

Bone & Cartilage Regeneration News 02|09

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BONE & CARTILAGE REGENERATION

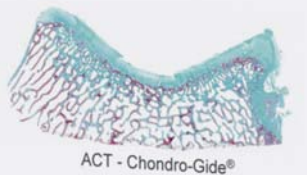
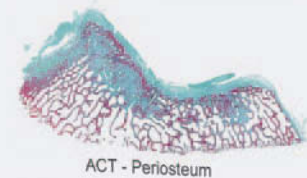
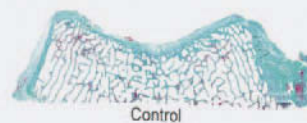
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Chondral bone densification Transplantation in sheep



ns. 319:133;2005

Geistlich
Surgery



Title Image: Mayron Spector, Ph. D., ICRS World Congress in Miami



Orthoss®, the natural choice in bone regeneration. The excellent biofunctionality makes Orthoss® the ideal bone graft substitute. Bone regeneration materials from Geistlich have been used successfully in more than three million patients.



Chondro-Gide®, the leading natural collagen matrix in cartilage regeneration. This standardised, easy to handle matrix can be used to treat cartilage defects using both AMIC® and ACI. The product now includes a sterile Aluminium Template, ideal for creating an accurate impression of the defect.

Introduction

Geistlich Surgery is pleased to present the 10th issue of its Bone and Cartilage Regeneration newsletter.

The highlight in this year's cartilage regeneration calendar was the 8th International Cartilage Research Society (ICRS) congress in Miami. Over 800 surgeons and scientists attended the 12 free paper sessions, 2 poster sessions, 17 special sessions, 5 plenary sessions, 6 industry satellite symposia and 8 workshops.

Geistlich Surgery, as a long term industry partner for the ICRS, was present in Miami as gold sponsor promoting Chondro-Gide®. Our leading collagen I/III matrix was referred to as the gold standard matrix in cartilage regeneration. In many of the various lectures, abstracts and papers, research groups presented the results of the successful clinical application of Chondro-Gide® in different cartilage repair strategies. A selection of the abstracts and poster summaries is included in this newsletter in their submitted form. Of special note are the results of Dr. A. Fontana (Monza, Italy). In a controlled retrospective study, he investigated 182 patients who were affected by hip chondropathy. Of these patients, 120 underwent arthroscopic ACI and the other 62 arthroscopic AMIC® surgery. The author concluded that no significant difference between the groups could be observed and that the AMIC® appeared to be the more valuable treatment option, as it was less invasive and more cost effective when compared to ACI.

During the well attended Geistlich satellite symposium, renowned scientists and surgeons presented the results and the benefits of using Chondro-Gide® in ACI as well as for AMIC®

during cartilage regeneration in the knee and in the talus. Insight into this symposium will be available soon in the members area of the ICRS website and on DVD from Geistlich Surgery. Further information can be found in the short summary of the symposium on page 18.

Geistlich Surgery, in association with the Royal National Orthopaedic Hospital NHS Trust in Stanmore, is organising a workshop in cartilage regeneration techniques with national and international speakers in September 2009. We have included details of the programme and would like to invite you to join us at this event.

We kindly thank Prof. Dr. Ruhnau and Prof. Dr. Bruns for providing their case reports to be shared with you. Prof. Ruhnau presents a case in bone regeneration of a patient with pseudarthrosis after a tibial osteotomy. Prof. Bruns describes a case of a young patient with a subchondral ganglion of the capitulum humeri.

We would again like to take this opportunity to invite you to present interesting clinical cases in both bone and cartilage regeneration in the form of case reports in future copies of this newsletter. Please contact us via surgery@geistlich.com for further details.

Geistlich Surgery is an innovative leader specialising in biological bone and cartilage regeneration. We implement our scientific expertise for the development of novel biological matrices for tissue regeneration in orthopaedic and trauma surgery.

**Geistlich Surgery
August 2009**

NOW AVAILABLE!

Chondro-Gide®

NEW: Greater Primary Defect Filling Sterile Aluminium Template

Description

To further improve the product characteristics of our gold standard matrix in cartilage regeneration, we have increased the thickness of the 20 x 30 mm and 30 x 40 mm Chondro-Gide® by up to 60%.

The Chondro-Gide® Collagen Matrix 40 x 50 mm, primarily used for ACI surgeries has not been changed.

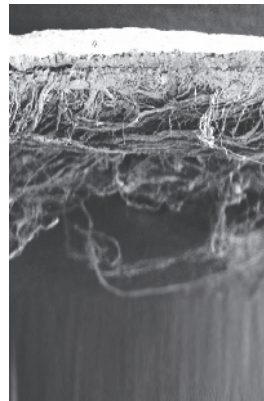
The new Aluminium Template now provided is used to create an accurate impression of the defect. The template is sterile and is delivered with the Chondro-Gide® in a double blister packaging.

These enhancements were implemented as a result of the requirements of many of our customers to further improve the handling properties of this unique matrix during cartilage regeneration procedures.

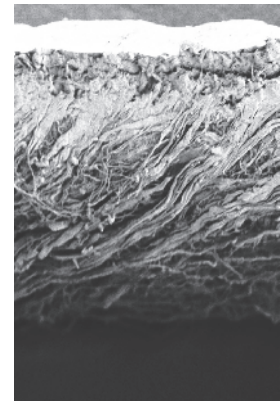
Pricing

Please contact your local representative for pricing and ordering information.

