

# **PROJECT BIOGEN HEART**

**Submitted by:**

**Vedala's Medical Vision Healthcare Services (VMVHS)  
Engineering Staff College Of India (ESCI)**

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## Introduction

### Vedala's Medical Vision Healthcare Services (VMVHS)

VMVHS is an organization pertaining to medical fraternity doing and rendering medical services, medical awareness projects, technical help and medical Research along with academics and clinical treatment.

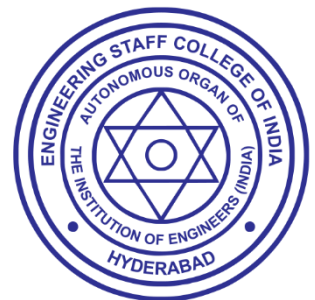
VMVHS has services pertaining to medical development, research about medical innovation and inventions and also added are medical services which are being carried out. This organization has been Present since more than a decade and has been conducting research on many medical diseases. Recently been doing research on invention of a Biogenic heart towards improvement for cardiac problems.

—VMV—  
HEALTH CARE



### Engineering Staff College Of India

Engineering Staff College of India (ESCI) is an autonomous organ of India's largest body of professional engineers, "The Institution of Engineers (India)". ESCI was established in the year 1981 with the mandate of providing quality training and education in engineering and techno management fields. Inspired by innovation and governed by excellent council, ESCI strives to offer high quality proficiency development programmes to engineers from industries, R&D labs, academics, public and private organizations. ESCI conducts programmes in core engineering domains, interdisciplinary fields, and customer-specified interdisciplinary areas and also in cutting edge technologies, at its Hyderabad campus and at customers' premises. Experienced faculty of ESCI, ably complemented by the adjunct faculty and external advisors, conduct training programmes in important fields such as additive manufacturing, climate change, engineering analysis and simulation, quality management, renewable energy, remote infrastructure management, smart grids, Human Resource Management including Soft skills and other management field in project & SCM etc. to induce industry-relevant skills among young engineers. Renowned personalities like Late Dr. APJ Abdul Kalam, Shri R. Venkataraman, Mr. Suresh Pachauri, Lt. Gen. (Dr) V.S. Sundaram, Padmashri Prof. R.M. Vasagam and other eminent engineers, academicians and scholars graced the ESCI's Programmes and enriched them. ESCI's operations are firmly grounded in its desire to act as a bridge between academic institutions, R&D laboratories and organizations in private and public sectors to promote the growth and increased availability of latest know-how and expertise to professional engineers, executives and managers in all these sectors.



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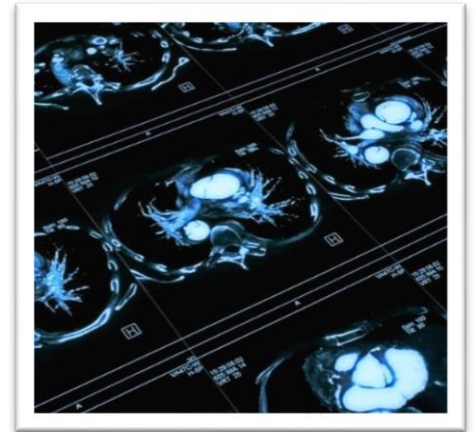
## Project Details:

### TITLE: BIOGEN Heart made using Stem Cells

**Objective:** “To develop an artificial organic & miniature heart & lung system using stem cells which would reduce the burden on the main heart & lungs and also reduce the free radicals.”

#### Introduction:

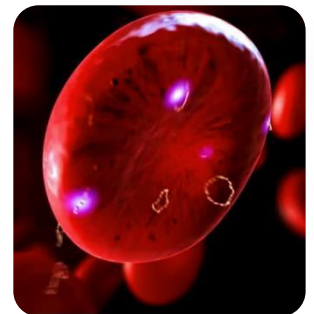
▪ **Image** - The BIOgen Heart, a 3D Bio-printed organ replacement process begins with a MRI procedure with the help of DICOM FILE – (digital imaging and communication in medicine), which is used to create a detailed 3D image of a patient's heart. Using this image a computer software program called Computer assisted design (CAD), will construct a digital model of a new heart for the patient, matching the shape and size of the original heart.

