Chondro-Gide® enhanced marrow stimulation – also for ankle and hip?

AMIC® – A promising approach in cartilage regeneration

GEISTLICH SURGERY SATELLITE SYMPOSIUM
INTERNATIONAL CARTILAGE REPAIR SOCIETY (ICRS) WORLD CONGRESS
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Articular cartilage, if damaged beyond a point, cannot heal itself, which affects a patient's level of activity and general quality of life. Marrow stimulation is a first-line cartilage repair technique which triggers a natural intrinsic repair mechanism. Understanding the mechanism of blood clot formation and subsequent biological regenerative processes is fundamental to improving results by therapeutic interventions. By stabilizing the blood clot through a matrix, chondrogenic differentiation of human mesenchymal progenitor cells may be enhanced and thus cartilage regeneration improved.

Autologous Matrix-Induced Chondrogenesis (AMIC®), an in-situ matrix assisted marrow stimulation technique, has proven successful in terms of restoration of joint function, pain reduction, and regain of mobility up to previous levels of physical activity. Below is a summary of the presentations of the Montreal Symposium, addressing the biology of clot formation and the technique and clinical results of AMIC® in the ankle and hip.

Blood clot biology after marrow stimulation

Prof. Caroline Hoemann (Montreal, Canada) provided an excellent elaboration of the process of clot formation and presented methods to modulate its behaviour so as to improve repair mechanism in higher grade cartilage defects.

Microfracturing (MFx) as described by Hoemann, is a first-line cartilage repair technique which aims to restore knee function, to reduce pain and to delay or avoid the need for prosthesis. Perforation of the subchondral bone enables release of mesenchymal progenitor cells, cytokines and growth factors which ideally fill the defect, leading to the formation of a superclot and ultimately cartilage repair tissue. However, in large defects, after MFx, capillary bleeding leads to clot formation over the holes, but blood dissipates into the perfusion solution and the synovium, without superclot formation.

Hoemann referred to two mechanisms in haemostasis. In primary haemostatis, platelets are activated which adhere to damaged endothelium to form a platelet plug. In secondary haemostasis, blood is also transformed from a liquid to a gel like substance through involvement of clotting factors and pro-coagulants. Adding a biomaterial during marrow stimulation helps to increase the volume and stability of the initial clot and to protect the clot from rapid degradation.

Hoemann's group used a chitosan-glycerol phosphate based scaffold which resulted in a more hyaline-like fill compared with microfracture alone. Since formation of a superclot is of fundamental importance in matrix-assisted cartilage repair techniques, Hoemann concluded that methods to enhance blood clot formation biology need to be optimized.

One option to obtain this enhancement is to cover the blood clot with a collagen matrix. This was shown in a study by Dickhut et al., where a collagen matrix (Chondro-Gide®) in combination with fibrin sealant strongly prevented shrinkage of the superclot and significantly enhanced proteoglycan deposition compared to that achieved by fibrin sealant alone. Thus, the collagen matrix seems to facilitate chondrogenesis from mesenchymal progenitor cells.

The next two speakers described in detail the surgical steps involved in AMIC® for the treatment of high-grade chondral and osteochondral lesions in the talus and the hip. Both speakers presented highly encouraging post-operative results. They emphasized the need to address other associated joint pathologies for successful outcome of the procedure.

AMIC® Talus - Surgical Technique and Clinical Results

Prof. Markus Walther (Munich, Germany), reported on his experience with AMIC® technique in the treatment of osteochondral lesions of the talus.

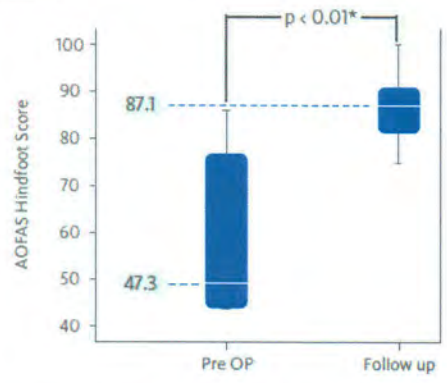
One major advantage of AMIC®, as pointed out by Walther, is that osteotomies can be avoided in most cases, and if found necessary, they can be performed outside the loaded

area. Other advantages of AMIC® are that it is a one-step procedure that can be prearranged, the matrix is an off-the-shelf product that is readily available, and no sutures are required for attaching the matrix to the defect, since it can be fixed firmly with fibrin glue.