REM Images (40x)



Chondro-Gide® 40 x 50mm



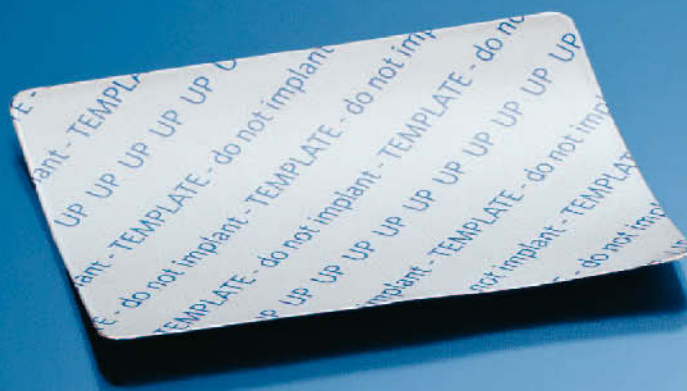
NEW Chondro-Gide®
20 x 30mm and 30 x 40mm.
Improved for greater
primary defect filling



Ordering details

- 30890.3 Chondro-Gide® Bilayer Collagen Matrix 20 x 30 mm
- 30915.5 Chondro-Gide® Bilayer Collagen Matrix 30 x 40 mm
- 30939.9 Chondro-Gide® Bilayer Collagen Matrix 40 x 50 mm

Chondro-Gide® is not sold in the U.S.A.



Bone Grafting in Pseudoarthrosis Surgery

Clinical Case by Prof. Dr. med. Ruhnau
Sankt Marienhospital Buer, Germany

Pseudoarthrosis is a commonly known complication in non-surgical and even operative fracture treatment. A pseudoarthrosis is a false joint and occurs when a bone fracture fails to unite and remains mobile at the fracture site. Pseudoarthrosis is still one of the most difficult conditions to assess as a source of symptoms, and not surprisingly the outcome of pseudoarthrosis repair intervention to treat patients is difficult to predict.

Patient History, Clinical Diagnosis

Five months prior to the presentation of the patient in our institution, an open wedge valgisation osteotomy had been performed on the left tibia of a 66 year old patient with a medial gonarthrosis. The osteotomy had been filled with autologous bone from the iliac crest.

The patient complained of pain in the leg depending on the weight load. When diagnosing the patient, the radiological assessment revealed incomplete bone formation in the osteotomy with pseudoarthrotic symptoms (Figure 1).



Figure 1: Pre-operative to the revision, incomplete bone formation is visible after open wedge osteotomy with pseudoarthrotic symptoms.

Treatment

In a revision intervention, the original osteotomy was debrided and the defect was completely filled with a mixture of autologous bone from the iliac crest and 2-4mm Orthoss® granules.

Results

The postoperative course was uneventful and no complications were reported. No signs of thrombosis or inflammations were visible. Despite the progressing medial gonarthrosis the patient was pain free after three months and showed a range of motion from 0-120 degrees. Three months post-operatively, new bone formation is clearly visible (Figure 2).

The Orthoss® bone mineral matrix proved ideal as augmentation material during autologous bone grafting in pseudoarthrosis surgery providing an ideal scaffold for new bone formation.



Figure 2: Defect completely filled with autologous bone and Orthoss® after 3 months.

Treatment of a subchondral ganglion at the elbow joint with a combination of autologous cancellous bone grafting and Chondro-Gide® according to the AMIC® procedure

Clinical Case by Prof. Dr. med. J. Bruns
Diakonie-Klinikum Hamburg Standort "Alten Eichen", Germany

In general, only little is known about subchondral ganglion cysts. The etiology of this disease is still under discussion. We report a case with such a subchondral ganglion of the capitulum humeri in a young woman.

Patient History, Clinical Diagnosis

A young 18-years old woman, a student and part-time waitress, was suffering from pain and locking of her right elbow joint. No previous trauma or other specific diseases were known.

At clinical presentation the patient exhibited a typical valgus angle of the elbow joint with slight joint effusion. No limitation of the passive motion of the elbow was detectable. The range of motion for flexion-extension was 130-0-10 and pronation-supination 90-0-90 on both sides.

Pre-op x-rays exhibited a large subchondral cyst, which was filled with a liquid substance (Figure 1). In addition, the cyst was covered towards the joint with a flat cartilage layer without any adjacent bone (Figure 2).



Figure 1: MRI coronal plane: A large subchondral cyst is visible in the region of the capitulum humeri.



Figure 2: MRI sagittal plane: The subchondral position of the cyst immediately under the cartilage layer is clearly evident.

Treatment

First, the elbow joint was opened via a lateral approach. Intraoperatively, a cartilaginous lamina without any adjacent bone covering the entrance of the bone cyst was found. After removal of the cartilaginous lamina, the cyst was curetted and drill-holes were placed in the surrounding bone of the capitulum humeri to stimulate bony ingrowth (Figure 3 and 4). For filling of the bony defect, cancellous bone from the ipsilateral iliac crest was harvested and the blood obtained during harvesting of the bone graft was sampled (Figure 5).

After transplantation of the bone graft and the sampled blood, a collagen I/III matrix (Chondro-Gide®, Geistlich Pharma AG, Switzerland) was placed over the treated area and glued by means of fibrin-glue (Tissucol®, Baxter, Germany) with the rough matrix surface facing the bone transplant according to the AMIC® procedure (Figure 6).

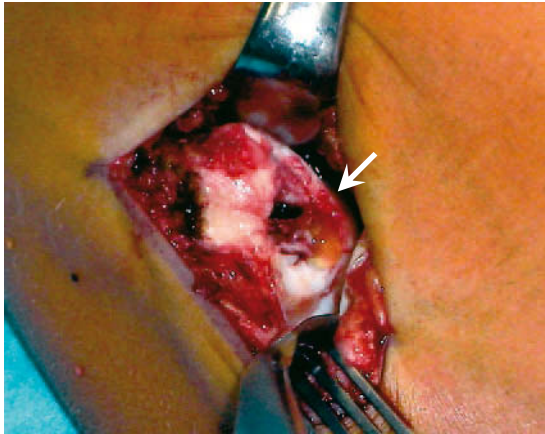


Figure 3: Intraoperative situs after removal of the subtotal loosened cartilage layer lying over the subchondral cyst with mucoid fluid filling the bony defect.

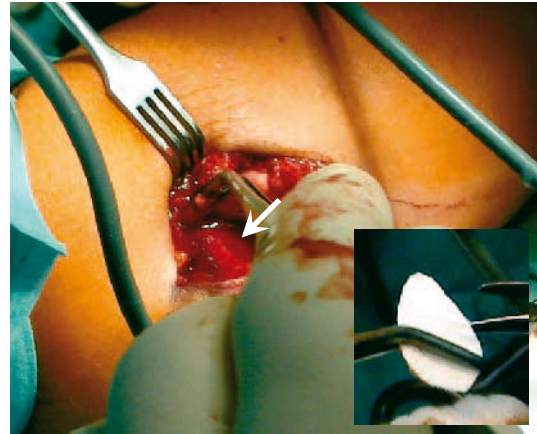


Figure 6: The cyst is completely filled with the bone graft and covered by the Chondro-Gide® Bilayer Collagen Matrix, which has been cut to the size of the cyst (small inset).

