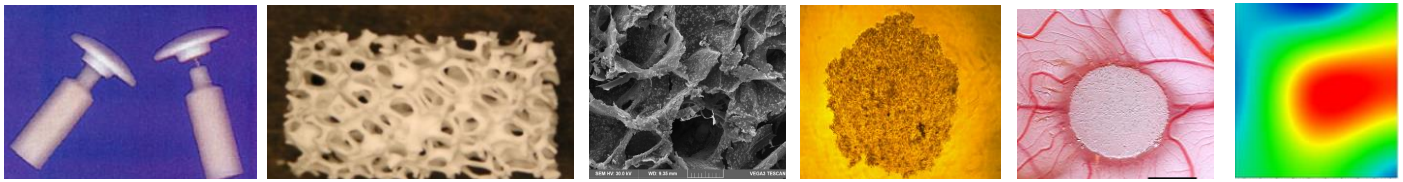
Bioengineering of Bone - repair to regeneration: *Materials from lab to patients*



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Professor of Bioengineering

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Outline

- Collaboration between UK and Pakistan – Time line
- Key research questions
- What are biomaterials
- Interdisciplinary research
- Bone repair, understanding hard and soft tissue
- Concept of bone repair – Bioactivity
- Bone Regeneration; Injectable and hybrid Scaffolds promoting angiogenesis
- Dental materials

Historical context:
Established Collaboration between UK and Pakistan

1989 to 2020

US$380M

Apatech®
Redefining orthobiologics

UKAS MANAGEMENT SYSTEMS

ISO 9001:2015

Queen Mary University of London

1989 – 2010

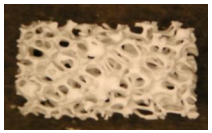
IRC in Biomedical Materials

Quality System Established
1990 - 1997

Chemical, biological, mechanical, and physical

HAPEX™
1998
85% WM

Porous HA
1999



2000

Abbonetics
Spinout

2005-10
Spinout

Affordable Healthcare
Lab to Patients

INTERDISCIPLINARY RESEARCH CENTRE IN BIOMEDICAL MATERIALS CIIT LAHORE

IRCBM

Three Key Research Questions

1. How the field of biomaterials have evolved from repair to regeneration

2. What have been the contributing factor

3. Where the research is heading now

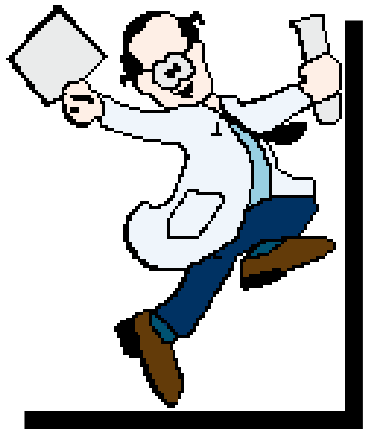
What are Biomaterials

"Biomaterials saves lives, relieves suffering and improves the quality of life for a large number of patients"

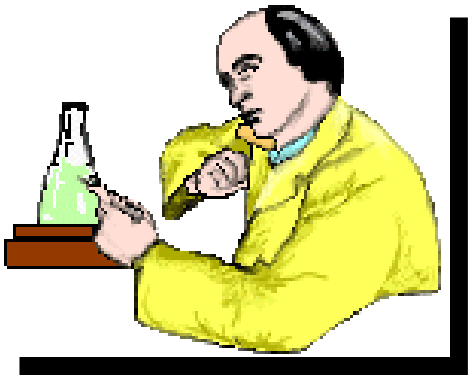
(Technology Foresight, UK)

Interdisciplinary Research

"From concept to the patient"



Engineer



Chemist

Physicist

Materials Scientist

…….working in partnership with Biologists and Clinicians ?

Bone Repair

- To mimic the properties of any natural material, it is important to understand the chemical, physical, mechanical and biological properties of that tissue.

- This provides a base line data for the synthetic material to be tailor made for a specific application.

