CLINICAL EXPERIENCE WITH MATRIX ASSOCIATED AUTOLOGOUS CHONDROCYTE TRANSPLANTATION (MACT).

RAMADANI F.[1], ORTHNER E.[1], KITZLER B.[1], WALLNER B.[1], BURGHUBER C.[1], FUSSENEGGER M.[2], MEINHART J.[2]

[1]*Department for Traumatology, Klinikum der Kreuzschwestern, Wels, Austria*

[2]*Institute for Tissue and Organ Reconstruction, Wels, Austria*

ABSTRACT

Introduction

Matrix associated autologous chondrocyte transplantation (MACT) represents a further development of the autologous chondrocyte transplantation (ACT) for the treatment of articular cartilage defects. Whereas several studies proved the clinical feasibility of ACT, only few clinical data are available for MACT. We summerize here the data of 100 consecutive patients which were operated in our department between 2001 and 2004 with igor-MACT, the system of the Institute for Tissue and Organ Reconstruction, Austria.

Patients and Methods

Autologous chondrocyte cell cultures were established from small cartilage biopsies and were grown until sufficient cell numbers could be obtained. Cultivation took place in an accredited cell culture laboratory. Shortly befor operation, the cultures were harvested and transfered to the operation theatre. After preparation of the defect, cells were mixed with a stabilized fibrin solution which was then allowed to polymerize on a collagen fleece. Before that, the fleece was trimmed to the shape of the defect. This cell-fibrin-collagen constructs could then easily be put into the defects where they tightly adhered to the surrounding tissue. The success of the transplantations was examined by using the knee evaluation score of the International Cartilage Repair Society (ICRS), by clinical, MRI and CT examinations.

Results

100 patients were treated by MACT based on stabilized chondrocyte-fibrin-collagen constructs. Median observation period was 18 months ranging from 1 to 38 months. MRI ans CT data demonstrated a progressive transformation of the chondrocyte-fibrin-collagen constructs to a mature tissue, producing a typical cartilage signal within one year. The subjective knee evaluation score was increased after the operation and reached pre-accidental values.

Conclusion

MACT based on stabilized chondrocyte-fibrin-collagen constructs is a clinically feasible method. Additionally, it is save and easy to use. Constructs adhere tightly to the surrounding tissue and can mature into cartilaginous tissue. The subjective knee evaluation score reached pre-accidental values, demonstrating a high level of patients satisfaction.

INTRODUCTION

Autologous chondrocyte implantation (ACI) has proven its clinical effectiveness for the reconstruction of articular cartilage. Thounsands of patients had been treated with this method so far (1,2). The method uses cultured autologous chondrocytes which are injected into the periostal flap covered cartilage defect. However, harvesting and sewing of the periostal flap is time consuming and difficult. Moreover, sealing of the flap covered defect appeared to incomplete with leakage and subsequent cell loss. Thus not all defects, especially those on the patella, could be treated with this method. Moreover, it has been shown that ACT tends to develop periostal hypertrophy and delamination (3). Matrix associated autologous chondrocyte transplantation (MACT) represents a further development of the autologous chondrocyte transplantation (ACT) for the treatment of articular cartilage defects. Whereas several studies proved the clinical feasibility of ACT, only few clinical data are available for MACT. We summerize here the data of 100 consecutive patients in a prospective cohort study, who were operated in our department between 2001 and 2005 with igor-MACT, the system of the Institute for Tissue and Organ Reconstruction (igor, Wels, Austria).

METHODS AND PATIENTS

We used the igor MACT system (igor, Wels, Austria) for the reconstruction of articular cartilage defects in 100 patients. The igor system utilizes 3 components for the formation of transplantable constructs. The first component is a collagen I/III fleece which provides structural stability and can be easily trimmed to the desired shape. The second component is a stabilized fibrin solution which provides a natural environment for cartilage maturation. It has adequate resorption properies and glues the construct tightly to the surrounding tissue. The thired component are cultured autologous chondrocytes which secrete specific matrix molecules and remodel the constructs to hyaline cartilage.