Walther outlined the surgical technique which involves debridement of unstable cartilage and cystic lesions, drilling into the sclerotic wall, harvesting of bone for grafting if needed, mostly from the ipsilateral calcaneous, preparing and cutting the matrix precisely to cover the defect without overlap onto the surrounding tissue, and finally fixing the matrix over the defect with fibrin glue. Walther also pointed out that, depending on the location of the lesion in the talus, several approaches to the ankle are available, namely, ventral (medial, lateral and central) and dorsal (medial and lateral), indicating also the appropriate positioning of the patients for the procedure. Details of postoperative measures to ensure success were also given. He emphasized the importance of addressing other concurrent joint pathologies such as hindfoot malalignment or ligamental instability. Failure to address and correct such defects often prevents successful cartilage repair interventions. Defects in deltoid and lateral ligaments should be corrected, ligament augmentation may be required and can be performed with plantaris longus tendon, peroneal tendons may need reconstruction and closing wedge osteotomy of the calcaneus may have to be performed for correcting hindfoot varus. In some cases, also supramalleolar ostoeotomy may be required. If bone graft is needed, autologous bone can be harvested from the ipsilateral calcaneous, with minimal secondary donor site morbidity in comparison to the illiac crest.

Walther presented his follow-up results of a total of 72 patients with Grade III and IV cartilage defects of the talus, treated with a minimally invasive AMIC® without an osteotomy of the malleolus. In a prospective study, 21 patients with a follow-up >30 months were analysed. The defect size was greater than 1.5cm² (ICRS Grade III and IV), mean patient age was 32 (20 – 54) and the mean BMI 23 (20.1 – 31.4). There was significant improvement in the average American Orthopaedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Scale from 47.3 to 87.1 points (Figure 1) with major improvements in the categories of pain and activity. There was no significant difference in the leg circumference and in the range of motion between the treated and the untreated ankle, which can be interpreted as indicators of normal leg function.

FIGURE 1



Average AOFAS Score preoperative and at follow up (30–40 months) of 21 talus patients [unpublished data, Walther 2012].

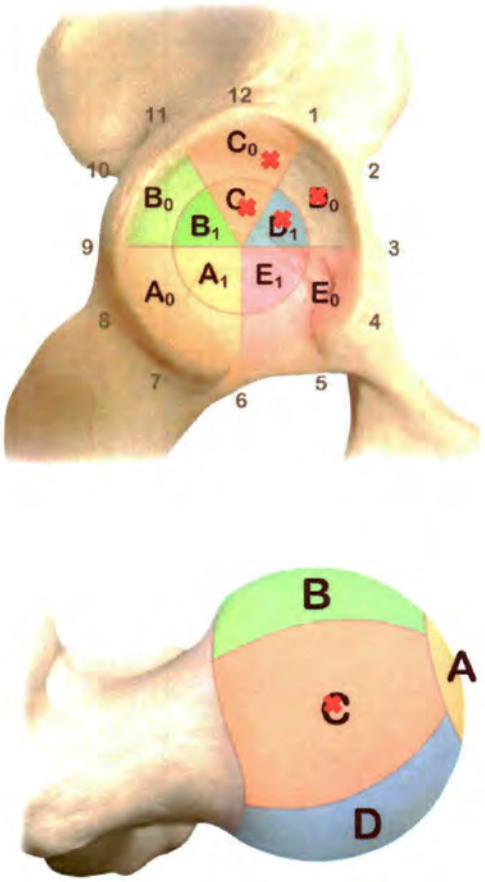
Walther concluded his talk by raising some very relevant questions relating to the necessary extent of debridement, choice of donor site with minimum donor site morbidity for bone graft harvesting is found to be necessary and finally, if involvement of autologous stem cells may be an option to further improve the results of AMIC®.

AMIC® Hip - Surgical Proceedure and 5-Year Clinical Outcome

According to Prof. Andrea Fontana, Milan (Italy), chondral lesions and labral tears are the consequences of femoroacetabular impingement (FAI) and frequently cause pain and functional limitations. Surgical treatment should aim at, according to Fontana, not only correcting the causative bone deformities, but also address all associated intraarticular chondropathies. Fontana presented a schematic area classification zonation of the acetabulum and the femoral head for localization of chondral lesions (Figure 2). According to his experience, the majority of the defects appear at the anterosuperior acetabulum and the superior segment of the femoral head.

