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Indian Institute of Science

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Certificate Course in

Healthcare Technology (CCHT)

Module 4: Technology-led advancements and innovations in healthcare

Tissue Engineering, Biomaterials and 3D Printing for Clinical Applications

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Tissue Engineering, Biomaterials and 3D Printing for Clinical Applications

Learning Objectives:

- Fundamentals of Biomaterials and Biocompatibility
- Introduction to Tissue Engineering
- Overview of Additive Manufacturing technique
    - High energy laser/e-beam
    - 3D inkjet printing
- Case study
    - Clinical study on the use of 3D printing in cranioplasty surgery
- Bioprinting

Overview of Session:

Tissue engineering

Tissue engineering is an emerging multidisciplinary research area at the interface of biology, engineering as well as medicine, with immense potential to recast our means of healthcare by offering potential solutions in terms of regenerative medicine for maintenance, restoration and amelioration of damaged tissues and hence, organ functions. Underlying this concept of tissue engineering for both therapeutic and diagnostic applications is the ability to exploit the functionality of living cells in diverse ways on engineered scaffolds. The ability to develop materials, which concert with tissues structurally, mechanically and bio functionally, i.e., biocompatibility, is of prime importance in regenerative medicine and all such materials, with appropriate biocompatibility property, are widely known as biomaterials. One prime approach for developing artificial constructs for tissue regeneration is autologous transplantation, i.e. direct transplant from the host only.

Although this method offers the 'gold standard' and promises the best clinical results by virtue of inherent reliability with the host, a lack of immune and disease related complications possible from external transplantation sources, it severely restricts large-scale application of such an approach. Efficacious design of a tissue-engineered scaffold requires sufficient understanding of the interplay among the cells, tissues and the extracellular matrix (ECM) at the molecular level. The scaffold should ideally provide an environment for tissue regeneration, evading hostile immunogenic responses, while degrading in a sustained manner, *in vivo.*

Additive Manufacturing

Phenomenologically, additive manufacturing is described as a layer-by-layer fabrication technology of 3D physical structures of a material, based on machine-readable design files, for example, stereolithography (STL) files. Rapid Prototyping (RP) is a broad term for several manufacturing techniques, where 3D structures can be developed in a layer-by-layer manner based on the computer-aided design (CAD) data. The main advantages of RP methods are the fabrication of complex 3D geometries with high reproducibility, waste minimization, extensive choice of materials domain (metals, polymers, ceramics, and composite), and customized product design. Furthermore, the RP processes can create micro- to nanometer details and are incapable of precisely controlling the pore size, shape, interconnectivity, and special distributions within the fabricated construct. There are several RP technologies available, such as STL, selective laser sintering (SLS), 3D binder printing, electron beam melting (EBM), and laser-engineered net shaping (LENS^{TM}).

Detailed reading content:

The following text has been reproduced and adapted from Prof. Bikramjit Basu's textbooks,

B1. Bikramjit Basu; Biomaterials Science and Tissue Engineering: Principles and Methods; Cambridge University Press; ISBN: 9781108415156; 2017.

B2. Ashutosh K. Dubey, Amartya Mukhopadhyay, Bikramjit Basu; Interdisciplinary Engineering Sciences: Concepts and Applications to Materials Science, CRC Press, Boca Raton, USA; 2020. (ISBN:9780367333935)

Tissue Engineering

The tissue interactions at the molecular level involve predominantly weak interactions: (hydrogen bonding, electrostatic interactions and solvation effects), manifested in hydrophobicity. Such lower energy couplings are responsive and adaptive, facilitating rapid assembly and disassembly as well as changes in protein conformation. The self-assembly of collagen, a primary component of the extracellular matrix (ECM) protein of hard tissues occurs sequentially from the expression of pro-collagen proteins to their eventual assembly into triple-helical fibres. The entire phenomenon is strongly dependent on the hydrophobic interactions within the physiological environment. The weak forces aid the dynamicity of tissues and the shock absorbing nature of cartilage can be attributed to the movement of water from a nexus of hydrophilic proteoglycan molecular chains. On the same note, the nucleation of hydroxyapatite into the nanodimensional gaps between collagen molecules tones up a bone. The proteins, like collagen and elastin, are stabilized by the enzymatic cross-linking of lysine, and the phenomenon, brought about by stronger covalent bonds between tissues, is known as covalent capture. However, apart from conglomerating the biological components into a structure, the ECM must essentially provide necessary instructive cues for sustenance of cell phenotype behavior.

A plethora of biomaterials have been developed for tissue engineering, including various natural and synthetic, polymeric and ceramic biomaterials, and their composites. The most widely used techniques are electrospinning, self-assembly, etc. Subsequently, the techniques for enhancing biocompatibility of the scaffold are also important. Bioactivity of a substrate can be augmented either by direct topographical patterning or by surface treatment techniques, whereby surface nanofeatures can be introduced. It has already been widely appreciated that the bone cells respond to multidimensional cues, including

topography. Along with this, patterned surfaces influence cell responses, protein adsorption plays a role of in manoeuvring cell-substrate interplay.

Tissue engineering combines the principles and methods of life sciences and engineering sciences to create materials and develop strategies to heal damaged tissues or create tissue replacement substitutes. The three main approaches of tissue engineering include the implantation of (a) engineered scaffolds, (b) only cells and (c) engineered scaffolds seeded and cultured with appropriate cells. The most ideal strategy for regeneration is tissue specific. For instance, cells are not always included in scaffolds for nerve repair as host axons need to connect with the target tissue to restore function. Cells injected directly do not survive, and invoke an immune response. The most common approach involves a scaffold with cells. The scaffold is a construct that supports cell growth and proliferation and allows adequate nutrient exchange, and ideally, degrades as it is gradually replaced by a functional tissue. Different biofactors (cells, genes, proteins) may be transplanted along with this scaffold, and stem cell and gene therapy approaches may be used to stimulate tissue repair. Depending on the type of tissue, the scaffold may be an elastomer (for soft tissue engineering involving skeletal muscles, skin etc.) or rigid polymers/ metals/ ceramics (for hard tissue engineering involving bones, teeth etc.)

Tissue engineering offers a potential solution to many problems. Tissue and organ shortage is a severe challenge worldwide, and this gap is bound to exacerbate in the wake of an aging population. One of the aims of tissue engineering is also to achieve artificial organs, as the availability of donor organs and tissues is very limited. Tissue engineering offers a possibility of eliminating (or at least reducing) the need for organs by generating organ scaffolds and by regenerating the organ. Products such as tissue engineered skin, bone, blood vessels and pancreas exist as already approved therapies. Success in the field of tissue engineering can create tremendous financial opportunity. In this regard, the sales of regenerative biomaterials, which exceed USD 240 million per year, also hint at the tremendous potential that the field beholds. However, the complexities and the challenges involved in generating whole organs have largely given way to smaller, attainable goals. For instance, the goal to make an artificial heart has been replaced by a more realistic goal to replace coronary arteries, valves and myocardium.

In a nutshell, tissue engineering is one of the most stimulating areas of interdisciplinary and multidisciplinary researchers today. Scaffold materials and fabrication technologies play a crucial role in tissue engineering, and are rapidly evolving. Many exciting materials

are developed for scaffold applications, and these include biodegradable and bioactive polymers, ceramics, glass-ceramics, hydrogels, electrospun nanofibers etc. As scaffolds play a vital role in tissue engineering, the feasibility of designing nanofeatured scaffolds is also studied. Although bone is a functionally diverse tissue, new biomaterials with promise to cure orthopedic problems are yet to be discovered. In conclusion, the promising arena of tissue engineering, unveiled via the usage of stem cells, in conjunction with the multitude of biomaterials and processing techniques, might bear possible solutions to therapeutic repair of bone tissues, both in preclinical and clinical human models. It can be envisaged that with relevant animal studies and coherent understanding of the principles governing cell-biomaterial interactions, the tissue engineering doctrine can be efficiently leveraged to revolutionize the current scenario of regenerative medicine.

Additive Manufacturing of Materials

Phenomenologically, additive manufacturing is described as a layer-by-layer fabrication technology of 3D physical structures of a material, based on machine-readable design files, for example, stereolithography (STL) files. Rapid Prototyping (RP) is a broad term for several manufacturing techniques, where 3D structures can be developed in a layer-by-layer manner based on the computer-aided design (CAD) data. The main advantages of RP methods are the fabrication of complex 3D geometries with high reproducibility, waste minimization, extensive choice of materials domain (metals, polymers, ceramics, and composite), and customized product design. Furthermore, the RP processes can create micro- to nanometer details and are incapable of precisely controlling the pore size, shape, interconnectivity, and special distributions within the fabricated construct. There are several RP technologies available, such as STL, selective laser sintering (SLS), 3D binder printing, electron beam melting (EBM), and laser-engineered net shaping (LENS^{TM}).

Although 3D printing can be accomplished in a number of different approaches, the generic process involves the following sequential steps. In the first step, a CAD model is created digitally, for example, using a CT scanner. Afterwards, from the CT scan data, the region of interest can be converted into a 3D design file, for example, STL file, by using MIMICS or CATIA. In the second step, the STL file is sliced (cross-sectioned) digitally into a number of 2D layers. In the slicing process, the layer thickness influences the model accuracy and the build time. Therefore, the layer thickness is an important parameter in this process. The model accuracy increases with a decrease in the layer thickness and an increase in the build time. In the third step, the design data for the sliced layers are sequentially passed to the 3D printing machine through a computer interface.

The prototype is made as a layer at a time over the top of earlier layers. Such a process is carried out until the entire model prints completely.

Depending on the prototype composition, the post-processing treatment is followed as a last step to obtain 3D-printed prototypes with desired physical architecture and mechanical properties. Infiltration, high-temperature sintering, chemical conversion or combinations of them are among the common post-treatment processes. The STL-based manufacturing process was first invented by Charles W. Hull in 1986. The process described the fabrication of a 3D solid geometry from the physical state of a fluid through selective photo-crosslinking in a layer-by-layer manner using UV radiation. The liquid phase used in STL is essentially a photosensitive resin or monomer solution (mainly acrylic or epoxy-based). The UV light (or electron beam) exposed onto the liquid resin layer is used to initiate the polymerization chain reaction within the monomers. The activated monomers are instantly converted to polymers and then, they solidify. The scanner system cured the liquid monomer by irradiating the UV laser beam, which is guided through the CAD modeling data.

The STL machine consists of a build platform, which is connected with the moveable table and mounted in a vat of photopolymers. Initially the UV beam solidifies the topmost layer of the exposed resin surface. Once the layer has been scanned, the moveable table moves downwards by exactly one layer inside the resin and the next layer is exposed to the radiated beam. The energy of the photo-radiation and the exposure time are the parameters, which control the layer thickness and ultimately determine the mechanical properties of the final product. After fabrication of the entire structure, the unreacted resins are removed from the final product through heating or photo-curing to get the desired mechanical strength. Not only polymer-based materials, but also ceramic materials can be constructed using this technique. Ceramic particles are suspended within the photocurable monomers or resins and using the UV laser beam, the monomers are polymerized in a layer-by-layer manner similar to the above-described method. After construction, the polymer binder is removed by pyrolysis and sintering provides the final strength.

SLS is an RP process, which allows us to generate a complex 3D structure using powders as raw materials. The machine consists of three major operative parts such as the powder delivery system, powder spreading roller, and the powder bed or build bed where the object is fabricated. The powder feed chamber is raised to supply the powder to the spreading roller (or scraper), which spreads the powder over the powder bed. The powder layers are selectively fused or sintered using the thermal energy of the laser beam. After

sintering of each layer, the fabrication piston is lowered and the powder delivery system is raised. The subsequent powder layers are spread over the top of the previous layer and sintered by using the laser beam. During fabrication, the entire powder bed is heated to provide thermal energy to the printed layers and facilitate fusion to the previous layer. In the commercial SLS system, either a CO_2 or Nd:YAG laser is used, of power in the range of 25–50 W and the laser power depends on the type of materials under construction.

The fabrication principle of 3D binder printing is similar to that of SLS. The binder printer consists of a moveable inkjet printhead, which selectively expels a stream of adhesive droplets to the powder layers. The binder binds the powder particles to form a solid shape. The main challenge of this process is to develop a suitable powder–binder system. After fabrication, the construct is heat treated for binder evaporation or chemically infiltrated, to get the final structure with desired mechanical strength.

EBM is a RP technology to fabricate fully dense 3D metal constructs directly from metal powder. An electron beam selectively scans the thin metal powder layer which is spread in a layer-by-layer manner in a high vacuum. The electron beam column is made up of an electron gun and magnetic lenses. A thermionic or field emission electron gun is used as a source of electron beam, which is focused by using the electromagnetic lenses. The specimen compartment consists of powder hoppers to deliver metal powder on the build table and the powder distributor spreads the powder to form a thin layer. The electron beam sinters the specific areas of each powder layer as directed by the CAD file. The mechanical properties of the fabricated construct depend on the sintering strength which is controlled by the accelerating beam voltage, beam diameter, and exposure time. The vacuum environment is created to reduce oxidation and contamination of the fabricating materials. Generally, the electron beam gun compartment is kept in a higher vacuum (~10−7 Torr) compared to the specimen fabrication compartment (~10−5 Torr).

Laser Engineered Net Shaping (LENS™) is another RP technology that was developed by Sandia National Laboratories and Stanford University, and was commercialized by Optomec for metal 3D geometries. Using this technology, fully dense metallic structures can be developed. The powder delivery nozzles transmit the powder particles through a gas flow jet and a laser beam is used to melt the powder particles. The mounted substrate moves in a raster manner on an X–Y stage according to the CAD model. The important parameters of these processes are the powder flow rate, laser power, and layer thickness. The main advantage of LENS™ is the multilateral deposition for *in-situ* alloying, composite

material formation, wear and corrosion resistance surface coating, asymmetrical welding, and functionally gradient structure development.

Most recently, 3D bioprinting has been investigated widely as a novel biofabrication method in regenerative tissue engineering to mimic the native-like tissue structure with specific dimensions and high reproducibility. Bioprinting technologies get enormous attention for the precise placement of living cells within biomaterials into preprogrammed geometries using a 3D bioprinter. The raw material of 3D bioprinting is called bioink, which is a combination of living cells, growth factors, nutrients, and printing media. Biodegradable biopolymers are the raw materials of 3D bioprinting. The biopolymers loaded with living cells are deposited in a layer-by-layer manner, similar to that done using a conventional additive manufacturing technique. Several types of bioprinting strategies, such as extrusion-based, inkjet/droplet-based, and laser/light-assisted bioprinting strategies have been developed in the past few years. Each of the printing technologies has some characteristic features which control the cell viability within the bioprinted construct. Extrusion-based bioprinting is considered as the most promising method because the process is simple; there is a large window of choice of materials and chemically relevant tissues and organs can be fabricated with high accuracy. This printing technology involves mechanical pressure to extrude the bioinks through the nozzle of a syringe in a controlled manner.

Living cells, growth factors, and microcarriers are loaded in the biopolymer and are inserted to the syringe barrel and printed as a continuous filament. Inkjet bioprinting is based on the drop-on-demand method, where hydrogel-encapsulated cells are placed within the inkjet cartridge, and bioink droplets are deposited in a controlled manner. The two different approaches developed to generate the ink droplets from the inkjet printhead are thermal and piezo-electric. For droplet bioprinting, thermal energy is applied to the bioink chamber to generate small air bubbles. The bubbles create a pressure pulse within the ink and inks are ejected as droplets with different diameters.

For piezoelectric inkjet bioprinting, an electric current is applied to a polycrystalline piezoelectric ceramic, which creates a transient pressure to expel ink drops to the building substrate. The main advantage of the piezoelectric printhead is that it can generate a more precise droplet size compared to the thermal printhead. However, many researchers prefer thermal inkjet printing over piezoelectric since the piezoelectric printing frequency within the range of 15–25 kHz can damage the cell membrane.

Laser-assisted bioprinting (LAB) is a nozzle-free approach, which allows bioprinting with a wide range of bioink viscosity (1–300 mPa/s) and high cell concentration in the order of 1×10^8 cells/mL without nozzle clogging, such as conventional extrusion or inkjet bioprinting·The printhead setup comprises a ribbon that is typically a transparent glass slide or quartz. The donor side of the ribbon is coated with a laser-absorbing media (such as Ag, Au, Ti, and TiO_2), and the cell-encapsulated hydrogels are sprayed on it. The absorbing media also protects the hydrogel encapsulated living cells from the high power laser pulse. The laser impulse focuses the absorbing media through the ribbon and the absorbing media is evaporated with the creation of high local pressure on the bioink film. The vapor pressure of the absorbing media generates cavitation-like bubbles toward the bioink film. The expansion and collapse of the bubbles creates jets within the bioink layer which leads to the creation of the bioink droplets, which are transferred to the printing substrate. The advantages of LAB are high printing resolution (≥20 μm) with no limitation on hydrogel viscosity and cell concentration. The process parameters of the LAB are the wavelength of the laser, pulse duration, beam focus diameter, viscosity and surface tension of hydrogels, and substrate properties.

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Additive Manufacturing

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Suggested Reading:

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Bikramjit Basu

Materials Research Center

Center for BioSystems Science and Engineering

Indian Institute of Science, Bangalore, India

CERTIFICATE COURSE IN HEALTHCARE TECHNOLOGY

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Bikramjit Basu is currently a Professor at the Materials Research Center, with joint appointment at the Center for Biosystems Science and Engineering, Indian Institute of Science (IISc), Bangalore. He also serves as Visiting Professor at University of Manchester, UK (2018-2023) and at the European Centre for Functional and Surface Functionalized Glass, Alexander Dubček University of Trenčín, Slovakia (2020-2021). After his undergraduate and postgraduate degree in Metallurgical Engineering from NIT Durgapur (1995) and IISc (1997) respectively, he earned his PhD in the area of Engineering Ceramics at Katholieke Universiteit Leuven, Belgium in March, 2001. Following a brief post-doctoral stint at University of California; he served as a faculty in Materials Science and Engineering at Indian Institute of Technology Kanpur (2001-2011) and moved to IISc in May, 2011.

Bikramjit has been pursuing interdisciplinary research at the cross-roads of Engineering Science, Biological Science and Medicine. Encompassing experimental discovery, theoretical predictions, computational analysis, and clinical translational research, his research group has laid the foundation for *biomechanically-compliant design of implants, 3D binderjet printing of biomaterials and* biophysical stimulation (intermittent delivery of electrical/magnetic stimulation) mediated stem cell functionality modulation on implantable biomaterials and in biomicrofluidic devices , to advance the field of biomaterials science and regenerative engineering; thereby impacting human healthcare. Over the years, he has created interactive and intensive collaborations with over a number of clinicians, one multinational company and 7 SMEs/start-ups to accelerate biomaterials science-to-biomedical device prototype development. During 2018-2020, a bicentric human clinical study on cranioplasty surgery to treat decompressive craniectomy is completed in one hospital and under progress at another hospital in India.

Bikramjit's contributions in Engineering Science have been globally recognised. He received Government of India's most coveted science and technology award, Shanti Swarup Bhatnagar Prize in 2013 for his significant contributions to the field of Biomaterials Science. A Chartered Engineer of the UK, he is an elected Fellow of the International Union of Societies for Biomaterials Science and Engineering (2020), Fellow of the Indian Academy of Sciences (2020), Fellow of the American Ceramic Society (2019), American Institute of Medical and Biological Engineering (2017), Institute of Materials, Minerals & Mining, UK (2017), National Academy of Medical Sciences, India (2017), Indian National Academy of Engineering (2015), Society for Biomaterials and Artificial Organs (2014) and National Academy of Sciences, India (2013).

- Published over 300 peer-reviewed research papers in leading journals (total citations: > 11,000 and H-index: 56)
- Co-inventor of 7 Indian patents.
- Authored/co-authored 7 textbooks, 2 edited books and one research monograph in the interdisciplinary areas of Biomaterials Science and Engineering Ceramics.
- Has been a primary advisor to 27 PhD students, 11 Masters students, 7 Post-Doctoral researchers, and has mentored 10 Project Scientists and 9 International researchers

CERTIFICATE COURSE IN HEALTHCARE TECHNOLOGY

NPTEL* courses

Outreach Course	Weblink for course content	National Program	Lecture hours
Biomaterials for Bone Tissue Engineering Applications	www.youtube.com/playlist?list=PLLj8usx87A_b16gYoCJclV9ADCgnre0tq	NPTEL, MHRD, India, 2016 and 2019	20
Introduction to Biomaterials	http://nptel.ac.in/courses/113104009/	NPTEL, 2011	40
Friction and Wear of Materials: Principles and Case Studies	www.youtube.com/watch?v=Bmj85Ihfv7w&list=PLLy_2iUCG87Bhld-RXqBIAwKCLaLjOzX	NPTEL, 2018 and refloated in 2019	20

*National Programme on Technology Enhanced Learning (NPTEL), a project funded by MHRD, Gov't of India

Acknowledgements: Text books / Reference Books

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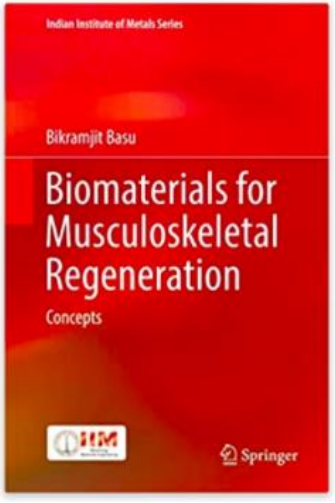
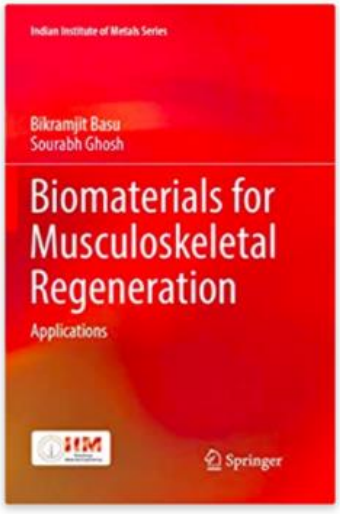
Biomaterials texts

- Bikramjit Basu; **Biomaterials for Musculoskeletal regeneration: Concepts**; Springer Nature, 2017 [ISBN: 978-981-10-3059-8]
- Bikramjit Basu and Sourabh Ghosh; **Biomaterials for Musculoskeletal regeneration: Applications**; Springer Nature, 2017. [ISBN: 978-981-10-3017-8], 2017.





