



Techniques for cartilage repair in chondral and osteochondral defects of the knee

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Many techniques are currently used in an attempt to regenerate cartilage surfaces in the presence of a chondral or osteochondral defect. Clinical results have been mixed and no single treatment has emerged as being superior. This article reviews the techniques previously and currently being used and evidence to support their use.

Keywords : chondral defects ; osteochondral defects ; chondral repair.

INTRODUCTION

The surgical management of chondral and osteochondral defects (OCD's) of the articular surface of the knee joint remains a controversial topic (27). William Hunter noted, in 1743, that articular cartilage has limited capability for repair once damaged (31). Articular cartilage may be lost due to trauma, osteochondritis dissecans or osteoarthritis, metabolic, haemorrhagic or rheumatological arthritides. Usually trauma or osteochondritis dissecans will result in a focal lesion but most other types of joint pathology will result in a more global pattern of cartilage damage at the joint surface. A discrete osteochondral lesion will sometimes result in a fragment of cartilage and underlying bone being partially or completely separated from the surrounding joint surface. The lesion can sometimes be repaired by retaining the fragment and fixing it *in situ* but if the osteochondral fragment is completely

detached or if it has degenerated to the extent where it can no longer function as joint surface, modalities of treatment to repair the defect with other tissue need to be considered.

The limited spontaneous capacity for repair of these defects once the fragment has become detached has driven surgeons to employ many different techniques in an attempt to establish a layer of soft tissue to take on the function of articular cartilage (20). The goal of these treatment modalities has been to re-create a tissue layer that is effective in load transmission, long term wear, joint lubrication and nutrition.

Large loads are placed on articular cartilage and at times these loads will reach up to 10 times body weight (33). The joint reaction force results from the combination of the force of bodyweight and also the force caused by ligament tension and muscular contractions around the knee. Any tissues that are formed in lieu of damaged articular cartilage in an

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osteocondral defect, will need to have sufficient inherent strength to withstand these loads. Not only does the tissue have to have the inherent strength to resist these loads but it also needs to be sufficiently well bonded to the surrounding bone and cartilage that it does not cleave from those tissues when loaded.

The wear characteristics of healthy articular cartilage are exceptional (23). Attempts to regenerate tissue in an OCD should therefore be aiming to create tissue with similar wear characteristics. This is the challenge facing surgeons in joint arthroplasty and also in cartilage repair surgery for OCD.

Healthy articular cartilage has a complex role in the lubrication of a synovial joint such as the knee. Boundary, fluid film and mixed forms of lubrication take place at different phases of the gait cycle. At heel strike, predominantly boundary lubrication will exist but there is also squeeze film lubrication (50). Boundary lubrication involves direct contact between joint surfaces coated in the glycoprotein, lubricin (50) and with surface active phospholipids (29) and hyaluronic acid (28). Elastohydrodynamic (and micro-elastohydrodynamic) lubrication predominate during stance phase progressing to boundary, elastohydrodynamic and weeping lubrication at 'toe-off'. Hydrodynamic fluid film predominates during swing phase and then during prolonged stance, boundary and boosted lubrication are the main types of joint lubrication (50). Any replacement tissue achieved in an OCD should be able to recreate these conditions as closely as possible and be capable of involvement with these types of joint lubrication.

Healthy cartilage receives nutrition from diffusion of nutrients in synovial fluid as it is essentially an avascular tissue. Its porous structure also allows diffusion of waste products of metabolism to be removed from the cartilage matrix. The regenerated tissue should be able to perform a similar role to support the replacement cartilage tissue and the existing osteochondral tissue around the graft.

Techniques for chondral repair

The techniques that have previously been employed in attempts to achieve tissue that meets

the above requirements include microfracture (54), drilling of subchondral bone (5,35,54) autologous chondrocyte implantation (4) osteochondral autograft and allograft transfer systems (2,47) and abrasion chondroplasty (19). The results have been mixed (40).

Abrasion chondroplasty uses a burr to remove unstable cartilage and cause bleeding of the subchondral bone. The blood clot that forms then allows blood borne fibroblasts to lay down fibrous tissue to replace the cartilage. Early results suggested that it was a useful technique for younger patients with cartilage damage, showing that 50 percent of patients improved (21). This technique is easy to perform, can be undertaken using a single-stage arthroscopic technique but the tissue that is formed is superficial, lacks adherence to the subchondral bone and therefore is subject to damage from shear forces with joint movement (1).