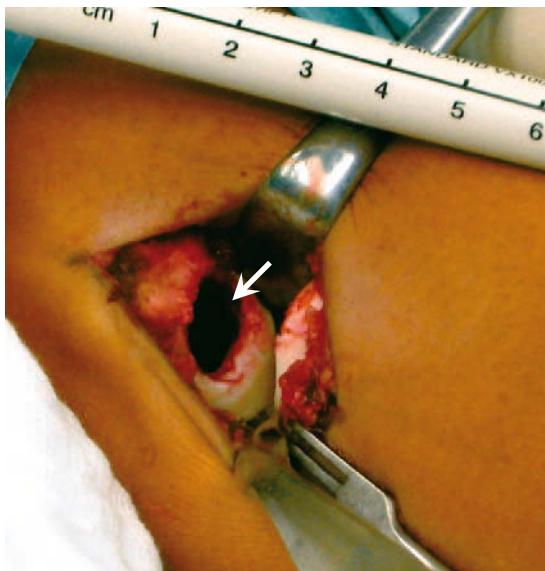


Figure 4: After removal of the mucoïd fluid and the cystic membrane, a large hole in the subchondral bone is visible.

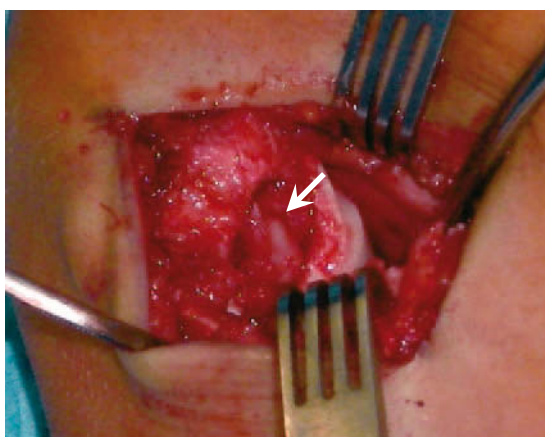


Figure 5: The cystic lesion is filled with autologous cancellous bone graft harvested from the ipsilateral iliac crest.

Finally a wound drainage was applied and the wound closed in layers.

The postoperative course was without any complication. The patient was advised to avoid loading of the right elbow for three months.

Follow-up

Routine follow-up examinations exhibited sufficient bony ingrowth of the transplant and tremendous pain relief within months. At the latest follow-up, one year postoperatively (Figure 7), the patient was free from pain and exhibited an unlimited range of motion of the operated elbow.

The latest X-ray of the elbow shows complete bony ingrowth with a normal articular surface.

Discussion and conclusion

Intraosseous ganglion cysts occur relatively often. They are most often found around the wrist joint, especially at the scapho-lunate joint. In addition, these lesions can be seen in the bones of the lower limb near to the joint space of the major joints of the leg.

Regarding the etiology, the reasons for development of such ganglia is still unclear. Subchondral cysts are common in cases of osteoarthritis and of rheumatoid arthritis. In some cases no other joint disease is detectable.

One theory includes the idea that preexisting clefts of the adjacent articular surface enable penetration of the synovial fluid into the subchondral cancellous bone and thus causing osteolysis due to the enlarged intraosseous pressure, similar to the development of Baker's cysts in the soft tissue.



Figure 7: One year follow up x-ray images showed new bone formation and cartilage repair tissue covering the capitulum humeri. The patient was pain free with unlimited range of motion.

In a few cases treated previously by the author it could be shown arthroscopically and fluoroscopically that there is such a cleft connecting the intraarticular space with the subchondral bone. Whether the cleft is a non-degenerative precondition or has developed in the course of degenerative changes of the involved joint is unclear.

Nevertheless, not much clinical evidence can be found for the treatment of this disorder in the recent literature and therefore there are no clear therapeutical recommendations.

In the case described, the use of autologous cancellous bone in combination with the AMIC® technique has proven to be a promising treatment option.

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Posters and Abstracts

Autologous Matrix Induced Chondrogenesis (AMIC®) for focal chondral defects of the knee – results at 2-4 years

Anders S., Schaumburger J., Wiech O., J. Beckmann J., Grifka J.
P238, Poster, 8th ICRS Congress, Miami, USA

Introduction

Autologous Matrix Induced Chondrogenesis (AMIC®) combines microfracturing with application of a cell-free collagen scaffold. No cultured chondrocytes are necessary. It was established for focal cartilage repair in the knee as a cost-effective one-step procedure.

Methods and Materials

38 focal chondral/osteochondral defects (ICRS III-IV°) of the femoral condyle, trochlea and/or patella in 35 patients (27 male, 8 female, mean age 35.8 (18-52) years) were treated by standardized microfracturing and application of a cell-free collagen type-I/III scaffold (Chondro-Gide®, Geistlich Pharma AG, Switzerland). The mean defect size was 3.8 (1.0-10.8 cm²). The results were evaluated prospectively by functional outcome scores, subjective clinical ratings and MRI with an average follow-up of 30.4 months (range 24-54 months).

Results

Significant improvements were seen in the Cincinnati-Score (50.4 to 87.3) as well as in the Lysholm-Score (59.6 to 88.6, each $p < 0.001$). Pain on a 10-point VAS decreased significantly from 6.2 to 1.8 while subjective knee function improved from a mean of 4.6 to 7.5.

In 5 revision cases at 4-26 months the repair tissue revealed reasonable results with regards to surface formation, filling and integration. The MRI follow-ups showed an adequate filling of the defect, no prolonged effusion occurred. 85% (30/35) of the patients were satisfied with the functional results (ICRS I°+II°).