Springer

"This book provides an encyclopedic coverage of biomaterials science which, at the same time, has enough to interest the biomedical scientists and engineers. Overall, the book emphasizes the enormous need for the supply of regenerated organs and tissues as the spontaneous capacity for regeneration is limited in the human body."
— **Marthanda Varma Sankaran Valiathan**, National Research Professor, Manipal University, India

"This book has a seminal collection of chapters. I especially liked the chapter on biocompatibility assessment. The case studies described are a good way for any learner to see how basic science can be translated."
— **Abhay Pandit**, Scientific Director, Centre for Research in Medical Devices, National University of Ireland Galway

"Professor Basu has successfully provided an excellent guide in the interdisciplinary frontier field, for students, biomedical engineers and scientists. The fundamentals of materials and biomedical sciences are comprehensively and scientifically detailed for holistic understanding. A rich collection of objective and subjective problems of different formats will greatly benefit the academic community around the world."
— **Kimihiro Yamashita**, Professor, Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental University, Japan

"Professor Basu has created a comprehensive textbook for Biomaterials Science and Tissue Engineering that provides both important fundamentals and application areas. The scientific community will benefit greatly from this new resource which highlights key principles in this rapidly growing multidisciplinary field."
— **Tejal A. Desai**, Professor of Bioengineering, University of California San Francisco

"New discoveries in Biomaterials Science and Tissue Engineering increasingly dominate the current scientific literature. The consistent progress in the field demands the training of the younger surgeons and scientists. The pedagogical contribution of this book towards this important mission would certainly help in developing a clear understanding of Materials and Biological Sciences for this societally relevant scientific and clinical field."
— **Guy Daculsi**, INSERM Research Director DRE, Université de Nantes, France

Bikramjit Basu is Professor at Materials Research Center and Associate Faculty at Center for BioSystems Science and Engineering, Indian Institute of Science, Bangalore. He is the recipient of the Shanti Swarup Bhatnagar Prize for Science and Technology by the Government of India and an elected Fellow of the American Institute for Medical and Biological Engineering, Indian National Academy of Engineering and National Academy of Sciences, India.

Cover image: Confocal image of a cell on a biomaterial (top left), 3D printing process description (top middle), volume rendered image of microporous ceramic scaffold obtained using micro-CT (top right), histology image of an implant / host-tissue interface (bottom left), AFM image of micro-patterned biomaterial substrate (bottom second from left), Cell-material interaction (bottom second from right), micro-CT image of a cylindrical implant (red) in animal defect model (bottom right)
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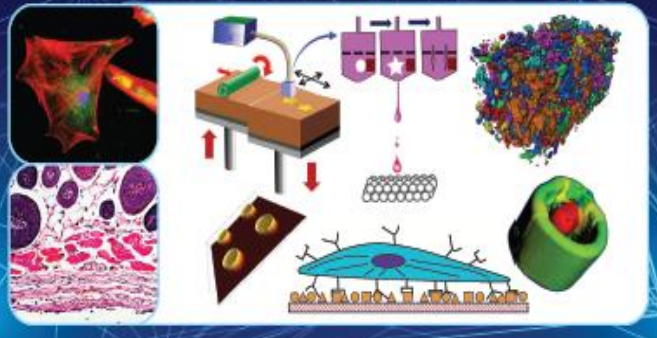

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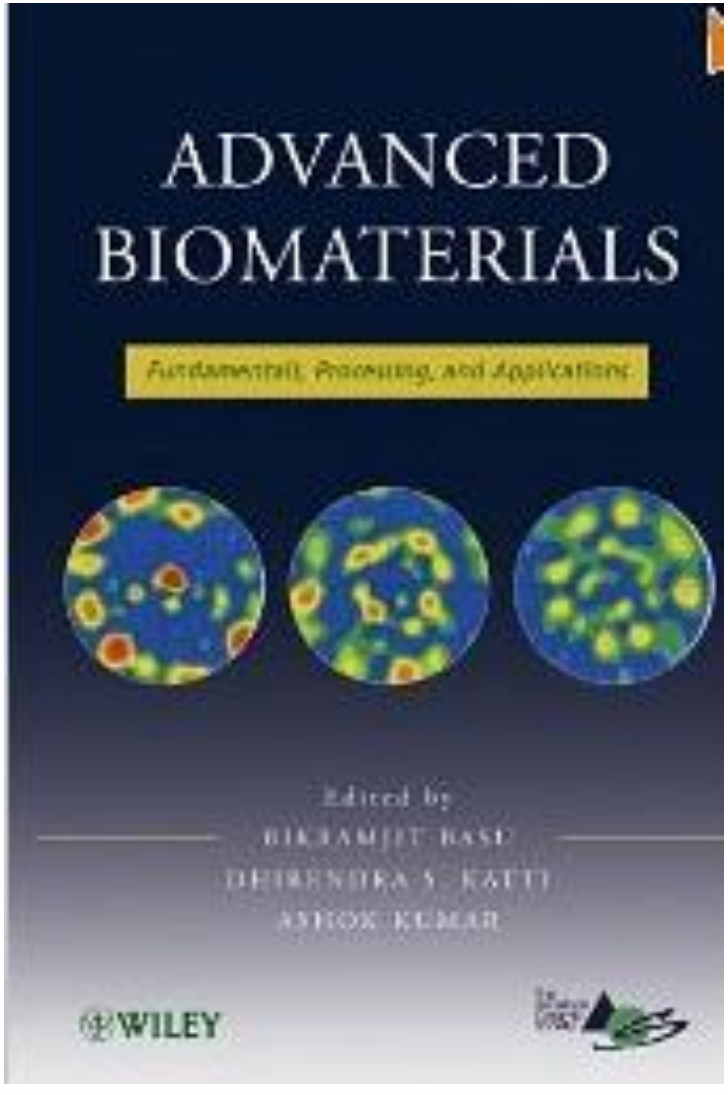
ADVANCED
BIOMATERIALS
Fundamentals, Processing, and Applications
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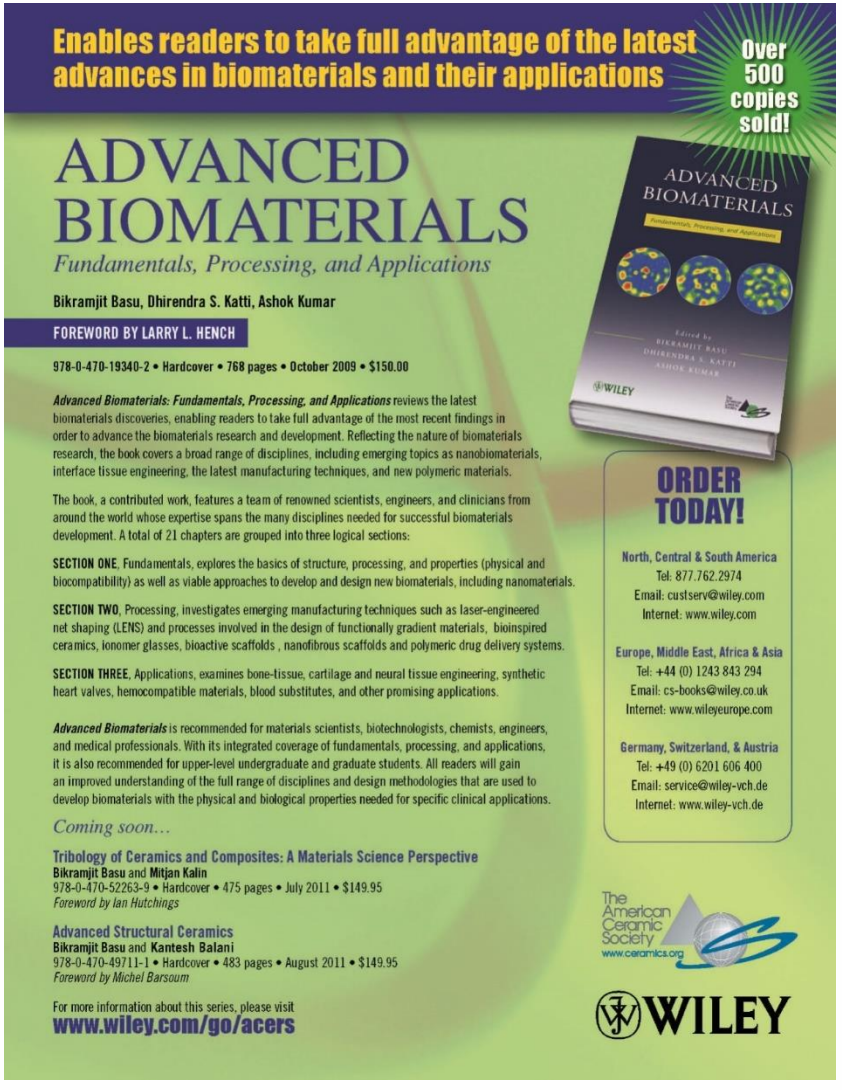
Enables readers to take full advantage of the latest advances in biomaterials and their applications
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ADVANCED BIOMATERIALS
Fundamentals, Processing, and Applications
Bikramjit Basu, Dhirendra S. Katti, Ashok Kumar
FOREWORD BY LARRY L. HENCH
978-0-470-19340-2 • Hardcover • 768 pages • October 2009 • $150.00
Advanced Biomaterials: Fundamentals, Processing, and Applications reviews the latest biomaterials discoveries, enabling readers to take full advantage of the most recent findings in order to advance the biomaterials research and development. Reflecting the nature of biomaterials research, the book covers a broad range of disciplines, including emerging topics as nanobiomaterials, interface tissue engineering, the latest manufacturing techniques, and new polymeric materials.
The book, a contributed work, features a team of renowned scientists, engineers, and clinicians from around the world whose expertise spans the many disciplines needed for successful biomaterials development. A total of 21 chapters are grouped into three logical sections:
SECTION ONE, Fundamentals, explores the basics of structure, processing, and properties (physical and biocompatibility) as well as viable approaches to develop and design new biomaterials, including nanomaterials.
SECTION TWO, Processing, investigates emerging manufacturing techniques such as laser-engineered net shaping (LENS) and processes involved in the design of functionally gradient materials, bioinspired ceramics, ionomer glasses, bioactive scaffolds , nanofibrous scaffolds and polymeric drug delivery systems.
SECTION THREE, Applications, examines bone-tissue, cartilage and neural tissue engineering, synthetic heart valves, hemocompatible materials, blood substitutes, and other promising applications.
Advanced Biomaterials is recommended for materials scientists, biotechnologists, chemists, engineers, and medical professionals. With its integrated coverage of fundamentals, processing, and applications, it is also recommended for upper-level undergraduate and graduate students. All readers will gain an improved understanding of the full range of disciplines and design methodologies that are used to develop biomaterials with the physical and biological properties needed for specific clinical applications.
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Bikramjit Basu and Kantesh Balani
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Biomaterials Science and Implants: Status, Challenges and Recommendations

ISBN: 978-981-15-6917-3

Springer

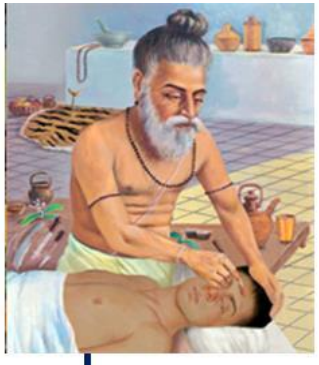
INDIAN NATIONAL SCIENCE ACADEMY
द्यावापृथिवी भर्गः सवितुर्वरेण्यम्

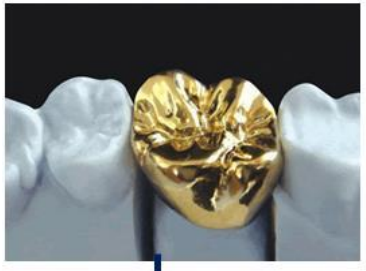
Upcoming book

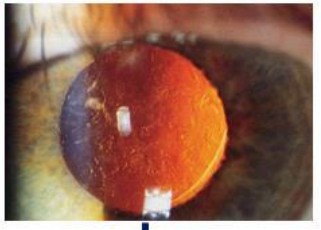
Plan of the sub-module presentation

- Fundamentals of Biomaterials and Biocompatibility
- Introduction to Tissue Engineering
- Overview of Additive Manufacturing technique
    - High energy laser/e-beam
    - 3D inkjet printing
- Case study
    - Clinical study on the use of 3D printing in cranioplasty surgery
- Bioprinting
- Closure

Historical Evolution of Biomaterials







1000-800 BC

Sushruta
Sutures of flax, hemp and human hair to close incisions

129-200 AD

Galen of Pergamum
Catgut sutures to close large wounds

166-201 AD

Romans
Dental implants made of Fe, Au, Cu

600AD

Myans
Nacre shells as teeth substitute

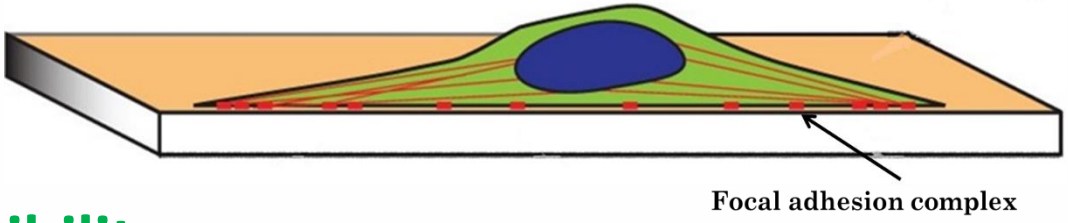
1940

World War II
PMMA shards in the eye - no inflammation or irritation

Defining terms...

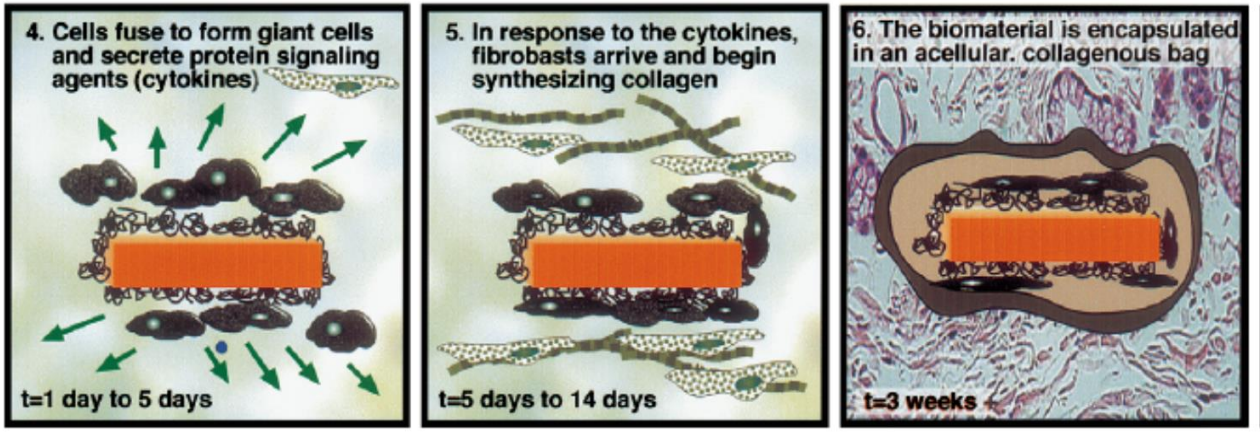
Biomaterial

- **Compatibility with living system (protein, blood, cell, tissue)**



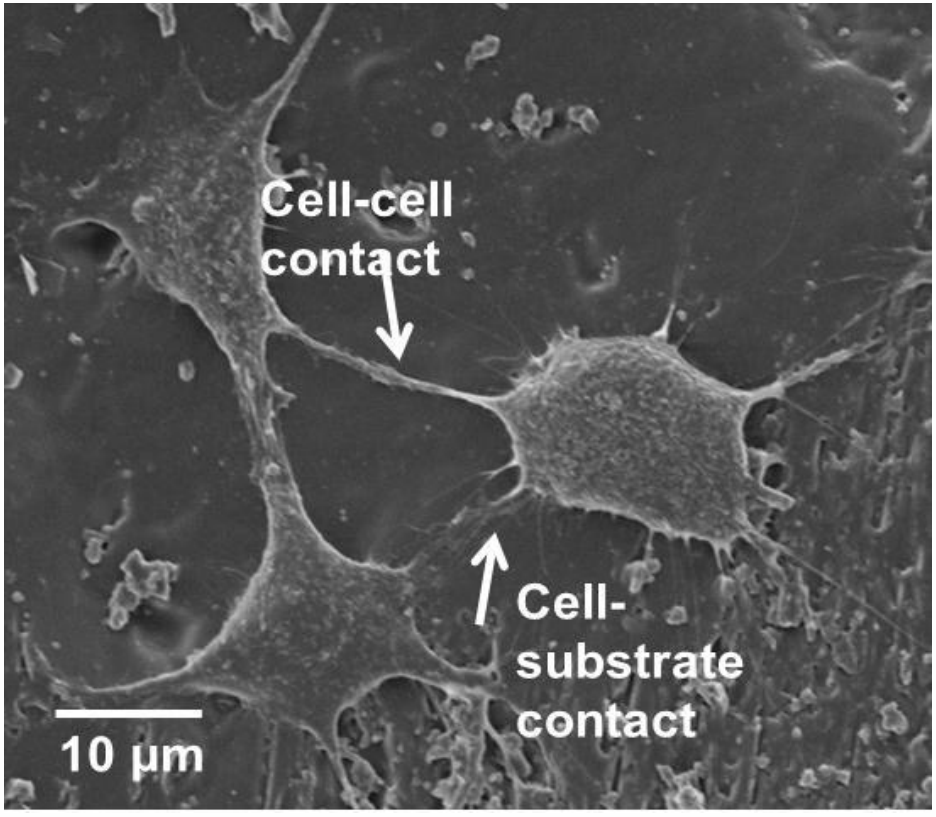
Biocompatibility

- **A holistic property rendering a biomaterial with most appropriate beneficial cellular/tissue response for targeted clinical application**



B. Basu; Biomaterials Science and Tissue Engineering; Cambridge University Press and IISc Press, 2017

Experimental result showing cell-cell interaction on a soft polymeric substrate



What is a Biomaterial?

'Biomaterials are those materials — be it natural or synthetic, alive or lifeless, and usually made of multiple components — that interact with biological systems.' Biomaterials are often used in medical applications to augment or replace a natural function [Ref.1].

A biomaterial is defined as a material of synthetic or natural origin with engineered structural features, which supports desired cellular functionality without any adverse local/systemic immune response, for a targeted clinical application. [IISc definition]

Ref 1: Biomaterials, Accessed 12 April 2017. http://www/nature.com/subjects/biomaterials

Biocompatibility: A recent definition

Biocompatibility refers to the ability of a biomaterial to perform its desired function with respect to a medical therapy, without eliciting any undesirable local or systemic effects in the recipient or beneficiary of that therapy, but generating the most appropriate beneficial cellular or tissue response in that specific situation, and optimizing the clinically relevant performance of that therapy.

Biocompatibility **describes the compatibility of material, both *in vitro* (experiments conducted in physiologically simulated conditions in glassware) and *in vivo* (*when tested in whole organism, like in any animal model*).**

David F. Williams, Biomaterials 29 (2008) 2941–2953.

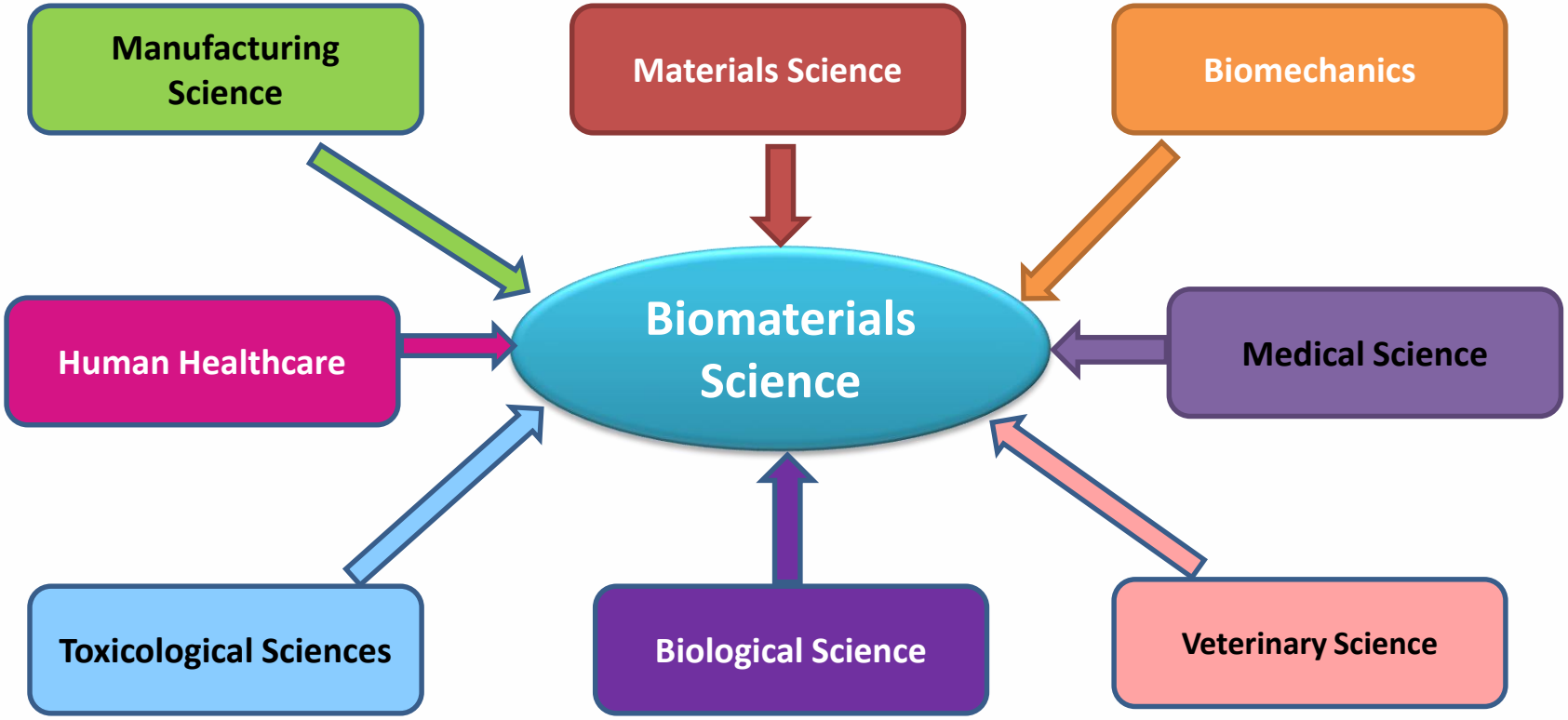
Biocompatibility – some facts

Biocompatibility is the application specific, i.e. a material, which may be biocompatible for bone replacement applications, may not be biocompatible in other application, e.g. blood contacting devices

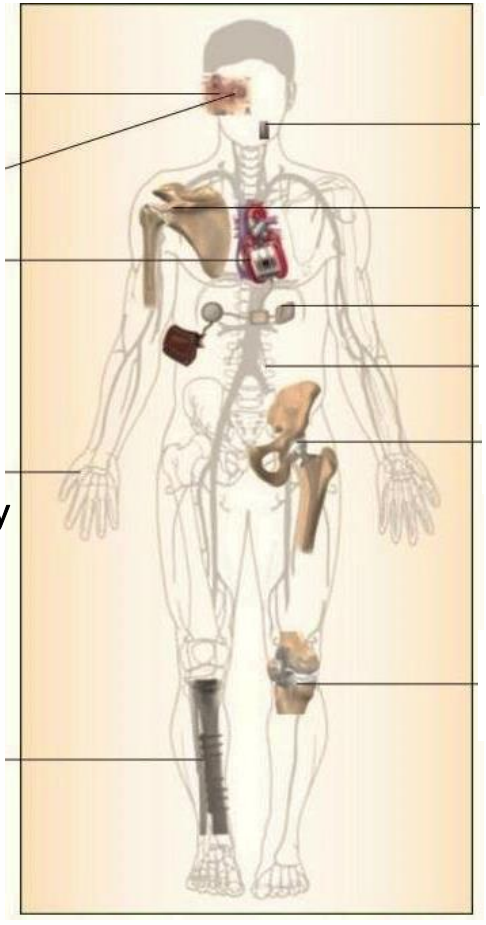
- **The phrase, Biocompatibility should be carefully used. If a material can support good cell adhesion/cell growth, it is better to describe it as 'Cytocompatible'. Similarly, if a material does not induce thrombus formation, when in contact with blood, such a property can be described as 'haemocompatibility'.**

- **Depending on targeted clinical applications, Biocompatibility can be experimentally evaluated using a spectrum of biochemical assays or molecular biology protocols involving specific cell types, blood, etc. (*in vitro*) and pre-clinical studies in animal models (*in vivo*)**

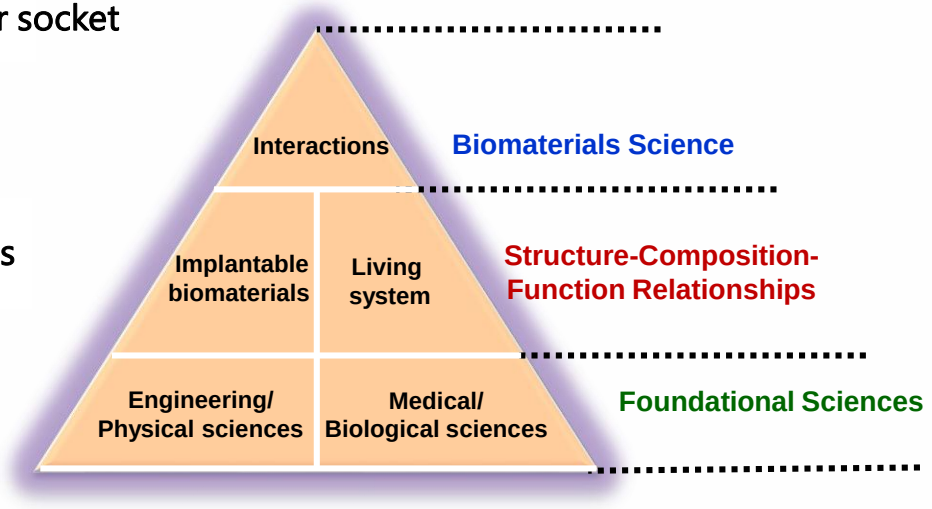
Interdisciplinary nature (Engineering, Biology and Medicine)



Current spectrum of clinical applications of biomaterials



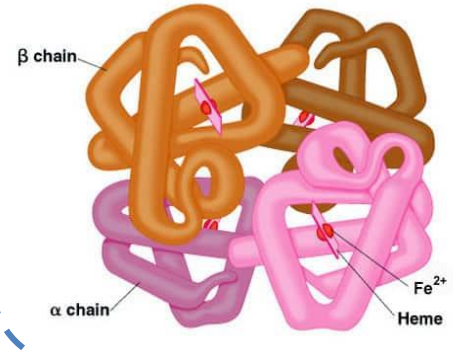
More than 75% of implants used in Indian hospitals/clinics are imported. Need for high quality indigenous implants!



