Abstract/Introduction

Chaired by Prof. Roland Jakob, Kantonsspital Fribourg, Switzerland, the Geistlich AMIC® Satellite Symposium took place during the 12th ICRS congress in Chicago, on May 10, 2015. Three top international cartilage surgeons gave a fast-paced update on the use and mid- to long-term outcomes of Autologous Matrix-Induced Chondrogenesis (AMIC®) using Chondro Gide® in the ankle, knee and hip. Prof. Markus Walther presented an update on the use of AMIC® in the ankle; Prof. Andrea Fontana relayed his experience in arthroscopic treatment of chondral defects in the hip; and Prof. Roland Jakob presented the long-term results of the use of Chondro-Gide® in the knee. AMIC® has proven to be a valid and long-lasting technique to ensure excellent clinical outcomes and allow patients to resume their usual lifestyles.
Mid-term Results of AMIC® in the Ankle

Prof. Markus Walther, Medical Director and Chief Surgeon at the Schön Clinic Munich, Germany, presented the 48-month results of a prospective follow-up study using AMIC® in the ankle. Introducing the topic, Prof. Walther summarized the recent developments in bone marrow-stimulation techniques, finding that smaller but deeper drilling into the cancellous bone was more beneficial, as it damaged the subchondral plate less and improved access to the bone marrow stem cells. Furthermore, it has been learnt that a membrane helps contain stem cells in the defect, as it stabilizes the super clot and improves tissue regeneration.

Prof. Walther treated 20 patients between 2009 and 2010 in a prospective trial using Chondro Gide®. The median patient age was 39 years (19–60), mean BMI 23 (20.1–31.4), and all patients had grade III and IV cartilage defects of ≥1 cm². Five patients required osteotomy (OT), 13 were treated without OT; 16 patients required bone graft.

Patients were assessed clinically using MRI and both the American Orthopaedic Foot and Ankle Society (AOFAS) and Foot Function Index (FFI) scores; Prof. Walther felt favourably about the FFI scoring system as a self-reporting questionnaire for patients. It retrieves feedback in two subcategories with 8 questions on pain and 10 on function. Standardised treatment for all patients involved debridement of unstable cartilage, removal and grafting of necrotic bone and cysts, graft sealing with fibrin glue, and then membrane fitting and attachment with fibrin glue. Careful attention must be paid when fitting the membrane; it should be within the defect boundaries but should also make good contact with the surrounding cartilage. Creation of a foil template greatly facilitates correct fitting.

Post-operative rehabilitation was achieved through 48-hour immobilization in a splint followed by continuous passive motion. Partial weight bearing (10 kg) began at 6 weeks, with 10 kg weekly load increases, up to full bodyweight. Cycling and swimming were resumed at 3 months; other non impact sports, at 6 months; and, eventually, running and impact sports were resumed no earlier than 12 months.

Patients showed significant improvements in FFI scores at 12 and 48 months, predominantly in the functional assessments (Figure 1). A clinically significant reduction in FFI pain scores was also recorded, with much of the improvement occurring during the first 12 months and slight-but-noticeable improvements continuing out to 48 months.

Significant improvements were also recorded when patients were assessed at 12 and 48 months using the AOFAS scoring system, with a median (SD) ± standard deviation increase from 64.2 ± 19.5 to 84.2 ± 31.

There was no correlation between patient age and FFI score, and it was postulated that the FFI, as a patient-reported score, more closely reflects patient expectation. For example, older age may be linked to lower expectation, meaning these patients are generally satisfied with the results compared to other cartilage-repair treatment options.

Objective results obtained through MRI (Figure 2) indicate that bone marrow (BM) oedema is a common occurrence, even in patients showing otherwise excellent clinical outcome, and that only severe BM oedema correlates to inferior clinical results, suggesting that mild-to-moderate BM oedema reflects the higher metabolism present in bone that is still healing.