Summary

The AMIC® procedure is a minimal invasive effective one-step therapy for focal chondral or osteochondral cartilage defects in the knee. It was shown to provide stable results at mid-term follow-ups.

The Treatment of Retropatellar Chondral and Osteochondral Defects with Autologous Matrixinduced Chondrogenesis (AMIC®)

Benthien J.P., Jakob M., Behrens P.

P212, Poster, 8th ICRS Congress, Miami, USA

Introduction

Retropatellar cartilage defects are difficult to treat. A regeneration of pristine hyaline cartilage is desirable but yet impossible. The AMIC®-procedure (Autologous Matrix Induced Chondrogenesis) is an option to facilitate regeneration of substitute cartilage. These case reports document the successful cartilage regeneration in patients with chondral and osteochondral retropatellar defects where other treatment options have failed.

The aim of this case control study is to evaluate the value of the AMIC®-procedure in retropatellar cartilage defects. The operative procedures are introduced.

Methods and Materials

A case control study introduces 2 cases in which retropatellar AMIC® was performed. One was a chondral, one an osteochondral defect. The follow up is 12 months. Pain reduction evaluating the Visual Analogue Scale (VAS) and range of motion of the affected joint were evaluated.

Results

In both cases a pain reduction in the VAS from 10 to 2 could be achieved. The range of motion improved in flexion from 90 to 130 degrees. X-ray and MRI document almost complete regeneration of bone and cartilage in both cases.

Summary

The AMIC®-procedure was successfully carried out in these patients where other options had failed. Matrix induced chondrogenesis may be an alternative in retropatellar chondral defects which are otherwise difficult to treat. Further studies are encouraged.

Autologous Matrix-Induced Chondrogenesis (AMIC®) – Treatment of Chondral and Osteochondral Defects in the Knee

Kursano T., Jacobi M., Hoogewoud H., Jakob R.

P231, Poster, 8th ICRS Congress, Miami, USA

Introduction

We present our experience of a microfractured defect covered with a collagen matrix (Chondro-Gide®, Geistlich Pharma AG, Switzerland) called Autologous Matrix-Induced Chondrogenesis (AMIC®) originally described by Behrens combined with discharging osteotomies. The idea behind is to maintain the stem cells that are mobilised through bleeding in the defect are maintained under the matrix to help to form a regenerate.

Methods and Materials

From August 2003 to July 2007 a number of 56 patients have been treated by AMIC® in Fribourg by the senior author. Patients were treated for chondral and osteochondral lesions (OCD) at the knee joint and for OCD of the talus. 38 patients (40 knee joints) with a minimum follow-up of 1 year (Ø follow-up 2.5 years, range 1-4 years) underwent retrospective analysis using clinical scores (ICRS, Lysholm). 17 patients had MRI which was analysed by Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) score. 11 second look arthroscopies were reviewed using the ICRS Cartilage Repair Assessment and Oswestry Arthroscopy Score. 5 biopsies have been examined histologically.

Results

23 men and 17 women with a mean age of 36 years (range 14 – 64) underwent the AMIC® procedure. Patients were treated for OCD (11), femoropatellar (20) and posttraumatic (9) lesions. Defects were located on the medial femoral condyle (16), lateral femoral condyle (3) and femoropatellar defects (21) with a mean size of 3.87cm² (range 0.72 – 12). ICRS and Lysholm scores improved especially for OCD and femoropatellar lesions. MRI showed 18% complete fillings and 24% by hypertrophy; complete integration to the border zone was observed in 47%, but surfaces were only intact in 12%.

Arthroscopically we found good fillings with some hypertrophies, but repair tissue was somewhat softer. ICRS Arthroscopy Score showed a mean of 9/12 and Oswestry a mean of 6/10 points. Histologically all biopsies showed fibrocartilage with some hyaline-like elements.

Conclusion

AMIC® improved the clinical outcome and decreased pain in the cartilage defects treated in this study. Arthroscopy showed good fillings with some hypertrophies. In the MRI the AMIC® zone was well integrated to the border zone but filling was mostly incomplete and surfaces damaged. Histology showed fibrocartilage with some hyaline-like elements. Especially in OCD and femoropatellar patients, but less in the purely cartilaginous lesions of the femoral condyle the AMIC® procedure is an interesting, one step technique.

Chondrocyte Transplantation: ACT or AMIC®?

Fontana A.

2.2.4, *Extended Abstract, 8th ICRS Congress, Miami, USA*

Introduction

Chondropathies of the acetabulum and the femoral head are a frequent cause of pain and functional limitation. The incidence of acetabular cartilage damage is estimated to be of 74% in a total of 736 hip arthroscopies. Furthermore, there is an association between cartilage damage and lesions of the acetabular labrum in 81% of the cases.

Currently, treatment of hip cartilage pathologies is based exclusively on arthroscopic debridement, microfractures, multiple femoral head perforations or fibrin glue injection for chondral delamination.

The purpose of this study was to report the results obtained in treating hip chondropathies using the arthroscopic ACT or AMIC® technique. A comparison between the two techniques and results was made to evaluate advantages and disadvantages of these two procedures.

Materials and Methods

A controlled retrospective randomized study was carried out on 182 patients affected by a hip chondropathy of 3rd and 4th degree, according to the Outerbridge classification, extended 2cm² or more.

120 of these patients underwent arthroscopic autologous chondrocyte transplantation (ACT), while the other 62 underwent arthroscopic autologous matrix induced chondroplasty (AMIC®).

The surgical treatment, in those cases treated by ACT, was always carried out in two steps. The first was a diagnostic arthroscopy used to evaluate the chondral damage and to take a cartilage biopsy from the area surrounding the pulvinar. In the second step the transplant was implanted by arthroscopy.

On the contrary the AMIC® procedure was carried out as a one step procedure. Once the chondral defect was located, the area was cleaned and microfractures were performed. Then the collagen membrane was applied to cover the defect.

In that cases treated with the ACT procedure, the chondrocyte culture was carried out on a polymer scaffold, which is a reabsorbable composite material of polyglactin 910 and poly-p-dioxanone, in 65 cases and on a Hyaluronic acid scaffold in 55 cases.

In all the cases treated with the AMIC® procedure a suine collagen membrane, added with autologous growth factors, was applied to cover the chondral defect.

