BONE REGENERATION

Yuxing M.D  PH.D

Biomaterials Laboratory, Department of Materials Science & Engineering, Tsinghua University

Orthopaedic center, Dongzhimen Hospital, Beijing University of Chinese Medicine
Over the course of the century, orthopaedic surgeons have used many synthetic materials (metals, ceramics, polymers, and plastics, etc) to replace human tissue and provide improved function.

Bone is the basic orthopaedic biomaterial, including host bone, allograft bone, xenograft bone, and bone graft substitutes.
summary

- Basic knowledge of bone
- A new bone material ---nano-HA/Collagen/PLA composite
- Clinical application of nHAC/PLA
Basic knowledge of bone
Function of bones

- Bone is a specialized connective tissue and have three major functions: to serve as (1) mechanical support, (2) sites of muscle insertion, and (3) a reserve of calcium and phosphate for organism.

- The supporting function of bone resembles a composite building system. There are short and long tubular bones, irregular bones, flat bones and bones of a highly specific form.
Function of bones

- The skeleton is both a structural support and a metabolic organ. It serves especially for the storage of calcium and phosphate, ensuring the equilibrium of these ions in the blood serum.

- A constant level of the blood calcium is essential for life and bone plays a decisive role in maintaining this level.
The bone consists of bone matrix and bone cells.
The bone matrix consists of 77% inorganic and 23% organic material.
The organic bone matrix—the osteoid—is 89% collagen and 5% protein, and is the site of bone mineral deposition.
Osteoid is produced by large polyhedral osteoblast.
Daily deposition of 1um osteiod (=collagen)
Total width of osteoid seam: 6um
Zone of provisional calcification: 4um
Fully calcified organic matrix (10um distant from cell wall)
structure of bone

- The bone consists of bone matrix and bone cells.
- The bone matrix consists of 77% inorganic and 23% organic material.

The inorganic component of the bone tissue consists of 90% calcium phosphate and 10% calcium carbonate. The most important mineral, calcium, is deposited in the organic matrix as hydroxyapatite crystals.
The crystals are hexagonal and embedded alongside the collage fibrils intervals of 68 nm.
structure of bone

- The bone consists of bone matrix and bone cells.
- All mature bone cells are derived from the preosteoblasts, which are derived from undifferentiated mesenchyme cells.
- Preosteoblasts mature to form osteoblasts, which are the true builders of bone. They produce collagen and regulate the mineralization of matrix.
- The origin of osteoclasts has not been fully established. Osteoclasts play an important part in bone resorption.
Bone is remodeled throughout life by the activation-resorption-formation (ARF) sequence by which the coordinated actions of osteoclasts and osteoblasts replace old with new bone.
Bone can be divided into two types: cortex and spongiosa.
Cortical bone is homogeneous and very densely structured. The typical lamellar structure of the bone is apparent in the onion-like arrangement of the osteons.
A maceration specimen of the cancellous scaffolding of a vertebral body.

The bony trabeculae constitute a honeycomb formation.

Between the bony elements, space contain the bone marrow.
A bone scaffold material and relative research

nano-HA/ Collagen/PLA composite
nano-HA/collagen/poly(lactic acid) (nHAC/PLA)

- The bone scaffold material was developed by biomimetic synthesis.
- In main composition and hierarchical microstructure, the bone material is similar to natural bone.
The three dimensional porous scaffold materials mimic the microstructure of cancellous bone.

Tests of cell culture and animal model showed that the composite material is bioactive.
The osteoblasts were separated from the neonatal rat calvaria and seeded into material at a concentration of $5 \times 10^5$ cells/cm$^2$.

Osteoblasts adhered, spread and proliferate throughout the pore of the scaffold material within a week.
15 mm segmental defect model in the radius of rabbit

15mm nHAC/PLA implanted, After surgery

Implant 12 weeks new bone grow up, cortical bone connected completely
Histology of the new bone tissue

There are some islands osteoid, which was regularly lined by many cubioidal osteoblasts, indicating bone-forming activity. (HE stain)

8 weeks

12 weeks
Lumbar Spinal fusion with nHAC/PLA and rhBMP-2 in a rabbit model
X-ray radiographs in Group nHAC/PLA and nHAC/PLA+rhBMP-2

2 weeks 4 weeks 6 weeks 10 weeks
the new trabecular bone distribute in the whole fusion mass area
Clinical application of nHAC/PLA
The clinical study began on January 15, 2003. Since then, we have completed 50 cases in orthopedic center, Dongzhimen Hospital.
The lateral and anterior-posterior radiograph and computed tomogram of a 55-year-old woman with degenerated lumbar disc disease, scoliosis, stenosis, lumbar spondylolisthesis at the L4–L5 level, which was refractory to medical care. Who had definitive neurological damage and was unable to ambulate.
Pedicle screw-plate system instrumentation

Medtronic Sofamor Danek Tenor System

Autogenous cancellous bone and Nano-bone granules
1 month post-op new bone began to form

4 month post-op bone fusion
Pre-op lateral radiograph and MRI (magnetic resonance image) of a 42-year-old woman with degenerated cervical disc disease at the C4 5 and C5 6 level, ventral intrusion into canal and spinal cord compressed,

Physical exam: myeloradiculopathy associated with incomplete paralysis
After discetomy, wedge graft implanted

Then, anterior titanium plate system instrumented
Post-op 2 weeks, low density in radiograph

Wedge Nano-bone graft

Cage filled with Nano-bone

graft density similar to vertebrae

Post-op 3 months, bone fusion
A 12-year-old boy with cerebral palsy right knee over extension 30 degree.

epiphyseal transverse cut and filled with autogenous iliac crest and nano-bone granules

Post-op 5 months, bone fusion in radiograph
A young man with burst fracture of calcanium, a large bone defect cavity filled with nano-bone granules.

Post-op six weeks.
conclusion

- Nano-hydroxyapatite/collagen composite has fine histocompatibility, without immunogenic responses from the host.
- The fusion period of nano-bone is about 4-6 months, a litter longer than autograft.
- It may be an relatively ideally alternative substitute to autograft
Hippocratic Oath

Thanks For Attention