Artificial bone as an alternative solution for halal bone implants

Assoc. Prof. Dr. Iis Sopyan¹,²
¹Biomedical Engineering Research Group
²Halal Industry Research Center
Kulliyyah of Engineering
International Islamic University Malaysia
Why do we need bone implants?

- Accident
- Diseases
- Aging
Orthopedic Implant Forecast

Orthopedic implant demand to rise ca. 10% annually to $23 billion in 2012.

The three major product segments:

- **reconstructive joint replacements**
  Eg: knees and hips

- **spinal implants**

- **orthobiologics**
  Eg: Growth factors, grafts, bone cements
Dental Implant and Bone Graft (Orthobiologics)

- US$ 2 Billion in 2006
- US$ 4.5 Billion in 2012 (15% annual increase)
Organ transplants in Europe and US: an example

- Number of patients awaiting transplant:
  - Western Europe – 40,000 patients (all organs)
    1) UK – 7,000 patients
      - 1,000 needs cornea grafts
      - 600 have received, 400 still on the waiting lists
    2) 15-30% of patients in needs of kidneys and livers die while awaiting an organ
    3) Average waiting time is 3 years

- US:
  1) 300,000 hip and knee replacement surgeries annually
      - 65% of HR and 70% of KR: > 65 age people
  2) 6,000 patients die annually while waiting kidney and liver transplants
Donation of body part

- Most civil societies:
  1. literally beyond price
  2. free of charge
  3. that donation should be altruistic

But...

A completely exploited, healthy single body can fetch **US$ 400,000 – 1,000,000** on black market
Usable components for transplantation

- heart valves
- lungs
- livers
- corneas
- pancreases
- bone (allograft)
- skin
- hair
- collagen
- ligaments
- blood
- embryos
- bowels
- stem cells
- placenta
Where do those body–parts go?..

- medical-school laboratories
- dissection rooms
- transplant theatres
- dentists surgeries
- orthopedic clinics
- ophthalmic grafting units
- multi-billion dollar cosmetics industry
- blood-donor centers
- stem-cell laboratories
- DNA data banks
- tissue bank
- surgical equipment companies
Which parties do supply grafts

- **LEGAL**: Tissue banks, hospitals, tissue companies
  Should be accredited, track of all organs recorded.

- **ILLEGAL**: Body brokers
  (selling and buying cadavers and body parts)
  - independent businessmen
  - crematoria
  - employees of morgues, funeral homes, pathology departments
Black market in body parts

- Shortages of implants
- Criminality
- Desperate Poverty
Over the past 19 years, more than 16,800 families have been represented in lawsuits claiming loved ones' body parts were stolen for profit. During that period, profits from the sales of thousands of suspected stolen bodies are believed to have topped $6 million...
Body parts trade: a lucrative business

- Selling body parts and dead body is illegal, but
- handling, procuring, storing, processing, and transporting human tissue are allowed
  (The American Uniform Anatomical Gift Act 1968 & 1987)

... parceling out an entire dead body then delivering it to the highest bidder (e.g. tissue service companies, body brokers) : $ US 5,000 – tens of thousands (as “processing fee” only).
Supply of body parts in the past

- Dead bodies of the poor or unclaimed persons were enough to meet the needs of science and education.

But now the need surpasses the supply...

- the hospital or medical school that acquires the dead body may legally sell it to others.
Inconsistency of Regulations

- Organs donated specifically for transplant are tightly regulated.

  the same scrutiny does not apply to bodies donated for research and education.

- Selling dead body is illegal but taking money for compensating storage and transportation of human tissue are legal.
The activities of black market in body parts

- Illegal harvesting and sale of body parts, tissue, and organs to gain profit
  
  E.g: people who sell their kidneys was paid about \textbf{US$ 1000}, but the recipients have paid up to \textbf{US$ 1,000,000}.