The two groups were similar in age, gender, degree and location of the pathology. The mean follow-up was 23.8 months (36 to 12) in the group of patients treated with the ACT procedure and 22.6 (36 to 12) in the group of patients treated with the AMIC® procedure. The mean size of the defects was 2.6 cm² (2.0 – 4.8) in the ACT group and 2.8 cm² (2.0 – 5.0) in the AMIC® group.

All the patients were assessed before and after the procedure with the Harris Hip Score (HHS).

Postoperatively all the patients underwent physiotherapist therapy. Exercises began from the 1st post-operative day. Patients were discharged on the 2nd day and were subject to both active and passive physiotherapy to regain complete range of motion without putting any weight on the articulation for 4 weeks. Partial load was allowed after 4 weeks, when exercises on a gym bike and swimming were recommended. After 7 weeks, crutches were no longer required and the patients were allowed to return to normal work activity. Jogging was allowed only after 6 months, while a complete return to sports activities was recommended only one year after the surgical procedure.

Results:

The mean preoperative HHS in the group of patients treated with the ACT procedure was 52 (32 – 60), similar to that of the patients treated with the AMIC® procedure that was 48 (28 – 56).

Mean post operative HHS results in both groups were also similar: ACT = 86 (58 – 92); AMIC[®] = 88 (56 – 98), showing no significant difference.

In both groups, unsatisfactory results were recorded in those patients suffering from a cartilage defect on the femoral head or where standard x-rays showed a reduced or compromised articular space.

Discussion

Knee arthroscopy has for some time now been able to show the present of chondral lesions and has allowed for the development of the current surgical techniques used for treating these lesions.

Even hip arthroscopy, although considerably less common, has allowed for chondropathies in this area to be detected. The therapeutic approach is different, however, since the hip is a deep articulation surrounded by large muscular masses that make surgical access difficult.

Hip arthrotomy exposes the articulation to the serious risk of aseptic necrosis of the femoral head, along with being a significantly invasive procedure.

The arthroscopic approach to the treating hip chondropathies, therefore, solves the serious problem regarding arthrotomy.

The AMIC[®] procedure has several advantages compared to the ACT. First of all it is a one step procedure, with no need to expose the patient to a second operation. The other advantage is that there is no need for a logistic support to the procedure, having no external laboratory support.

Considering that the post operative results obtained with the two procedures showed no significant differences, the AMIC[®] appears to be much less invasive and more cost effective compared to the ACT.

The cartilage defects located on the acetabulum can be treated with athroscopic ACT or AMIC[®] procedure. This study shows the effectiveness of the AMIC[®] procedure with respect to the ACT.

1 Step Cartilage Repair: Mesenchymal Stem Cell Implantation

Gobbi A.W.

13.1.3, Extended Abstract, 8th ICRS Congress, Miami, USA

Articular cartilage lesions, with their inherent limited healing potential, remain a challenging problem for orthopaedic surgeons. Various techniques, both palliative and reparative have been used to treat this pathology with variable success rates. In recent years regenerative techniques, such as ACI, have emerged as a potential therapeutic option. Recent studies [1, 2] suggest the durability of this treatment, especially at long-term follow-up, due to its ability to produce hyaline-like cartilage that is mechanically and functionally stable, and also allows integration with the adjacent articular surface.

However, despite the favourable clinical results obtained by many authors, the use of classic ACI (first generation) has been associated with several limitations related to the complexity and the morbidity of the surgical procedure, as well as the frequent occurrence of periosteal hypertrophy. Also some recent randomised studies [3, 4] report controversial results regarding the better performance of the first generation ACI technique compared to other procedures used for cartilage repair.

To address these problems Second generation ACI has been developed and biodegradable polymers as temporary scaffolds for the in vitro growth of living cells and their subsequent transplantation onto the defect have become widely used.

Second generation ACI represents a modern and viable technique for cartilage full thickness chondral lesion repair [5, 22, 23]. However second generation ACI is a two step procedure which includes an arthroscopic biopsy for cell culture and implantation. Aside from the risk of harvest site morbidity and two surgical procedures, the total cost of the operation, scaffold and chondrocytes cultivation is still very high. Future directions in cartilage repair are moving towards the possibility to performing one step surgery. These could include the use of stem cells and growth factors. The use of autologous mesenchymal stem cells (MSC) and growth factors represents an improvement on the currently available techniques as this avoids the primary surgery for cartilage biopsy and subsequent chondrocytes cultivation and seeding on a scaffold.

Many authors have recognized that nucleated cells found in bone marrow are a useful source of cells for restoration of damaged tissue [6, 7]. Once MSC are cultured in the appropriate microenvironment, they can differentiate to chondrocytes and form cartilage. The onset of chondrogenesis requires a chemically defined serum free medium supplemented with dexamethasone, ascorbic acid and growth factors such as TGF- β [8]. In conjunction with appropriate scaffolds, these has been demonstrated that cells can be used to regenerate cartilage in a variety of applications [6].

However, some animal and laboratory studies have shown the chondrogenic potential of MSC but only few clinical human studies have been published [9, 10].

Wakitani et al. [11] used autologous culture of expanded bone marrow for repair of cartilage defects in osteoarthritic knees; they chose 24 knees of 24 patients with knee OA who underwent a high tibial osteotomy; patients were divided into cell transplanted group and cell free group. After 16 months follow-up, they concluded that MSC were capable of regenerating a repair tissue for large chondral defects.

Ochi et al. [12] observed that in a rat model the injection of cultured MSC combined with bone marrow stimulation can accelerate the regeneration of articular cartilage; they noted that this cell therapy was a less invasive treatment for cartilage injury. In their animal study [13] they introduced a MSC delivery system with the help of an electromagnetic field, enhancing the proliferation of cartilage inside the chondral defect after intra-articular injection, decreasing ectopic cartilage formation.

Fortier et al. [14] concluded in animal studies that development of patient-side configuration techniques for intra-operative stem cell isolation and purification for immediate grafting have significant advantages in time savings and immediate application of an autogenous cell for cartilage repair.