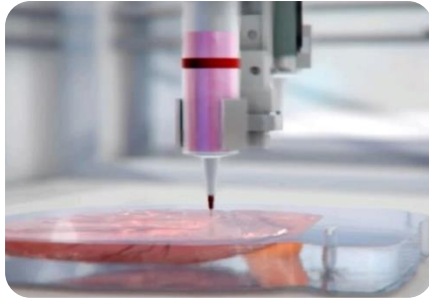


▪ **Cells** – A miniature heart is created through the bio printing process starting with the patient's own stem cells. Doctors take the cells from the patient via blood sample with aseptic precautions by using growth factor (GF) and also leveraging recent stem cells research inventions. The next step is to reprogram those blood cells which are taken and convert them to create specialized heart cells named Cardiomyocytes from the induced pluripotent stem cells (IPS'c). This is done by a process called as differentiation. Heart tissue grown on spinach leaf wherein researchers turn the vascular system of plants to solve a major bioengineering problem blocking the regeneration of human tissues and organs. The scientists turn to plants culturing beating human heart cells on spinach leaf. In this sequence a spinach leaf is stripped of its plant cells, which is a process called decellularisation using a detergent. This process leaves behind the leaf's vasculature. This looks like a shape of SCAFFOLD.



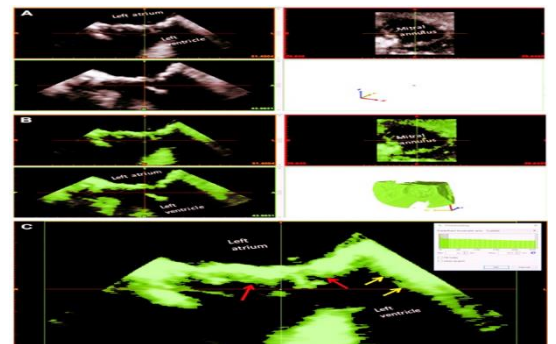
▪ **Ink and Bio printing** - The Bioink is created using specialized heart cells (Cardiomyocytes), combined with nutrients in a liquid environment (hydrogel ) along with other materials which help the cells to survive the bio printing process. The Bioink will then be loaded into a bio printer in a highly specialized 3D Printer designed to protect living cells during 3Dprinting process. This is done by printing one layer at a time, guided by CAD following the specific dimensions obtained from MRI. As the heart cells will not be fused together at this point biocompatible and biodegradable scaffolding will be included. This is done to support the cells and hold them in place.





## ▪ End Process

Step 1 - When the process of procurement of cells is completed the cells will be shifted into a bio reactor which will create the appropriate conditions required for nutrition and oxygen rich environment. The individual cells would begin self-organizing and fusing into networks which will connect to form living healthy tissue. The cells in this tissue will even begin to work in unison and in fact the mass beats.



Step 2- The Bio-printing process is the stage where a miniature heart is developed using Bio-Printer. This heart will remain in the bioreactor until it reaches a desired level of strength and maturity.

Step 3-A successful patient deployment would be then possible under aseptic precautions and minimal anesthesia. This should be carried out by vascular and CT surgeons, with the help of adherent glue. This glue is combination of new heat sensitive gel & glue which will enable blood vessels to be reconnected without puncturing or cutting them with a needle and thread. This is a thermos reversible polymer which is biocompatible. This is named as POLOXAMER 407 which is approved by FDA. Similarly derma bond, which is a surgical sealant, is also used to attach ends of blood vessels together. This is a novel approach to anastomosis which could play a valuable role in microvascular surgery and beating heart surgery instead of suturing, where there is reconstruction of vessels and anastomosis. Suturing work is not





needed at any point, internal or external at the deployment site. The miniature BIOgen heart is aptly fit and a perfect genetic match for the patient and is free from risk of rejection, infection or the need for immunosuppressant therapy which is generally used for organ transplant procedure.