Subchondral drilling was described in animal models initially in 1986 (59) and was first described in orthopaedic practice in the ankle joint (5). Drilling generates heat and there is, therefore, a risk of thermal necrosis and sub-chondral bone necrosis has been noted following subchondral drilling (35). Chen *et al* have recently refuted these findings, showing that there was actually more osteocyte death in peri-microfracture lacunae than in peri-drill hole lacunae in a rabbit model (16).

Microfracture was first described by Steadman (55) and involves placing multiple 0.5-1.0 mm holes in the exposed subchondral bone at the base of the cartilage defect using a sharp pick. These holes are placed 3-4 mm apart taking care not to disrupt the integrity of the sub-chondral plate. This can be performed arthroscopically. The results from this technique have been shown to create at best a hybrid tissue cover of mixed hyaline and fibrocartilage (55) but the good clinical results have been reproduced by other authors in other centres with good to excellent results in 67% and poor results in only 8% (43). The fibrocartilage may provide temporary cover of bone with a soft tissue layer but may not have sufficient loadbearing capacity to be of value in terms of long term load transmission to the other joint surface as some have reported declining function in high-demand patients after one year (62).

Experimental studies have shown that patches of perichondrium and periosteum can be sewn onto an osteochondral defect and pluripotential cells from the cambium layer can differentiate into chondrocytes and form a 'hyaline-like' tissue covering the defect at follow-up (14,45). Peterson *et al* subsequently investigated the outcome of injecting cultured chondrocytes underneath periosteal patches (46). Cartilage is harvested from the joint with an arthroscopic technique, chondrocytes are isolated from the matrix in the laboratory and are then cultivated and their numbers increased between 20 and 50 times (46). The second stage requires an arthrotomy to suture the periosteal patch on to the surrounding articular cartilage and inject the chondrocytes *in situ*. This technique of autologous chondrocyte implantation (ACI) is expensive but has had some popularity and has been shown in some studies to have favourable outcome when compared to other techniques such as mosaicplasty (6,10). ACI is technically more difficult than microfracture and involves two-stage surgery. The tissue created has been shown to contain hyaline-like cartilage and chondrocyte-like cells but it is not clear that the recreated tissue functions in the same manner as articular cartilage in terms of load distribution. To take biopsies of adequate size for mechanical testing would cause chondral damage and therefore is not possible in a human subject following ACI. The chondrocyte-like cells may come from the cultivated chondrocytes injected underneath the periosteal patch, they may be from the chondrocyte precursors in the periosteum or from mesenchymal stem cells from sub-chondral bone bleeding into the OCD (7,51). Jones and Peterson have also described the sandwich technique for defects deeper than 8 mm whereby the base of the defect is bone grafted and then covered by a double periosteal layer and the cultured chondrocytes are then injected between this double layer (34).

Saris *et al* achieved improved structural repair of chondral surfaces with characterised chondrocyte implantation (CCI) as assessed by histomorphometry and histological evaluation when compared to microfracture but did not show significant improvement in functional outcome (52). The technique of CCI uses an autologous chondral cell therapy aimed

at optimising its biological potency to form stable cartilage tissue when cultured and transplanted. Techniques such as this may show superior results to standard ACI in the longer term.

In an attempt to encourage the growth of chondrocyte-like cells in a stable matrix to obtain hyaline cartilage in a more physiological pattern, matrix induced ACI (or MACI) was developed (4). This technique uses cultured chondrocytes, as in ACI, but implants these cells within a type I/III collagen disc. This can be stabilised with fibrin glue and has been shown to lead to a stable tissue construct in the original defect on MRI scan as much as two years later (3). Various types of matrix are available but most require an arthrotomy for their implantation. The demand for arthroscopic techniques has driven the development of third generation types of carrier/matrix which allow arthroscopic implantation. Although only early clinical results are available, the outcomes appear comparable with earlier 'open' techniques (9). Phase III, multicenter, randomised clinical trial of the co.don chondrosphere[®], a three-dimensional autologous chondrocyte transplantation product is underway, which will be comparing microfracture in the treatment of cartilage defects of the knee joint (9).