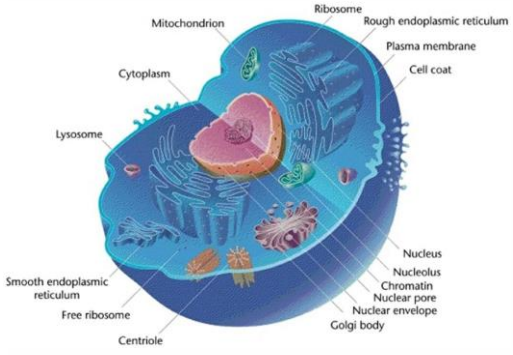
Interaction of a synthetic material with living system

Living system components

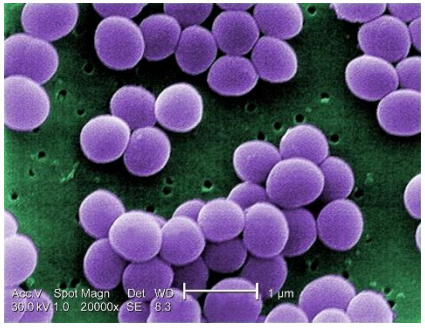
Protein



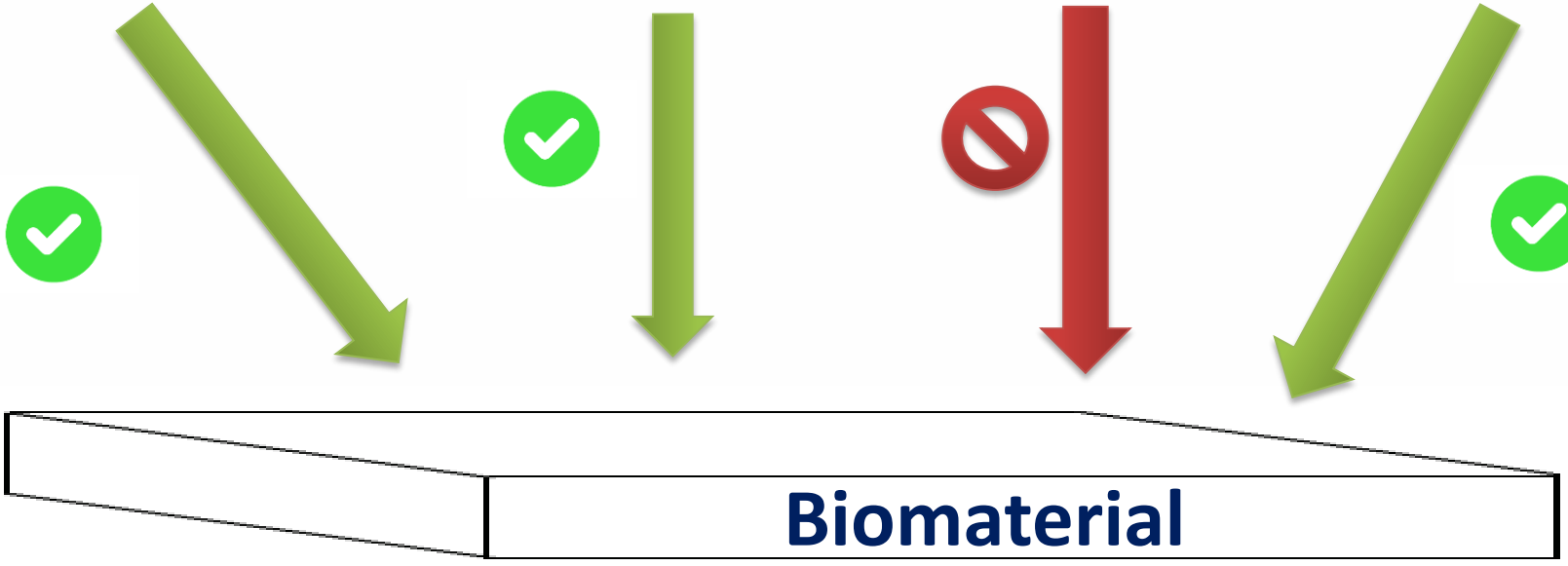
Cell



Bacteria



Red blood cells



Important Points to be Noted

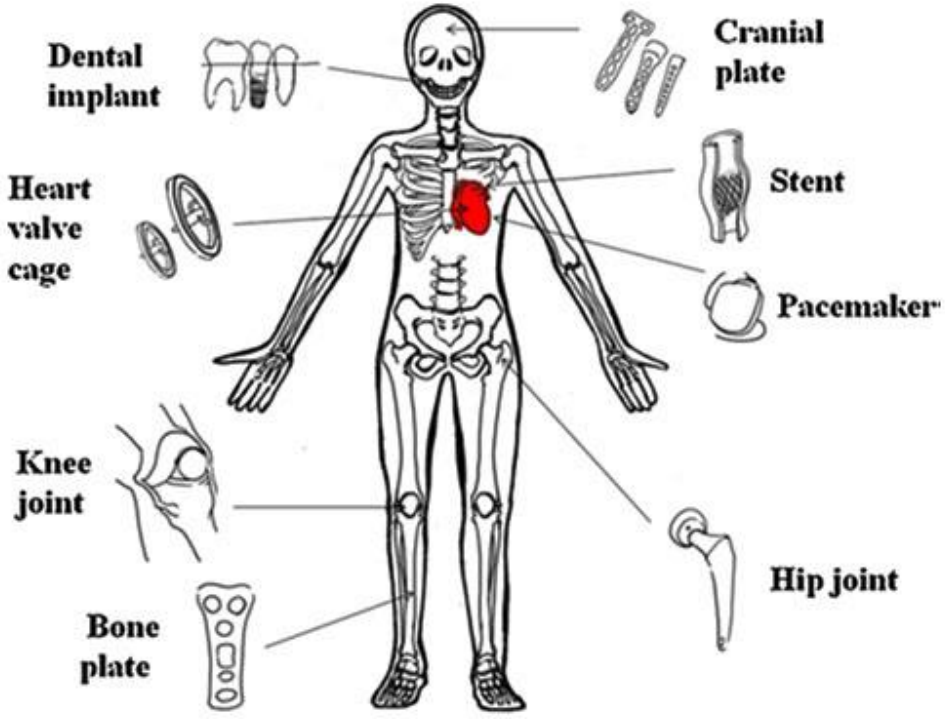
Any human disease is the outcome of the abnormal or temporal variation in numbers or functionality (expression) of the components of the living system.

Biomaterials, implants, scaffolds (often loaded with antibiotic or drugs) used for disease treatment or restoration of the functionality of anatomical parts.

A biomaterial is NOT a pharmaceutical drug!

Medical devices used for diagnostics. Example- blood sugar measurement, cancer, other diseases.

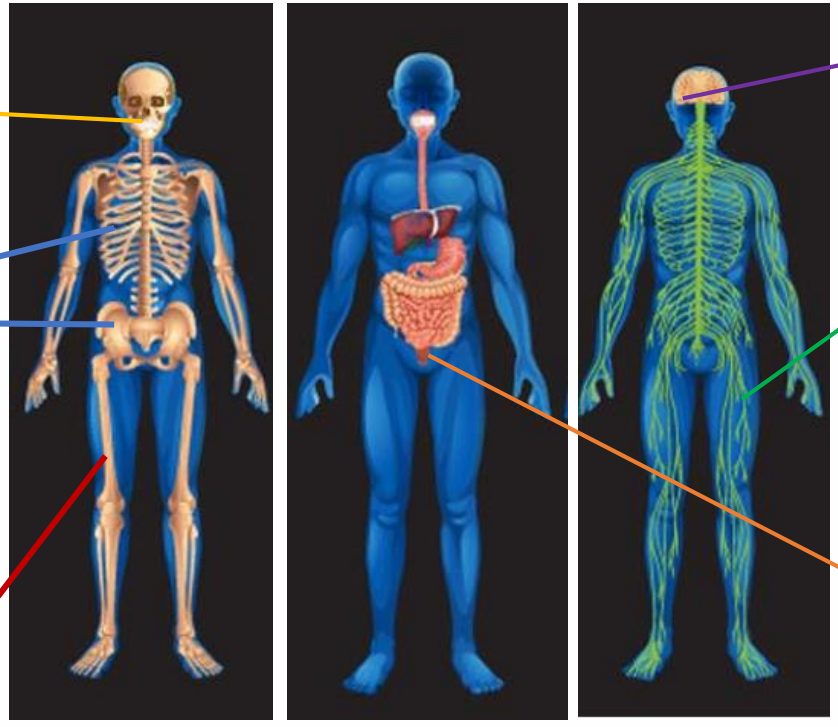
Example - Titanium and its alloy as Implants



- **High strength**
- **Low density and better specific modulus or strength**
- **Resistance to corrosion**
- **Acceptable biocompatibility**

Ref: Orient J Chem 2016;32(6)

Biomaterials Research landscape at IISc



Dental Implants

Biomaterials/ Implants for Musculoskeletal Reconstruction and Regeneration

Electrical/magnetic stimulation for Bioelectronic Medicine

Cranioplasty Surgery

Stem cells-based Regenerative Engineering

Urological neo-bladder reconstruction

Image courtesy: https://www.livescience.com/37009-human-body.html

Plan of the sub-module presentation

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    - High energy laser/e-beam
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- Closure

Tissue Engineering

Tissue Engineering

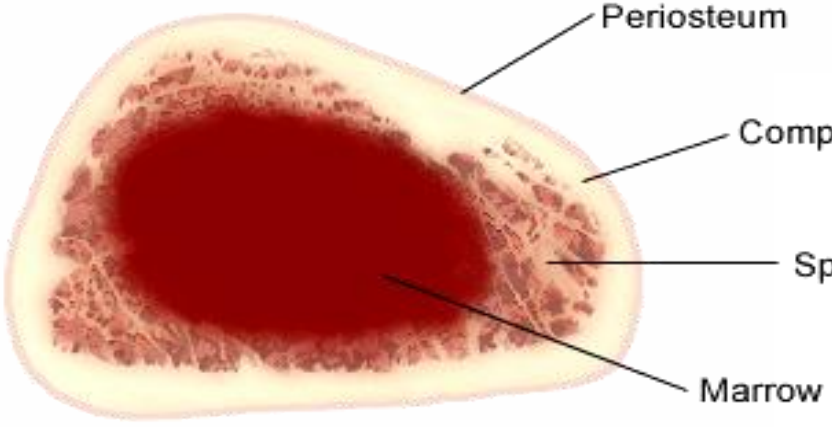
- **Tissue engineering is defined as a concept encompassing the modulation of organ specific multi-cellular functionality towards tissue regeneration and integration through vascularization and angiogenesis, aided by biophysical/ biochemical cues. [IISc definition]**

- Tissue engineering can be conceptualized as the means of orchestrating cells, engineering materials and suitable biological factors to enable relevant biological functions.

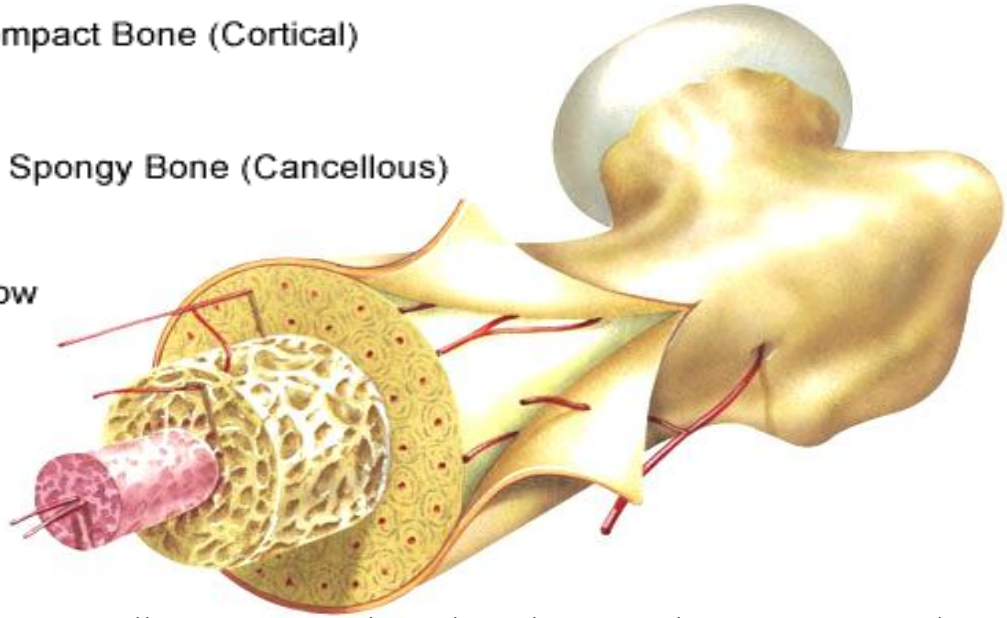
Bone: Functionally graded biocomposite

- Natural bone, a composite of hydroxyapatite and collagen, known for its **gradient porosity** from cortical to cancellous side.

- Porosity gradient also in 3D space (shape, size and distribution).



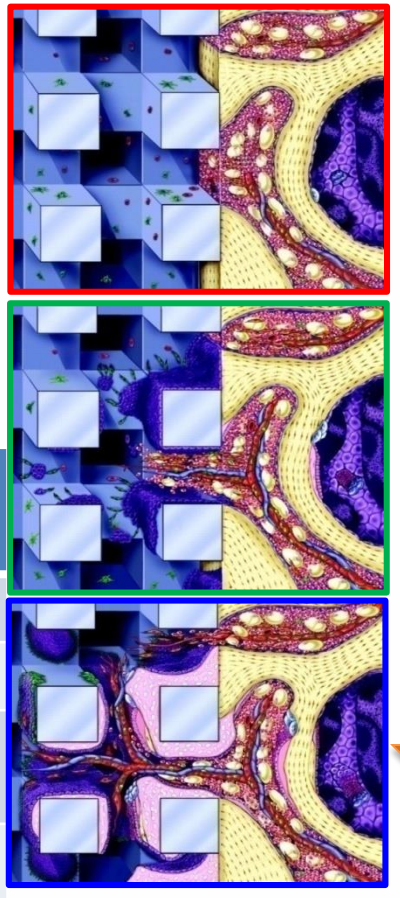
http://www.georgetownhospitalsystem.org/stw/images/125431.jpg



http://www.wellcome.ac.uk/stellent/groups/corporatesite/@msh_publishing_group/documents/image/wtdv033058.jpg

Cell functionality/Strength vs. Porosity

*Osteogenesis** is governed by vascularization and is determined by **pore size and total porosity**; however at the expense of **mechanical properties**. For example, increase in porosity from **32 to 62%** in TCP scaffolds decreases compressive strength from **37 to 0.43 MPa.**



***Barralet et al. Biomaterials 2002;23(15):3063–72**

Pore size (µm)	Biological response
20 - 50	Physiological liquid exchange
50 - 150	Hepatocytes cell functionality
150 - 400	Fibroblast cell colonisation and vascularization leading to tissue formation
400 – 1200	Extensive osteoblast functionality, substantial bone formation with bone in-growth

S. Simske, R. Ayers, T. Bateman, Mater Sci Forum 250 (1997) 151-182
E. Damien, K. Hing, S. Saeed, P. Revell, J Biomed Mater Res A 66 (2003) 241-246
S. Hollister, Orthod. Craniofac. Res. 8 (2005) 162-173
Zhang t al.,J Biomed Mater Res 54 (2001) 407-411

Nature Materials 4, 518–524 (2005)

REVIEW

nature biotechnology

Science 338 (6109), 2012, 921-926

Science

AAAS

REVIEW

Printing and Prototyping of Tissues and Scaffolds

Brian Derby

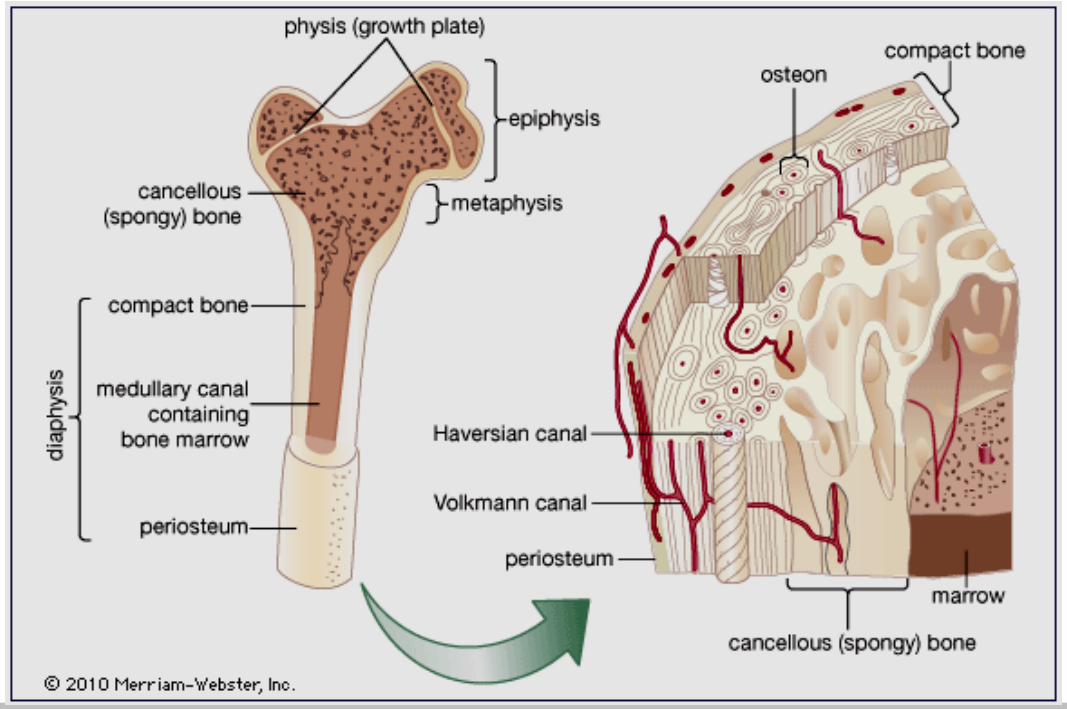
New manufacturing technologies under the banner of rapid prototyping enable the fabrication of structures close in architecture to biological tissue. In their simplest form, these technologies allow the manufacture of scaffolds upon which cells can grow for later implantation into the body. A more exciting prospect is the printing and patterning in three dimensions of all the components that make up a tissue (cells and matrix materials) to generate structures analogous to tissues; this has been termed bioprinting. Such techniques have opened new areas of research in tissue engineering and regenerative medicine.

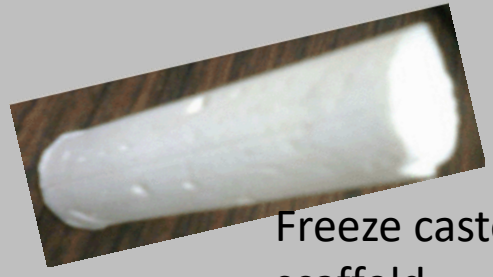
Biomaterials

Porous scaffold for orthopedic application

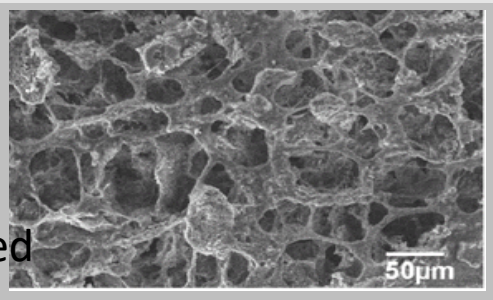
- **Bone is a vascularized tissue with various level of porosity and pore architecture**

Ideally, scaffold architecture, mechanical and physical properties, and efficacy of diffusion of nutrient allows cells to penetrate into pores, migrate, proliferate, and differentiate.