STEP 4- The patient will then be kept under continuous monitoring for evaluation.

### **Key Words:**

**RESPIRATORY PROCEDURE** - We inhale and exhale up to a thousand breaths in a day. The methodology by which a circuit board functions will be exhibited by a tissue which acts as lungs (bronchiolar unit and alveolar unit) which we can name as PULMON breathing, which means mimicking lung functions. Internal respiration is transfer of gas in between blood and cells which are present in the body whereas external respiration is transfer of gas in between lungs and outer environment and external respiration takes place prior to internal respiration. This process shows taking oxygen from the air into lungs and expelling carbon dioxide from the lungs into the air. Internal respiration is called as METABOLIC PROCESS IN WHICH OXYGEN IS RELEASED TO THIS TISSUES AND CARBON DIOXIDE IS ABSORBED BY THE BLOOD, APART FROM THE RELEASE OF ATP (ADENOSINE TRI PHOSPHATE) WHICH IS ENERGY.

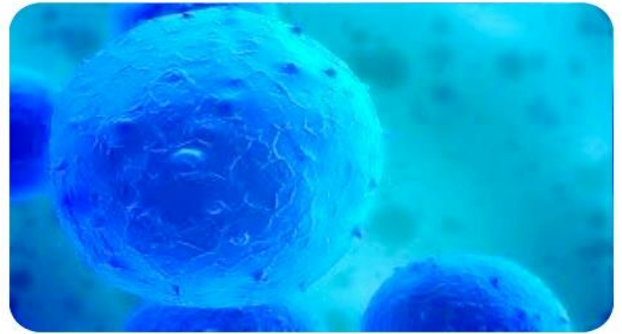
**PACEMAKER** - The pacemaker is an electronic biomedical device which regulates human heart beat. The pumping action is synchronized by pacemakers starting from SA node, AV node and PF. The electrical impulse is created by the diffusion of calcium ions, sodium ions and potassium ions. Pacemakers are created during the bio printing process or if necessary we can incorporate sensors also. SA Node cardiomyocytes function as a biological pacemaker. The pacemaker comprises of few myofibrils.

**TISSUE OXYGEN** - Oxygen is one of the most important keys to good health and its level is hundred percent. Levels below 90 percent are considered to be low. Oxygen is the spark of life which is carried from the lungs to tissues by RBC. When the body has ample oxygen without free radicals, which produces more energy to optimize metabolism and eliminate toxic wastes. Detoxification occurs when oxygen is introduced into the system. Oxygen carries Hemoglobin and iron.

**BIOPRINTING** -Welcome to the age of bio printing - A device pertaining to 3D tissue bio printing will decrease the burden of artificial organs into reality and the latest advance in regenerative medicine with the help of refined CAD software where ink will be used by our own cardiomyocytes. 3D Modelling software are DICOM format or OSIRIX format (it is a viewer which enables you to convert and post process the file into 3D. Other software using are 3D-DOCTOR, MEDICAL DESIGNING STUDIO, OSSA 3D, D2P. 3D Bio printing for fabricating biological constructs typically involves dispensing cells onto a bio compatible scaffold using a successive layer by layer approach to generate tissue like 3 dimensional structure. Post bio printing is done with the help of bio reactor

**CARDIAC MUSCLES** - Cardiac muscle tissue is associated with actin, myosin, troponin and other protein namely MYH7 and LDB3. Cardiac output is related to the quantity of blood delivered to various parts of the body whereas physical exercise requires more oxygen. Cardiac output is measured by stroke volume and heart rate. Therefore Cardiac output (CO) = Stroke volume (SV) \* Heart Rate (HR).

**STEM CELLS** - Stem cells are the foundation for every organ and tissue in our body. There are many different types of stem cells which include ESC- embryonic stem cells which exist only at earlier stages of development, TSS (Tissue specific stem cells) which appear throughout life. The pluripotent stem cells have got affinity to convert into cardiomyocytes. stem cells are preserved under the technology of cryopreservation where cells are susceptible to damage caused by chemical kinetics and are preserved by cooling minus 80 degrees centigrade to minus 196 degree centigrade using liquid nitrogen.



