COMPARING THE REGENERATIVE CAPACITY OF DIFFERENT SIZE BONE CHIPS

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Abstract
Bone chips are used in many orthopedic and orthodontic surgical applications. The regenerative capacity of these bone chips is not well understood. In this study, the different sizes of bovine bone chips were created using different bur designs. Both cell viability and potential for mineralization of these surgically cut bone chips were compared. The temperature generated by the different bur designs were also observed for its potential role in bone regeneration.

1. Introduction
Autologous material is the gold standard material for bone regeneration, because the native growth factors and cells are available for bone healing1,2. During orthopaedic surgery, bone cells are subjected to many factors that could affect their regeneration. Due to heat generated by surgical instruments (e.g. drilling, bur, cutting), bone cells will undergo apoptosis and necrosis3. Autologous bone chips are commonly used in number of regenerative applications such as acetabular revision and maxillary sinus floor augmentation4. Other factors affecting regeneration include mechanical forces and infection5,6,7,8. The addition of growth factors and/or antibiotics into the bone chips could improve bone regeneration. However, the regenerative capacity of surgically cut bone is not well understood and requires further investigation.

The characteristics of osteoblasts in regenerative bone chips (Fig.1) are (1) the ability to proliferate and mature into osteocytes, which are vital cells for new bone formation, and (2) bioresorbability of bone chips for bone healing. It has been proposed that the size of bone chips and donor site can influence its resorbability into the healing bone tissue9,10. However, the optimal bone chip size and shape is not yet known for new bone formation.

![Bone chip with emigration of osteoblast cells](image1)

**Fig.1** CULTURED bone chip with emigration of osteoblast cells, which are needed for new bone formation.

In this study, two different donor sites and bone chip sizes were compared to investigate the role of bone chip size and morphology for dictating the regenerative capacity of autologous bone chip material.

2. Methods
Bone chip experiments: Bone samples will be harvested from bovine animals. Different types of bone bur, supplied by Stryker Instruments, will be used to produce bone chips of different sizes. Thermal imaging will be carried out to investigate the temperature gradient experienced by the bone chips during the production of the bone chips, specifically to determine whether temperatures exceed the thresholds (e.g. 44°C) for cellular apoptosis and necrosis (Fig.2)11.

![Bone chip experiments](image2)

**Fig.2** MC3T3-E1 cells were stained with phalloidin and DAPI after 24 h heat treatment of (a) 37°C, (b) 45°C, (c) 47°C, and (d) 60°C (from Dolan et al., 2012).

Micro-CT scanning: Using a micro-CT scanner (Scanco MCT 100), the morphology of bone chips will be imaged to determine the precise size and morphology of the bone chips generated using the bone bur.

In vitro bone regeneration experiments: Using an Alamar Blue assay (Invitrogen), the viability of cells within bone chips will be analysed at time points 0, 5, 10, 15 and 20 days. The bone chips will also be cultured to determine the regenerative capacity of cells from the outgrowth from cultured bone chips; osteoblasts, osteoclasts, and mesenchymal stem cells. An alkaline phosphatase (ALP) assay (Sigma) will be used to analyse their potential for mineralization, which will also be quantitatively measured using alizarin red S3. ALP activity will be analysed at 0, 5, 10, 15, and 20 days post-bone chip production.
**Future Directions**

The regenerative capacity of bone chips with different sizes will depend on the viability and phenotype of cells present within bone chips after production. It is expected that larger chips should have enhanced viability directly after harvesting, as the cells within the centre of the chips will be protected from the temperature elevations and mechanical abrasion at the periphery. For the same reason it might be expected that these chips have a superior regenerative capacity. The chip shape may also be expected to have an important impact on the cellular activity. The results from this study will be used to design approaches combining human bone chips with growth factors and/or anti-inflammatory drugs, in order to investigate the factors, which may aid in the improvement of bone healing.

**8. References**