Bone Repair

- Bone is a composite material
  - Inorganic
    - Ceramic and mostly hydroxyapatite…?
  - Organic
    - Collagen, fibres, fat cells, elastin

Hard Tissue Repair

- Bone is regarded as nano-composite of minerals and proteins /collagens. The minerals include

- Hydroxyapatite
- Fluroapatite
- Carbonate-apatite

HA: $Ca_{10}(PO_4)_6(OH)_2$

The minerals are distributed in the collagen matrix in the microcrystalline form

Biomaterials ~ Bioceramics

Ceramic:

A "bioactive Material" which is phase-pure as bone mineral, containing no secondary phases and bonds to the natural bone

Repair – Synthesis of Hydroxyapatite

Inorganic: Initially used for repair

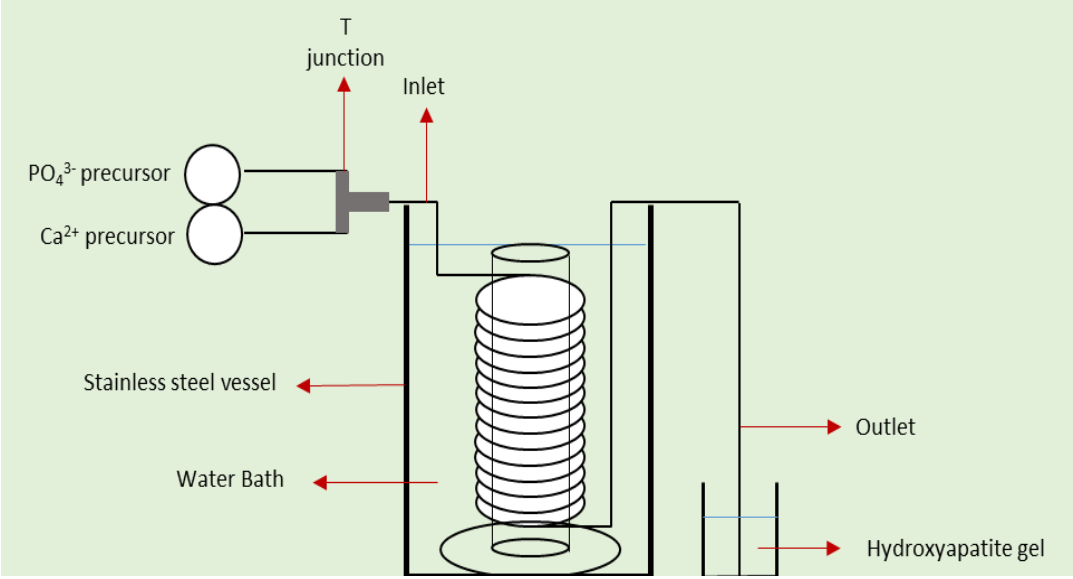
- Controlling ionic substitution, particle size, shape and form of substituted hydroxyapatites
- Improved bioactivity and biocompatibility

Organic:

- Polymers (natural and synthetic)

Composites:

- Bioactive scaffolds for bone regeneration
- Different fabrication routes to control porosity
- Functionalisation



Continuous hydrothermal flow method for HA synthesis

Affordability is the key and especially in Pakistan:

