AMIC® technique for cartilage repair, a single-step surgical intervention as compared to other methods

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Source: 8th EFORT Congress, 11-15 May 2007, Florence, Italy

Introduction: As a single surgery technique we adopted the "Autologous matrix induced chondrogenesis" (AMIC®) proposed by Behrens. Microfracture results in intrinsic repair of cartilage defects. Breinan et al (2000) have shown that the fibrocartilaginous filling of a microfracture treated defect is superior when covered with a collagen membrane to when left uncovered.

Materials & Method: We find this technique especially useful in OCD. We curette the defect and apply microfractures to the base of the osseous defect. Then we obtain cancellous bone from the tibial plateau and mix it with fibrin glue, of which 50% of the thrombin portion is replaced by the serum of the patient as a source of growth factor. This paste of bone and enriched fibrin glue is filled in the defect which is then covered by the Geistlich Chondro-Gide® membrane that is glued on and which we can as well suture to the defect. The AMIC® technique in combination with microfractures can be utilised for the coverage of pure cartilage defects alone, where the membrane is glued alone or fixed on the defect in combination with 5-0 resorbable sutures. In the first two weeks following surgery, after treatment is very defensive to avoid loss of the membrane. After two months of crutch walking with 15 kg of weight we observe a nice osseous integration of the graft and a covering layer that looks promising. After 4-6 months activity can be increased depending on the size of the defect.

Results: This is a young technique that we adopted in mid 2003 with 45 cases treated so far. Femoro-patellar joint with OA due to chronic subluxation or OCD: 23 cases; pure femoro-condylar cartilage lesions: 8 cases; OCD lesions: 8 cases; talar lesions: 6 cases; total 45 cases. OCD lesions showed a nice healing process of the osseous implant that was maintained by the matrix coverage in situ. 2 of the 8 patients having received coverage of a mere cartilage defect on the femur showed hypertrophy and were subsequently debrided. Of the 6 OCD lesions of the talus resorption of the graft was observed in 2 patients. Re-operation was combined with an implant of cancellous bone mixed with granules of hydroxyapatite (Geistlich Orthoss®), after which integration was successful. Strict observation is required over the upcoming years regarding clinical results and durability and also the composition of this neocartilage, mainly also to see whether it is superior to Microfracturing alone.

Conclusion: So far it seems to be an interesting alternative to Mosaicplasty or Microfracturing alone since it combines principles of cell therapy with an artificial and instant biological containment that acts against the loss of cells thus acting as a internal bioreactor with the patients own growth factor support.

Comments: The treatment of OCD lesions has always posed a challenge. The use of the AMIC® technique in conjunction with bone graft and PAF (Partial Autologous Fibrin Glue) gives us another option for this condition. In areas where the resorption of autologous bone is likely to be rapid, the use of Orthoss® will allow remodelling without the loss of bone stock.

Posters/Abstracts

Autologous Matrix Induced Chondrogenesis (AMIC) for focal chondral defects of the knee - first clinical and MRI results

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Introduction: Focal chondral defects of the knee joint can be dealt with by bone-marrow stimulating techniques like microfracturing (MF). By penetrating the subchondral layer emerging Mesenchymal stem cells are used for the repair process. Microfracturing shows good results for smaller defects up to 2 cm^2 while in larger defects early secondary degeneration has been observed. Autologous Matrix Induced Chondrogenesis (AMIC) combines MF with the application of a collagen matrix for covering the defect, hosting of the stem cells and mechanically stabilizing the blood clot.

Methods: 43 patients (30m, 13f, mean age 37y (18-53y)) with focal chondral defects of the knee joint (ICRS III-IV) of condyle, trochlea or patella were treated by standardized MF and application of a porcine collagen type-I/III bilayer matrix (Geistlich Biomaterials, Wolhusen, Switzerland). Clinical
Scores and MRI scans were evaluated with a follow-up of 6 to 24
months. 33 patients had at least one intervention (1-4) of the knee before. The mean defect size was 3.2 cm^2 (1.3-7.5cm^2).19 defects were caused by trauma.