For the establishment of autologous chondrocyte cultures, small biopsies were harvested from non weight bearing parts of the knee articular cartilage. The biopsies were transferred to the accredited cell culture laboratory Institute for Tissue and Organ Reconstruction There the chondrocytes were isolated and cultured until a sufficien cell number (>30 . 10^6) was reached. After a mean cultivation period of 3 weeks, the cells were ready for transplantation.

After defect preparation, the collagen fleece was trimmend to the sizee of the defect. Then the cultured cells were resuspended in the fibrinogen component and were applied onto the trimmed collagen fleece. The cell loaden fleece was then placed in the defect. By applying thrombin, polymerisation was started, which therefore took place at the site of the defect. The constructs adhered tightly to the surrounding tissue (Fig. 1).

The inclusion criteria for our study were: Age under 55 years, lesions stage III or IV, defect size over 2 cm^2 and defect localization on the femur condyls, patella or trochlea.

Our 100 patients were 40.2±12.2 years old. 65 patients were male and 35 female. 21 patients were treated for stage III lesions and 79 for stage IV lesions. The defects were located on the condyls (87) or on the patella (13). In 59 patients, the treated knee had previous operations like mosaic plasty, debridements, sub chondral drilling etc. Patients had to comply to a specific rehabilitation program. The success of the transplantations was examined on a regular basis by using the knee evaluation score (IKDC) of the International Cartilage Repair Society (ICRS), by clinical, MRI and CT examinations. Nine patients agreed to have their reconstructed defects biopsied after 6 months. Biopsies were histologically examined at the Department for Traumatology of the Medical University of Vienna.