Limited cartilage resurfacing with metal implants has been described and implants for this exist. As it involves replacement of deficient cartilage with a metal disc, it is of course not cartilage repair as such. Animal testing in a goat model has shown that the implants can appear stable on radiographs with normal joint range of motion and no joint effusion at 4 weeks post operatively (36). There was however noted to be cartilage damage on the opposing joint surface (at the tibial plateau) when the medial femoral condyle was re-surfaced with a cobalt chromium implant (36). This type of cartilage damage to the opposing joint surface has been reported in other animal studies (18). Further work is required to ensure that this type of procedure will be safe for use in clinical practice.

Osteochondral transplantation or 'mosaicplasty' involves taking one or more autografts (full thickness bone and cartilage graft) from a 'non-weightbearing' portion of the joint and transferring it to the area of the osteochondral damage (8). This

is usually done by taking cylindrical cores of cartilage and underlying sub-chondral bone and impacting them into cylindrical holes drilled into the base of the lesion.

This is the only technique which recreates type II collagen hyaline cartilage in normal cartilage matrix. This is however obtained at the expense of removing joint surface elsewhere in the joint. There is also the issue of the areas in between the cylindrical grafts and the fibro-cartilagenous tissue which develops here. It is also essential to get the grafts to fit in at the correct depth to avoid the point loading which will occur if part of the graft is 'proud' of the surrounding cartilage surface. This will increase wear rates and secondary cartilage damage. Cell death at the margins of the graft is also known to occur, leading to a reduction in graft tissue of as much as 24 percent (32). Mosaicplasty is best reserved for small to medium-size defects of less than 25 mm in diameter (8).

Allograft of osteochondral tissue has also been used with some success for full thickness cartilage defects (63) and avoids the problems of donor site morbidity required with osteochondral autograft. Studies have shown statistically significant improvement up to 3 years as measured by several knee specific scoring systems including IKDC, Knee Related Quality of life scores, Sport and Recreation Function Score and SF12 Physical Component score (42). Overall patient satisfaction rates of 84% with allograft transplantation have also been reported (42). Some grafts have done well, surviving up to 25 years but equally there is still a significant rate of early failure (25). Equally good results for allograft in terms of imaging characteristics, biomechanical properties and histology have been achieved in animal (dog) models when compared to autograft (24). There are however the issues of greater cost and lower availability of allograft tissues for implantation but using allograft does avoid the potential for donor site morbidity (11).

Cartilage regeneration with type II collagen and a highly sulfated proteoglycan matrix has been the goal of many of the treatments for full thickness cartilage loss but this has not been reliably achieved with histological specimens often revealing 'hyaline-like' cartilage and fibro-cartilage cover of

defects on follow-up biopsies (40). It is this focus on developing techniques which can reliably produce healthy chondrocytes and type II collagen in an extra-cellular matrix which has characteristics which allow adequate load transmission and involvement in joint lubrication and nutrition that has driven interest and research in tissue engineering techniques and led to the development of synthetic scaffolds for the purpose of cartilage repair. The basic concepts of tissue engineering dictate that for new tissues to form and remain viable, cells need both a stable scaffold to grow in and the appropriate biological signals to determine cellular differentiation and tissue type. The goal of scaffold replacement for OCD's is that bleeding into the scaffold will allow pluri-potential mesenchymal marrow cells to migrate into the implant. Responding to inductive biological signals from the surrounding injured bone and cartilage, collagen deposition and cellular infiltration and differentiation will allow the formation of hyaline cartilage within the surface layer of the 'plug' and ossification of the deep 'bone' layer of the implant. Advances in tissue engineering have led to improvements in biomaterials including natural and synthetic hydrogel polymers which have been used as scaffolds for the purpose of cartilage repair in chondral and osteochondral defects (60).