Results: All patients considered their knee as abnormal (78%) or severely abnormal (22%) pre-operatively in comparison to the contra-lateral knee. The ICRS functional status showed an improvement from 100% ICRS III/IV to 66.7 % ICRS II/I. For 63.7% of all patients knee function was perceived as improved, for 27.2% unchanged and for 9.0% worsened after self-evaluation. Pain decreased considerably from 5.7 to 1.9 (10=max.) on the visual analogue scale. The MRI follow-ups showed a reasonable filling of the defect with no prolonged effusion.

Conclusion: Microfracturing in combination with a collagen matrix (AMIC) can be considered feasible as a minimally invasive single step procedure for the repair of focal cartilage defects without using cultured chondrocytes. The first results concerning clinical functional improvement, pain reduction and patient satisfaction as well as defect filling in MRI are promising.

Comments: Despite the small cohort of patients; limited follow-up (6 months in some cases) and a variety of chondral injury sites including the patella, the improvement in pain relief is very promising.
We know from experience with previous publications that repaired and regenerated cartilage may take up to two years to mature, and so would expect to see these functional and subjective scores improve over the next 12 to 18 months.
This is one of the first presentations of the new AMIC (Autologous Matrix Induced Chondrogenesis) technique, which is a logical evolutionary step on from microfracture. By trapping the first few millilitres of bone marrow blood in the Chondro-Gide® membrane, a higher concentration of Mesenchymal stem cells is stabilised in the defect than with the traditional microfracture technique.

MR imaging protocols for optimized visualization of a collagen matrix used for cartilage repair

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Objective: To compare the performance of different MR pulse sequences for high-contrast and high-spatial-resolution imaging of collagen matrices.

Material and Methods: Chondral resection 2cm² in size was carried out resembling a grade- IV defect of a porcine femoral condyle. A bilayer matrix consisting of collagen I/III (Chondro-Gide®, Geistlich Biomaterials, Switzerland) was dissected and fixed with fibrin glue. MR-imaging was conducted using a 1.5T device (Siemens, Germany). 27 pulse sequences were varied with regard to their main properties (T1- and T2-weighted spin-echo or gradient echo), mode of volumetric data acquisition (2D, 3D), image matrix, slice thickness (1.3–2mm) and the choice of fat saturation techniques. Signal intensities were measured in the subchondral layer, collagen matrix, adjacent cartilage and fluid. Contrast-ratios were computed.

Results: Contrast-ratios of the matrix vs. adjacent fluid/subchondral layer were calculated with values 0.05- 0.88 ± 0.04 and 0.03-0.99 ± 0.05 respectively. While highest contrast was achieved using PD-weighted TSE-sequences with low echo-time, high image matrix and thin sections without fat saturation, T1-weighted IR-sequences yielded an intermediate contrast-ratio with optimal depiction of the defect depth. 5 sequences were unable to differentiate between subchondral layer and matrix.

Conclusion: Appropriate MR imaging parameter selection is crucial for optimized visualization of the matrix and has the potential to provide information about matrix integrity and success of cartilage repair.

Comments: As cartilage repair and regeneration procedures emerge from the realm of research and into everyday clinical practise, we need to develop efficient and accurate non-invasive means of monitoring the repair tissue in-vivo.
MRI has emerged as the modality of choice for visualising soft tissues, including cartilage. Unfortunately the T1 and T2 images routinely used do not give the optimum information and detail we now routinely demand. This has led radiologists to explore and describe alternative protocols such as FSE (Fast Spin Echo) and the PD-weighted TSE-sequences described above.
As not every patient is willing or suitable for dGEMRIC contrast scanning and 3T scanners are still a long way off for most hospitals, it is vital that we are able to achieve the best resolution and contrast from the current technology.