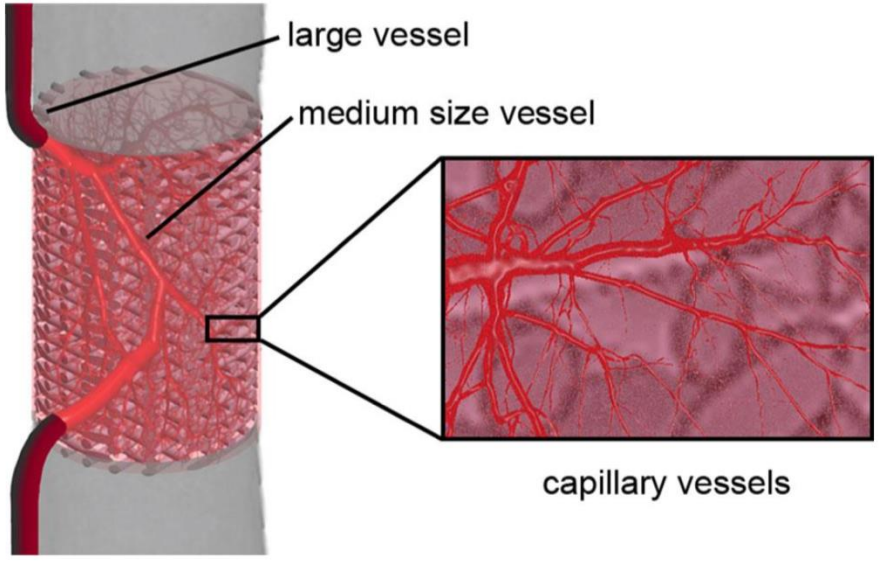


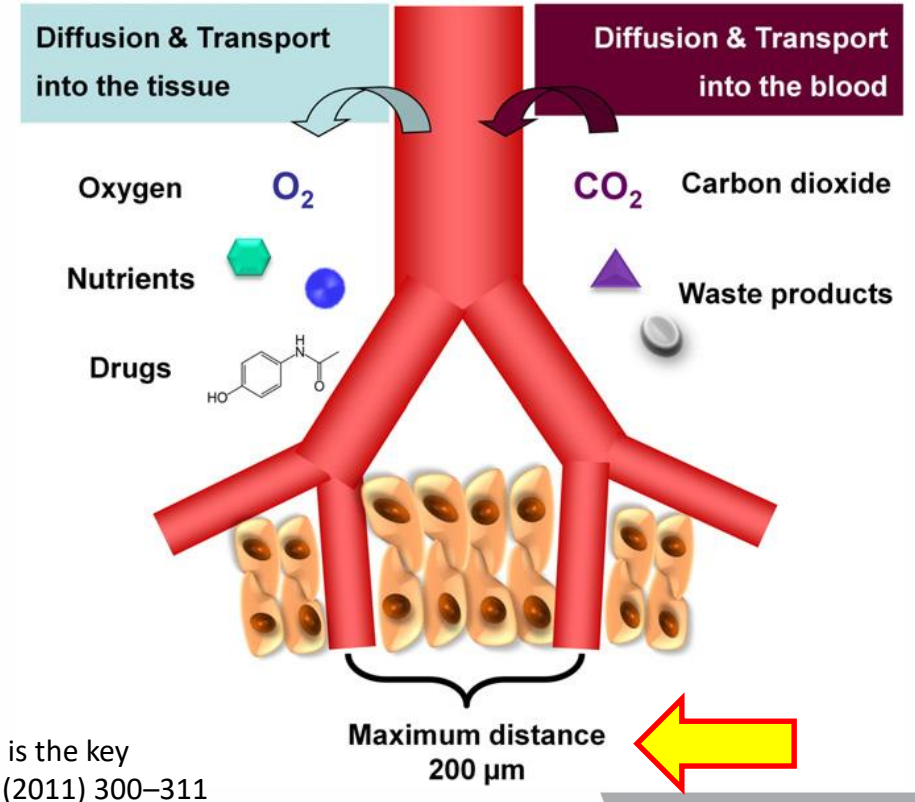


Freeze casted scaffold



Vascularization in tissue and relation of diffusion length of oxygen with distance between blood capillaries





Esther C. Novosel , Claudia Kleinhans, Petra J. Kluger, Vascularization is the key challenge in tissue engineering. Advanced Drug Delivery Reviews 63 (2011) 300–311

Implants and Scaffolds

Scaffolds are defined as a physical structure of synthetic/biological materials or both, wherein the biological cells are often implanted or 'seeded' with an aim to facilitate three-dimensional tissue formation *in vitro*.

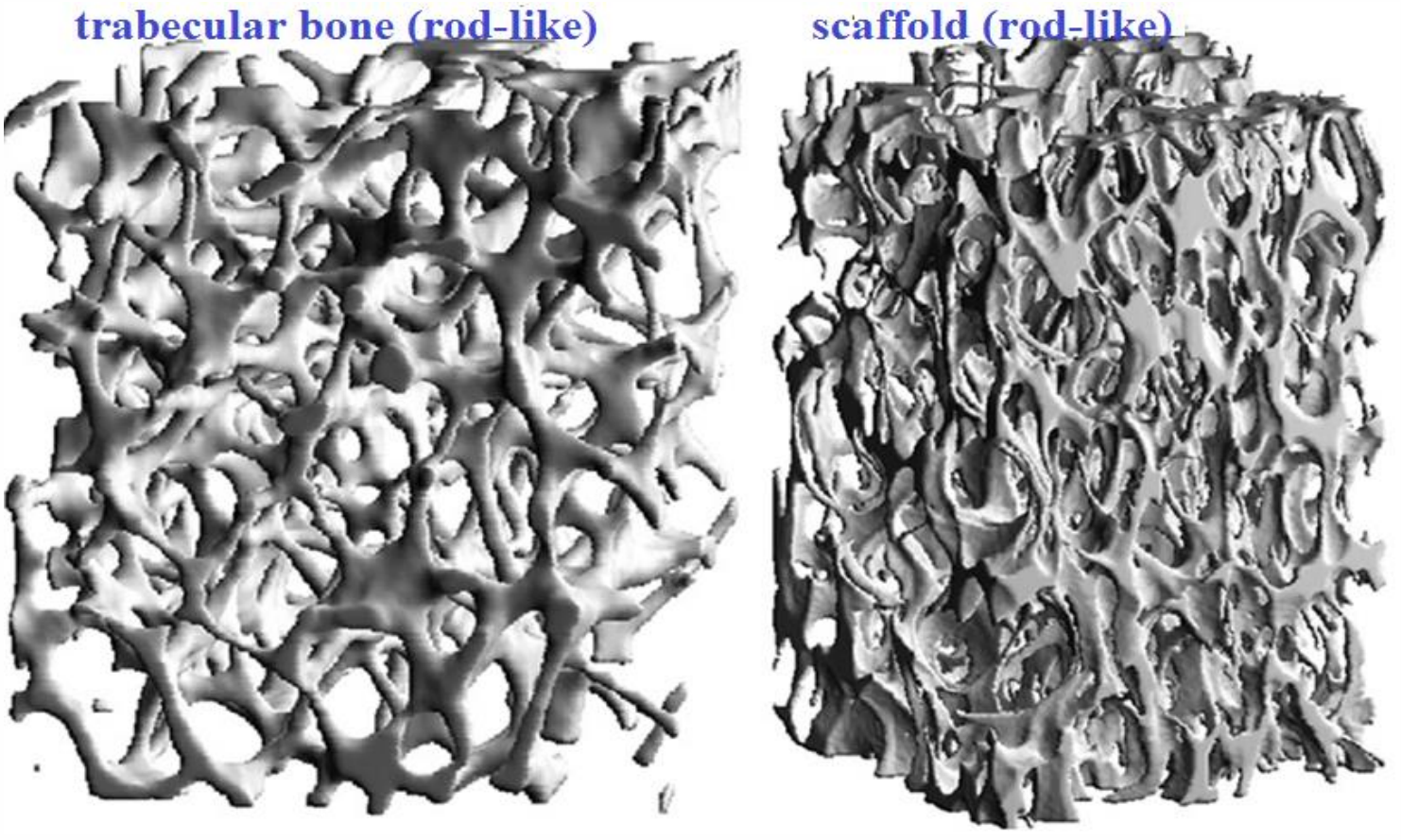
An implant is a synthetic biomaterial, which restores the physiological function of damaged/injured tissues. [IISc definition]

A scaffold is a 3D biomaterial platform with interconnected porosity, which supports cell functionality and aids tissue ingrowth. [IISc definition]

Implant vs. Scaffold

Implant	Scaffold
An implant is a synthetic non-porous biomaterial, which would remain in a living system for a longer timescale, unless it fails under biomechanical stresses.	A scaffold is a porous implantable biomaterial platform, which would support cell functionality.
An implant provides biomechanical support to the surrounding osseous system.	A scaffold is non-permanent and degradable in a biological system.
Depending on porous architecture, a scaffold has weaker mechanical properties, but has better biocompatibility than an implant.	

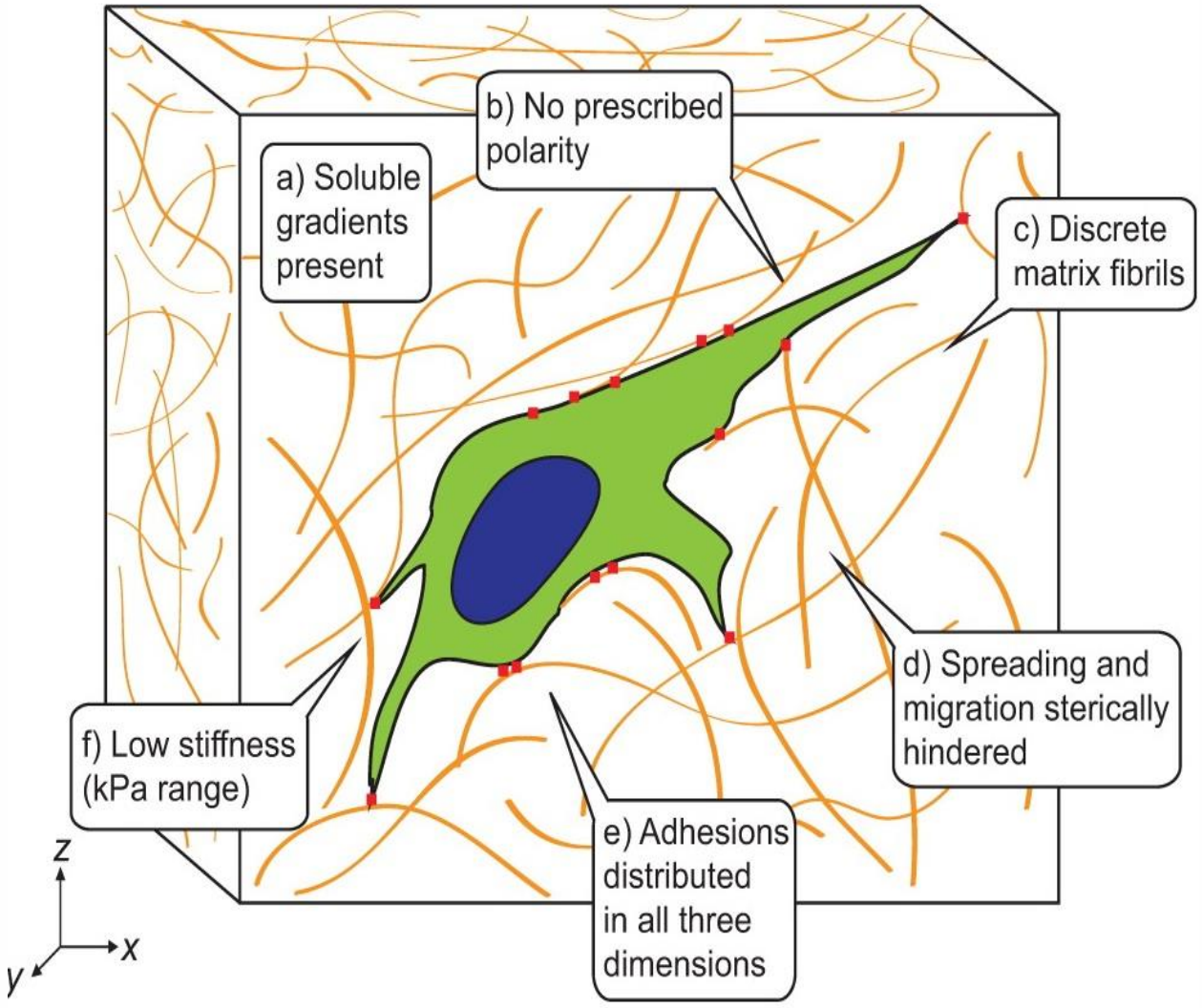
An example of a scaffold



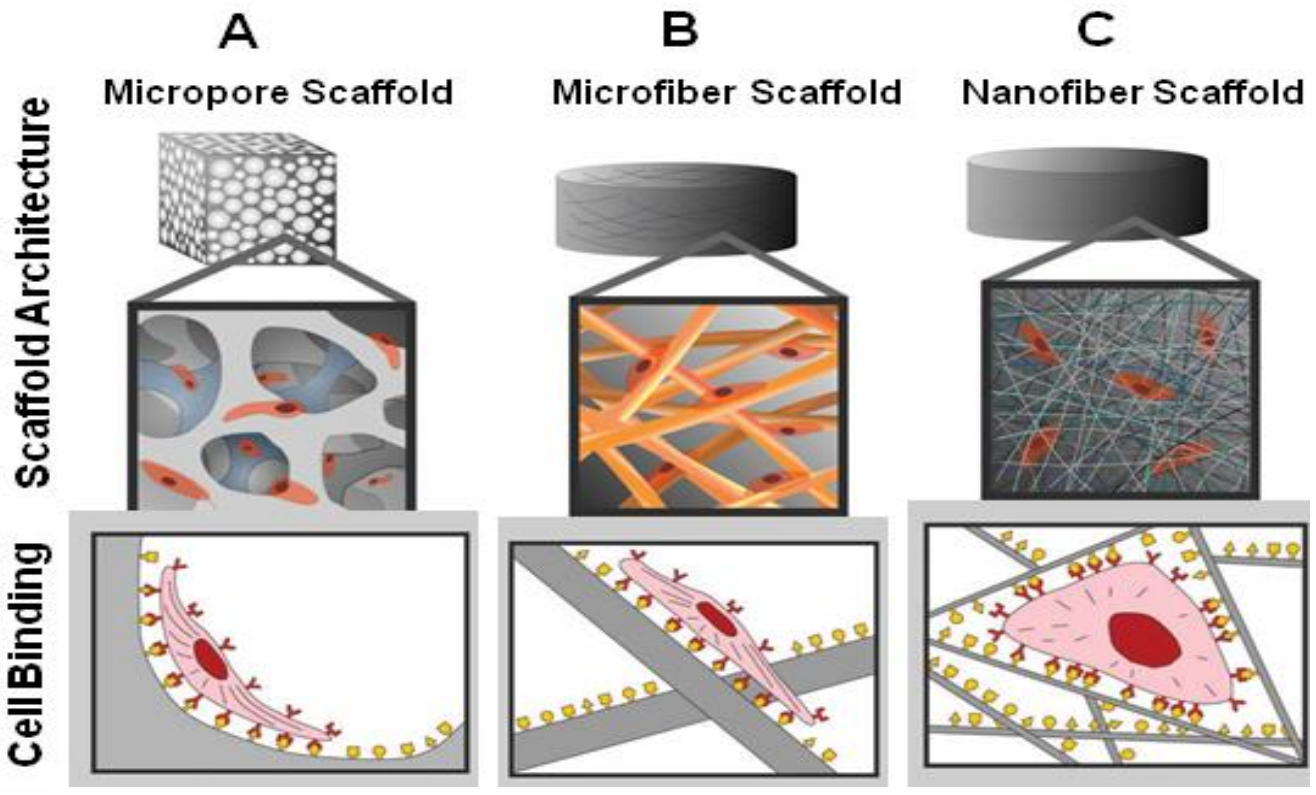
Similarity with cancellous bone structures

G. Harry van Lenthe, Henri Hagenmuller, Marc Bohner, Scott J. Hollister, Lorenz Meinel, Ralph Muller,, Biomaterials 28 (2007) 2479–2490.

Schematic of interaction of cells in a 3D scaffolds



Scaffold architecture and cellular orientation



• Electrospinning affords easy functionalization of fibers by surface conjugation or by direct incorporation of proteins and genes and thereby, boosts sustained delivery of bioactive molecules (cytokines, proteins, drugs etc.) to cells over longer duration.

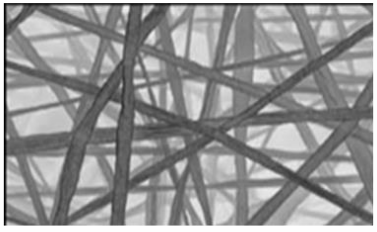
Stevens, M.M., and George, J.H. Exploring and engineering the cell surface interface. Science 310, 1135, 2005

Different Bone Graft Materials

B-TCP Ceramics

Hydroxyapatite –based materials

Bioactive Glasses



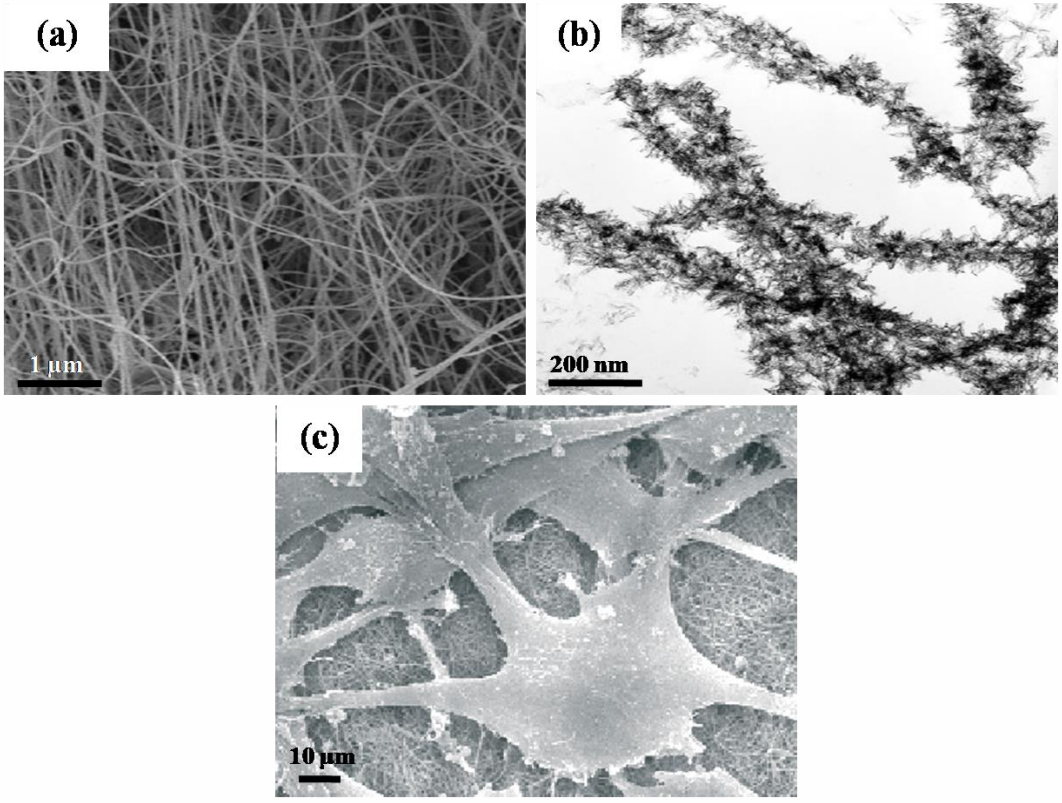
Nanofibrous Scaffolds

Stevens, M.M. Biomaterials for bone tissue engineering. Mater Today **11**, 18, 2008

Biomineralisation and cell functionality

Electrospun inorganic nanofibers

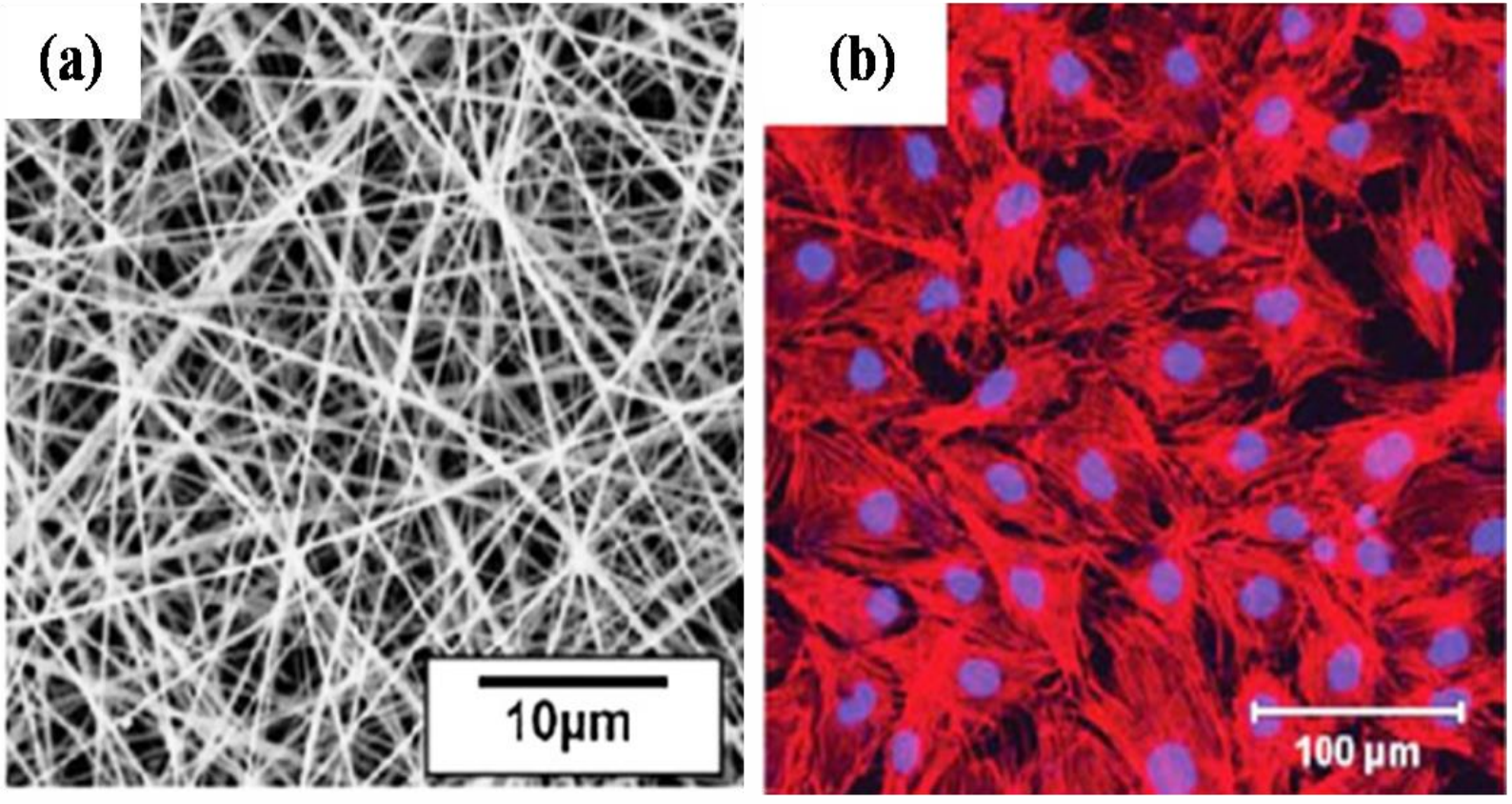
Bone-mineral like apatite



Morphological features of rat BMSCs

H.W., Kim, H.E., and Knowles, J.C. Production and potential of bioactive glass nanofibers as a next-generation biomaterial. Adv Funct Mater **16**, 1529, 2006

Gelatin-Siloxane Nanofibers



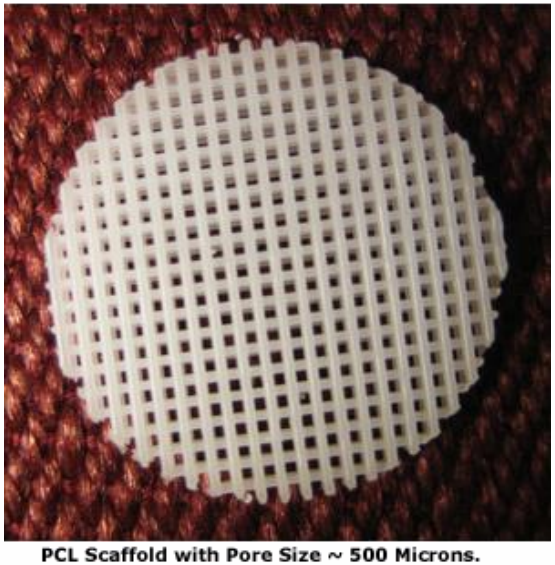
Song, J.H., Yoon, B.H., Kim, H.E., and Kim, H.M. Bioactive and degradable hybridized nanofibers of gelatin–siloxane for bone regeneration. J Biomed Mater Res Part A **84A**, 875, 2007

Additive manufacturing in tissue engineering

Complexity in 3D scaffolds cannot be introduced using traditional scaffold fabrication methods.