MRI findings in this cohort also included mild-to-moderate synovitis, usually in the anterior joint area, which links more closely to pain than BM oedema. Patients experiencing severe pain attributable to synovitis were initially treated with hyaluronic acid or, in more severe cases, platelet-rich plasma (PRP). Failing these approaches, a patient might be managed with arthroscopic surgery including synovectomy.

The severity of BM oedema was seen to shift from moderate-to-severe in pre-clinical assessments to generally mild at 48 months. A similar trend is noticed for effusion, with a general decrease over time, although even some patients with excellent outcomes had some effusion.

Prof. Walther summarised that AMIC® treatment of cartilage defects in the ankle leads to good mid-term results, with significant improvements in pain and articular function. However, the healing process takes longer than 12 months, and continual improvement can be expected at least out to 48 months. Patient education is crucial to ensure that activities that might reduce the probability of achieving the best possible outcome are not undertaken.

Questions

Upon being questioned about dealing with cysts and oedema, Prof. Walther clarified that cysts are repaired with bone grafts and that, for the oedema, as long as there is no clear link to clinical issues, it will usually reduce over time and is not cause for worry. Prof. Walther concluded that drilling 8–10 mm deep addresses these issues of bone metabolism.

“Before you do the surgery you have to think about location: if it is the dorsal, place the patient on the side and take a medial- or lateral-dorsal approach. Otherwise you have regular access from the ventral side and then you can get a bone space of about 5–8 mm, which is sufficient in most cases.”
The Arthroscopic Treatment of Chondral Defects in the Hip

Dr Andrea Fontana of COF Lanzo Hospital, Lanzo d’Intelvi, Italy, started by taking the audience back to basics. He introduced his experience from 359 patients to explain that chondral lesions in the hip, and especially on the acetabulum, are more common than is often expected. In fact, acetabular chondral lesions were present to some degree in 96.1% of patients treated, compared to only 68% of cases involving femoral head lesions.

In treating these deformities, Dr Fontana highlighted that it is important to not only seek to repair damaged cartilage, but also – and more importantly – to regenerate tissue. Among current treatment techniques, microfracture (MFx) is seen as the gold standard. Microfracture requires the formation of 3–5 mm deep holes at ~5 mm spacing; these should be perpendicular to the articular surface. These requirements render MFx a technically challenging procedure not always applied with the necessary precision. Moreover, MFx is indicated for defects <2 cm², and clinical results show a decrease in success after just 2–4 years.

Dr Fontana went on to report the results of a trial recently published in Bone Joint Journal, wherein he compared the 5-year results of the use of AMIC® with MFx in 147 patients with grade III to IV acetabular chondral lesions of 2–8 cm². Patients were assessed using the modified Harris hip score (mHHS) pre-operatively, at 6 months, and then annually from 1-5 years. Although both techniques showed marked improvement and good scores at 6 months, the durability of these outcomes was significantly greater for the AMIC® patients (Figure 3). The decline in clinical outcome was particularly noticeable in MFx patients with lesions >4 cm² (Figure 4).

Dr Fontana also highlighted his findings from another study published in International Orthopaedics. In this study, Dr Fontana compared the use of AMIC® with Matrix-Induced Autologous Chondrocyte Implant (MACT) in 31 and 26 patients, respectively. Both techniques afforded very good clinical outcomes, again assessed on the modified Harris hip score, and no significant difference between the outcomes was determined over the 5-year follow-up. However, the single-step AMIC® procedure reduced operating times compared to the two-step MACT protocol, and Dr Fontana opined that this reduction reduced total treatment time and can be associated with improved patient morbidity and cost-effectiveness.

Dr Fontana’s presentation was of such comprehensive and compelling strength that he fielded but a single question at the end of his talk. Asked by Chairman Prof. Jakob to offer typical incidence values for acetabular and femoral head lesions, Dr Fontana responded that roughly 90% of patients present with acetabular lesions compared to about 65–70% with femoral head lesions.
Long-term Results of AMIC® in the Knee

Prof. Roland Jakob was the final speaker to present, treating the audience to a pictorial tour de force of his experiences using Chondro-Gide® in the knee over the last 10 years. Prof. Jakob concentrated on just a few cases that he felt best illustrated the excellent outcomes that are possible using Chondro-Gide®, the great variety and severity of cases that can be successfully treated, and the long-term outcomes that can be expected.

