Comparative study between perichondrial graft and tissue engineered cartilage in reconstruction of articular cartilage defects

Thesis

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INTRODUCTION

Articular cartilage is an avascular, alymphatic, aneural tissue with a relatively high matrix to cell volume ratio **(Schumacher *et al.*, 1994)**. It is a hyaline type of cartilage. Owing to its histological structure, this hyaline cartilage performs two functions: increase the area of load distribution to reduce the static and dynamic loads imposed on the bone ends, and allow relative movement of the opposing joint surfaces with minimal friction and wear **(Armstrong and Mow, 1980)**. Hyaline cartilage is distinct from most tissues because it has only limited self-regenerative ability due to its vascular deficiency **(Mauck, 2003; Ramallal *et al.*, 2004)**. This limited ability to self-repair is somewhat modulated by the size, location, and depth of the cartilage lesions **(Mankin, 1982)**.

Numerous strategies have been employed to repair cartilage defects with an end goal of filling the defect with tissue having biochemical and biomechanical properties approximating surrounding native tissue. Such clinical and experimental efforts include subchondral drilling or microfracture technique **(Blevins *et al.*, 1998)**, perichondrial grafts **(Homminga *et al.*, 1990)**, periosteal grafts **(Poussa *et al.*, 1980)**, osteochondral grafts **(Burks *et al.*, 2006)**, cell transplantation therapy in the form of single cell suspensions of either terminally differentiated chondrocytes **(Brittberg *et al.*, 2003)** or undifferentiated bone marrow–derived mesenchymal stem cells (MSCs) **(Wakitani *et al.*, 1994)**, and tissue-engineered constructs **(Fragonas *et al.*, 2000; Fuentes-Boquete *et al.*, 2004; Jiang *et al.*, 2007)**.

Subchondral drilling or microfracture technique involves breaching the subchondral bone to allow pluripotent stem cells from the marrow to remodel the fibrin clot in the defect into fibrocartilage **(Johnson, 1989)**. This technique, while advantageous over other treatment options due to reduced donor site morbidity, its usage have been very limited because it contribute to a large amount of fibrocartilaginous tissue which fail to withstand the mechanical demands of articular cartilage **(Steadman *et al.*, 1997)**.

Soft tissue grafts involving the transplantation of periosteum and perichondrium to full thickness defects of articular cartilage have been used extensively both in animal models and in human clinical trials. The results have been variable, although hyaline-like tissue had been reported **(Carranza- Bencano *et al.*, 1999)**.

The use of rib perichondrium for articular cartilage reconstruction was introduced and investigated by many authors **(Engkvist *et al.*, 1979, Kwan *et al*, 1989 and Homminga *et al.*, 1990)**. Compared with ear perichondrium, **Homminga *et al.*, 1990** found that the perichondrium of the rib produced a repair tissue that closely resembles hyaline cartilage. Accordingly, the rib perichondrium was widely used in repair of articular cartilage defects with reasonable results **(Skoog and Johansson, 1976 and Sully *et al.*, 1980)**.

Free periosteal grafts were found to stimulate an enchondral bone formation **(Poussa and Ritsila 1979)** and in a chondrotropic environment it favors cartilage formation **(Poussa *et al.*, 1980)**. The chondrogenic potential of the periosteum is attributed to chondrocyte precursor cells in its cambial layer **(Rubak *et al.*, 1982; Zarnett and Salter, 1989; O'Driscoll *et al.*, 1999; Ito *et al.*, 2001)**.

Osteochondral transplantation involves harvesting one large graft or multiple smaller cylinders (mosaicplasty) from minimal load-bearing portions of the joint and transplanting them to cover defects in higher load-bearing areas **(Hangody *et al.*, 1998)**. But, this graft is limited by donor tissue availability required to fill large osteochondral defects **(Jakob *et al.*, 2002)**, the questionable viability of the chondrocytes from the donor tissue following graft harvest, whether tissue derived from a non-load bearing source can withstand the stress of a load-bearing area, and the extent of donor site morbidity **(Evans *et al.*, 2004)**.

Due to the inconvenience of all previous traditional techniques, a more sophisticated treatment option in the form of cell transplantation therapy was introduced. Autologous chondrocyte transplantation (ACT) was first described by **Brittberg *et al.*, in 1994**. The procedure involves harvesting chondrocytes from a non-load bearing region of the articular cartilage which expanded in culture media, and second procedure is then performed by taking a periosteal graft from the medial tibia, sutured over the defect; and cultured chondrocytes are then injected into the defect. The use of matrix scaffolds in tissue engineering has paved the way for use of periosteal patch and the two-stage procedure **(Tuli *et al.*, 2003)**. **Horas *et al.*, 2003** documented that the neocartilage consisted primarily of fibrocartilage with small localized hyaline-like regions near the subchondral bone **(Kurkijarvi *et al.*, 2007)**. In addition to this, there are other disadvantages; like being too much expensive, difficult technique, and two stage procedure **(Wood *et al.*, 2006)**.

Another source of the cell transplantation therapy is the bone marrow-derived mesenchymal stem cells (MSCs). These cells were proven to have the potential to facilitate osteochondral differentiation when implanted in vivo. The neotissue contained hyaline-like cartilage and its

composition is similar to the surrounding native tissue **(Ashhurst *et al.*, 1990)**. This resulted in an increased interest in the use of these cells in cartilage tissue engineering **(Wakitani *et al.*, 1994)**. Its usage was based on the fact that MSCs are multipotent stem cells that have the ability to self-renew and intrinsically repair and regenerate the tissue in which they reside **(Roufosse *et al.*, 2004)**.

The use of MSCs has advantages over chondrocytes implantation due to limited donor site morbidity, a less invasive procedure is required to obtain MSCs than native chondrocytes, only one surgical procedure on the damaged joint is required, and that MSCs have a greater proliferative capacity than differentiated chondrocytes **(Wakitani *et al.*, 2007)**. So current research focused on the use of bone marrow-derived MSCs as a recent strategy in the repair of cartilage defects, and now many alternative sources of MSCs such as the synovial membrane, blood, adipose tissue, muscle, and trabecular bone have been considered **(Raghunath *et al.*, 2010)**.

A number of studies have investigated all these treatment options, in an attempt to bypass articular cartilage's limited ability to self-repair, and to achieve tissue similar to native surrounding tissue. Nevertheless, controversy and uncertainty remain with respect to the best available treatment option. Perichondrial grafting and the use of bone marrow-derived MSCs in reconstruction of full thickness articular cartilage defects are known to build up hyaline like tissue in the reconstructed joints without any donor site affection. Clinically, they have been studied with reasonable results; however, no previous studies compared between both techniques in reconstruction of full thickness articular cartilage defects.