In this context, additive manufacturing methods such as 3D plotting, 3D powder printing, and high energy beam melting are found suitable to produce the tissue specific implantable 3D porous scaffolds.

Conventional 3D porous scaffold



PCL Scaffold with Pore Size ~ 500 Microns.

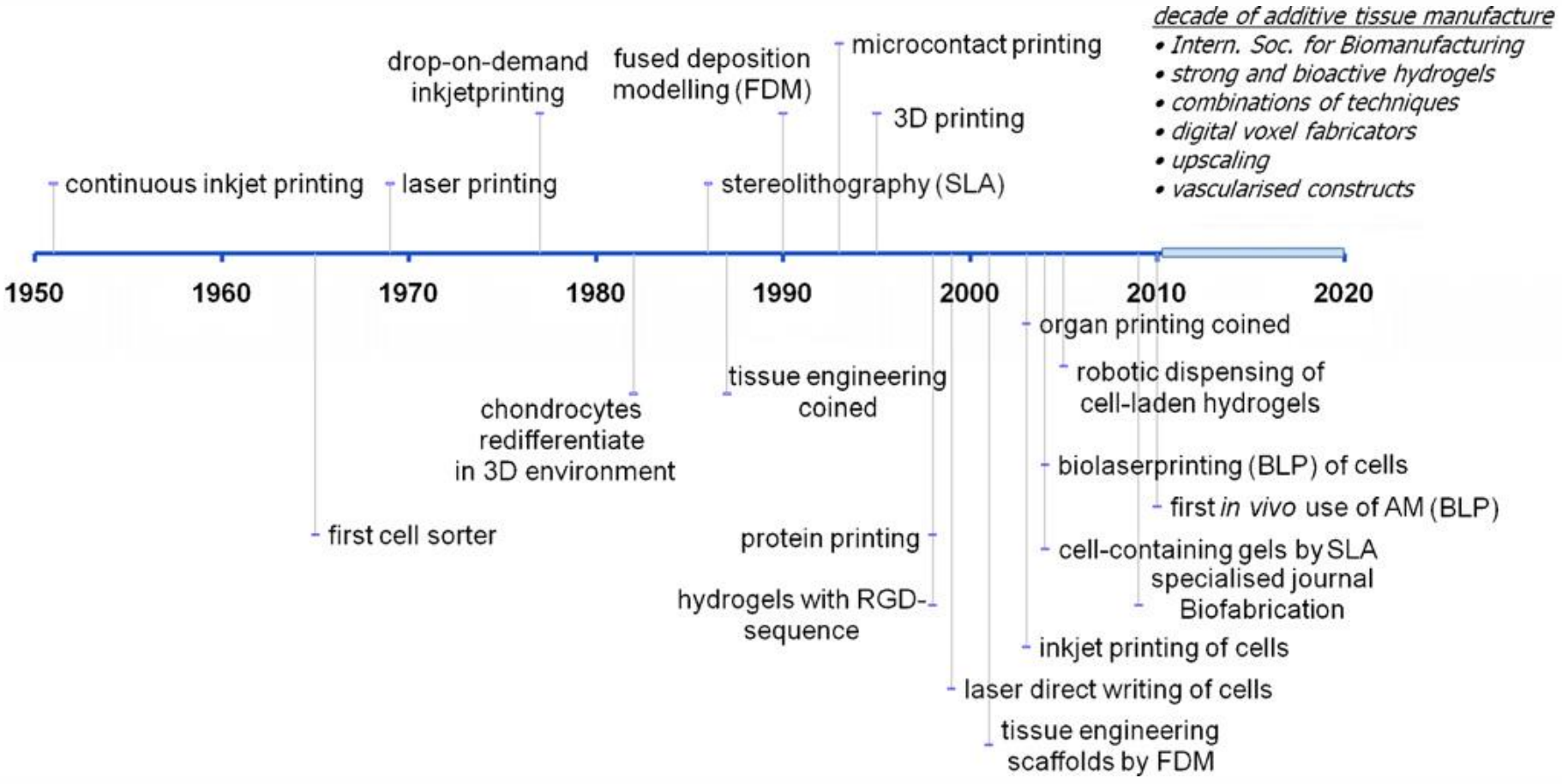
3D printed porous scaffold

http://www.cellsupports.com/
http://www.techno-isel.com/LMS/ApplicationStories/Biotek.htm

Advantage of rapid prototyping over conventional processing

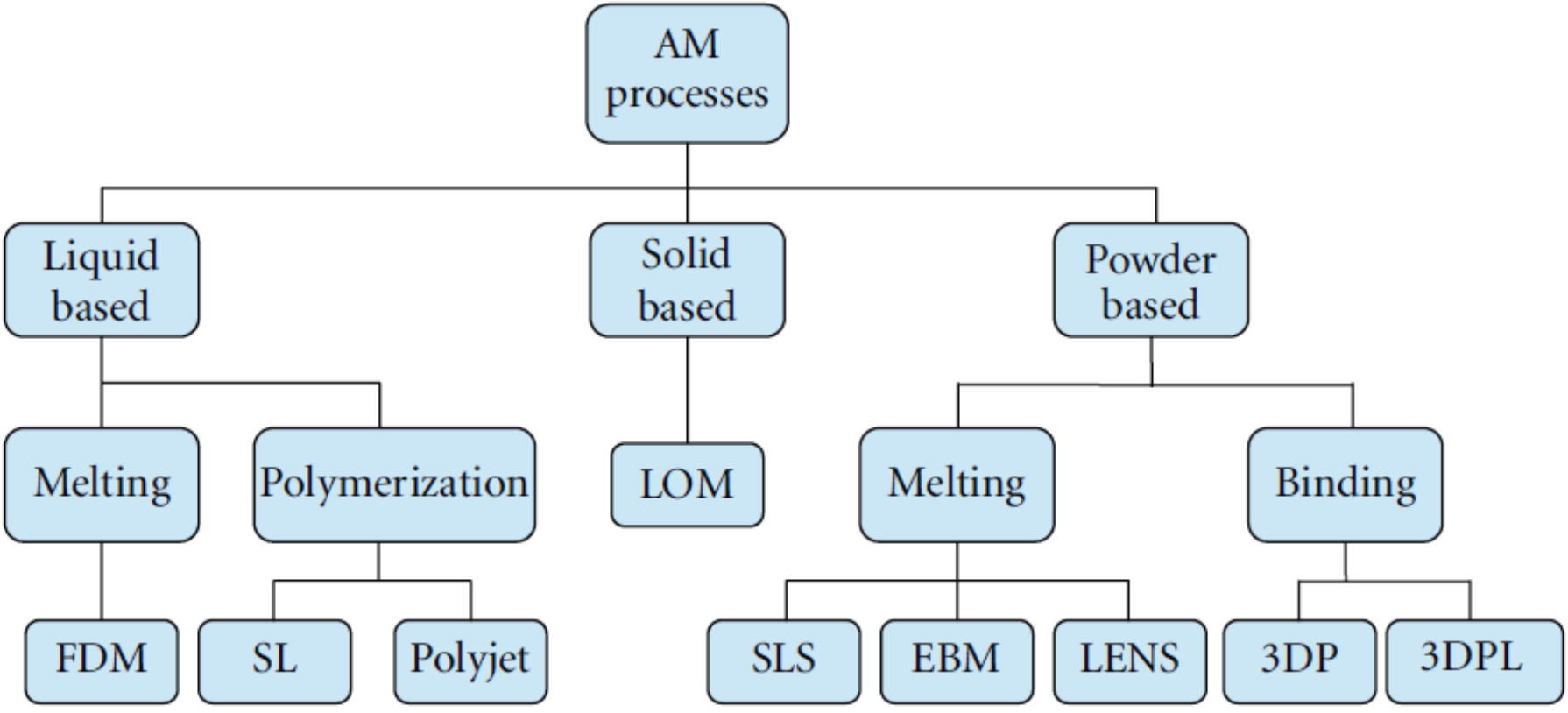
Properties	Conventional processing	Rapid prototyping
Approach	Replacement of affected bone with implant with limited integration with living tissue	Better integration with living tissue around the scaffold due the presence of deep interconnected pores at the surface
Structural complexity	Very limited	Can produce very complex structural features
Porosity	Difficult to control the porosity distribution	Gradient porosity can be introduced
Mechanical strength	Generally stronger than 3D printed prototype	Porosity and absence of sufficient pressure during scaffold design is responsible for decreased strength
Time	Time consuming process	Build speed is faster

Evolution of additive manufacturing



Melchels et al, Progress in Polymer Science, 37 (2012) 1079– 1104

Variants of additive manufacturing

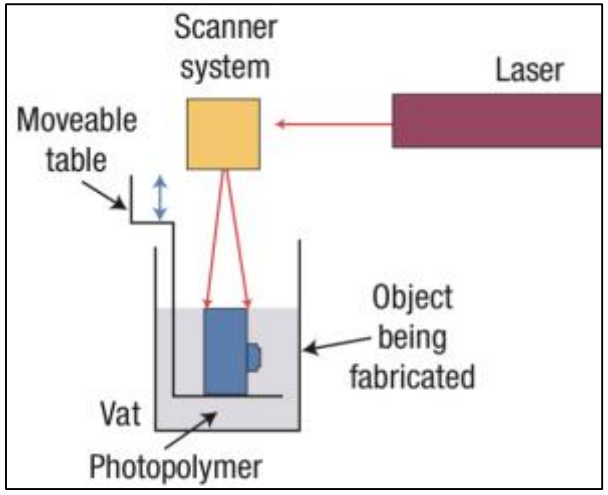


AM represents a wide spectrum of manufacturing techniques, computer aided design (CAD) driven layer-by-layer addition of materials in a programmed manner.

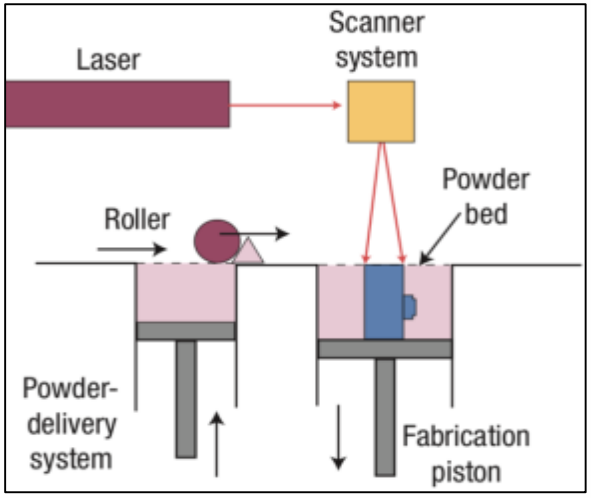
Wong et al, ISRN Mechanical Engineering, Volume 2012, Article ID 208760

Rapid prototyping techniques

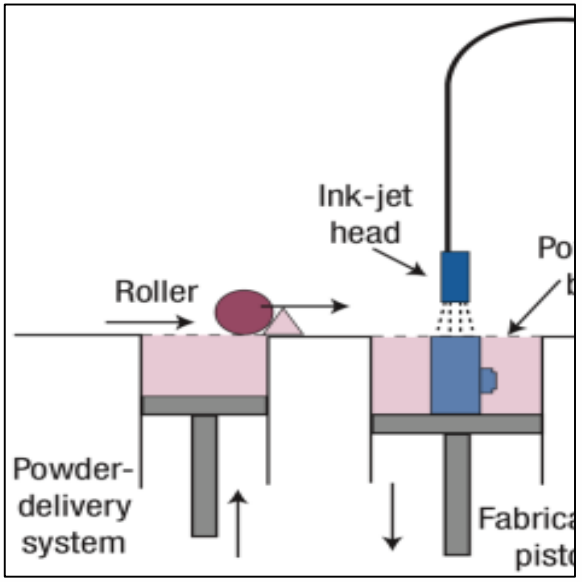
Stereolithography



Selective laser sintering



3D printing



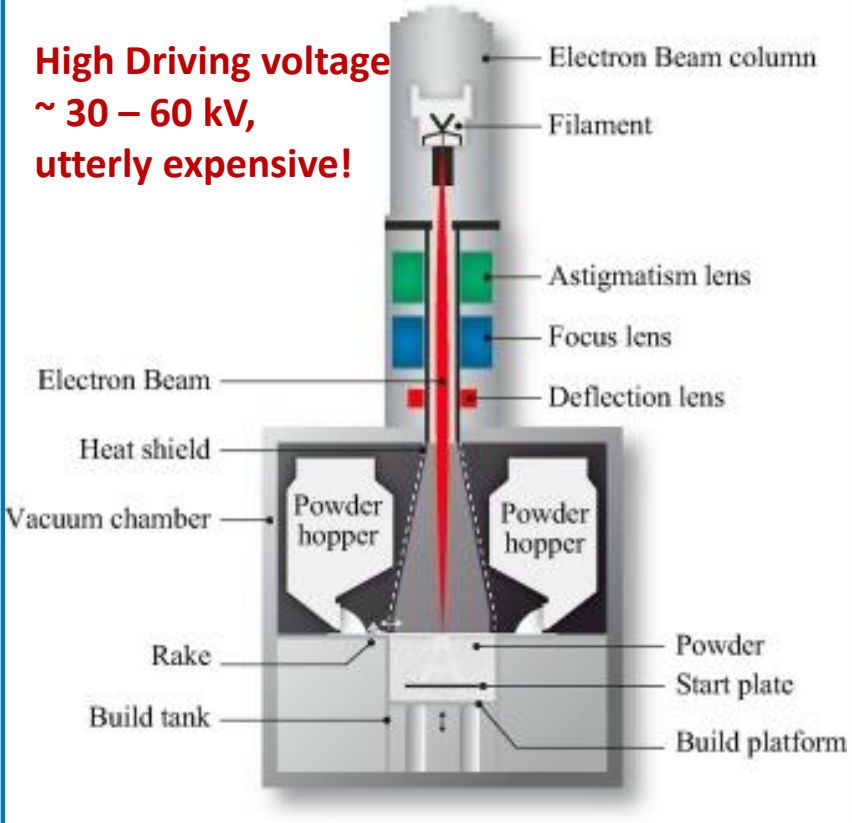
3D printing can be adopted for scaffold fabrication at ambient condition.

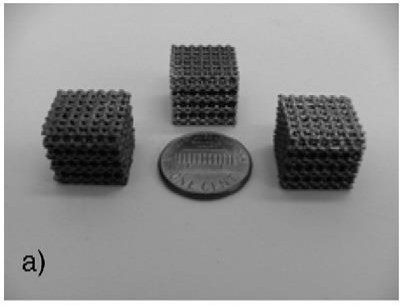
However, universal binder formulation and quantitative understanding of the process physics poorly appreciated!

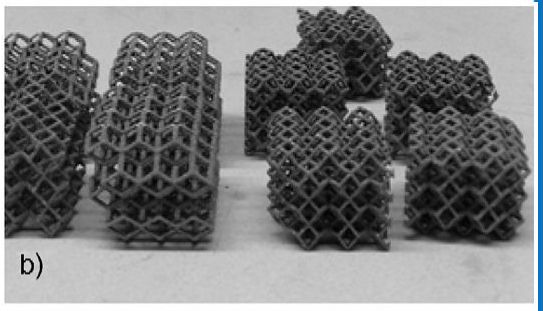
Scott J. Hollister, Nature Materials, Vol . 4, July 2005

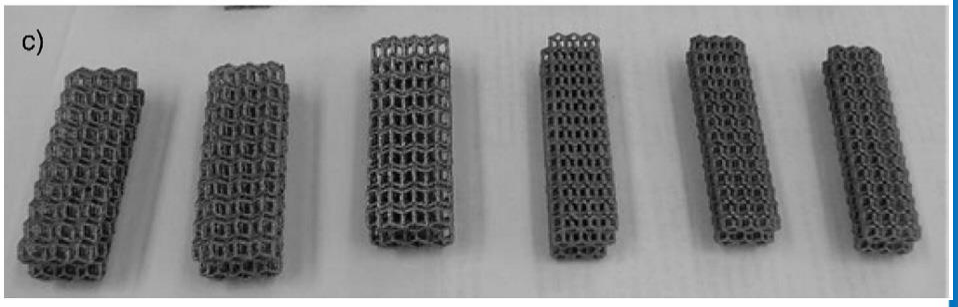
Electron beam melting, 1997

High Driving voltage ~ 30 – 60 kV, utterly expensive!







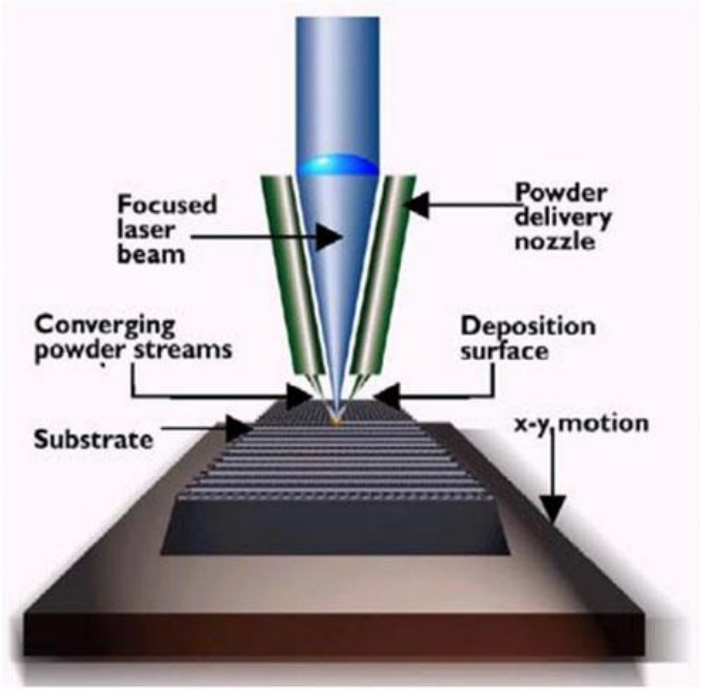


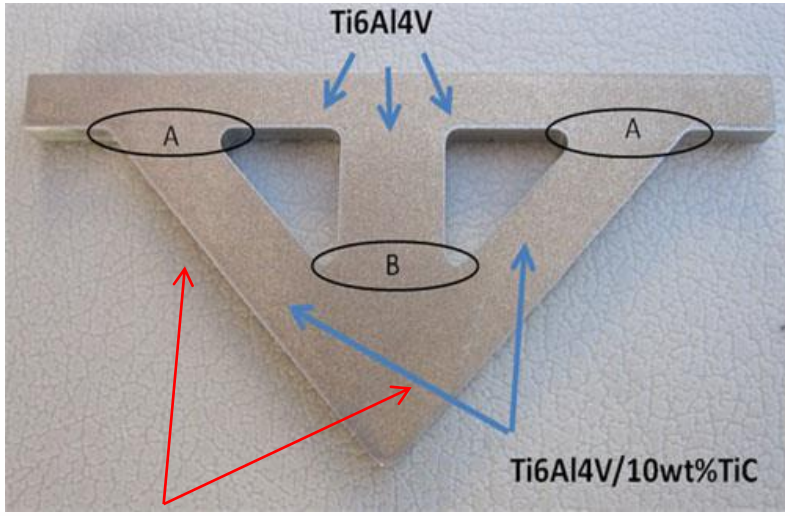
(a) Cubes with 40% relative density (60% porous)
(b) Cubes with relative densities of 8.0%, 5.0%, and 3.8%
(c) Bending specimens with 8 mm and 6 mm cell sizes (7.3% and 11.9% relative density)
(d) hip stems with mesh configuration, hole configuration, and solid

Rest process methodologies are identical as SLS/DMLS

Koike et al, Journal of Materials Processing Technology 211 (2011) 1400–1408
Harrysson et al, Materials Science and Engineering C 28 (2008) 366–373
Manuela et al, Additive Manufacturing 19 (2018) 1–20