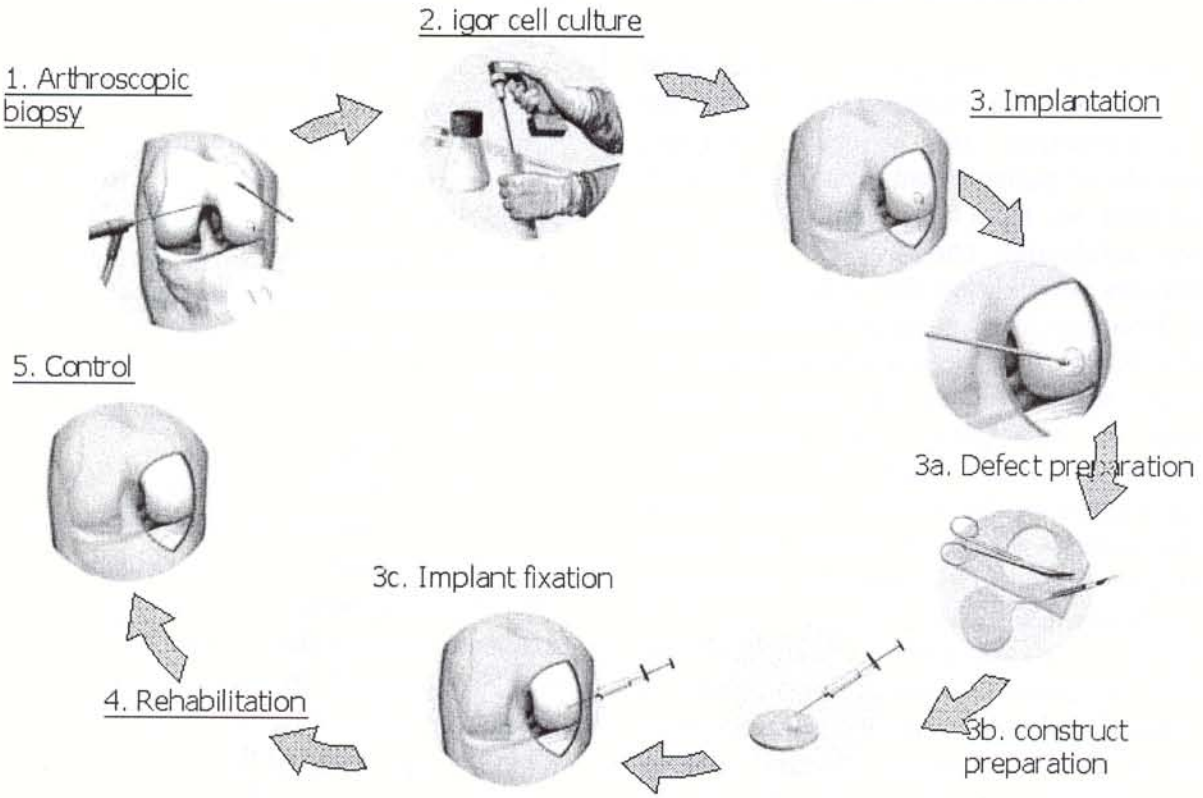

Fig. 1. Schematic drawing of the igor matrix associated autologous chondrocyte (MACT) system

RESULTS

Median follow up time was 18 months (2 to 38 months). The average defect size was 5.7 ±3.9 cm^2. Only one transplant was lost and this patient had a knee prosthesis implanted. Both the objective (clinician's, Fig. 2) and the subjective (patient's, Fig. 3) IKDC knee evluation score showed good increasing results as compared to the preoperative scores, after 1, 2 and 3 years. Especially patients which had been treated for patellar defects evaluated their knees as excellent after 1 and 2 years (Fig. 4). All patients showed increasing daily activities over time as documented by the activity index, which nearly reached pretraumatic values (Fig. 5).

MR images documented a gradual maturation of the constructs over time, showing already a typical hyaline cartilage signal at 1 year with stable conditions up to 3 years both for defects at the condyls (Fig 6) and the patella (Fig 7) with excellent integration and only minor irragularities. This corresponded well with the histological findings of the 9 biopsies. After 6 months typical hyaline cartilage was found in all samples (Fig 8). In some samples, remnants of the collagen/fibrin components could be found (Fig 9).

DISCUSSION

Matrix associated autologous chondrocyte transplantation (MACT) represents a further development of the (ACT) for the treatment of articular cartilage defects. All systems used so far used preseeded matrix constructs of different origin (4,5).The method we used has demonstrated its high potential to produce typical cartilage tissue in vitro (6) and in vivo (7). The handling of the transplants was simple. A major advantage of the system is the fact, that the constructs are freshly prepared during operation guaranteeing a high number of vital cells for the reconstruction. Moreover, the transplant is moldable and can fill easily also more complicated defects.

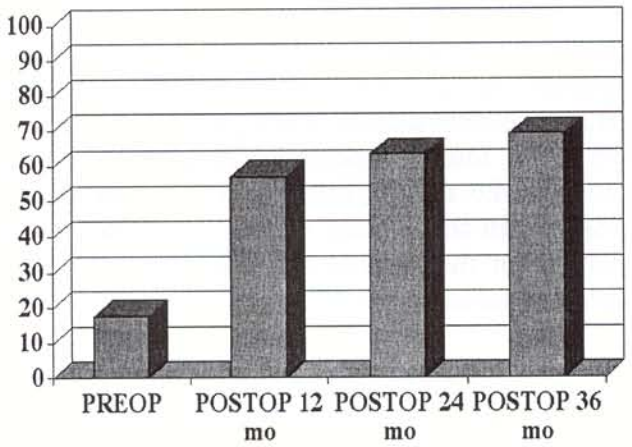

Fig 2: Objective IKDC score for patients with patellar reconstructions.The higher the score, the better the clinician has evaluated the patient knees

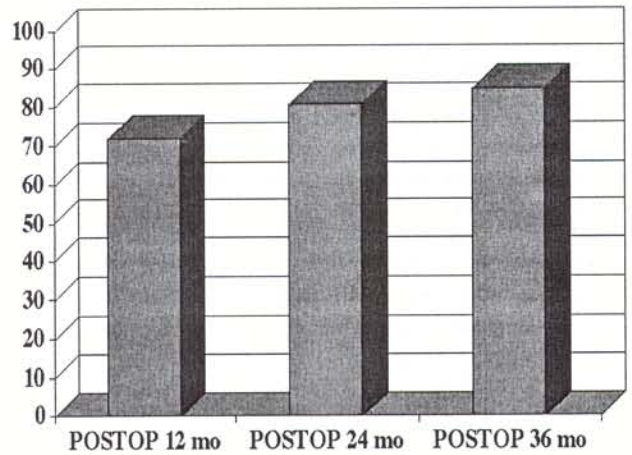

Fig 3: Subjective IKDC score for MACT patients.The higher the score, the more activity patients can perform in daily life, at work and in sports and the less pain the experience