Fontana presented data of patients with cartilage lesions of the hip which he treated since 2005. In this collective, 81 patients were treated with the AMIC® technique and 80 patients with Autologous Chondrocyte Implantation (ACI). Demographic characteristics like age and sex, and pathological features such as grade, location and size of lesions in the two groups were comparable. Fontana pointed out that a comparison of ACI- and AMIC®-treated patients revealed no significant differences between the two groups of patients. The mean modified Harris Hip Score (HHS) value improved from 46 ± 7 preoperatively in both patient groups to 85 ± 6 (AMIC® n=81) and 81 ± 6 (ACI n=80) 5 years postoperative (Figure 3). He described that the arthroscopic surgical procedure involves chondrectomy to remove defective cartilage, exposure and microfracture of the subchondral bone, shaping the margins of the defect to have a round shape and insertion of the matrix previously cut to shape. Microfracture in the hip can be difficult when perpendicular access to the subchondral bone is not given. In these cases, Fontana recommends scratching the surface to make grooves which

FIGURE 2



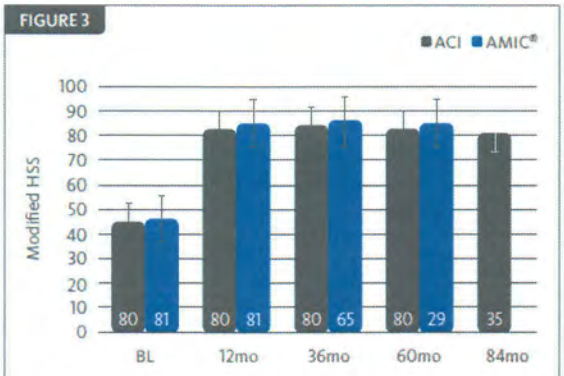
The most frequent cartilage defects are localised at the anterosuperior acetabulum (top) and the superior segment of the femoral head (bottom) [Fontana 2012].

establish contact between the bone marrow cells and the joint. He emphasized the importance of placing the rough side of the bilayer Chondro-Gide® matrix towards the subchondral bone. Fontana added that he did not use fibrin glue to stabilize the matrix in the lesion. In case the matrix was not flat, he took recourse to a simple trick of inserting a catheter into the joint and by inflation firmly pushing the matrix against the defect surface.

The main disadvantages of ACT, according to Fontana, are that two surgical steps are involved in the procedure, that it requires additional work in logistic and planning and that chondrocyte culture may not always be successful.

For Fontana, the advantages of the innovative technique of AMIC® are that it is a one-step surgery that can be well planned without additional logistic work. Additionally he concluded that AMIC® is highly cost-effective, and is as efficacious as ACI. For these reasons, Fontana said that he discontinued ACI in favor of AMIC® for cartilage repair.

FIGURE 3



Post-operative course evaluated by a modified Harris Hip Score (HHS) for AMIC (n=81) and ACI (n=80). Mean values and SD at baseline (BL) and 12–84 month post-op. [unpublished data, Fontana 2012].

Conclusion

At the ICRS satellite symposium, successful outcomes following AMIC® treatment of severe chondral and osteochondral defects of the ankle and hip were reported. Restoration of joint function, pain reduction, regain of mobility as well as return to previous levels of physical activity were achieved, documenting the highly promising potential of this procedure. AMIC® as an easy-to-plan, single-step procedure is both cost efficient and clinically effective and thus has distinct advantages compared to other techniques currently in use in the treatment of severe cartilage lesions.

The satellite symposium was recorded by the ICRS and can be viewed on the ICRS educational services website (ICRS 2012 Session 10.1) or on the Geistlich Surgery website.

Chondro-Gide®

AMIC®

Autologous Matrix-Induced Chondrogenesis

An innovative, biological technique for the treatment of cartilage defects in the talus, knee and hip

- A minimally invasive, one-step surgical technique for the treatment of chondral and osteochondral defects larger than 1cm²
- Based on microfracturing, the established first-line treatment
- Natural protection of the superclot resulting from Chondro-Gide®'s unique bilayer structure
- Positive influence of the chondrogenesis through Chondro-Gide®
- Promising clinical results
- Straightforward, cost-effective surgical technique
- Over 7 years clinical experience

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Clinical results and scientific studies confirm the effectiveness of Chondro-Gide®, the leading collagen matrix in cartilage regeneration.

Chondro-Gide® is not available in all markets. Availability is subject to the regulatory or medical practices that govern individual markets.

CARTILAGE REGENERATION

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