Currently research is focusing on manipulating the material properties of the scaffold implant in order to regenerate tissue that is as physiological as possible. As more research is published, it becomes clear that the factors such as the Young's modulus (stiffness) of the implant, the relative porosity (for nutrition of cellular components and removal of waste products of local cellular metabolism) and ease of degradation of the scaffold material have both quantitative and qualitative impact on the tissue that regenerates within the scaffold (49). For osteochondral defects, the challenge in scaffold engineering remains focused on encouraging the growth of osseous tissue at the base of the defect firmly attached to cartilaginous tissue at the most superficial part. The solution has been the development of biphasic implants with two adherent layers. It has become apparent that the porosity of the implant and therefore the stiffness of the implant

can be manipulated to determine the tissue type that grows within it (38,49,64). It is therefore possible to encourage cartilaginous tissue differentiation in the surface layer of the implant and osseous tissue differentiation in the deep layer.

TruFit® CB plugs (Smith and Nephew) are one example of commercially available and licensed, synthetic resorbable biphasic implants made of a patented composite hydrophilic polymer composed of polylactide co-glycolide, calcium sulphate and poly-glycolide fibres. The TruFit® CB plug is licensed for chondral and osteochondral defects in Europe but only for bone void filling in the USA (61). It is designed as a cylindrical scaffold with two layers, one with a similar trabecular network to cancellous bone and a superficial 3 mm layer designed to simulate the matrix of articular cartilage. The plugs are available in three different diameters of 7 mm, 9 mm and 11 mm. Clinically, a cylindrical hole of 18 mm depth is drilled into the osteochondral defect (usually in a femoral condyle) and a plug of the same depth undergoes a press fit into the defect. Osteo-progenitor cells can migrate (from surrounding osseous bleeding) into the basal layer with resultant ossification in the basal layer. Histology from a goat model has shown osseointegration of the deep part of the implant, with resorption of the implant material and 'hyaline-like' cartilage formation in the surface layer (61). Authors have reported the potential for cyst formation and delayed incorporation at the site of plug implantation which may persist for 24 months or more (12).

Increased interest in tissue engineering techniques has driven a significant increase in the number of materials and implants being assessed for use as a scaffold for the repair of cartilage in chondral and osteochondral defects. Large numbers of resorbable hydrogel polymers such as polylactide co-glycolide (PLG), similar to the TruFit CB plug, have been assessed in recent years (17,26,44,53). Kon *et al* showed that a composite biomaterial scaffold composed of hydroxyapatite nucleated type I collagen fibrils was used in 13 patients with a significant improvement in outcome scores but incomplete integration on MRI in up to 47% of patients at 6 months follow up (37). Other materials used as

scaffolds include medical grade polycaprolactone (often with Tricalcium phosphate and collagen mesh), porous tantalum and carbon fiber (13,41,56). Cellulose sponges have also been used in laboratory studies but have not been successful as the matrix formed has been soft and unlikely to have withstood loading *in vivo* (48). Allogenic cartilage has also been harvested, shattered and de-cellularized and then reconstituted to form a neo-cartilaginous scaffold for cartilage repair but this has been confined to laboratory and animal studies to date (65). Recent studies have reported the use of silk-worm and spider silk scaffolds for use as a scaffold support for chondrocytes in cartilage repair (22). A wide range of cellular pretreatment of scaffolds has been attempted using ACI techniques, autograft of cultured chondrocytes, allograft chondrocytes, mesenchymal stem cells and the addition of biological and biochemical factors such as fibroblast growth factor, platelet derived growth factor, bone morphogenetic protein (rhBMP 2) and hydroxyapatite (15,39,57,58,60).

The ultimate aim in 'cartilage repair' surgery is to achieve type II collagen in a stable tissue matrix which is capable of performing as load bearing articular material under physiological loading conditions. The techniques described above have all been used in the treatment of full thickness cartilage loss but many have simply delayed the need for more definitive treatment, which often requires partial or total joint arthroplasty. The current focus is on developing techniques which lead to long lasting cartilage repair which will obviate the need for joint replacement.

At this stage, many of the techniques for chondral repair have been used with some success. None have consistently shown superiority in clinical trials and as such, no recommendation regarding treatment can be made at this time. High-quality clinical trials are needed to evaluate new treatments and more research is needed but with new tissue engineering techniques, the prospect of developing long lasting cartilage repair tissue with good wear characteristics that is capable of involvement in load bearing, nutrition and lubrication of the joint is increasingly realistic.

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