Autologous Matrix Induced Chondrogenesis - A One Year Follow-Up With Clinical And MRI Results *

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Introduction: The technique of microfracturing is well described and is shown to provide a clinically acceptable outcome in terms of pain relief and function for the majority of patients. Microfracture is however known to generate a high percentage of fibrocartilage which is well documented as being inferior to hyaline cartilage in terms of stiffness and stress resistance.
We describe a novel method of chondral repair using Mesenchymal stem cells released into the defect following microfracture. The cells are then stabilised by and within a Chondro-Gide® collagen I/III bilayer membrane (Geistlich biomaterials, Wolhusen, Switzerland).
Materials & Method: Between March 2002 and December 2003 eleven (11) patients were operated on for traumatic chondral defects using the AMIC technique and followed prospectively. The mean age was 29 years (19-40 years) and all patients had undergone at least one previous surgical procedure for the chondral defect (range: 1-9). Lesions were located on the patella (1); MFC (4); LFC (3); Trochlea (1) and Tibial Plateau (2). 10 Patients were available for follow-up and MRI scanning at 12 months.
Results: At 12 months post-op the mean subjective functional score had improved from 3.5 to 6.6 (max 10) and the pain had decreased from 6 to 2 on a 10 -point VAS. MRI demonstrated: No marrow oedema (8 patients); normal graft-host interface (7); full -thickness graft integration (10); smooth contour of articular surface (7); remaining effusion (4); sub-chondral sclerosis (5) and 75-100% graft fill in 7 patients.
Discussion: AMIC (Autologous Matrix Induced Chondrogenesis) is an exciting new technique utilising the bodies own Mesenchymal stem cells supported by a Chondro-Gide® matrix to repair a chondral defect. This study has shown a clear improvement in both pain and function, even at 12 months post-op when repair tissue is still remodelling.
This cohort of patients will continue to be followed prospectively.

Comments: It always takes a leap of faith to begin using any new technique or product, and this does not usually happen unless you are satisfied with the scientific principles underlying this. The AMIC (Autologous Matrix Induced Chondrogenesis) technique certainly has a strong heritage. Microfracture is clinically well proven to generate healthy fibrocartilage, while the Chondro-Gide® membrane has been extensively used in ACI and is the original collagen I/III membrane with an excellent track record, having been utilised in all of the ACI trials reporting medium to long term results, including those by Bentley et al and Ackland et al. It was from these two seemingly opposed repair technologies that AMIC was born.
When considering the results of this cohort of patients it is worth noting that each patient had undergone not only previous surgery for their chondral lesion, but also for numerous other pathologies such as ACL reconstruction, meniscectomy, re-alignment procedures and ORIF. These patients were all desperate to regain a pain-free functional knee. It has been postulated that all of the previous chondral surgeries failed due to the multiple intra-articular pathologies generating such forces that the repair fibrocartilage could not stand up to them and broke down. Despite the lack of histology in this cohort, the MRI scans demonstrate that the chondral repairs are solid and stable, even at this early stage. There is no reason to think they will not continue to improve as the repairs mature.

- (This abstract was revised after the ICRS by Dr. Kili)

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Autologous Matrix-Induced Chondrogenesis (AMIC®) for focal cartilage defects of the knee – First Clinical and MRI Results

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Introduction: Bone marrow stimulating techniques such as microfracture are frequently used to treat focal chondral defects of the knee. These techniques release Mesenchymal Stem Cells (MSC's) from the bone marrow cell pool to participate in the regeneration. One of the limiting factors of this technique is the defect size, which if over 2cm^2 runs the risk of premature degeneration. The AMIC technique combines microfracture with the application of a collagen matrix to cover the defect and provide mechanical stabilisation of the MSC 'super-clot'

Method: 26 Patients (6 Women, 20 Men, Age 18-52 years, mean age 38, 7 years) with 28 focal partial or full-thickness chondral defects (ICRS III-IV) of the medial condyle (20), Lateral Condyle (4), Trochlea (3) and the Patella (1) were treated with standard microfracture and application of a collagen I/III Matrix (*Chondro-Gide®, Geistlich Biomaterials*). Patients were prospectively followed clinically and using MRI. The mean defect size was 3,45cm^2 (1 – 5,9 cm^2). 6 Patients had OCD defects which were treated with autologous bone grafting. 4 Cases underwent simultaneous ACL reconstruction.