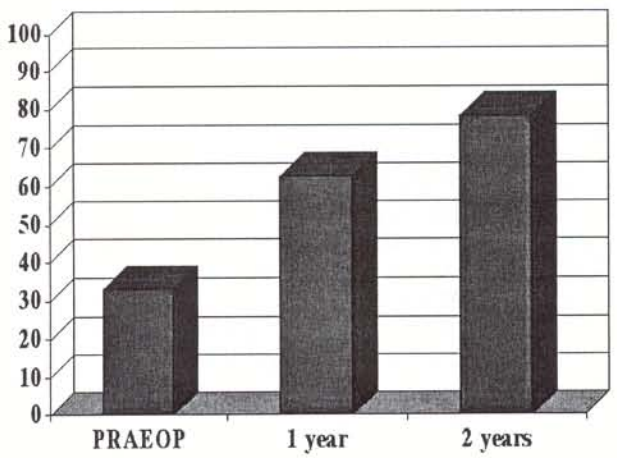

Fig 4: Subjective IKDC score for patients with patellar reconstructions.The higher the score, the more activity patients can perform in daily life, at work and in sports and the less pain the experience

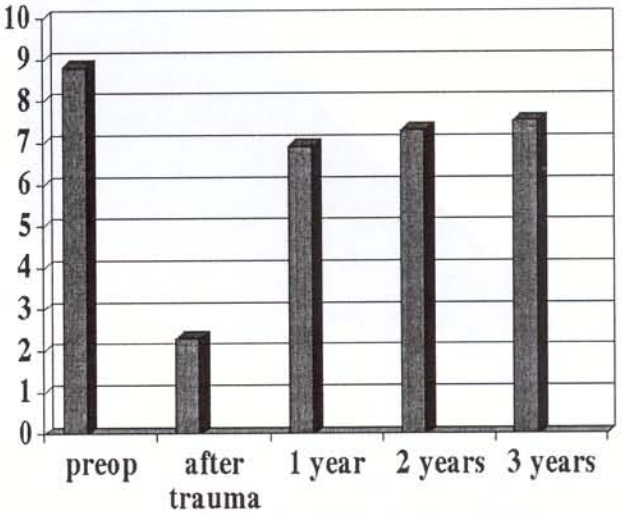

Fig 5: Activity index, score range 0-10, the higher, the more activity patients can perform with their knee

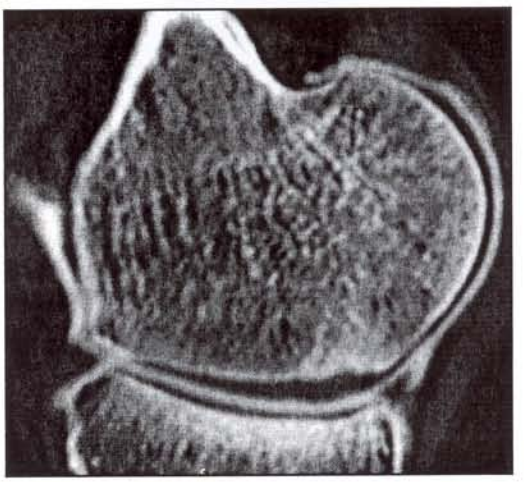

Fig 6: Excellent reconstruction at the medial femur condyl, minimal cartilage thickening and cortical subchondral reaction. MRI 3 years postoperativly.