Stem Cells

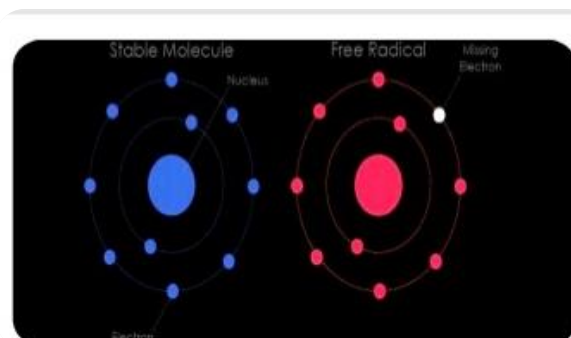
**SCAFFOLD** - It means a framework or structural element that holds cells or tissues together and maintains tissue contour. In our research we are using spinach leaf as a scaffold.

**HEART** - The main aim is to get rid of free radicals from the body through second phase systemic respiration followed by flow of pure oxygen without free radicals with the help of tiny miniature heart which is deployed at the place of the body where a cushion like aponeurosis is present. Aponeurosis is a type of connective tissue which supports the body and helps the body move. This is made of collagen fibers.



**FREE RADICALS** - Oxygen consists of 8 electrons (2, 6) and if external electrons have been lost from outer shell then it's called free radical oxygen. Oxygen electron configuration is 1:2:2p4.

Free radicals are molecules with unpaired electrons. They rob other cells of their existing electrons and cause damage wherein oxidative stress occurs when an oxygen molecule splits. Free radicals can cause damage to parts of cells such as proteins, DNA and cell membranes by stealing their electrons through a process called as oxidation.



Free radicals have gained importance due to central role in various physiological conditions and their implication ranges in diverse pathological diseases. These free radicals occur due to exogenous sources like pollution, alcohol, smoking, industrial solvents, pesticides, radiation and drugs like paracetamol and halothane. Free radicals affect various molecules like nucleic acid, mitochondria, lipids and proteins. Thereby by altering the normal redox status leading to