Beginning with a brief history of his AMIC® experiences, Prof. Jakob explained how, in 2003, his team began working with AMIC®. Prof. Jakob noted that their goal was to achieve the same kind of healing observed in the spontaneous healing of a traumatic cartilage defect; i.e. healing associated with bleeding. He pointed out that microfracturing creates a blood clot, which is replaced by vascularized, scar-like fibrocartilage and potentially hyalin-like tissue³, and believes that fibrocartilage repair has lower chance of providing a durable solution when not combined with unloading through OT.

Prof. Jakob extended the procedure to osteochondritis dissecans (OCD) explaining the procedure, published in 2012 Kusano et al., involving multiple, deep perforations by drilling into the cancellous bone, followed by bone grafting to reconstitute condylar convexity. Prof. Jakob remarked that not only did the bone reform well, but also thick strong neo-cartilage was produced.

The 8- to 10-year follow-up of the patients involved in the study published in 2011 is now under way, and Prof. Jakob presented one complicated case of a 24-year-old construction worker with bilateral OCD. Post-operative assessments at the time (Figure 5) suggested an excellent outcome, the patient returned to work after 4 months, and the 8 year MRI follow-up suggested consistent filling of bone and good cartilage formation.

Prof. Jakob indicated that a full presentation of the 10-year results from the study would be given in the near future, but he shared some preliminary data. A total of 40 lesions (38 patients) were treated with a mean age at surgery of 38 years and a mean age at follow-up of 47 years.

The study³ included 20 full-thickness chondral defects of the patella, 11 osteochondral defects of the femoral condyle due to osteochondritis dissecans (OCD), and 9 full-thickness chondral defects of the femoral condyle. Overall, the 2 and 10-year functional scores show remarkable consistency and durability with excellent clinical outcomes; mean Lysholm 83.78 (SD 17.74) and 84.72 (SD 12.76) at 2 y and 10 y respectively, and mean VAS of 2.12 (SD 2.28) and 2.00 (SD 1.63), again at 2 y and 10 y respectively, (Figure 6).

Figure 5: Before and after images of left and right knee; upper images intra-operative, lower images left and right knees at 24 and 18 months post-operative, respectively, of patient treated for severe bilateral OCD

Figure 6: Ten-year mean Lysholm and VAS scores and standard deviations for all subjects treated with AMIC®
Prof. Jakob finished by presenting the complicated case of a 44-year-old woman from the 20 cases in the femoropatellar branch of the study. The case involved a tuberosity OT with medialisation and slight advancement, a cartilaginous reconstruction procedure using Chondro Gide® for the patella and periosteal coverage over microfractures on the trochlea.

This complicated hybrid solution was chosen to highlight the successes possible by using Chondro Gide® even in what appear to be salvage situations. The comparison between the pre-operative and 12-month X-ray images (Figure 7) are a testament to the excellent clinical and radiological results possible, and highlight the continued success of Chondro Gide® in a wide variety of clinical situations.

When asked why he does not perform only the OT, Prof. Jakob responded that, although there was some evidence to suggest that OT alone might induce a certain degree of regenerative action in the cartilage, a more certain approach is to perform at least MFx and use a matrix to support chondrogenesis.

In summary, Dr Jakob reported that AMIC® shows constant good results at 10 years of follow-up after procedures in the knee suggesting that AMIC® is a more enduring treatment for cartilage lesions of the knee in the long term compared to microfracturing alone.

