INTRODUCTION: Meniscal fibrocartilage, like articular hyaline cartilage, has limited healing capabilities, caused, at least in part, by the limited vascularity and the limited capacity for recruiting cells to participate in repair. Menisci play an important role in the biomechanics of the knee joint with respect to compressive load transmission, shock absorption, and knee stability. [1]. Therefore, total and partial meniscectomies have been strongly associated with the development of early osteoarthritis. Clinical and basic science researchers in the last years have been intensifying their efforts in order to find different approaches to save this important structure. Nevertheless, meniscal repair is a challenging task, since the meniscus is vascularized only in the outer third, and lesions occurring in the inner two thirds rarely repair spontaneously. In previous studies, we demonstrated that isolated chondrocytes seeded on scaffolds were able to bond articular cartilage matrices in vivo [2] with mechanical integrity [3,4]. Following studies have demonstrated the ability of chondrocytes to adhere to meniscal matrix and repair a lesion made in the inner third of the meniscus in an ectopic model in nude mice [5 Peretti ORS 2000]. The purpose of the present study was to assess the capacity of chondrocyte-seeded cartilaginous scaffold to repair a bucket-handle lesion of the knee meniscus orthotopicly in a large animal study.

METHODS: From the longitudinal aspect of a cross section of pig menisci, meniscal slices (10mm x 2mm x 0.5mm) were sectioned. Meniscal specimens were treated with five devitalizing freeze-thaw cycles in order to kill all the innate cells. Twelve three-month-old Yorkshire pigs have been employed for this study. Cartilage specimens were surgically harvested from the patellar groove of the left knee of the pigs belonging to the experimental group. As shown in the experimental diagram, chondrocytes were isolated by enzymatic digestion and seeded by suspension culture onto the previously processed allogeneic meniscal slices. After in vitro culture, in a second surgery, using an anteromedial approach, the left medial meniscus of the same pig from which chondrocytes were harvested was exposed and a one-centimeter bucket handle lesion was produced at the margin of the inner third and the outer two thirds of the meniscus. The cell-seeded meniscal construct was secured in the lesion in three pigs of the experimental group (Group A). Identical lesion was performed all other pigs. In three pigs the lesion was treated with an unseeded scaffold (group B); in three the lesion was sutured without insertion of any other material (group C); in three the lesion was left untreated. Animals were sacrificed after nine weeks and the menisci were harvested. The specimens were examined grossly, fixed in buffered formalin, processed, sectioned, and stained with hematoxylin and eosin for histological analysis.

RESULTS: Results showed gross bonding of lesion margins in the specimens of the group A, whereas scaffold was still present in the lesion site (fig. 1A). Macroscopic analysis of the control specimens indicated still presence of a not repaired lesion (fig. 1B). Histological analysis showed complete adherence between the margins of meniscal fracture and the cell-seeded scaffold in several areas in the specimens of group A menisci (fig 1C). Other areas of the same specimens showed interruption of continuity between the seeded scaffold and the native meniscus lesion edges. Where repair was achieved, newly formed cartilage matrix was involved in the bonding process. On the other hand, no matrix formation nor signs of repair was seen in the specimens of all control groups (fig. 1D).

DISCUSSION: The meniscus is an important structure for knee function and for the maintenance of articular surface integrity. This work evaluates the capability of a cell-based therapy for repairing a lesion in the avascular area of the meniscus in a large animal study. Based on previous studies that showed the capability of isolated articular chondrocytes to repair a lesion in the inner third of the meniscus in an ectopic in vivo model [5 Peretti ORS 2000], we have investigated the possibility of translating this model into a orthotopic large animal study. As well as in the previous model, in the present study, devitalized allogeneic meniscal implants were chosen as the scaffold for delivering the autologous chondrocytes. In this investigation, the tissue engineered cell-scaffold composite was able to achieve repair of a bucket-handle lesion in the avascular zone of the pig knee meniscus. Although the repair was not omnipresent, the results are encouraging, because a complete integration of the scaffold material with the native meniscus was noted in numerous surfaces by the formation of new cartilage matrix. We believe that these results represent a positive answer to the potential of a cell-based therapy for repair a tear in theinner third of the meniscus, a region thus far considered to have no healing potential. Future studies will determine the strength of this bonding and analyze the influence of different culture conditions, different cells source or the use of diverse scaffold material on the adhesion mechanism.

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