificial Pancreas (Biopancreas)

The artificial pancreas is a technology developed to help diabetes people. It automatically

controls blood glucose level by providing the substitute endocrine functionality of a healthy

pancreas. There are several important exocrine (digestive) and endocrine (hormonal)

functions of the pancreas, but it is the lack of insulin production, which is the motivation to

develop a substitute.

Different approaches (Different insulin administration systems of artificial pancreas)

under consideration include:

1. The medical equipment approach (Insulin pump) -- using an insulin pump under

closed loop control & real-time data from a continuous blood glucose sensor.

2. The bioengineering approach (The Bio-artificial pancreas): -- the development of a

bio-artificial pancreas consisting of a biocompatible sheet of encapsulated beta cells.

When surgically implanted, the islet sheet will behave as the endocrine pancreas and

will be viable for years.

3. The gene therapy approach -- the therapeutic infection of a diabetic person by a

genetically engineered virus which causes a DNA change of intestinal cells to become

insulin-producing cells.

Bio-artificial pancreas:

This involves harvesting insulin-producing cells from pigs, encapsulating the cells in

dissolvable “microreactors” (a tiny, dissolvable, spherical cage) and then injecting them into

the abdomens of people with diabetes. The microreactors float freely and producing insulin as

needed. This is a living drug-delivery system where pancreatic cells have a biochemical

mechanism that continuously monitors blood glucose, releasing only enough insulin to keep

blood sugar within a normal range. The microreactors permit life-sustaining oxygen and

nutrients to flow in and wastes and insulin to flow out, keeping cells healthy and nourished.

Capillary Bio-artificial Pancreas (Extracorporeal artificial pancreas):

In extracapillary space, pancreatic cells are being cultured. The pancreatic cells are islet of

Langerhans, which secrets hormone insulin and assimilate glucose. Glucose rich blood in

diabetes patient are passed through the capillaries (made of silicone rubber, Teflon, Dacron,

etc.). Glucose from the blood diffuses through the membrane to the extracapillary site and

insulin is released from pancreatic cells and also passes through the membrane into the

intracapillary site. Insulin converts the glucose into glucagons and ultimately, glucose level in

blood decreases by a significant level. The blood is circulated through capillary till the

desired level of glucose in blood is achieved.

**Artificial skin**

Artificial skin is a synthetic covering with two layers for regeneration of skin and is used to

treat burn victims. The material contains microcapsules filled with a special healing agent.

Like human skin, it bleeds and heals itself, offering a potential breakthrough in vital materials

used in surgical implants.

Trancyte is a bilayer skin substitute. Outer epidermal analog is a thin nonporous silicone

film with barrier functions. Inner dermal analog is layered human fibroblast products mainly

collagen type 1,fibronectin and Glycosaminoglycan. Subsequent cryo-preservation destroys

fibroblasts but preserves activity of fibroblast-derived products. Thin water layer at surface is

maintained for epidermal cell migration. It is removed after re-epithelialization (or prior to

skin graft or excised wound). Silicone provides flexibility. It must be kept frozen until use.

Biobrane is a bilayer synthetic skin substitute. Outer epidermal analog constructed of a thin

silicone film with barrier functions comparable to skin Small pores present in silicone to

allow for exudates removal, permeability to topical antibiotics. Inner dermal analog

composed of a three dimensional irregular nylon filament weave upon which is bonded type I

collagen peptides

Surface binding of inner membrane potentiated by collagen-fibrin bonds as well as fibrin

deposition between nylon weave. Subsequently fibronectin, produced by migrated

fibroblasts, enhances binding to the fibrin entrapped in mesh .New epithelial cells growing

along mesh measures adherence. Thin water layer at surface maintained for epidermal cell

migration. Removed after re-epithelialization (or prior to skin graft on excised

wound).Silicone and nylon weave provides flexibility.