- WHO reported 6,000 received illegal kidney transplants from living donors
  
  \textbf{Donors:} Egypt, Pakistan, Brazil, India, China
  
  \textbf{Recipients:} US, Saudi Arabia, UK, South Africa and other European countries

- More than \textbf{1,000 corpses} were illegally carved up over a four-year period in US for
  
  - orthopaedic treatments
  
  - dentistry
  
  - beauty products such as collagen
Issues on organ transplants

- Religious beliefs
- Availability of the organs (absolute shortage!)
- Permission or objections of donors’ family
- The hardships to get to the top of the waiting list
  - not on the basis of first come, first served, nor even purely on life-saving emergency
  - but based on the assessment by doctors and nurses over a period of weeks
- Unknown health risks to the recipients after the transplants (HIV, hepatitis, syphilis etc.)
- Black market
BONE IMPLANTS

- The needs of bone implants especially in US arose as the population is aging.
- More than 300,000 hip and knee replacement surgeries have been conducted which mostly to the people over the age of 65.
- The number of hip fractures is expected to exceed 500,000 annually by the year 2040.
- However, this practice caused severe pain to the patients after surgery and finally led to secondary operation to ease the pain.
- Hence, the motivation to end the suffering has driven to the study on the production of artificial bones from ceramics.
A solution...

ARTIFICIAL IMPLANTS: Biomaterials

- Ceramics
- Metals
- Polymers
- Composites
Artificial Bones Implant

- Made from hydroxyapatite, $\text{Ca}_5(\text{PO}_4)_3\cdot\text{OH}$, which has the same chemical formula as bone itself
- However, it is neither as porous as real bone nor as strong
- Pores are important:
  - conduits for blood flow
  - allow bones to be strong without being too heavy
  - provide a way for living bone to attach itself permanently to an implant
- Other potential candidates as a bone substitute: sea coral
  - porous enough but lack of strength, mostly used for cranial restructuring
- Hence, **it is very crucial to synthesize ceramics materials with the right combination of strength and interconnected pores to mimic real bone**
Biomaterials

- Used to direct, supplement or replace the functions of living tissues

- Selection criteria for bone implants:
  - High compatibility
  - Appropriate strength and stiffness
  - Economically viable

Metals

- E.g.
  - Titanium
  - Cobalt-Chrome-Molybdenenum
  - Stainless Steel (obsolete)
- High elastic modulus
- Biocompatible
- Concerns regarding release of harmful ions
- Issues with stress shielding
Ceramics

- E.g.
  - Alumina
  - Zirconia

- High strength

- Good biocompatibility

- Stable in physiological environments

- Lack of chemical bonding between material and bone

Composites

- Functionally graded composites
  - Continually graded composition

- Polymer-ceramic composites
  - E.g. Carbon fibre reinforced, bioactive glass, hydroxyapatite,
  - Mechanical properties comparable to that of bone
  - Can be tailored for specific stress and strain distributions as well as for specific requirements and applications
  - High strength and physiological strain distribution – low risk of fracture under high impact conditions
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Developing calcium phosphate bioceramics for artificial bone implants
Our business...

- Production of porous bioactive bone implants
- Production of porous ceramic microcarriers
- Production of nanosized calcium phosphate based powders:
  1. Hydroxyapatite
  2. Tricalcium phosphate
  3. Biphasic calcium phosphate
Lab Facilities (Kulliyyah of Engineering):

• **Materials Characterization Lab**
  (HRTEM, FESEM, AFM, SPM, FIB, XRD)

• **Biomaterials Lab**
  (Powder and porous materials preparation, High temp furnace, nanosizer, zetasizer, ellipsometer, dissolution tester, etc)

• **Polymers Lab**
  (TG/DTA, FTIR, DSC, DMTA, UV-vis, GC, mini spray dryer, UTM, surface area analyzer)

**Kulliyyah of Medicine**: Animal test, clinical test, *in–vitro* test
Examples of commercial products of bioceramics

Injectable bone fillers  Powder

Porous scaffolds  Granules
Commercial application of the product

- **Orthopedic and Maxillofacial/Dental**: bone substitute, injectable bone fillers, porous blocks, and metallic implant coatings

- **Pharmaceutics**: bioresorbable carrier material for controlled drug delivery in the treatment of diseases such as cancer, osteoporosis, osteomyelitis and diabetes

- **Chromatography**: separations and purification of proteins, nucleic acids and enzymes

