COMMENTARY

Commentary on "Third-Generation Autologous Chondrocyte Implantation Versus Mosaicplasty for Knee Cartilage Injury: 2-Year Randomized Trial"

In the clinical outcomes study reported in this issue of the *Journal of Orthopaedic Research*, Dr. Clavé and colleagues compared Cartipatch, a third generation autologous chondrocyte implantation (ACI) technique with autologous osteochondral mosiacplasty for the treatment of focal femoral chondral defects.[1] We would like to compliment these authors on designing and completing a Level 1 clinical trial examining a topic of high interest and importance in orthopaedic surgery. Treatments for large ($>2.5\,cm^2$) cartilage defects in the knee (and other joints) need to be critically evaluated for safety and efficacy. Head-to-head (Level 1) comparisons among treatments, as performed in this study, provide the most valid method for determining appropriate indications and evidence-based outcomes for accurately communicating to patients. Here, the mosaicplasty performed better than Cartipatch at the 2-year follow-up interval. This study highlights the difficulties investigators face enrolling for randomized trials, resulting in the study being underpowered. Nonetheless, these studies are particularly important in younger patient populations such as the one examined in this study. The peer-reviewed evidence clearly shows that for patients <60 years old, total knee arthroplasty (TKA) does not provide highly functional outcomes or sufficient therapeutic longevity and is associated with a high failure rate, such that multiple TKA revisions must be expected.[2,3]

With respect to the results of this study, we feel that it is critical to point out that both treatments were associated with clinically significant improvements in function (IKDC score) such that both would independently be considered successful. It is interesting and informative that mosaicplasty was associated with superior 2-year outcomes compared to Cartipatch, a tissue engineered autologous chondrocyte plug for osteochondral repair. Prior studies on this topic have reported mixed results.[4,5] We agree with the authors that longer term outcomes and assessment of secondary osteoarthritis will be necessary for conclusive evaluation of these and other techniques. However, this is the first Level 1 comparison reported for these treatments and provides valuable clinical data.

The specific differences between the two techniques evaluated in this study that may influence outcomes center on Cartipatch being a two-stage, cell-based, cartilage-only scaffold with long maturation time, compared to autologous osteochondral mosaicplasty being a one-stage, osteochondral tissue graft with native biomechanical properties. The authors suggest that these differences are responsible for the superior 2-year outcomes reported in their study, and we agree. One noteworthy difference of the Cartipatch implant over other autologous chondrocyte implantation techniques (ACI) lies in the creation of an osteochondral defect, whereas standard ACI techniques preserve the subchondral plate. While an osteochondral graft appropriately restores the subchondral portion of this osteochondral defect, Cartipatch introduces cartilage into the bony portion of the defect, leading to a significant alteration of the osteochondral unit. Restoration of tissue biomechanics in the defect appears to be of importance to a successful outcome and this involves recapitulation of the functional articular cartilage–subchondral bone unit with re-establishment of tissue composition, zonal architecture and material properties. Osteochondral autografts and allografts provide immediate restoration of each of these components. Autografts have the advantages associated with use of autogenous tissue. Allografts have the advantages of anatomic matching, the lack of donor site morbidity and the amount of useable tissue. Two-stage, cell-based, cartilage-only techniques—with or without scaffolds—do not allow for immediate restoration of these components and are dependent on in situ extracellular matrix synthesis and remodeling if they are to recapitulate a functional articular cartilage–subchondral bone unit. This is a very "big ask" in a pathologic joint and as such these techniques have consistently been associated with production of a mix of hyaline and fibrocartilage repair tissue,[6–10] as seen in this study. Procedures that provide immediate restoration of tissue biomechanics in the defect—with recapitulation of the functional articular cartilage–subchondral bone unit and re-establishment of tissue composition, zonal architecture and material properties—provide faster rehabilitation when compared to cell-based, cartilage-only techniques (with or without scaffolds). Current technologies that possess these capabilities include osteochondral autografts and osteochondral allografts.[6,8,9,11–13] Technologies that may fulfill these criteria in the foreseeable future include tissue engineered osteochondral constructs.[10,14]

With increased availability, osteochondral allograft transplantation has seen increased popularity and prominence in cartilage repair algorithms. However, published head-to-head studies between advanced cartilage repair techniques—such as osteochondral and chondrocyte-based procedures—remain limited. Therefore, we challenge surgeons and researchers, including

ourselves, to design and complete these types of studies to provide more evidence regarding these biologic techniques for the millions of patients for whom metal and plastic are not optimal. These studies are sorely needed for convincing third-party payers, determining decision-making algorithms, and educating patients in order to achieve optimal outcomes.

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