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Treatment of chondral defects with AMIC[®] technique (Autologous Matrix Induced Chondrogenesis) compared to AMIC[®] enhanced by concentrated bone marrow

Volpi P., de Girolamo L., Cervellin M., Bait C., Galli M., Schoenhuber H.
15.3.5, Free Paper, 8th ICRS Congress, Miami, USA

Introduction

It is well established that cartilage lesions up to 2 cm² can be successfully treated by bone marrow stimulating techniques.

AMIC[®] (Autologous Matrix Induced Chondrogenesis) combines the microfracture technique with the use of a collagen matrix for the treatment of lesions >2 cm². After microfracture, the defect is covered by a collagen I/III matrix, Chondro-Gide[®], which stabilizes and protects the blood clot, containing bone marrow elements, stem cells and growth factors.

Methods and Materials

We present the preliminary data of a prospective randomized clinical study, comparing AMIC[®] to AMIC[®] combined with concentrated bone marrow for the treatment of larger defects in the knee (2-8 cm²), with a minimum follow up of 6 months. Clinical evaluation of the results are based on Lysholm Knee Score, IKDC score and VAS pain scale. For each patient MRI has been performed preoperatively as well as 6 and 12 month postoperatively.

Moreover, a small fraction of bone marrow samples, both from iliac crest and retrieved from MF, has been processed to isolate, characterize and culture the mesenchymal stem cells population.

Results

Significant differences between pre- and post-operative values have been observed for all patients, but without distinction between the groups. MRI showed a good healing process of the cartilage defects. A difference in term of concentration, surface marker expression and differentiation potential have been found between the two samples, with an enrichment of these features in the iliac crest cells.

Conclusions

AMIC[®] technique alone or combined with bone marrow allow to obtain good results in this kind of chondral defects.

Joint reconstruction of femoral epiphyseal necrosis by two different scaffolds: Comparative results

Dallari D., Del Piccolo N., Rani N., Raimondi A., Roseti L., Stagni C.

9.4.6, Free Paper, 8th ICRS Congress, Miami, USA

Introduction

We present the comparative results obtained by two different scaffolds engineered with autologous chondrocytes in joint reconstruction of femoral epiphyseal necrosis (ARCO 3b, 4). The technique involved removing the chondromalacic area and recovering the necrotic zone, followed by reconstructing the epiphysis with bioceramic cylinders (TruFit[®]), lyophilized bone chips soaked in packed stromal cells and platelet gel, and finally, covering with engineered scaffold with autologous chondrocytes.

Methods and Materials

Thirteen patients with a total of 14 femoral epiphyses were treated. In the first 7 cases we used Hyaff-11 as the scaffold; subsequently we replaced it with Chondro-Gide[®] because of its better mechanical properties. The two groups had matching etiopathogenesis, lesion size, and age, but the follow-up varied.

The analyses performed on engineered scaffolds showed that chondrocytes were viable (viability ranged from 89 to 98%) and expressed the typical hyaline cartilage molecules, in particular collagen type II and aggrecan.

Results

At a mean follow-up of 24 months (18-30) in the Hyaff-11 group and 10.5 months (6-16) in the Chondro-Gide[®] group, the joint line was preserved similarly in both groups, and pain resolved in 93% of the cases. The only case of failure was in the Hyaff-11 group due to a co-existing rheumatic disease. Functional limitation occurred in 4 cases with Hyaff-11 and 3 cases with Chondro-Gide[®], caused by coxofemoral impingement secondary to the difficulty in reconstructing the normal spherical morphology of the femoral epiphysis.

Summary

In conclusion, Chondro-Gide[®] facilitated articular reconstruction with results analogous to those of the group treated with Hyaff-11.

8th ICRS Congress, Miami

International cartilage experts met during the ICRS world congress in Miami to discuss and present developments in research as well as clinical results in cartilage regeneration. Geistlich Surgery was present as gold sponsor, celebrating the development from periost to Chondro-Gide® Gold Standard Matrix.

The International Cartilage Repair Society (ICRS) was founded in 1997 in Switzerland as a specialised society, which enables the exchange of knowledge between scientists, physicians, industry and patients in the field of cartilage regeneration.

To provide continuing education and training to physicians and scientists, the ICRS organises various educational skill courses, scientific meetings and congresses. One of the highlights is the world congress which is held every 18 months.

Since the establishment of the society, these world congresses have been held at varying international locations:

- 1997: 1st ICRS World Congress, Fribourg, Switzerland
- 1998: 2nd ICRS World Congress, Boston, USA
- 2000: 3rd ICRS World Congress, Gothenburg, Sweden
- 2002: 4th ICRS World Congress, Toronto, Canada
- 2004: 5th ICRS World Congress, Ghent, Belgium
- 2006: 6th ICRS World Congress, San Diego, USA
- 2007: 7th ICRS World Congress, Warsaw, Poland

With over 800 participants, the 8th ICRS world congress in Miami, Florida in the USA, presented a platform for all leading scientists and clinicians to present their results in the field of cartilage regeneration.

Overall, this year's conference was a very successful meeting where Geistlich Surgery could strengthen its foremost position in cartilage regeneration with various groups presenting scientific and clinical results to substantiate the efficacy of Chondro-Gide® as the leading natural collagen matrix in cartilage regeneration.

Geistlich Surgery was present in Miami as gold sponsor with almost the entire team from Switzerland (Figure 1). It was an excellent opportunity to meet with experts in cartilage regeneration and to promote cartilage repair using Chondro-Gide® among young scientists and clinicians.



Figure 1: Members of the Geistlich Surgery team (left-to-right): Jo Liesenborghs (Head of International Sales), Dominique Tepper (Assistant for the Business Unit), Dr. Katja Martin (Head of Business Unit Surgery and Head of Clinical Research), Dirk Kuhlmann (International Product Manager), Adrian Schnyder (Clinical Research Scientist), Holger Klöß (Clinical Research Scientist).

Various of the lectures, abstracts and papers showed the good mid-term results of the AMIC® technique. This procedure was described as a minimal invasive effective, cost efficient, one-step therapy option. The AMIC® approach has been shown to be successful where other options had failed, offering a viable alternative especially in the difficult to treat retro-patellar chondral defects.