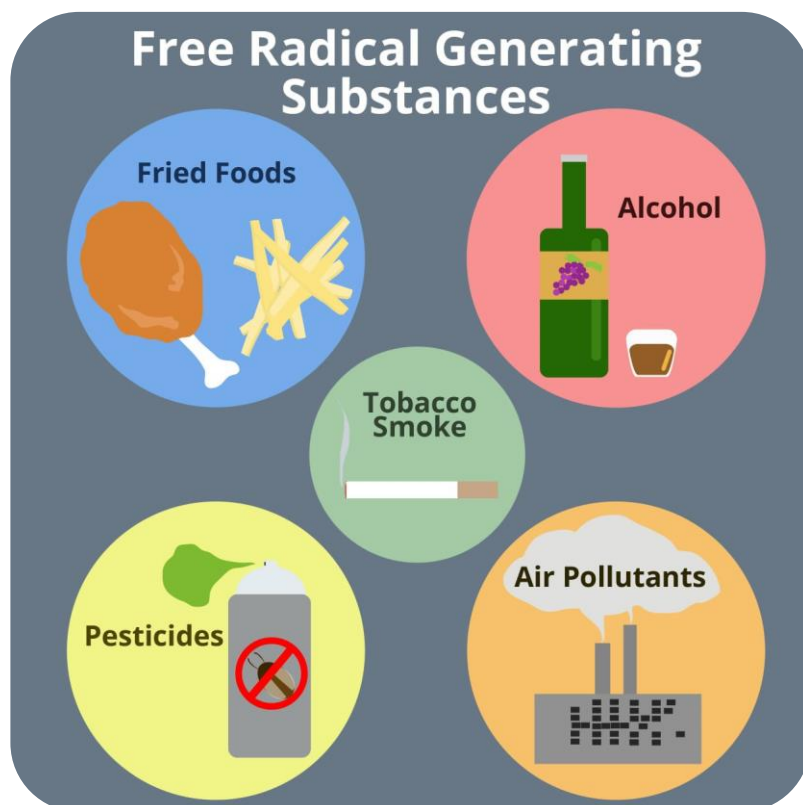


increased oxidative stress, the innumerable diseases which affects are Diabetes mellitus, Parkinsonism, Alzheimer's disease, Multiple sclerosis, Hypertension, Atherosclerosis, Ischemic disease, Asthma, Cataract, Rheumatoid arthritis and various cancers starting from colorectal, breast, prostate and bladder cancers. There is no particular drug which removes the toxicity of free radicals, but usage of anti-oxidant drugs like vitamin E, Selenium may play a minute effect on eradicating the toxicity of free radicals but it is not clinically and scientifically proved fully.

Infact free radicals which we inhale are formed due to all the pollutants present in the atmosphere which damage cell immunity and mitochondria.

If we induced the miniature heart made by stem cells at a certain place by reconstructing different vessels with anastomosis which we have molded and have attained after a thorough research which has been in the process. The place where we shall create secondary

respiration point, with the help of tissue which is enriched with vessels acts like the lung and also makes pure oxygen without free radicals. Here the last electron from the outer shell is





again incorporated to oxygen atom. During this period most of the free radicals maybe eliminated from the body. As this being a prototype, the results which are expected will be shown gradually.

The aggregate of enzymatic processes in the tissue respiration are the byproducts of the breakdown of carbohydrates, fats and proteins and subsequently they become oxidized into carbon dioxide, water and also convert into a large amount of energy (ATP). This pure oxygen without free radicals will travel to the right side of the human heart, through the means of major veins.

This part is important to know because oxygen is essential element for life and every cell in our body requires its presence for cellular metabolism and the oxygen without free radicals is a boon to every cell of the body.

The main point which we have to know here is although there are two variants of blood going on, which are pure blood without free radicals and blood with carbon dioxide (venous blood), oxygen which is present in pure blood without free radicals is a vasoconstrictor whereas blood with carbon dioxide is a vasodilator.

During the process of normal blood flow into the right side of major heart from the BIOgen Heart, it is seen that although there are two variants of blood ( blood with oxygen and blood with carbon dioxide), there will not be any fusion of these both as the flow of blood for both is antagonist to each other.

We have had succeeded to procure homologous hematopoietic stem cells from the donor by giving GF (growth factors) and also created stem cells in a spinach leaf which acts as a scaffold. Biomedical engineers and scientists will take over the mantle and will create this Biogen heart with the help of 3D printer.

**STEM CELL INOCULATION IN THE HEART** - This is a saying as stem cell technology is the futuristic modality pertaining to a newer invention and innovation in the medical fraternity. Usage of stem cells in the heart has had started from 2010 onwards, where millions of embryonic stem cells have been injected into the human heart by the methodology of STEMAID, where it has shown a quality of repair and replacement of damaged cardiac stem cells. Research is going on regarding the embryonic stem cell process to boost heart repair.

## **Background:**

- Top 10 causes of death globally 2015 according to WHO records
  - Ischemic Heart disease 8.76 million
  - Stroke 6.24 million
  - Lower respiratory infections 3.19 million
  - Chronic obstructive pulmonary diseases 3.17 million
  - Trachea, bronchus, lung cancers 1.69 million
  - Diabetes mellitus 1.59 million
  - Alzheimer's disease 1.54 million
  - Diarrhoeal diseases 1.39 million
  - Tuberculosis 1.37 million
  - Road injury 1.34 million