Laser Engineered Net Shaping (LENS™), 1997





Transition joints

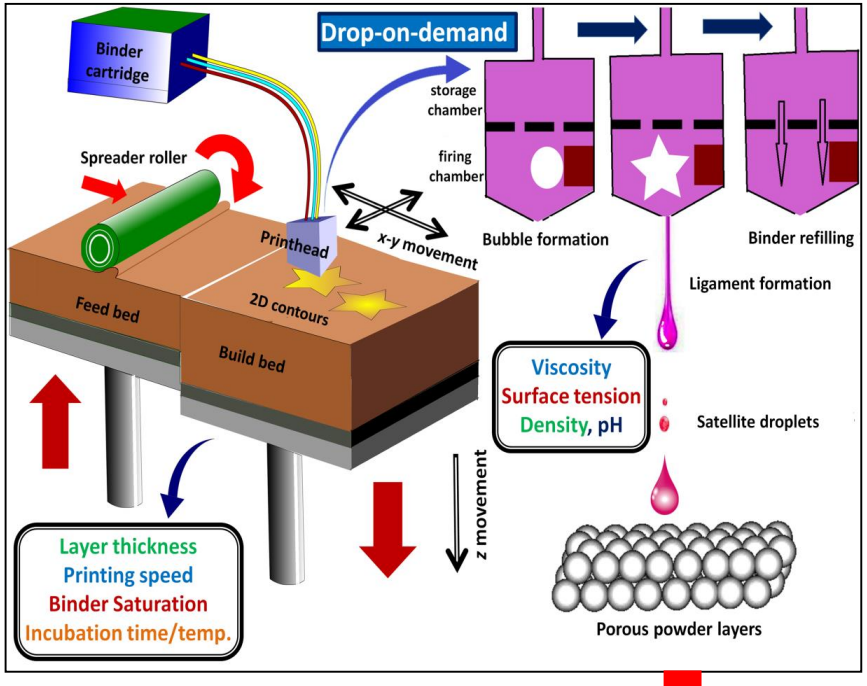
LENS-fabricated dual-material structure

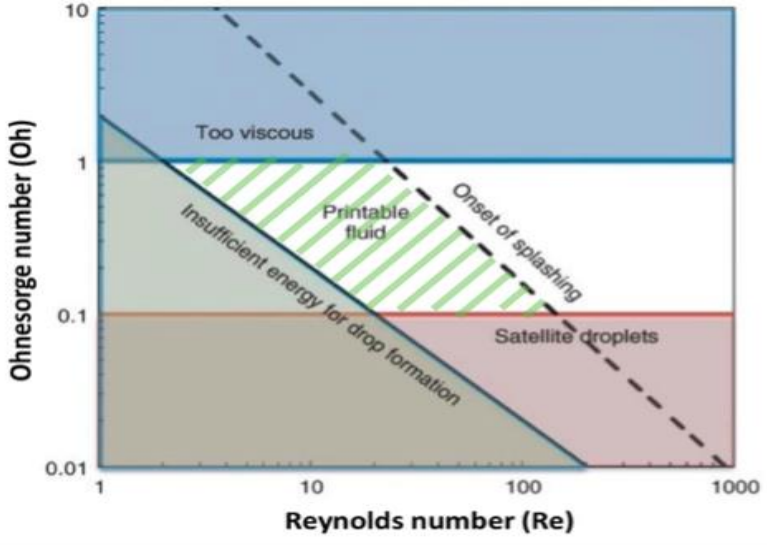
Multimaterials: *in-situ* alloying, composites, asymmetric welding of different class of materials

https://www.youtube.com/watch?v=3KrfIBEOuvw

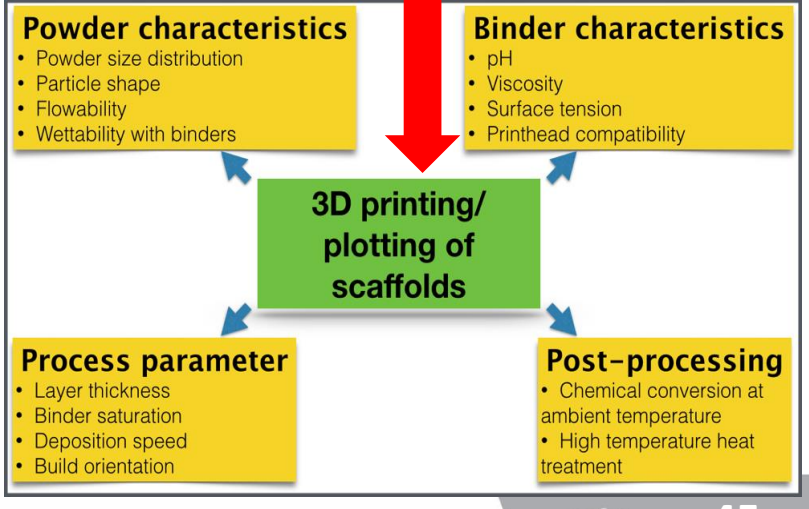
Obielodan et al, Int J Adv Manuf Technol (2013) 66:2053–2061

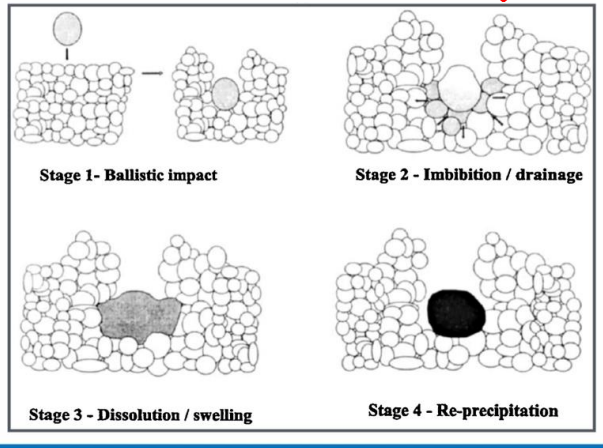
Thermal 3D inkjet powder printing, 1993





I.M. Hutchings, G.D. Martin, John Wiley & Sons, 2012





B.M. Wu, Dept. of Materials Science and Engineering, PhD thesis, Massachusetts Institute of Technology, 1998, p. 246.

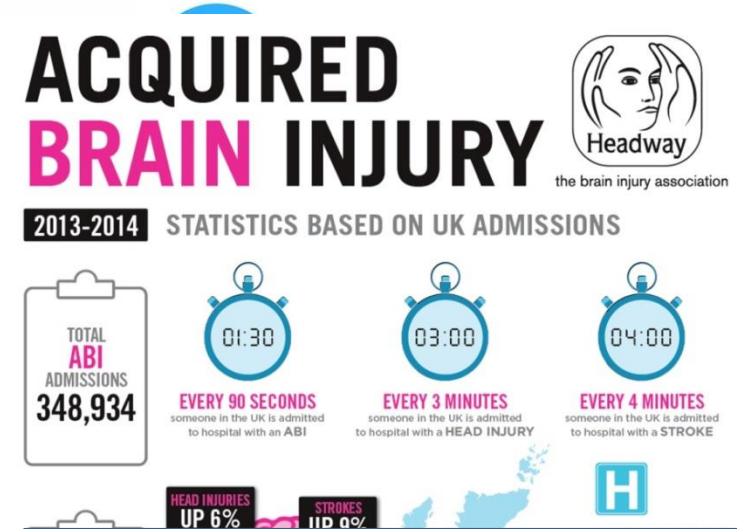
Plan of the sub-module presentation

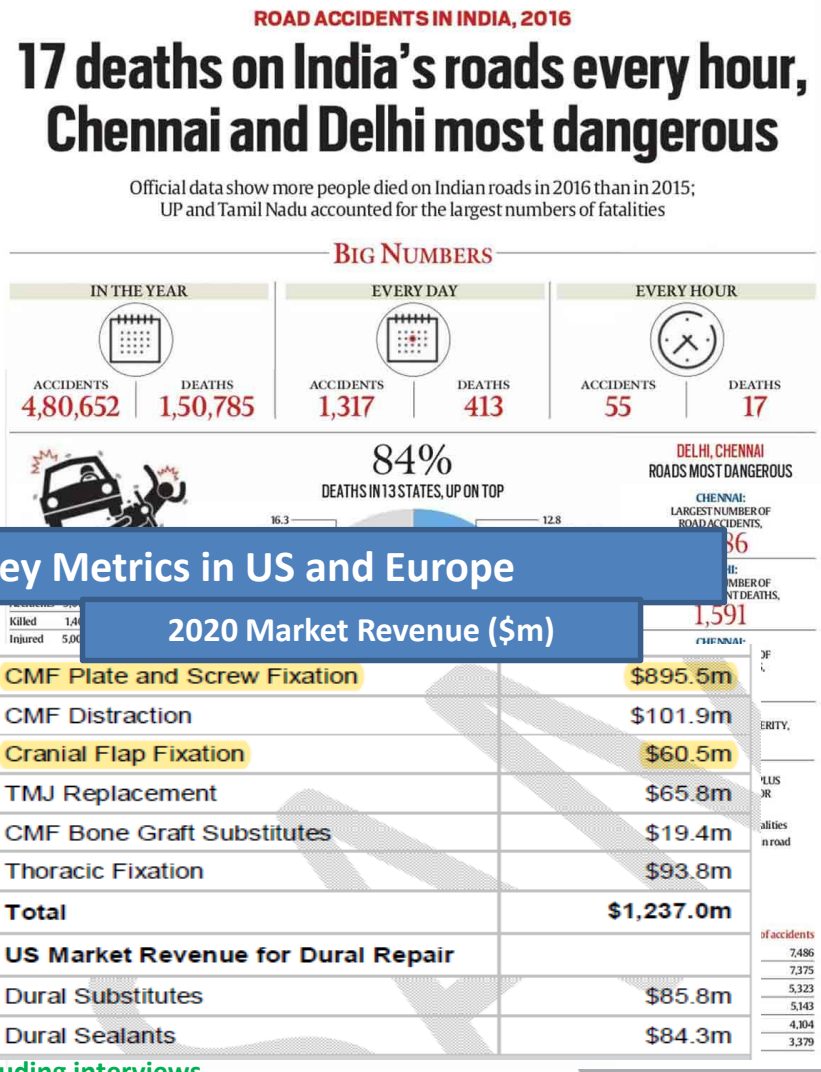
- Fundamentals of Biomaterials and Biocompatibility
- Introduction to Tissue Engineering
- Overview of Additive Manufacturing technique
    - High energy laser/e-beam
    - 3D inkjet printing
- Case study
    - Clinical study on the use of 3D printing in cranioplasty surgery
- Bioprinting
- Closure

An example of a clinical study

Evaluation of Implant Properties, Safety Profile and clinical Efficacy of Patient-Specific Acrylic Prosthesis in Cranioplasty Using 3D Binderjet Printed Cranium Model: A Pilot Study

Clinical relevance for cranioplasty





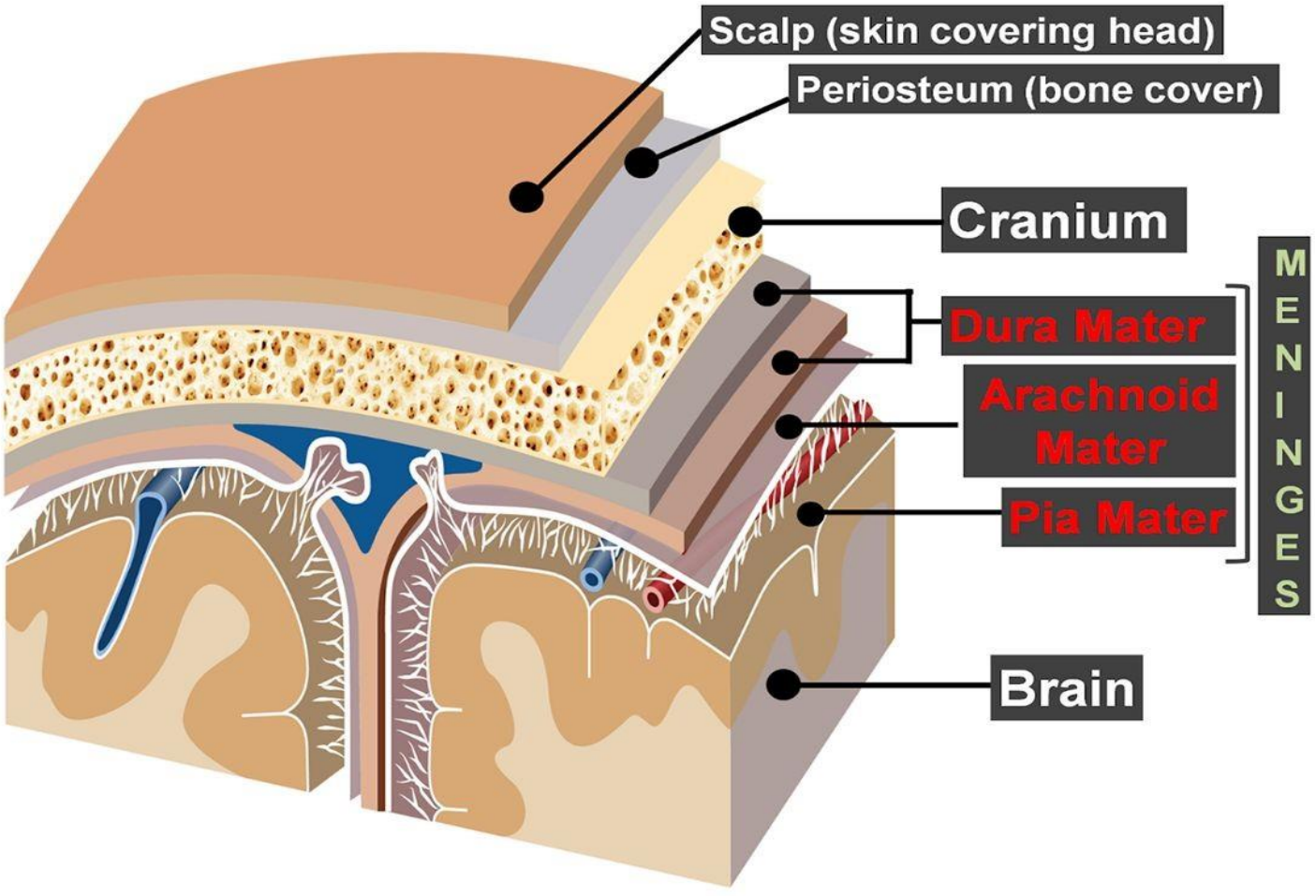
Craniomaxilliofacial Devices: Key Metrics in US and Europe

	2013 Market Revenue ($m)
CMF Plate and Screw Fixation	$587.0m
CMF Distraction	$58.5m
Cranial Flap Fixation	$50.9m
TMJ Replacement	$26.7m
CMF Bone Graft Substitutes	$15.4m
Thoracic Fixation	$65.1m
Total	**$803.5m**
US Market Revenue for Dural Repair	
Dural Substitutes	$73.2m
Dural Sealants	$72.8m

	2020 Market Revenue ($m)
CMF Plate and Screw Fixation	$895.5m
CMF Distraction	$101.9m
Cranial Flap Fixation	$60.5m
TMJ Replacement	$65.8m
CMF Bone Graft Substitutes	$19.4m
Thoracic Fixation	$93.8m
Total	**$1,237.0m**
US Market Revenue for Dural Repair	
Dural Substitutes	$85.8m
Dural Sealants	$84.3m

Source: Global Data, based on secondary research and primary research, including interviews.
https://www.prnewswire.com/news-releases/global-cranial-implants-market-2017-2021---key-tend-in-the-market-is-growing-demand-for-3d-printingmodeling-300560974.html

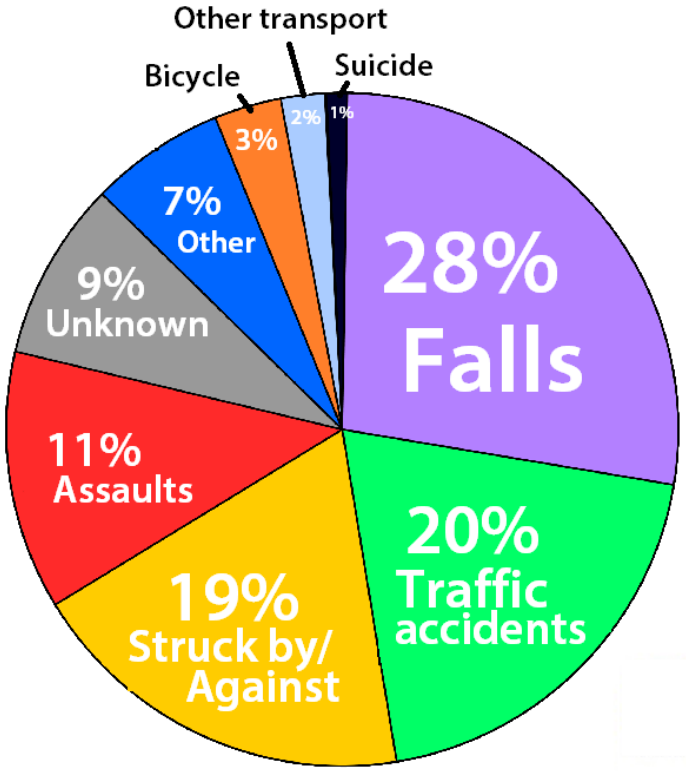
Structure of Brain



Ref: https://www.toppr.com/content/story/amp/meninges-of-the-brain-2707/

Traumatic Brain Injury (TBI)

Disruption in the normal function of the brain

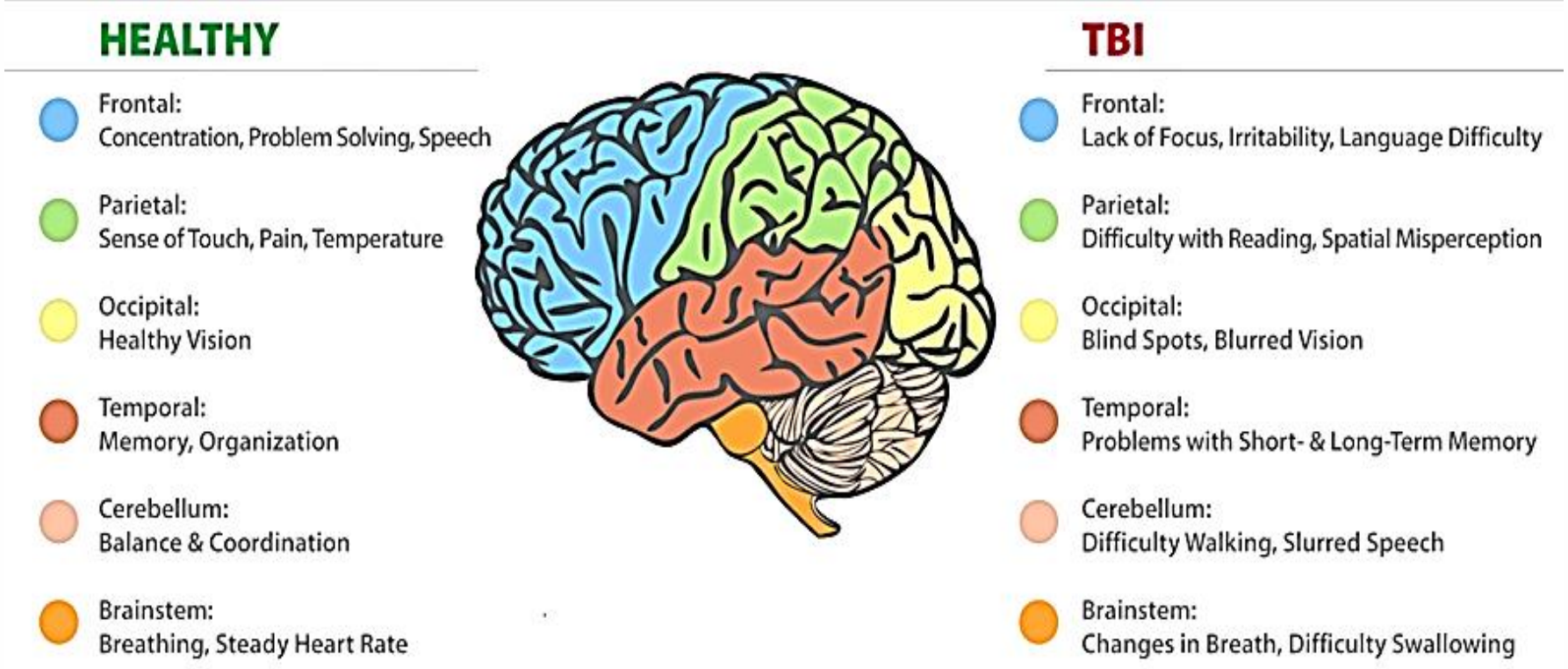


In India,

- **1.5–2 million persons are injured and more than a million succumb to death every year.**
- **Road traffic accidents: leading cause (60%) followed by falls (20%–25%) and violence (10%).**
- **Alcohol involvement is known to be one of the confounding factors among 15%–20% of TBIs at the time of injury.**

Ref: Kirankumar et al., 2019. DOI: 10.4103/JCSR.JCSR_65_19;

How TBI affects daily life?

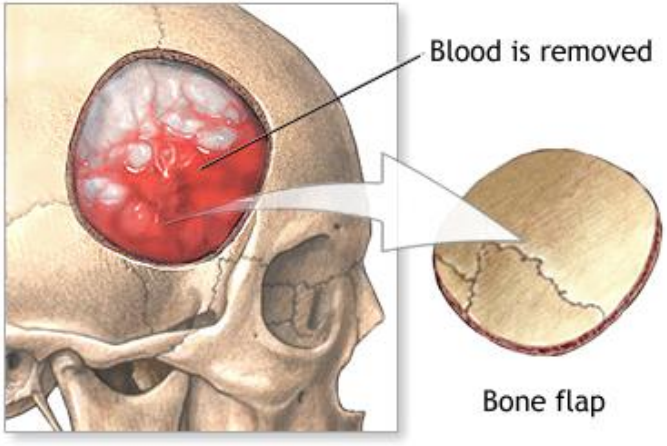


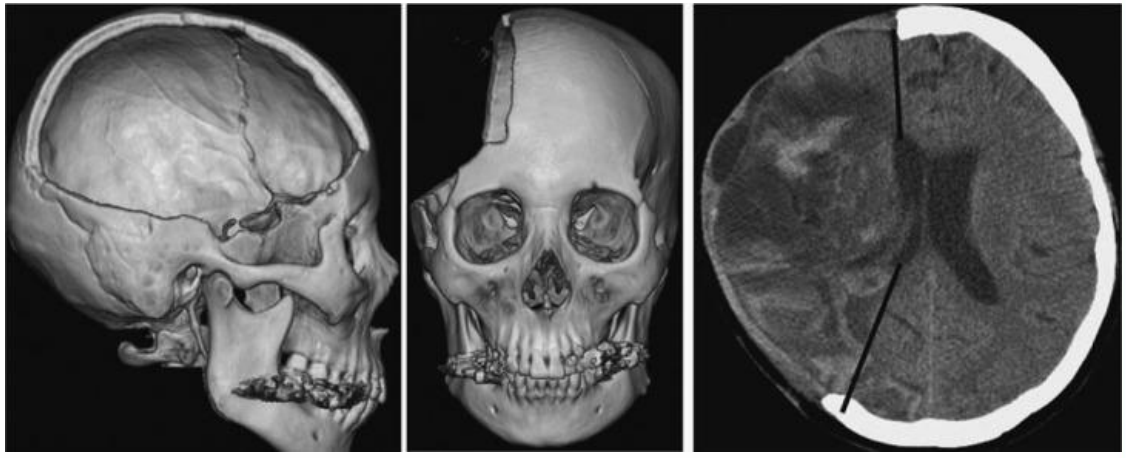
Symptoms of a TBI can be mild, moderate, or severe, depending on the extent of damage to the brain.
As a result of TBI, intracranial hypertension causes major complications and death.