- **Cosmetics**: skin fillers
Production of porous calcium phosphate for human cancellous bone substitutes
FESEM images showing the microporosity of pure BCP (a) and 10 mol% Mg-BCP (b).
3-D morphological measurement of porous Mg-doped BCP with a 10 mol% Mg (a and b) and 0.25 mol% Mg (c and d).
Top view of porous Mg-doped BCP with a 10 mol% Mg (a) and 0.25 mol% Mg (b)
Production of hydroxyapatite nanopowder using eggshell as the raw materials
Conventional Production of CaP

- **Methods**: Precipitation, sol-gel, mechanochemical, wet chemical

- **Materials**: Ca(NO$_3$)$_2$, Ca(OH)$_2$, H$_3$PO$_4$ (Reagent Grades)

- **Disadvantages**: Lengthy process, complex, relatively expensive materials, high temperature, pH control
Our Technology...

- **Method**: Newly developed low temperature hydrothermal method (90°C)
- **Raw Materials**: Eggshell, cockle shell (for Ca precursor)
- **Advantages**: Fast and simple, composition of CaP types can be controlled
Raw Materials

- Any organic solid wastes which contain calcium carbonate: eggshell (95%) and cockle shell (98%).

- National annual wastes:
  - 65,000 tons (cockle shell)
  - 40,000 tons (eggshell)

Example Data:
- One Company (Lay Hong Bhd.): 950,000 eggs per day.
- 2008’s National production: 7421 million eggs
  ( ~ 900 millions exported to Singapore).
- Four egg processing plants produce pasteurised liquid whole egg, liquid white, and liquid yolk
Commercial Powder Hydroxyapatite

- Sigma Aldrich (Germany)
- Fluidinova (USA)
- Himed (USA)
- A & Z Nutraceutical Co., Ltd (China)
Problems

- No local manufacturer, all specialty grade CPs are imported
- Need to fulfill very strict standard (ISO 13779-1 and ASTM F1185-03).
- Expensive.

Our solution...

- Solving the local need of medical and pharmaceutical grade of CP materials, at the same time, solving environmental problems.
- The method of synthesis is very simple and fast.
- Much cheaper
The method

- **Materials**: CaCO$_3$ containing solid organic wastes, ammonium di-hydrogen phosphate, water.

- **Processing time**: 3-5 h to get non-sintered CPs nanopowder and 5-6 highly crystalline CPs nanopowder.
  - 1 h for burning of wastes.
  - 2-4 h for the reaction at as low as of 90°C.

- No controlling of pH, no high temp. heat treatment, no filtration: a simple, fast procedure.

- Can control composition ratio of HA and TCP
Product Features

Microstructure of commercial HA (left) and the eggshell derived hydroxyapatite nanopowder (right)

- Size: 30-70 nm
- Purity: ~100%
- No heavy metal contained (< 0.1 ppm)

Commercial HA Powder:
- Bigger average particle size
- Lower surface area

XRD patterns of CaCO$_3$, CaO, commercial HA and seashell derived HA before calcination
Control of CaP composition

stable, non-dissolved CaP

degradable CaP
CONCLUSIONS

- Usage of allografts should be reduced.
- Most of world implants market are still occupied by advanced countries.
- Preparation of “halal” implants (in terms of the properties itself and the process of getting it) is a must.
- More efforts needed by all Muslim countries to overcome the shortage of implants.
Awards

- ITEX 2006, Kuala Lumpur (Malaysia): Gold
- IENA 2006, Nurenberg (Germany): Gold
- ITEX 2007, Kuala Lumpur (Malaysia): Silver
- PECIPTA 2007, Kuala Lumpur (Malaysia): Silver
- EUREKA 2007, Brusselss (Belgium): 1 G, 1 S
- BIS 2007, London (UK): Gold
- ITEX 2008, Kuala Lumpur (Malaysia): 2 Gold
- IENA 2008, Nurenberg (Germany): 2 Gold
- MTE 2009, Kuala Lumpur (Malaysia): Gold


Iis Sopyan and Toibah Abd Rahim, *Biphasic Calcium Phosphate Scaffold Containing Magnesium and a Preparation Method Thereof, Malaysia Patent*, PI No. 20084585 (November 2008).

Publications

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