- The major diseases linked to free radicals

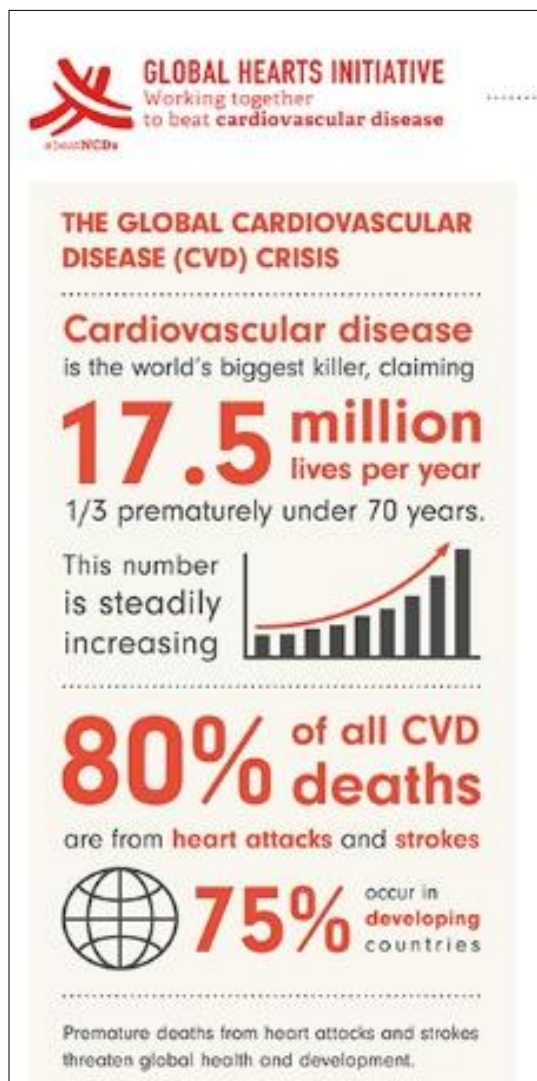
- Cancer
- Heart attack
- Cardio vascular diseases
- Emphysema
- Diabetes mellitus
- Rheumatoid arthritis
- Osteoporosis
- Aging senility

TOP 10 CAUSES OF DEATH		
	% of total deaths	% change 2005 to 2015
Heart attack/failure	16	+17
Lung disease (COPD)	10	+4
Stroke/brain hemorrhage	8	+7
Bronchitis/Pneumonia	5	-23
Diarrheal diseases	5	-32
Tuberculosis	5	-31
Diabetes	3	+35
Chronic kidney disease	3	+21
Preterm birth	3	-40
Road injuries	3	-3

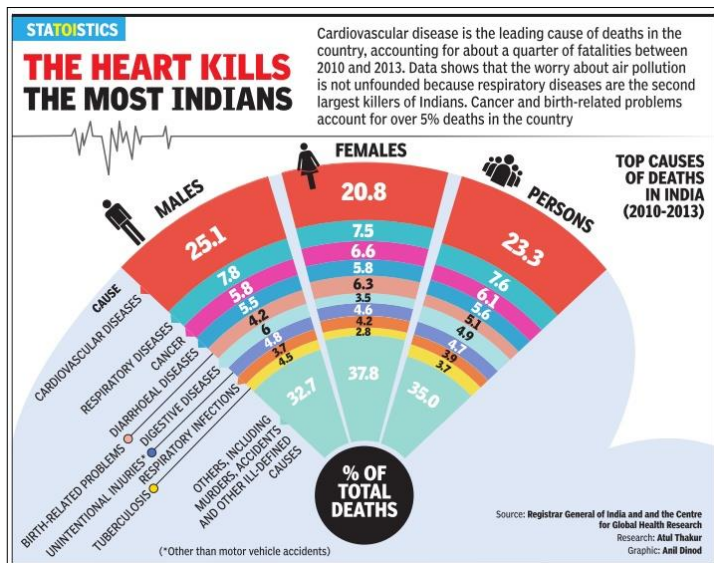
Source: TNN

- Leading causes of death in India

- Cardiovascular diseases -24.8 % of total deaths in between age 25-69
- Respiratory diseases – 10.2 % of total deaths in between age 25-69
- Tuberculosis – 10.1 % of total deaths in between age 25-69
- Malignant and other tumors – 9.4 % of total deaths in between age 25-69
- Ill defined conditions – 5.3 % of total deaths in between age 25-69
- Digestive diseases- 5.1 % of total deaths in between age 25-69
- Diarrhoeal diseases – 5.0 % of total deaths in between age 25-69
- Unintentional injuries- 4.6 % of total deaths in between age 25-69
- Intentional self harm – 3.0 % of total deaths in between age 25-69
- Malaria – 2.8 % of total deaths in between age 25-69