Ref: https://www.hopeforthewarriors.org/newsroom/the-daily-effects-of-traumatic-brain/

Decompressive Craniectomy

- **Strategy for managing intracranial pressure in patients with TBI.**
- **Removal of the portion of the skull that is causing the pressure on the brain. This is usually area of the skull that covers the injury.**
- **Reduce the risk of severe brain damage (life-saving).**



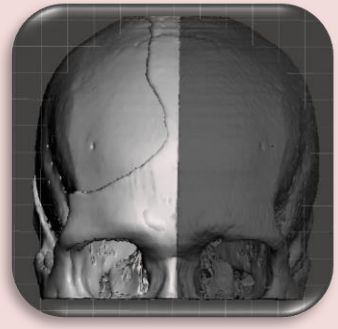


Ref: Journal of the Mechanics and Physics of Solids 96, 2016, 572-590

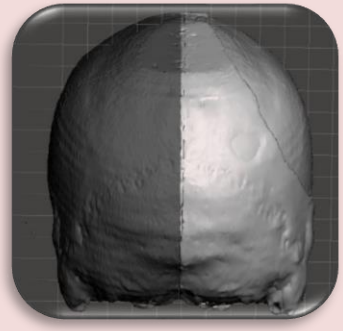
Clinical study on cranioplasty surgery in Bangalore

I

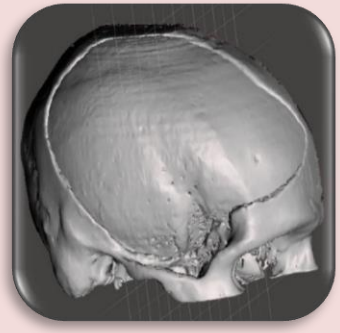
3D CT Scan Images showing craniotomy defect



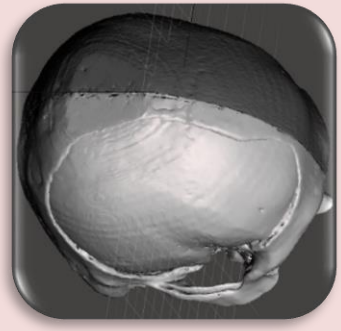
Front View



Back View



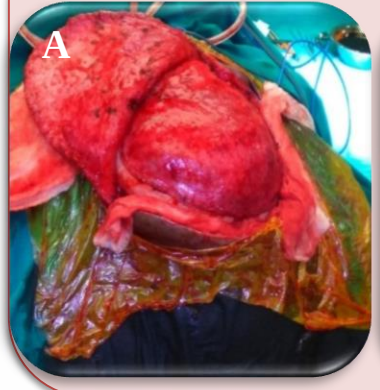
Lateral View

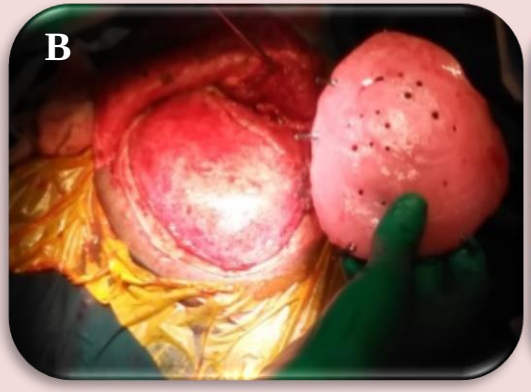


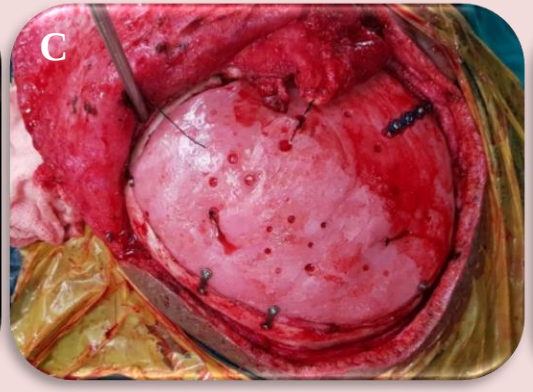
Superior View

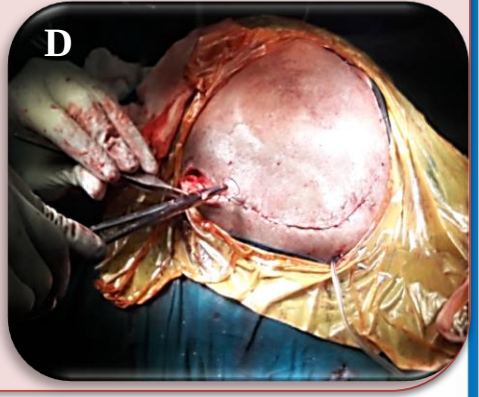
II

Intraoperative Implant Fixation





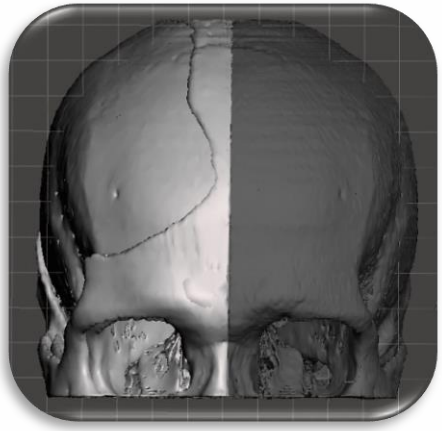




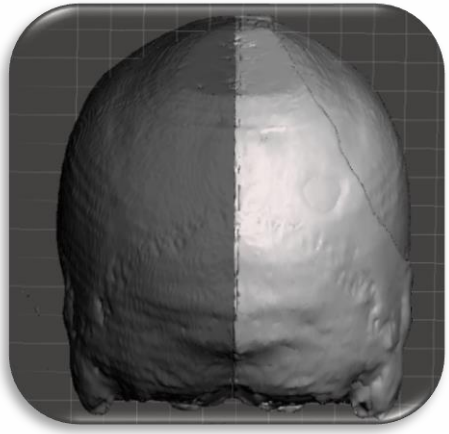
Fabrication of customised PMMA implant

3D CT Scan Images

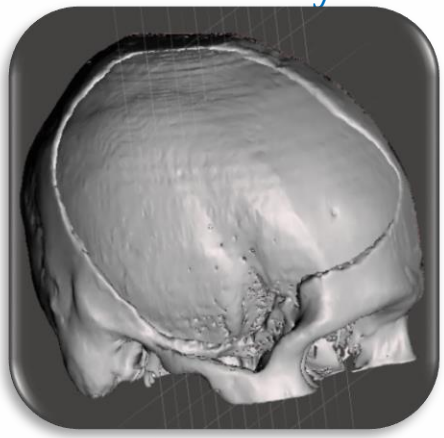
Conversion of DICOM data to *.stl file by 3D Slicer



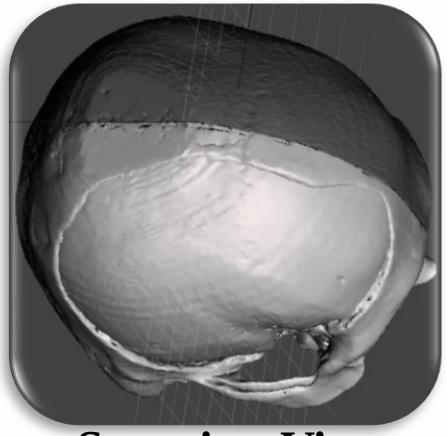
Front View



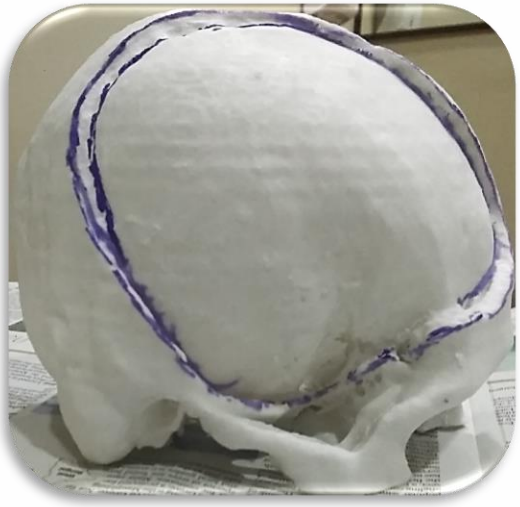
Back View



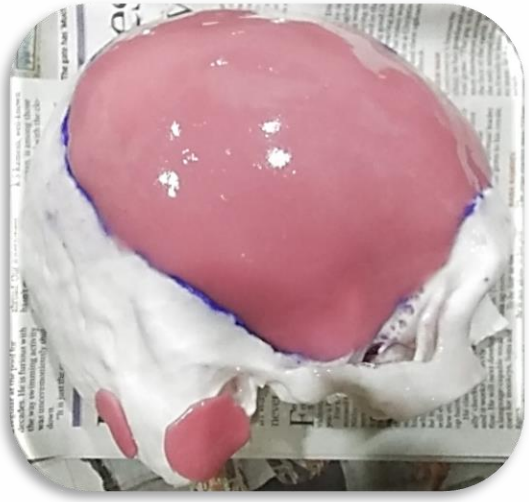
Lateral View



Superior View



3D Printed Skull model



PMMA prosthesis fabrication

Materials in Cranioplasty

An ideal cranioplasty material must have the following features:

- It must fit the cranial defect and achieve complete closure
- Radiolucency
- Resistance to infections
- Not dilated with heat
- Strong to biomechanical processes
- Easy to shape
- Not expensive
- Ready to use

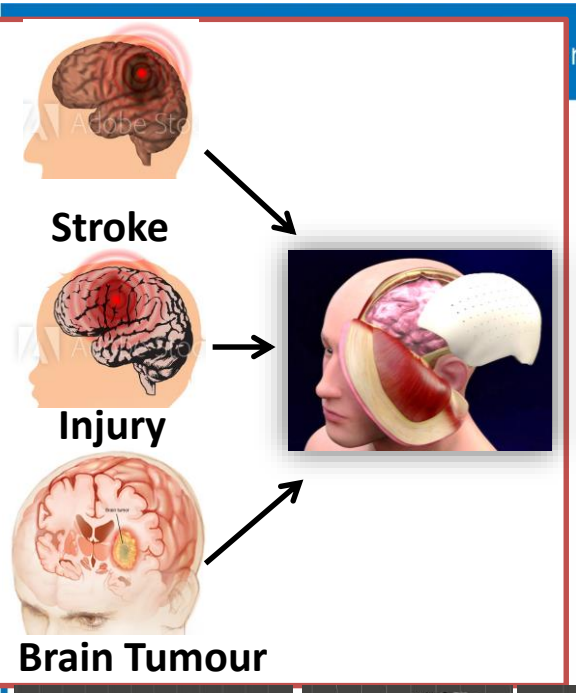
Polymethylmethacrylate (PMMA):acrylic bone cement

Advantages:

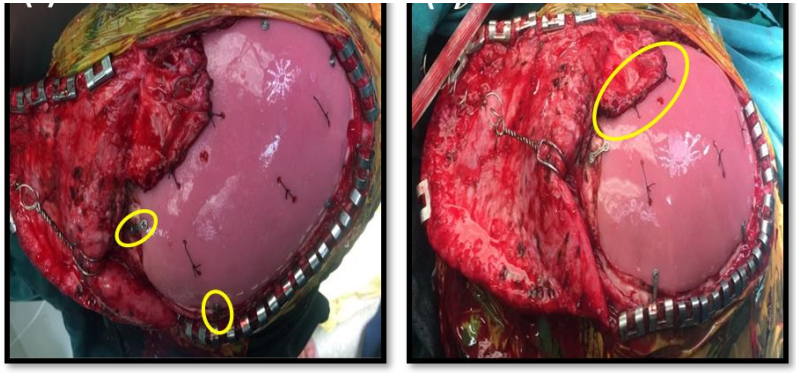
- **Cost-effective**
- **Easily available**
- **Radiolucency**
- **Acceptable biocompatibility**
- **Minimum reaction**
- **Tight adherence**
- **MRI compatible**
- **Prepare intra-operatively**
- **DPI – RR Cold Cure powder was mixed with methylmethacrylate (MMA) solvent to produce a viscous translucent plastic material with strength comparable to native bone.**

PMMA used for present study

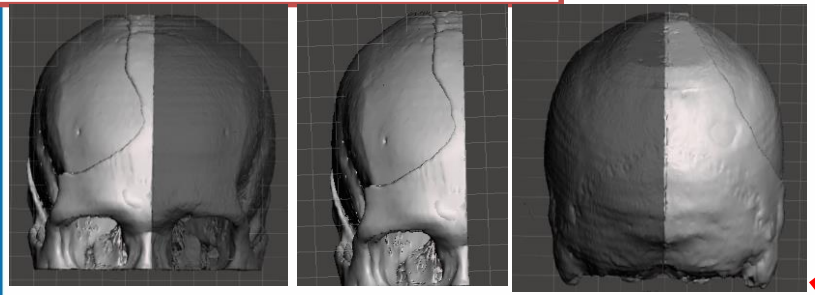
3D binderjet printing in healthcare



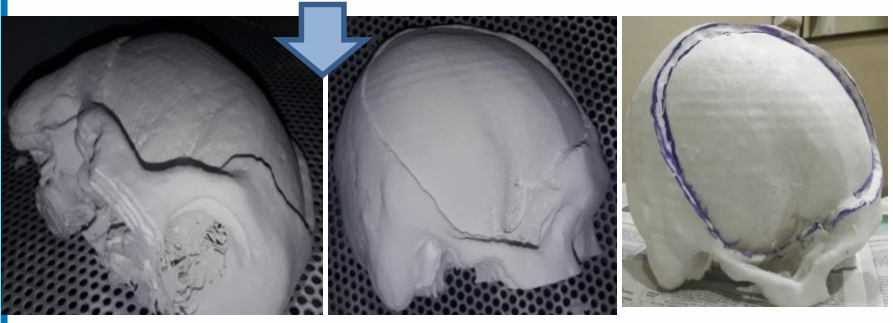
10 patients



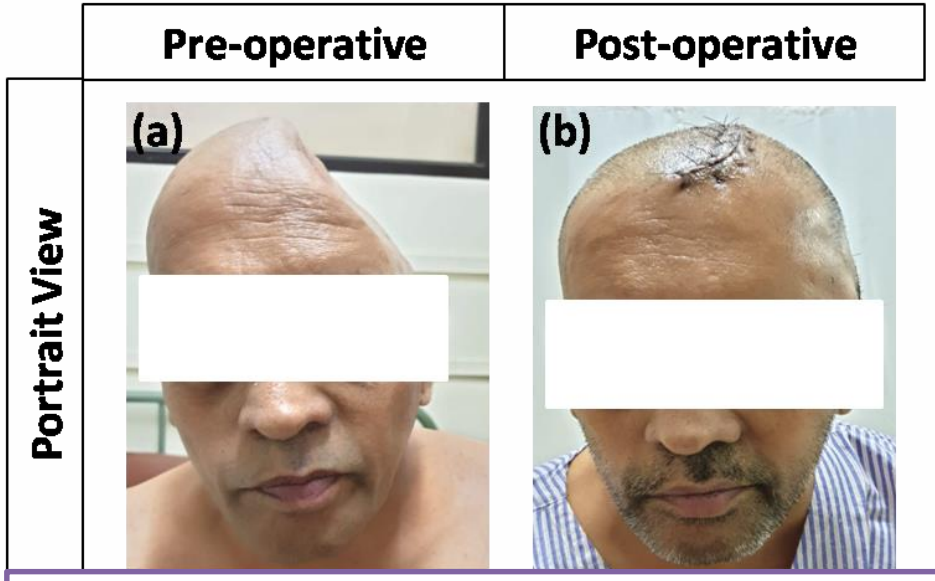
Intra-operative clinical images during Cranioplasty surgery



Conversion of DICOM data to *.stl file using 3D Slicer



3D Printed defective half skull mould



Clinical trial performed at two hospitals in India

The Telegraph
online edition

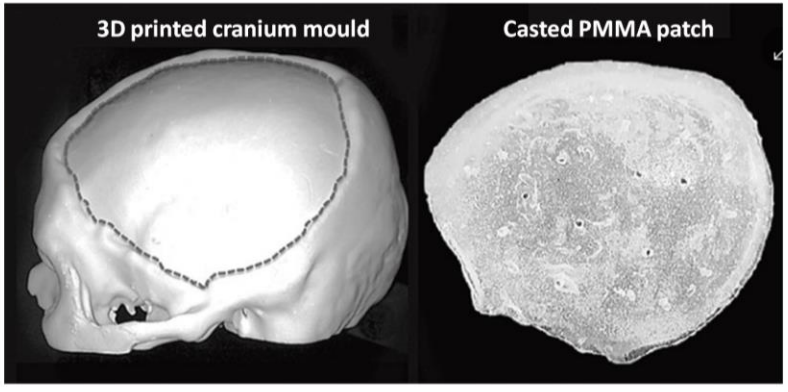
Home Opinion India States World

A printout to patch up the skull

Indian scientists are now using 3D printed parts to repair damaged craniums

By Prasun Chaudhuri

Published 1.03.20, 2:11 PM • Updated 1.03.20, 2:11 PM



Cut-outs

Traumatic brain injuries affect millions of people across the world every year. This includes victims of falls or road accidents and soldiers or security personnel injured in the line of duty. Soon after such a serious blow to the head, there's a cascade of immune responses that results in the swelling of the brain, which gets compressed in the skull. This often leads to a life-threatening condition.

The IISc team collaborated with neurosurgeons at M.S. Ramaiah Medical College in Bangalore to place the 3D printed bone flaps on the skulls of 10 patients through cranioplasty. It has now been over a year and all 10 patients have fully recuperated, showing accurate restoration of the symmetrical contours and curvature of the cranium.

The printing of the cranium model is then done in a unique binderjet printing process protocol, innovated by the IISc team. The technique employs inkjet printing technology — which dispenses a binder, droplet-wise, onto a powder and leaves a solid body behind — and the entire model is printed layer by layer. The fabrication process follows the contour or design profile generated by a computer-aided design of the skull defect. "The importance of 3D powder printing lies in its ability to fabricate a patient-specific model of the cranium with complex defect morphology at room temperature using a binder," says Basu.

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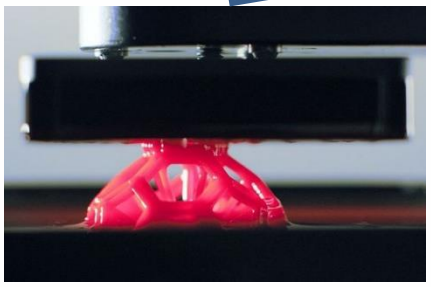
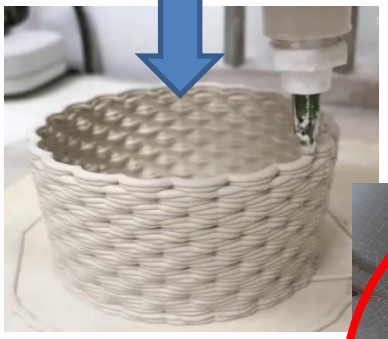
3D Printing



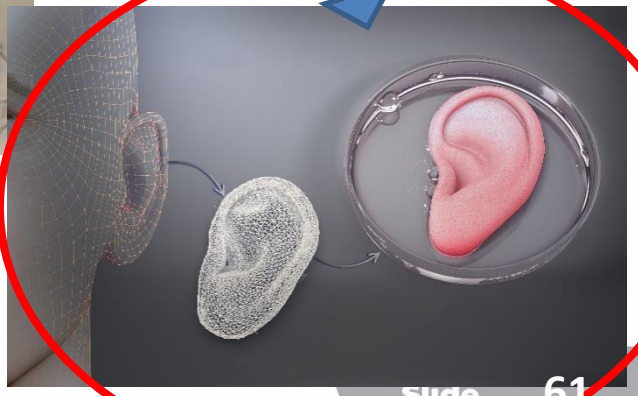
Polymer

Metal



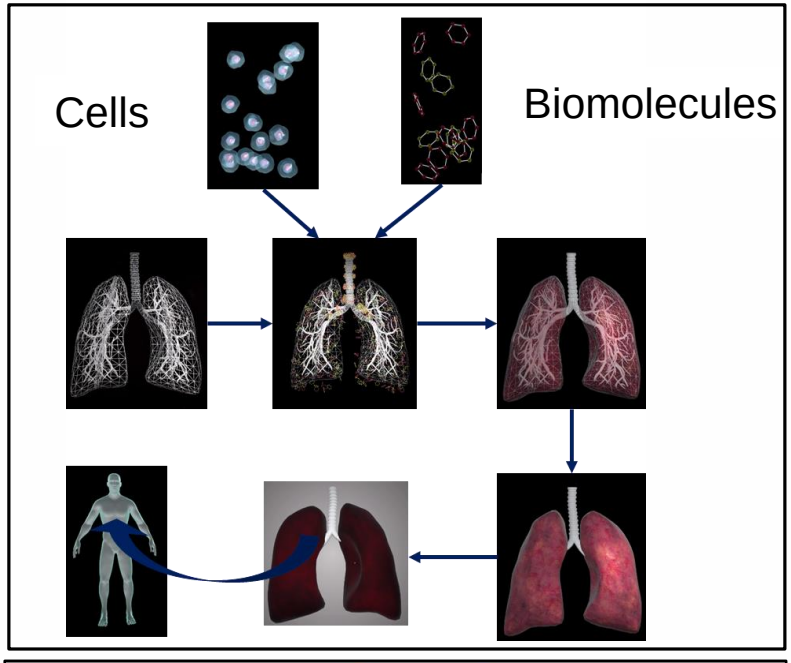
Ceramic

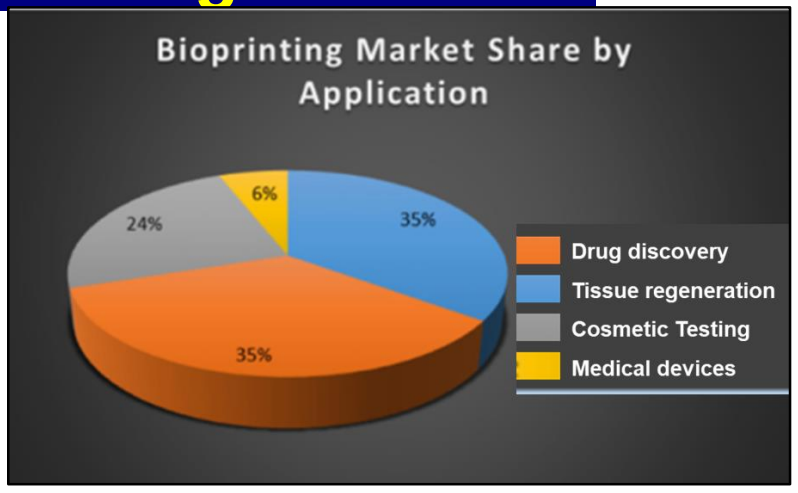
3D bioprinting

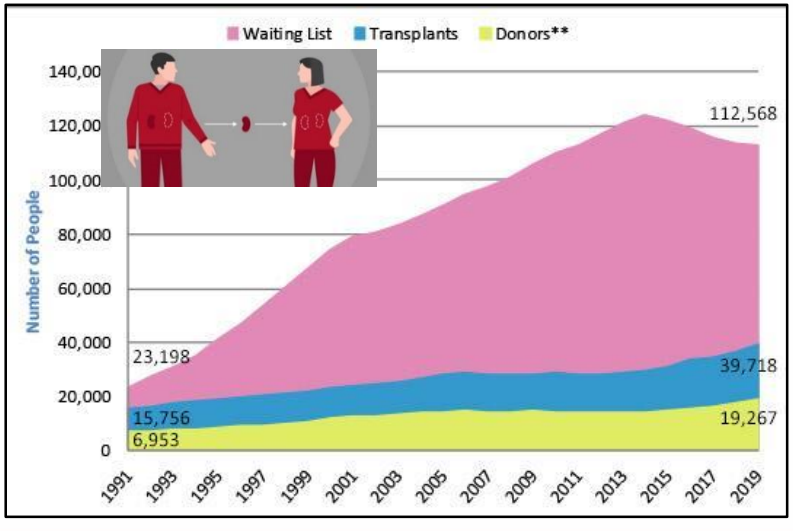


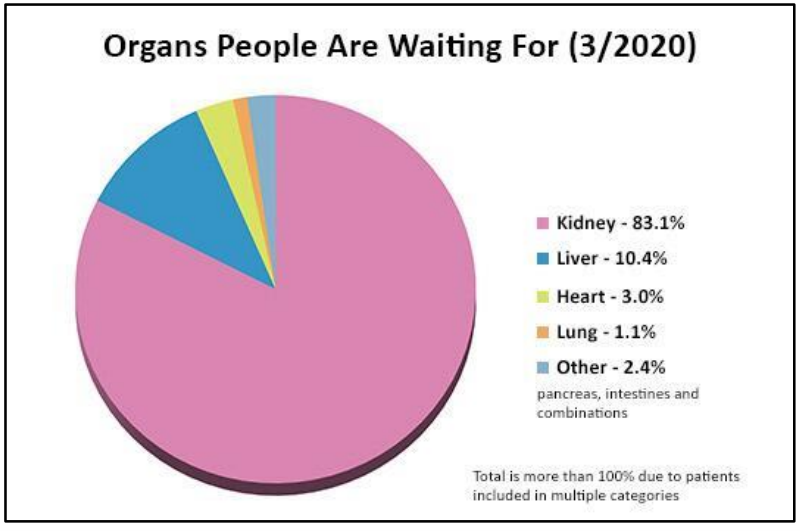
Living cells

Bioprinting in Tissue Regeneration





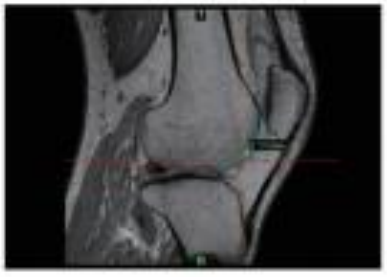




1. www.smartechpublishing.com; www.unos.org
2. https://www.organdonor.gov/statistics-stories-statistics.html;
3. Bajaj et al. Annual review of biomedical engineering 16 (2014): 247-276.