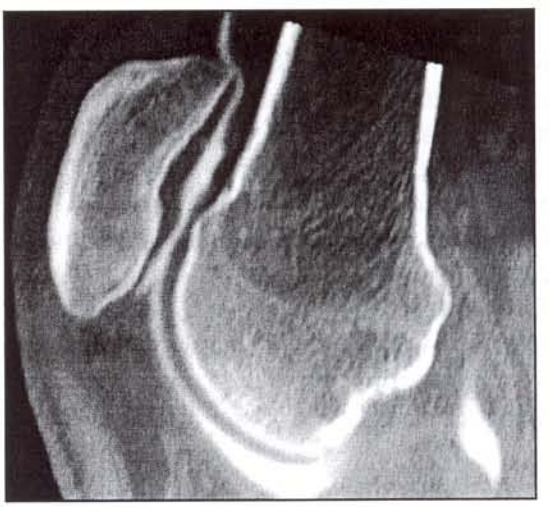

Fig 7: Excellent retropatellar reconstruction. MRI 3 years postoperativly.

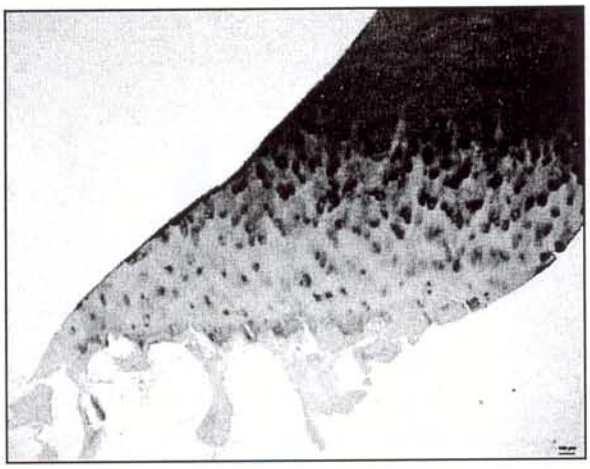

Fig 8: Hyaline cartilage, cells situated in thir lacunae surrounded by cartilge specific extracellular matrix (Alcian, digitally magnified)

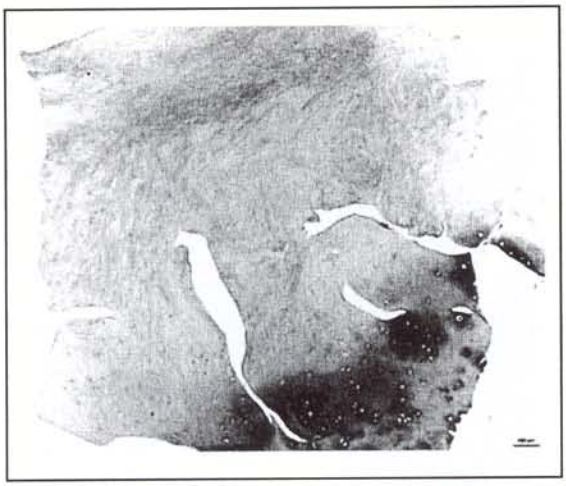

Fig 9: Partially hyaline cartilage clearly visible, partially the collagen/fibrin matrix is still present with typical signs of beginning cartilage maturation. (Alcian digitally magnified)

We included our patients according to the guidelines of the German and Austrian Associatiens for Traumatology. The indications were an intact cartilage surrounding the defect, an intact meniscus, stable ligaments, a correct foot axis and free joint movement. We treated 100 patients for articular cartilage defects. In our series only one transplant was lost. The IKDC scores showed a high level of patient satisfaction. MRI evaluation demonstrated a gradual maturation of the transplanted constructs to hyaline cartilage. Nine biosies harvested after six months could be studied. We found either fully developed and matured hyaline cartilage or predominatly hyaline cartilage with remnants of the transplanted matrices. In earlier studies with ACT poor results for patellar reconstructions have been reported (9). In contrast to that, our results for patellar reconstructions were particularily good. We also found especially good results for patients who strictly followed the rehabilitation program. In conclusion, we can recommend this method for the reconstruction of large articular cartilage defects.

LITERATURE

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