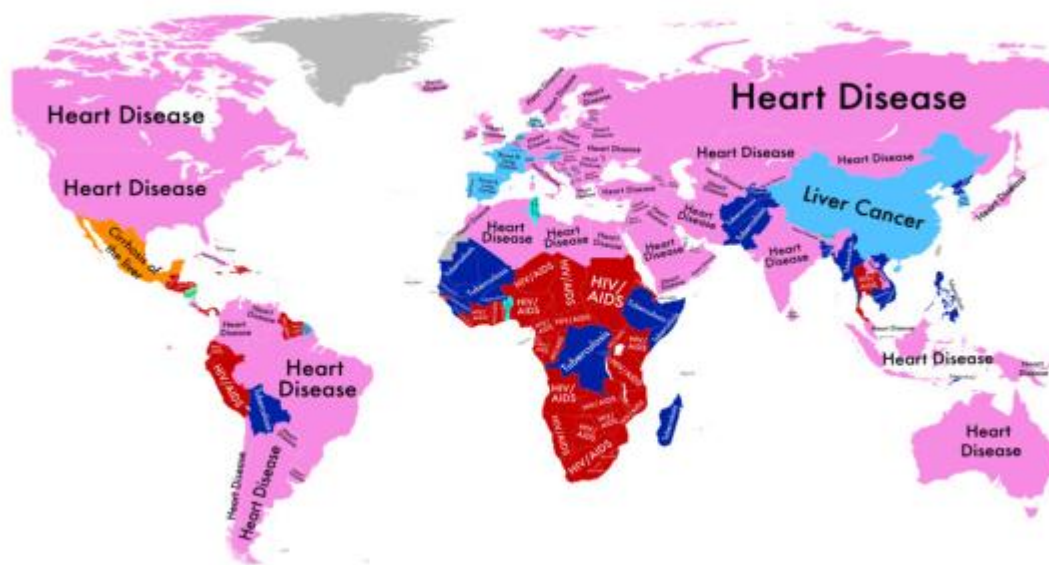






## COSTS DOUBLE OR MORE

Procedure	Old Treatment	New Treatment
<b>Arthritis: Joint/knee replacement</b>	Cemented/uncemented implants cost <b>₹50,000-60,000</b>	Coral synthetic implants (ceramic/oxinium) cost approx <b>₹1.2 lakh</b>
<b>Spinal cord surgeries</b>	Avg cost of India-made stainless steel implants around <b>₹30,000</b>	Imported implants (German/Korean) cost around <b>₹60,000</b>
<b>Heart stroke</b>	Implants using mechanical valves cost <b>₹60,000</b> on an average	Avg cost of implants using tissue heart valves is <b>₹1 lakh</b>
<b>Coronary stents</b>	Metallic version cost around <b>₹40,000</b> , drug-eluting ones <b>₹1.5 lakh</b>	New biodegradable stents cost more than <b>₹3 lakh each</b>



## Activities & Financial Estimates:

These estimates are for **Proof of Concept of the Pilot Project** (5-10 cases) and for a period of **08-12 months**:

1. **Medical:**
  - a. **Stem Cell Procurement**
  - b. **Stem Cell Growth**
  - c. **Bio-Printing**
  - d. **Health Checkup**
  - e. **Heart Insertion**
  - f. **Hospitalization**
  - g. **Medication & Monitoring**
  - h. **Ethical Committee**
2. **Administration:**
  - a. **Documentation**
  - b. **Information Security**
  - c. **Legal & IP Protection**
  - d. **Coordination**
  - e. **Financial Management & Logistics**
  - f. **Human Resources Management**
  - g. **Insurance**
3. **Technical**
  - a. **Equipment**
  - b. **Experts**

<b>Estimates:</b>	<b>INR    80, 000, 000.00</b> <b>(Taxes extra)</b>
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## CORE OPERATIONAL TEAM

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