1- Raw materials – affordable and available in Pakistan

2- Synthesis and fabrication

3- Clinical collaborators – understanding and procedures

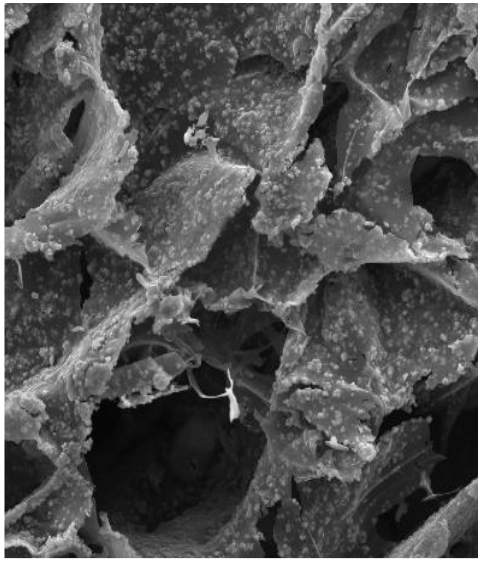
4- Regulatory protocols

5- Commercialisation – industrial partners

Bone Regeneration; Bioactive Hybrid Scaffolds

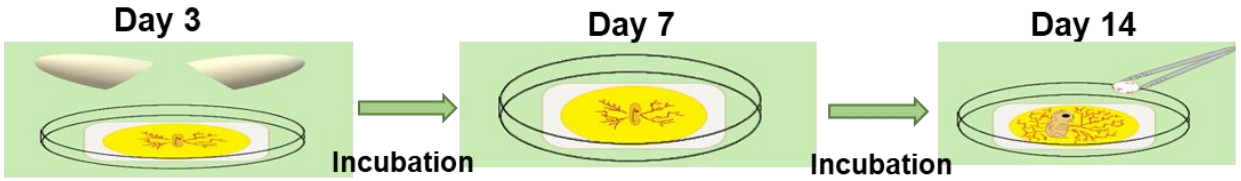
Angiogenesis

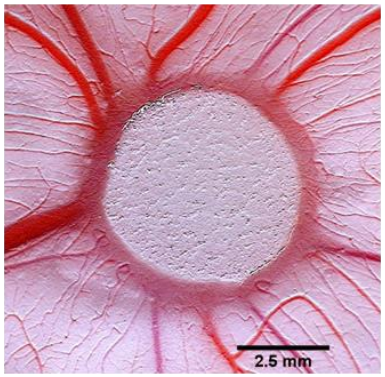
Chick Embryo Chorioallantoic Assay (CAM)