The three experts presented compelling clinical evidence on the efficacy and versatility of Chondro-Gide® AMIC®-based procedures to treat a variety of osteochondral and full-thickness chondral lesions in the talus, knee and hip. More importantly, the excellent clinical outcomes reported are proving to be durable, without the steady decline in efficacy over time reported for MFx techniques. Finally, as a procedure, AMIC® is simpler and more cost-effective than chondrocyte-transplant procedures, resulting in reduced operating times and improved morbidity.

Figure 7: Pre-operative and 12-month post-operative X-ray images after complex femoropatellar chondral reconstruction using Chondro Gide®

Conclusions
Biographies

Prof. Dr Roland Jakob
Prof. Dr Roland P. Jakob is emeritus professor at the Medical Faculty, Berne University, and at Hôpital Cantonal de Fribourg, Department of Orthopaedic Surgery, Switzerland. His long and illustrious career in orthopaedic surgery began in the early 1970s, training in orthopaedic Surgery in Switzerland, Finland, and Canada from 1968 to 1974 and serving with the Red Cross during the Yemin war. He has held many high profile posts in international orthopaedic societies including Founding President of the International Cartilage Repair Society (ICRS) 1997-1999, and leading roles in ISAKOS (President), European Society of Sports Traumatology (Head of Scientific Committee) Knee Surgery and Arthroscopy (ESSKA). His clinical interests include sports medicine and reconstructive knee surgery, paediatric orthopaedics, and post-traumatic reconstruction.

Prof. Dr Markus Walther
Prof. Dr Markus Walther has been the Medical Director & Head of Department from 2012 and 2005, respectively, at the Center for Foot and Ankle Surgery, Schön Klinik, München Harlaching. Prof. Walther studied at Friedrich-Alexander University, Erlangen/Nuremberg, graduating in 1992, receiving his doctorate in 1993 and license in 1994. He has held posts at Erlangen University Surgery Clinic in the Trauma Surgery Department, Outpatient Center and Department for Plastic and Hand Surgery (1992-1996), and at the Würzburg University Orthopaedic Clinic from 1996-2005 where he was Assistant Senior Speciality Registrar at the König-Ludwig-Haus Orthopaedic Clinic and Quality Management Director, and Physician in Charge of the Foot and Ankle Surgery Division Specialist Registrar for Orthopedics from 1999. Completing his postdoctoral qualification (Habilitation) in 2001, he later became Speciality Registrar for Orthopaedics and Trauma Surgery at Schön Klinik München Harlaching in 2005 and remains at the Schön Klinik to this day. A member of many national and international orthopaedic societies, president of the German Society for Foot and Ankle Surgery, Prof. Walther has received numerous prizes and has published extensively in the field of orthopaedic surgery.

Dr Andrea Fontana
Dr Andrea Fontana studied medicine at the University of Palermo, Italy, graduating in 1986. Specializing in orthopaedics in 1992, and completing a clinical research fellowship at the prestigious Cambridge BUPA Lea Hospital, Hip and Knee Unit, Cambridge, UK, Dr Fontana has been chief of Department at both Polyclinico di Monza (from 2001) and Casa di Cura Santa Rita (from 2006) hospitals in Milan, Italy, and is currently at the COF Lanzo Hospital, Lanzo d’Intelvi, Italy. Dr Fontana has been a leading investigator in a number of orthopaedic hip surgery trials, is a member of numerous international societies including ICRS, ESSKA, EHS, ISHA and SIOT, and has published prolifically.

References


Geistlich Pharma do Brasil
Av. Brig. Faria Lima 628, 9º andar – Pinheiros
São Paulo – Brasil
TEL: (11) 3097-2555
FAX: (11) 3097-2550
info@geistlich.com.br

France
Geistlich Pharma France SA
Parc des Nations – Paris Nord II
385 rue de la Belle Etoile
BP 43073 Roissy en France
FR-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-surgery.com

Italy
Geistlich Biomaterials Italia S.r.l
Via A. Fogazzaro 13
I-36016 Thiene VI
Phone +39 0445 370 890
Fax +39 0445 370 433
surgery@geistlich.com
www.geistlich.it

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-surgery.com