Results: The minimum follow-up period was 6 months with 15 patients having more than 1 year follow-up. Pre-operatively all patients rated their knee as abnormal (57, 7%) or severely abnormal (42, 3%), while post-operatively 78, 2% of patients rated their knee as normal or nearly normal. The mean modified Cincinnati score improved from 53,4 to 79,8 points, while the subjective pain rating using a VAS dropped from 6,0 to 2,0 and function improved from 4,3 to 7,6. These score improvements were significant. The MRI assessment demonstrated good defect filling without any signs of an effusion.

Conclusion: Microfracture in combination with a collagen I/III matrix (AMIC®) is a very attractive minimally invasive treatment method for medium to large focal chondral defects. The first experiences with AMIC demonstrate clinical improvement, pain reduction and a subjective improvement, making this an extremely promising therapy.

Comments: Despite still being a relatively new procedure, the AMIC® technique continues to show great promise. It borrows from both microfracture and ACI, using the best of both worlds. From microfracture it makes use of MSC's to enable a single stage repair, while the use of a Chondro-Gide® membrane borrowed from ACI provides the mechanical and biological protection to the friable "super-clot", enabling the cells to attach to the sub-chondral bone and begin differentiating into chondrocytes which will form a healthy repair.

Translated by: Dr. Sven Kili, Senior Medical Advisor, Geistlich Biomaterials

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Mosaicplasty and AMIC technique as single time surgery for cartilage repair

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The past ten years have generated much research and technical innovation in the field of cartilage repair. The common aim of all methods is to produce a stable, quality cartilage repair or regenerate. Unfortunately, clinical, radiological and histological results analysing the different techniques are somewhat contradictory. The various lines of research have focused on:

1. Techniques to generate the mobilisation of progenitor and mesenchymal stem cells from the cancellous bone into the defect to develop a hyaline-like cartilage.
2. Transplantation of osteochondral auto-grafts (Mosaicplasty, OATS, SDS) or allograft.
3. Autologous chondrocyte Implantation and periosteal coverage (ACI) for larger defects has been followed by 2nd and 3rd generation ex vivo products. (Chondrocytes cultured on membranes, gels, 3-D de novo cartilage disk or even engineered osteochondral grafts)

Much of today's research is focusing on the culture of a patients own chondrocytes or his own stem cells. Clinically, some methods may be applied in all indications regardless of size, localisation, depth up to the age of 50 and this is valid for lesions in the knee, shoulder, talus, elbow etc. Other methods like OATS should not be used for lesions over 2cm in diameter due to donor side morbidity. All methods claim *an 85% outcome success rate*. Microfracture produces a fibrocartilage repair which looks similar to the hyaline-like cartilage of ACI at two years. Mosaicplasty plugs remain hyaline, provided they are inserted without being prone or deep sunken and the surface convexity of the femoral condyle is restored and provided they are inserted tightly next to each other. There is agreement that this is more difficult arthroscopically. Results are dependent on the alignment of the limb and if the compartment treated is overloaded, there is less chance of integration. The ability to perform an osteotomy is therefore a requirement for the cartilage surgeon- up to 50% of our cases receive an osteotomy as part of their treatment regardless of which technique is utilised.