Figure 2: Dr. Alberto Gobbi, Scientific Programme Co-Chair for the congress and orthopaedic surgeon from the University Hospital of Milan, Italy, with Dr. Katja Martin in discussion at the Geistlich Surgery stand.



Figure 3: Myron Spector, Ph.D., Director of the Tissue Engineering Laboratories in Boston, Professor of Orthopaedic Surgery (Biomaterials) at Harvard Medical School and Senior Lecturer at the Massachusetts Institute of Technology, as Chairman of the Geistlich Surgery Satellite Symposium.

From Periosteum to Chondro-Gide® Gold Standard Matrix

The Geistlich Surgery satellite symposium, with **Prof. Dr. Myron Spector** as chairman, was one of the highlights of the industry organised symposia. Prof. Spector presented the scientific basis as well as the clinical relevance for the progression from using periosteum to using a collagen I/III matrix in ACI surgery.

Prof. Dr. Wiltrud Richter illustrated the positive effect of the collagen matrix as a carrier for cells as well as the influence of Chondro-Gide® on the chondrogenic differentiation of BMSCs. She further showed that the collagen matrix in combination with fibrin glue has a positive influence on chondrogenic differentiation of BMSCs and that it stimulates chondrocytes to enhance proteoglycan deposition.



Figure 4: Prof. Dr. rer. biol. hum. Wiltrud Richter, Head of the division of experimental orthopaedics at the university hospital in Heidelberg, Germany, illustrating the chondrogenesis of mesenchymal stem cells in a biphasic collagen I/III - fibrin matrix.

Test results showed lower proteoglycan deposition when using partial autologous fibrin compared to commercial fibrin glue. This is possibly the result of the presence of some inhibitory soluble factors in the serum from the patient. It can therefore be recommended to use commercially available fibrin glue instead of a partially autologous equivalent.



Figure 5: PD Dr. med. Peter C. Kreuz from the university hospital in Munich, Germany, discussed the clinical experience in using Chondro-Gide® versus periosteum.

Dr. Peter C. Kreuz presented his clinical experience in using the Chondro-Gide® for ACI and showed a decrease in hypertrophies when compared to periosteum.

Of the techniques used, 52 cases (14.9%) were periosteum-covered ACI, 215 cases (61.6%) ACI using Chondro-Gide® and 82 cases (23.5%) a 3-dimensional matrix-associated ACI (BioSeed-C, Biotissue Technologies, Freiburg, Germany). In 52 patients, revision surgery was performed for persistent clinical problems.

The overall complication rate of patients treated with revision surgery was highest in the periosteum group (26.9%), followed by the BioSeed-C group (14.6%) and was lowest in the Chondro-Gide® covered ACI group (12.1%).

The incidence of insufficient regenerative tissue in the defect area was lowest in the Chondro-Gide® group with 1.9%, with 3.7% in the BioSeed-C group and 3.8% in the periosteum group.

In his presentation, **Dr. Victor Valderrabano**, described diagnostic options and treatment alternatives for osteochondral lesions (OCL) of the talus. The majority of the posteromedial OCL resulted from malalignment and the anterolateral lesions through trauma.



Figure 6: PD Dr. med. Dr. phil. V. Valderrabano from the university hospital in Basle, Switzerland, during his talk on the benefits of using the AMIC® technique in treating osteochondral lesions of the talus.

The diagnostic methods used were weight bearing x-ray for determining the mechanical axis and MRI to detect signs of instability, however often also revealing a significant amount of bone bruising. Additional to these methods, the university hospital in Basle implements CT-SPECT technology. Dr. Valderrabano reported that this novel diagnostic method is used to determine the biological activity of the bone under the osteochondral lesion. A biologically active area of bone bruising was mentioned to be indicative of the source of the patients pain. Therefore, for the therapy, individualised treatment plans were suggested depending on whether the cartilage or the bone or both were affected. The most common indications included both the bone and the cartilage requiring bone grafting in combination with AMIC®.

Dr. Valderrabano concluded that the AMIC® technique in combination with a correction of the pathobiomechanics offers promising results with an excellent cost/benefit ratio.

The satellite symposium was recorded by the ICRS and will be available soon. For a complimentary copy, please contact us via surgery@geistlich.com.

Please find below a full list of the abstracts, papers and posters presented that give reference to the use of Chondro-Gide® or the AMIC® technique.

The 9th ICRS World Congress

The 9th ICRS world congress will be held in Sitges near Barcelona, Spain, in September 2010.

Extended Abstracts:

2.2.4: Chondrocyte Transplantation: ACT or AMIC®?; A. Fontana

5.2: 2nd Generation ACI M.; Marcacci, E. Kon, M. Delcogliano, G. Filardo, A. Di Martino, F. Zoffoli, F. Iacono

12.1.2: Stem Cell based Therapy in Chile - From the Lab to the Patients; R. Martinez, R. Mardones

13.1.3: 1 Step Cartilage Repair: Mesenchymal Stem Cell Implantation; A.W. Gobbi

Free Papers:

15.3.5: Treatment of chondral defects with AMIC® technique (Autologous Matrix Induced Chondrogenesis) compared to AMIC® enhanced by concentrated bone marrow; P. Volpi, L. de Girolamo, M. Cervellin, C. Bait, M. Galli, H. Schoenhuber

15.3.6: Long term results after cartilage repair of the knee with MACI and AMIC® procedures comparing clinical and MRI scores; J. Gellissen, J. Wimmer, M. Kaiser, P. Behrens

9.2.7: Treatment of Full Thickness Chondral Defects with a Collagen Scaffold, Mesenchymal Stem Cells Compromised to the Chondrocyte Lineage and Platelet Rich Plasma; A. Vaisman, D. Figueroa, R. Calvo, M. Espinoza, M. Gallegos, P. Conget

9.4.6: Joint reconstruction of femoral epiphyseal necrosis by two different scaffolds: Comparative results; D. Dallari, N. Del Piccolo, N. Rani, A. Raimondi, L. Roseti, C. Stagni

15.3.3: Decreased surgical re-intervention rate for hypertrophy after ACI with use of the Bio-Gide® collagen membrane; A. Gomoll, C. Probst, T. Bryant, T. Minas