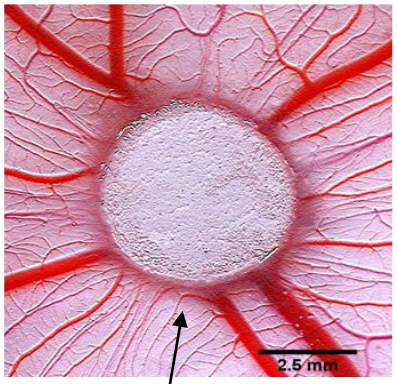


100 microns

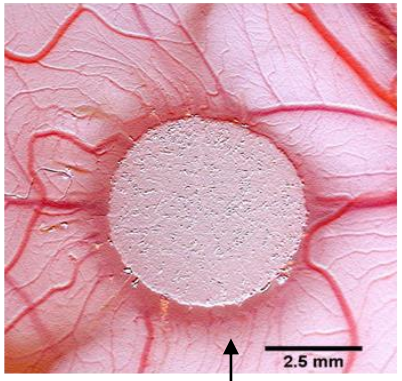
HA and Chitosan composite







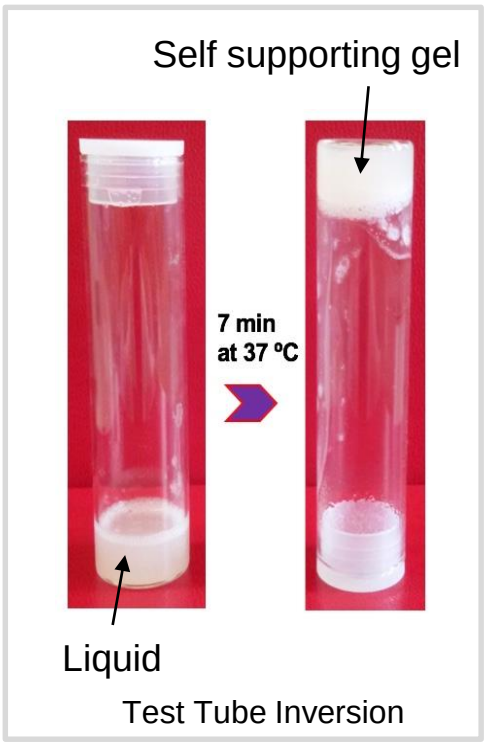
Note the growth of Micro-vessels

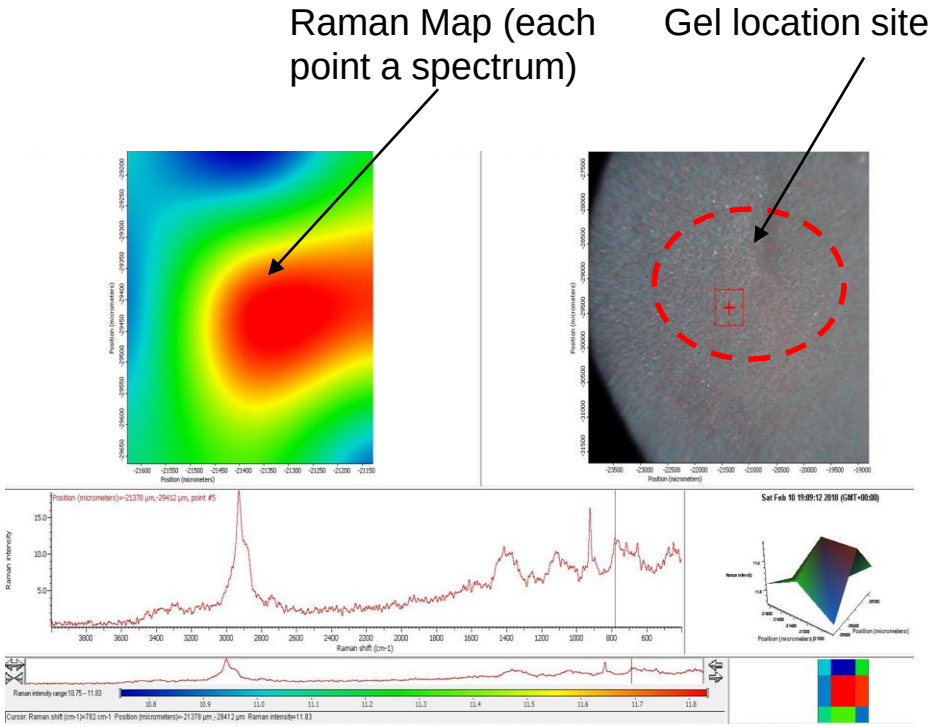


Note the release of growth factors and vascularisation

Biomaterials for Bone Regeneration

Pro-angiogenic pH/thermosensitive injectable hydrogels





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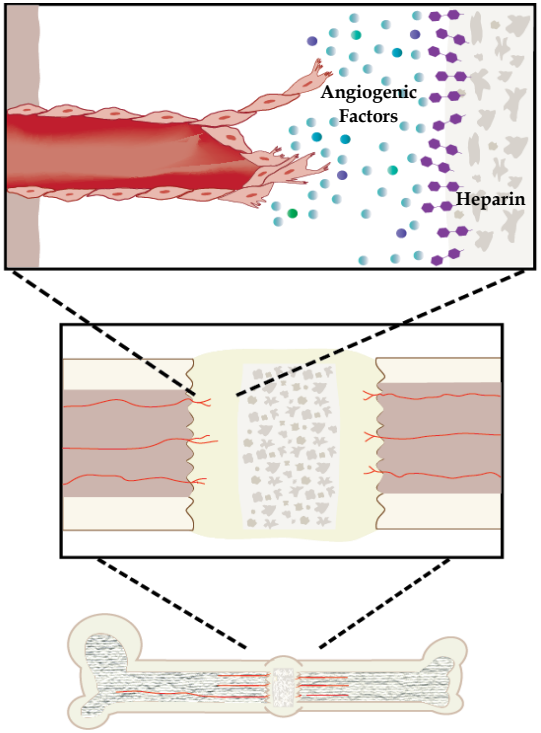
https://doi.org/10.3390/ijms21051633

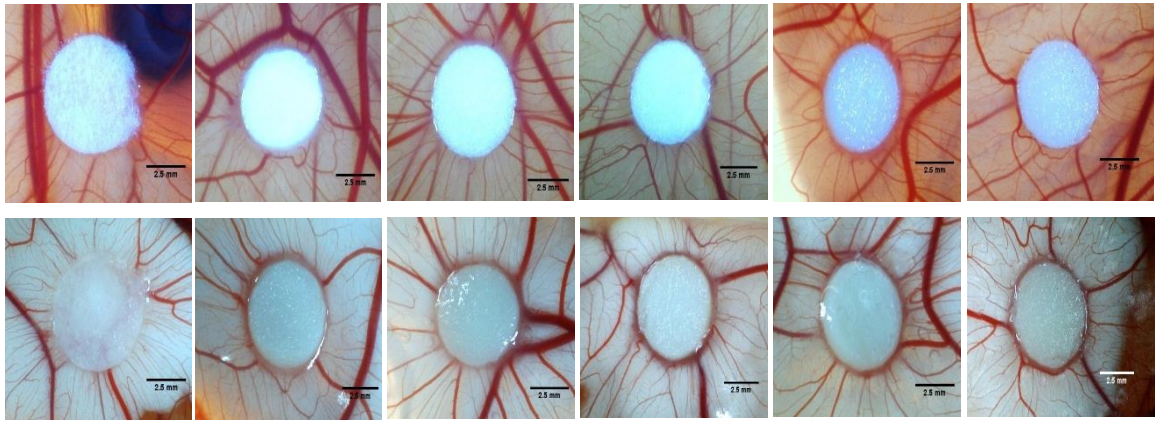
Bone Regeneration using Heparinized Chitosan/Hydroxyapatite scaffolds

- Formation of blood vessels during bone regeneration represents a major challenge for tissue engineered constructs.
- Poor revascularization can lead to scaffold failure and consequently, improper or no healing.
- Heparin is known to bind angiogenic growth factors influencing the process of angiogenesis.