Complications in mosaicplasty include: hyaline cartilage cap damage, non integration and pseudarthrosis or fractures of the cylinders (of special risk are smokers), especially when grafts are not inserted tightly to each other with fluid leakage from the cartilage caps. Rarely ossification is observed. Donor site morbidity is an issue of concern especially if more than six plugs are removed from the patellofemoral joint. This alone can create clinical symptoms.
Nicotine abuse decreases the rate of success of cartilage repair and osteotomy healing.
Roughly 300 cases have been treated during the last 10 years. The results were reported in 2002.
As an *alternative single surgery technique*, we adopted the "Autologous Matrix induced Chondrogenesis" (AMIC) technique proposed by Behrens. We find this especially useful in OCD. In this relatively young technique, we curette the defect and microfracture the base of the osseous defect. Cancellous bone is then harvested from the tibial plateau and mixed with fibrin glue, of which 50% of the thrombin portion is replaced by the serum of the patient as a source of growth factors. This paste of bone and enriched fibrin glue fills the defect which is then covered by the Chondro-Gide® membrane (Geistlich). This is glued on or may be sutured to the defect. The AMIC technique may also be used to treat pure cartilage defects. After two months PWB we observe good osseous integration of the graft and a covering layer that looks promising. After 4-6 months, activity may be increased depending on the size of the defect. This is a young technique that we adopted in mid 2003 with 30 cases treated so far, therefore strict observation is required over the upcoming years regarding clinical results and durability as well the composition of this neocartilage. So far it seems to be an interesting alternative to Mosaicplasty since it combines principles of cell therapy with a natural and instant biological containment that acts against the loss of cells acting as an internal bioreactor with the patients own growth factor support.

Autologous matrix induced chondrogenesis (AMIC®) for focal chondral defects of the knee – First results

Anders S, Wiech O, Schaumburger J, Grifka J
Source: 8th EFFORT Congress, 11-15 May 2007, Florence, Italy

Introduction: Bone-marrow stimulating techniques like microfracturing for focal chondral defects of the knee joint are widespread utilizing mesenchymal stem cells (MSC) for an autogenous repair process. Microfracturing shows good results for smaller defects up to 2cm² while larger defects tend to an early secondary degeneration. Autologous Matrix Induced Chondrogenesis (AMIC®) combines microfracturing with the application of a porcine collagen type-I/III bilayer matrix (Geistlich Chondro-Gide®) to host the MSC and to stabilize the blood clot.

Methods: 32 patients (25m, 7f, mean age 37.4y (18-52y)) with 35 focal chondral defects of the knee joint (ICRS III-IV°) of the condyle, trochlea and/or patella were treated by standardized microfracturing and application of a Chondro-Gide® matrix (Geistlich Biomaterials, Wolhusen, Switzerland). The outcome was evaluated prospectively by clinical scores and MRI with a follow-up of 6 to 24 months. The mean defect size was 3.86 cm² (1.0 - 6.8 cm²). 22 patients (68%) had at least one operation (1-8) on the knee before. 9 defects were caused by trauma. All 7 patients with osteochondritis dissecans had an autologous bone grafting. In 5 patients an ACL stabilization was performed simultaneously.

Results: All patients considered their knee as abnormal (ICRS III° (70%)) or severely abnormal (ICRS IV° (30%)) preoperatively according to the ICRS functional status. The Cincinnati-Score improved from 52.9 to 81.1 points while the Lysholm-Score rose from 60.4 to 85.9 points (each $p<0.001$). Pain decreased significantly from 6.1 to 2.2 (10=max.) on the visual analogue scale. 4 biopsies (4-21 months) revealed reasonable results with regard to surface formation, filling and integration in the Brittberg score (Ø10.25 pts., 12 pts.=max.) The MRI follow-ups showed an adequate filling of the defect, no prolonged effusion occurred.

Conclusion: Microfracturing in combination with a collagen matrix (AMIC®) is a minimal invasive, effective technique for the repair of focal cartilage defects of the knee joint. Not using cultured chondrocytes, it can be performed cost-effectively as a single-step procedure. Both primary and secondary treatments are possible. The first results concerning clinical functional improvement, pain reduction and patients' satisfaction as well as defect filling in MRI are promising.

Comments: Despite still being a relatively new procedure, the AMIC® technique continues to show great promise. It borrows from both microfracture and ACI. From microfracture it makes use of MSC's to enable a single stage repair, while the use of a Geistlich Chondro-Gide® collagen Matrix borrowed as in ACI provides the mechanical and biological protection to the friable "super-clot", enabling the cells to attach to the sub-chondral bone and begin differentiating into chondrocytes which will form a healthy repair tissue.