19.3.1: An ACI-like approach for guided tissue regeneration of the avascular meniscal defect: a preclinical goat study; H. Julke, B. Schäfer, D. Nestic, W. Brehm, K. Martin, P. Mainil-Varlet

Posters:

P133: Engineering functional osteochondral tissues with human articular chondrocytes and clinically used biomaterials; C. Scotti, D. Wirz, F. Wolf, D. Schaefer, V. Valderrabano, M. Jakob, D. Daniels, I. Martin, A. Barbero

P208: Evaluation of cell-loaded scaffold transplants; S. Nürnberger, C. Albrecht, P. Bartko, V. Vilmos, S. Marlovits

P212: The Treatment of Retropatellar Chondral and Osteochondral Defects with Autologous Matrix Induced Chondrogenesis (AMIC®); J.P. Benthien, M. Jakob, P. Behrens

P231: Autologous Matrix-Induced Chondrogenesis (AMIC®) – Treatment of Chondral and Osteochondral Defects in the Knee; T. Kursano, M. Jacobi, H. Hoogewoud, R. Jakob

P239: "Plateau Effect" of 3-year post-operative results in Autologous matrix-induced chondrogenesis (AMIC®); J. Wimmer, N.O. Wendler, J. Gellissen, W. Zoch, P. Behrens

Invitation to the UK Workshop on Cartilage Regeneration

Geistlich Surgery, in association with the Royal National Orthopaedic Hospital NHS Trust, invites you to a two day course in cartilage regeneration. The course, which is suitable for consultant orthopaedic surgeons, scientists and specialist registrars, will provide you with an update on the latest scientific and clinical techniques on cartilage regeneration and includes workshops on AMIC[®] and ACI.

Date:	02.-03. September 2009
Venue:	Sir Herbert Seddon Teaching Centre Royal National Orthopaedic Hospital Brockley Hill, Stanmore, Middlesex. HA7 4LP
CPD:	Applied for 7 points
Registration Fee:	£150 This fee includes registration fee, 1 nights accommodation, course material, refreshments & course dinner.

Lecture Topics

- > Direction of clinical cartilage cell transplantation
- > Lessons from the ACTIVE study
- > Cell-seeded Chondro-Gide[®] covered (ACI-CS)
- > AMIC[®] – One step procedure with Chondro-Gide[®]
- > Legislation & licensing
- > Interpretation of structure & function of the repair tissue
- > AMIC[®] in the Hip
- > AMIC[®] in the Talus
- > Cartilage repair methods, failures and successes

Workshops

- > ACI – Cell Seeded
- > AMIC[®] and arthroscopic AMIC[®]

Invited Speakers

- Prof. George Bentley – RNOH, Stanmore, UK
- Prof. James Richardson – RJAH, Oswestry, UK
- Mr. Tim Briggs – RNOH, Stanmore, UK
- Prof. Sally Roberts – RJAH, Oswestry, UK
- Ms. Imogen Swann – HTA, UK
- Prof. Damian Griffin – Coventry, UK
- Dr. Ph. Niemeyer – Germany
- Dr. S. Anders – Germany
- Dr. L. De Girolamo - Italy
- Prof. Dr. R. Jakob – Switzerland

Further Information

For further information please contact the Education Centre of the Royal National Orthopaedic Hospital NHS Trust on

Phone	+44 (0)20 8909 5326 or 5319
Email	courses@rnoh.nhs.uk
Website	www.rnoh.nhs.uk/education



Congress Preview 2009

Geistlich Surgery will be present at a number of events during the remainder of this year. We look forward to meeting you during our symposia and congresses.

Events for 2009

02. - 03. September 2009

Stanmore, UK - UK Workshop on Cartilage Regeneration in collaboration with the Royal National Orthopaedic Hospital

07. - 11. September 2009

Lausanne, Switzerland - ESB 2009 (European Conference on Biomaterials)

15. - 18. September 2009

Manchester, UK - BOA (British Orthopaedic Association)

17. - 19. September 2009

Leipzig, Germany - 26. AGA Kongress

01. - 03. October 2009

Rome, Italy - XIX Conresso Nazionale SIA (Società Italiana di Arthroscopia)

21. - 24. October 2009

Berlin, Germany - DGU/DGOOC (Deutscher Kongress für Orthopädie und Unfallchirurgie)

We invite you to visit us at our Stand 86/11 in the main foyer and to participate in our lunch symposia about bone and cartilage regeneration.

07. - 11. November 2009

Milan, Italy - 14° SIOT (Congresso Nazionale della Società Italiana di Orthopedia e Traumatologia)

09. - 13. November 2009

Paris, France - 84. SOFCOT (Société Française de Chirurgie Orthopédique et Traumatologique)

Further Information

Please consult our web page for further information and invitations to the lunch symposia.

www.geistlich.com



France

Geistlich Pharma France SA
Parc des Nations – Paris Nord II
385 rue de la Belle Etoile
BP 43073
F-95913 Roissy CDG Cedex
Phone +33 1 48 63 90 26
Fax +33 1 48 63 90 27
surgery@geistlich.com
www.geistlich.fr

Germany

Geistlich Biomaterials
Vertriebsgesellschaft GmbH
Schneidweg 5
D-76534 Baden-Baden
Phone +49 7223 96 24 0
Fax +49 7223 96 24 10
surgery@geistlich.de
www.geistlich.de

Italy

Geistlich Biomaterials Italia S.r.l
Via Castelletto, 28
I-36016 Thiene VI
Phone +39 0445 370 890
Fax +39 0445 370 433
surgery@geistlich.com
www.geistlich.it

United Kingdom

Geistlich Sons Ltd.
Long Lane
GB-Chester CH2 2 PF
Phone +44 1244 347 534
Fax +44 1244 319 327
surgery@geistlich.com
www.geistlich.co.uk

Distributor

Headquarters Switzerland

Geistlich Pharma AG
Business Unit Surgery
Bahnhofstrasse 40
CH-6110 Wolhusen
Phone +41 41 492 55 55
Fax +41 41 492 56 39
surgery@geistlich.com
www.geistlich.com