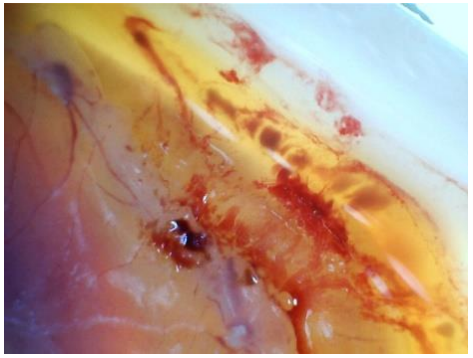


Schematic representation of the heparinized scaffold. The scaffold inserted to the bone defect zone, heparin then will interact/bind with the angiogenic growth factors from the surrounding bio-environment, inducing an angiogenic response.

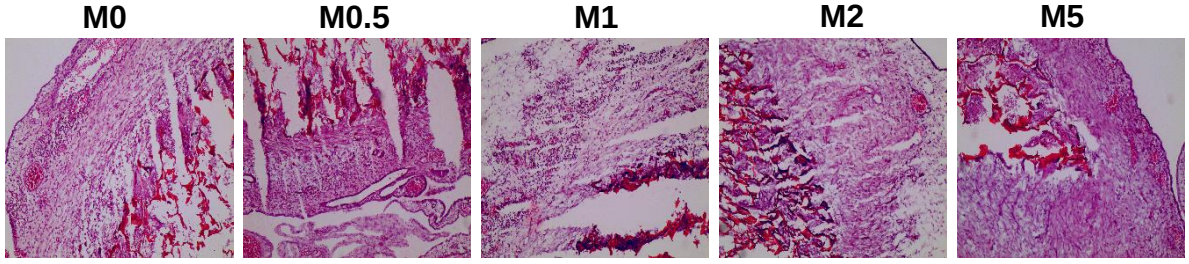
Bone Regeneration using Heparinized Chitosan/Hydroxyapatite scaffolds



Samples containing different concentrations of heparin after 3rd and 6th day of implantation in CAM assay



Spontaneous bleeding of an embryo implanted with the scaffolds with the highest concentration.



H&E staining of the samples for the different sample concentrations.

Sample	VIx
M0	33.5
M0.5	36.8
M1	32
M2	33
M5*	28.5

Vascular index: according to loading concentration.

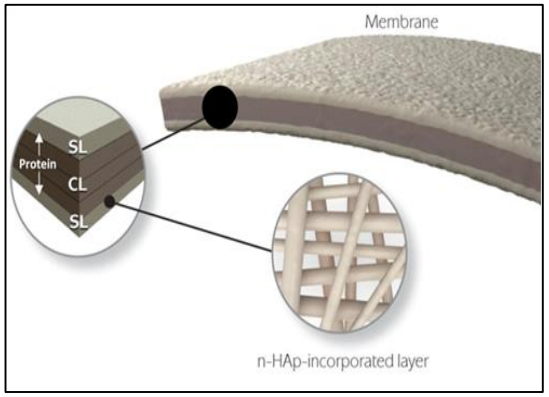
Next Generation Dental Materials

Guided tissue regeneration membrane

The treatment of periodontal diseases is estimated to cost the NHS approximately £2.78 billion per year* and 15-20% of worlds adult population is affected

Design:

- Biologically active
- Spatially designed
- Functionally degradable
- Occlusive membrane



Three Key Research Questions

1. **How the field of biomaterials have evolved from repair to regeneration**

- **Materials – identifying new methods of synthesis that are rapid, cost effective and reproducible**

2. **What have been the contributing factor**

- **Understanding chemical, physical, mechanical and biological aspects**

3. **Where the research is heading now**

- **Vascularisation – understanding angiogenesis**
- **Functionalisation and spatially designed scaffolds**
- **New "smart materials" that are self healing**

Interdisciplinary Collaboration

Interdisciplinary Research is the key to success in Translational Research

We must

Connect to form partnerships / collaborations

Discover for a common and targeted goal

Inspire each other with research

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