Tissue Regeneration Using Bioprinting

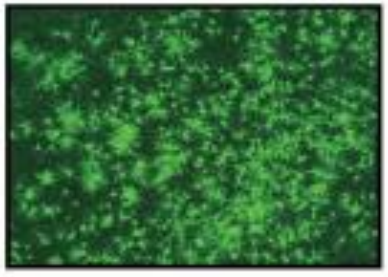
Step 1
imaging



Step 2
design approach

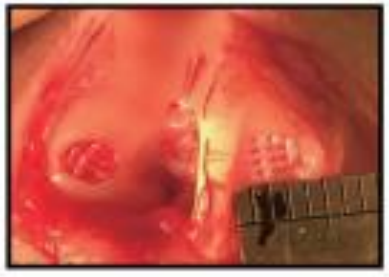
Step 3
material selection

Step 4
cell selection



Step 5
bioprinting

Step 6
application



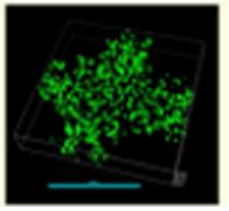
1. Park et al. *Tissue engineering and regenerative medicine* 13, no. 6 (2016): 622-635.
2. Datta et al. Biotechnology advances 36, no. 5 (2018): 1481-1504.

Process Control and Parameters

Before bioprinting → **During bioprinting** → **After bioprinting**

choice of technique

optimization of parameters



regulation of microenvironment

Bioink characteristics
- ✓ Origin
- ✓ Biocompatibility
- ✓ Viscosity
- ✓ Shear thinning
- ✓ Gelation kinetics
- ✓ Cell adhesion
- ✓ Biodegradation

Cell characteristics
- ✓ Nature
- ✓ Density

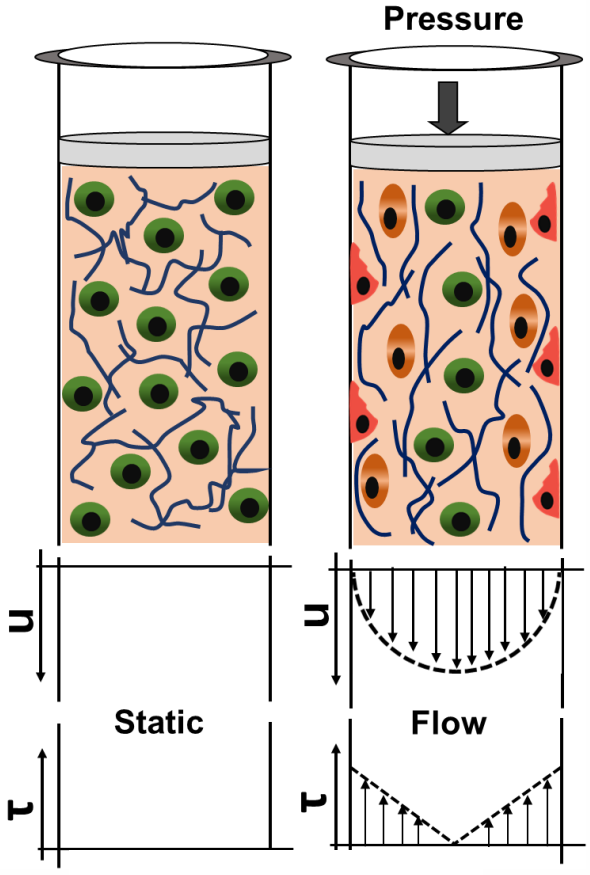
Printer characteristics
- ✓ Type of printer
- ✓ Resolution
- ✓ Printing speed
- ✓ Nozzle dimension
- ✓ Buildability

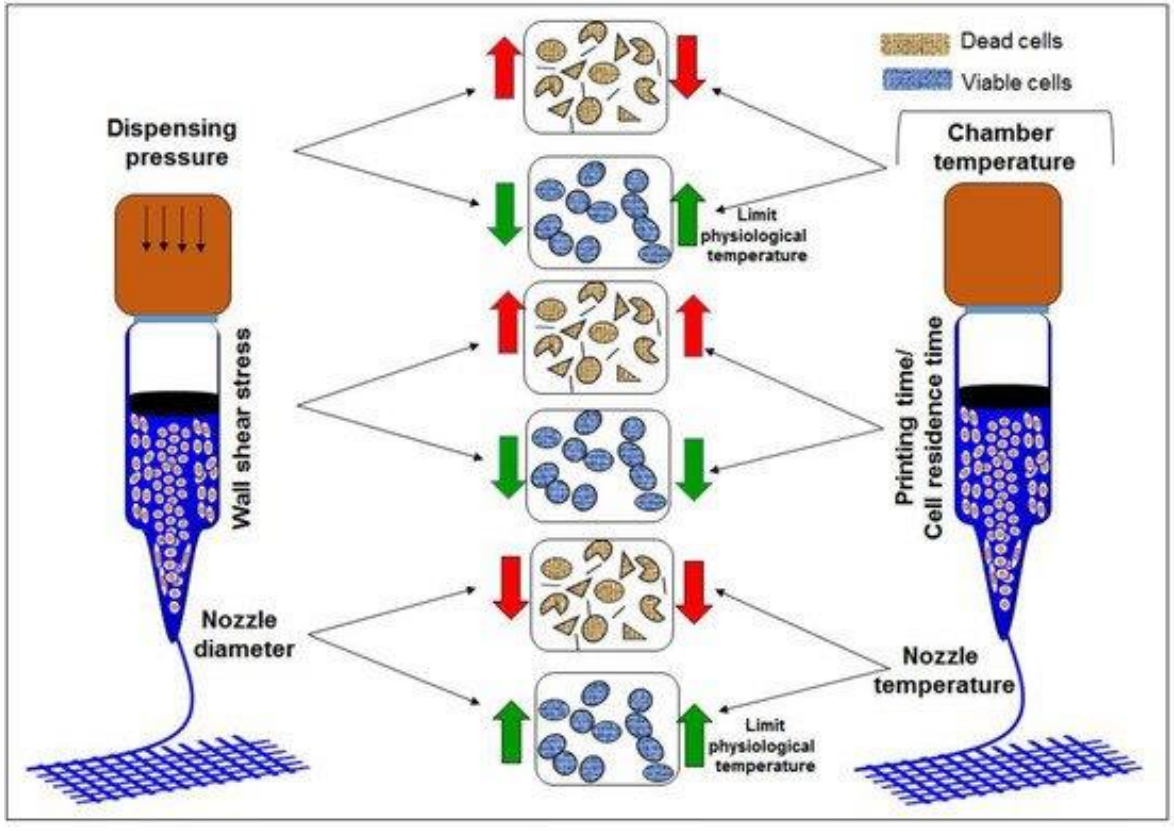
→

- ✓ Balance between cell-ECM, cell-cell interaction
- ✓ Cell proliferation, and differentiation
- ✓ Structural stability, and biodegradation

1. Ding et at. *ACS Biomaterials Science & Engineering* 4, no. 9 (2018): 3108-3124.
2. Adapted from: He et al. *Scientific reports* 6 (2016): 29977

Process Physics of Extrusion Bioprinting





Viable cells

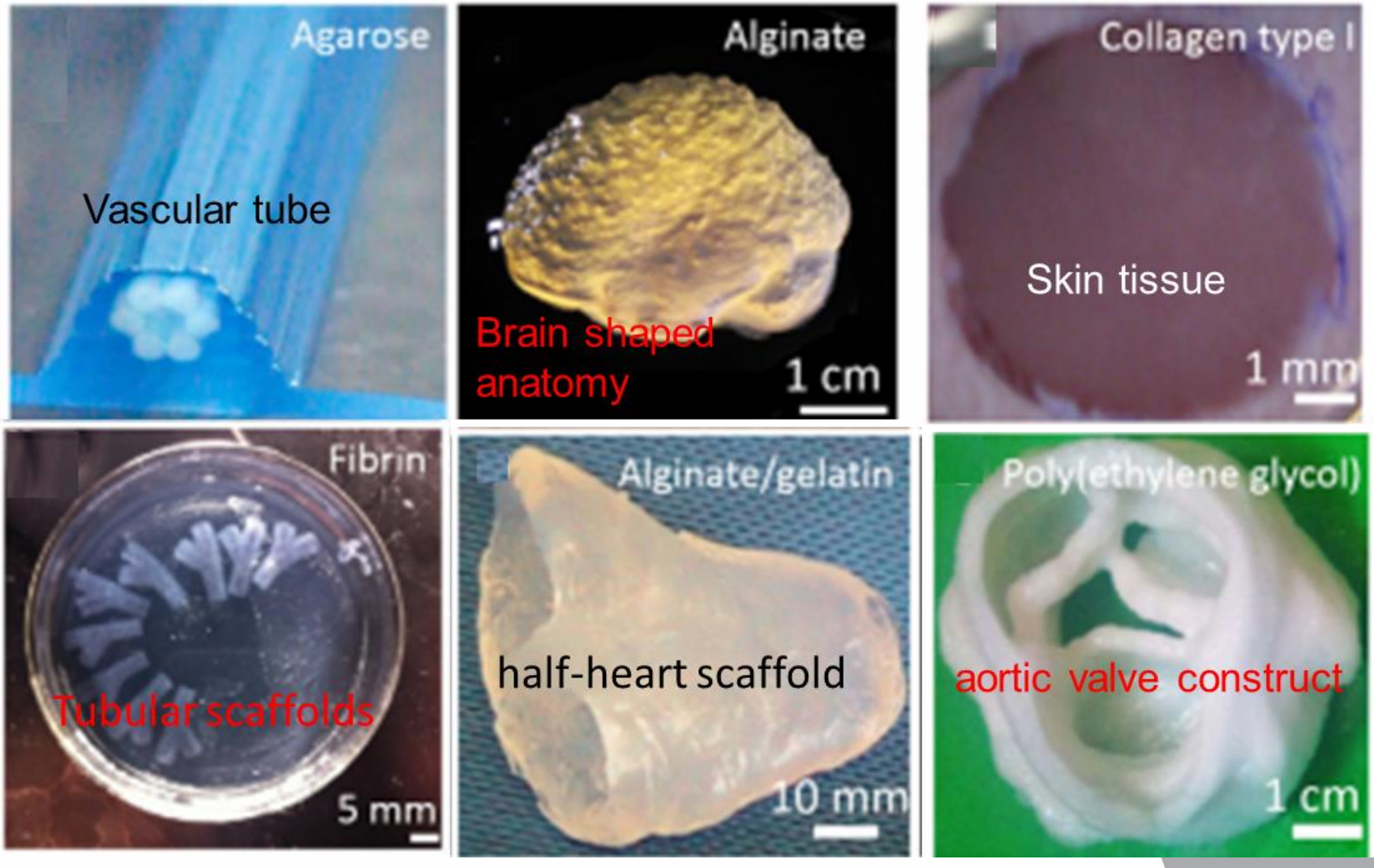
Stressed cells

Dead cells

Hydrogel molecules

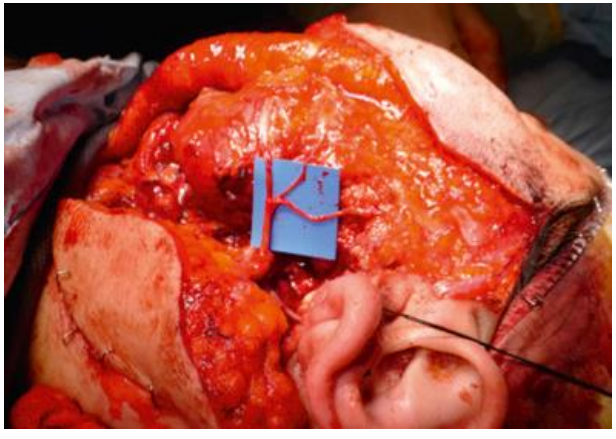
1. Adapted from: Shafiee et al. *Applied Physics Reviews* 6, no. 2 (2019): 021315.
2. Adapted from: Zhang et al. *Applied Physics Reviews* 5, no. 4 (2018): 041304.
3. Panwar et al. *Molecules* 21, no. 6 (2016): 685

Bioprinted hydrogels

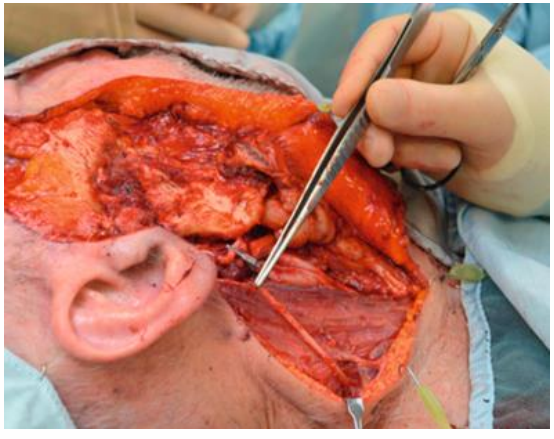


Nerve graft

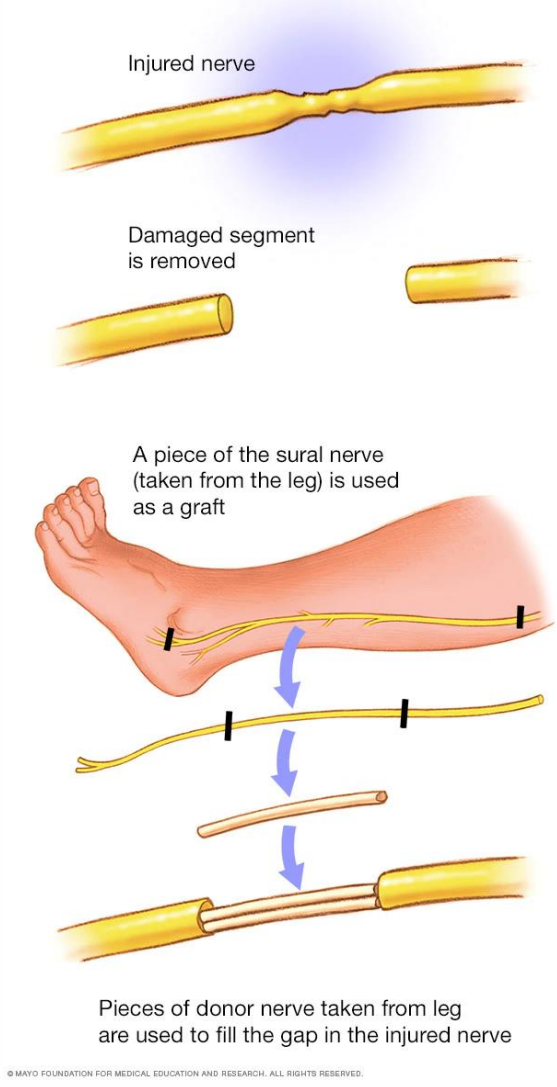
- A nerve from another source that matches the damaged nerve in terms of size and structure and stitching the appropriate ends together to bridge the gap.



41-year-old female patient with adenoid cystic carcinoma of the parotid. A vascularized nerve to vastus lateralis was harvested

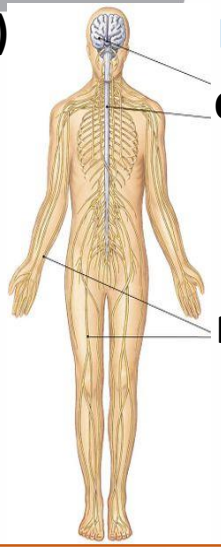


Great auricular nerve a local option for donor nerve graft.

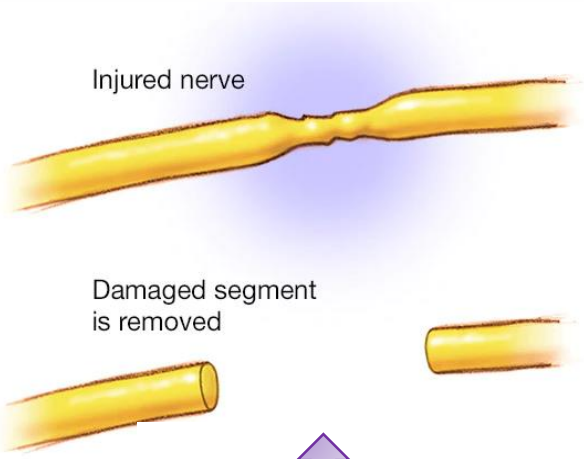


Ref: *Peripheral nerve conduits: Technology update, Medical devices, 2014:7, 405-424

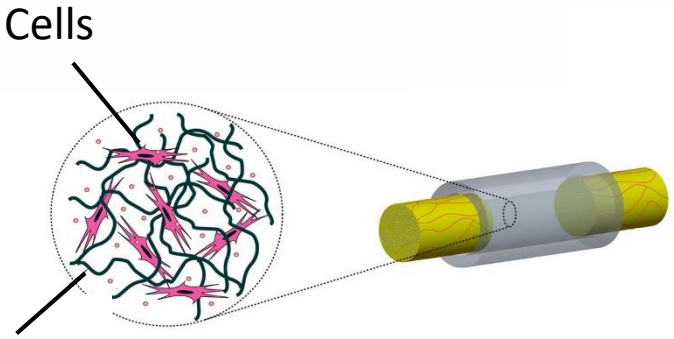
(a) **Nervous System**



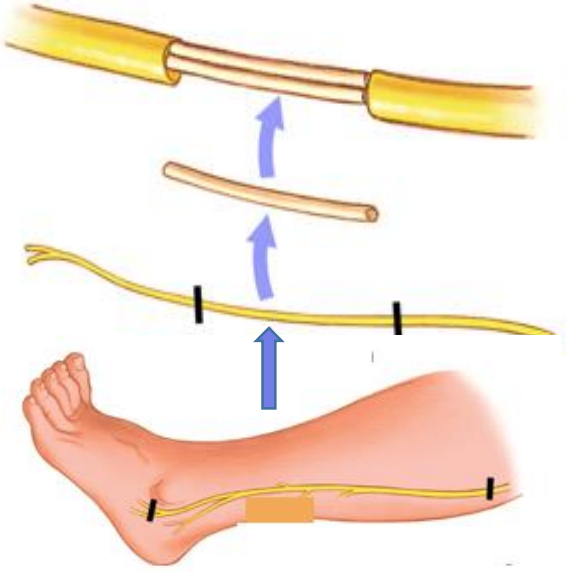
(b) **Peripheral nerve injury**



(c) **3D Bioprinting approach**



(d) **Autograft/allograft approach**



Acknowledgements: The Team

Calcium Phosphate Bioceramics for Musculoskeletal Applications


Asish Subhadip Shekhar Prafulla Naresh Alok

Polymer-Ceramic Hybrid Biocomposite based Acetabular Liner

Clinical Collaborator: D. Sundaresh, Q. Zahiruddin
Academic Collaborators: S. Bose, S. Kanagaraj


Vidushi Santhosh Garima Shekhar Subhadip

Ceramic Femoral Head for Total Hip Joint Replacement

Clinical Collaborators: D. Sundaresh, S. Nikose, Q. Zahiruddin

Academic Collaborator: D. Sarkar


Santhosh Nitu Subhomoy

Dental Implants and Restoration

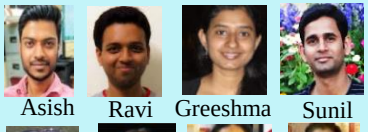
Clinical Collaborators: V. Shetty, B. V. S. Murthy S. Gupta


Srimanta Deepa SanthoshSubhomoy Atiar

Biophysical Stimulation Mediated Stem Cell Functionality Modulation on Biomaterials and in Biomicrofluidic devices for Regenerative Engineering

Academic Collaborators: A. Sharma, V. Kumaran, D. Saini, H. Pandya

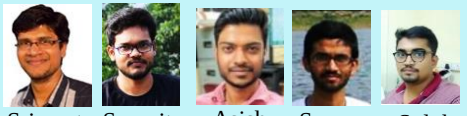
Neuroscientist Collaborators: B. Mehta, Y. Markandeya


Asish Ravi Greeshma Sunil


Sharmishta Ashutosh Indu Shilpee

3D Binder jet printing of Implantable Biomaterials and 3D/4D Bioprinting of Tissue Engineered Scaffolds

Academic Collaborators: B. Derby, S. Basu


Srimanta Soumitra Asish Sourav Sulob

Bioceramic Coating for Cardiovascular Applications and Biodegradable polymers for Drug Delivery

Academic Collaborators: M. Kosinova, S. Bose, R. Bhat


Nitu Ranjith Yashoda

Biomechanical Analysis, MD Simulation & Machine Learning

Academic Collaborators:
P. Talukdar, C. Bhattacharyya


Gowtham Subhadip

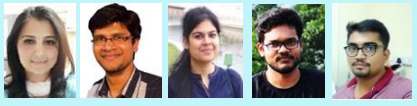
Polymer blends and 3D bioprinted scaffolds for urological reconstruction

Clinical Collaborator:
A. Mandhani


Swati Sulob

Clinical study on Cranioplasty Surgery

Clinical Collaborators:
A. Jagannatha, K. Khanapure, P. Hegde, P. Perikal, M. Shivakumar, S. Iratwar, Q. Zahiruddin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