Yet another key learning point in the quest universal cartilage repair and restoration

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One of the greatest challenges that continue to confront orthopaedic surgeons today is the management of large osteochondral defects of the knee. Despite great advances made in the last 3 decades, a well-defined, complete, and easily applied solution has not yet been demonstrated. Use of osteoarticular allograft is one such proposed solution that has been used since the 1980s with variable reported success (1). With clinical experience it became quickly apparent that the viability of both bone as well as chondrocytes was vital for radiographic incorporation and clinical success (1). The observation that short-term clinical experience quickly influenced the shift of using frozen osteochondral allograft (OCA) to fresh is supported by the exclusivity of studies fresh OCA investigations published to date. It was probably not the intent of the authors to highlight that use of decellularized OCA (DOCA) would be associated with high failure, but simply to report and inform. The groups' findings demonstrated a clinically important distinction that the use of acellular grafts in an already compromised recipient is probably not judicious.

There could be other factors involved in the failure of this DOCA that cannot be determined from the publication as it is beyond the articles' scope or from the proprietary tissue processing and sterilization methods utilized by the manufacturer that is not available for review that could be at play. It is well known that typical sterilization techniques that could be used for OCA such as use of ethylene oxide, gamma irradiation, and/or freezing techniques can result in tissue that is devoid of viable functional cells (2). Although the majority of studies reporting the short, mid-, and long-term clinical outcomes have focused on the use of fresh OCA, it is known from clinical experience that the less the cellular viability of the OCA grafts implanted, greater are the chances for failure in all time frames (3), hence increased cellular viability are equated with improved graft incorporation and possibly clinical outcomes. Based on the current published data available, the outcome of this current investigation probably could not have been predicted, and therefore this work is probably critical in defining the future direction of research as well as treatment platform development in that cellular viability of the implant whether harvested or manufactured most likely should include a highly viable cellular component. This assumption is currently being challenged with the use of number of biomimetic manufactured materials being clinically approved for use displaying good early term results (4) in some, but additional failures in others (5,6).

Another important distinction that has been defined as a result of this publication is the need for better regulation/testing/validation of allograft tissue that is currently exempt from regulatory body review. In this case, the review guidance is found in the United States Food and Drug Administration (US-FDA) Title 21, Part 1,271 of the Code of Federal Regulations (CFR) regulating human

cells, tissues, and cellular and tissue based products (HCT/Ps) being implanted, transplanted, or infused in human recipients. Additionally, in Section 361 of the Public Health Service Act (PHSA) that stratifies allograft tissue as low risk and, therefore exempts it from premarket approval, and clinical validation demonstrating long-term clinical safety and efficacy (6). The only FDA requirements are for tissue donor screening for blood borne viruses and bacteria, and establishment of maximum levels of sterilizing agents allowed to be found in the final product of which are known to be imperfect. The sterilization process could have had an impact on the clinical outcome that has been demonstrated, and this can only be investigated, only if a more rigorous evaluation of allogenic tissue existed (2).

Currently there has been great interest in the use of biological augmentation to enhance current orthopaedic procedures to repair articular cartilage defects (7,8). This strategy could be used with either manufactured 3D scaffolds, or DOCA implants to improve performance (9). The use of expanded cultured chondrocytes used with periosteal patch has demonstrated mixed results (10-12). Additionally, cultured mesenchymal stem cells (MSCs) demonstrated equivalence in comparison to expanded autologous chondrocytes with periosteal patch for treatment of symptomatic osteochondral defects (13). Platelet rich plasma (PRP), bone marrow aspirate (BMA), bone marrow aspirate concentrate (BMAC), stromal vascular fraction (SVF), culture expanded mesenchymal stem cells (CE-MSCs) bone marrow or adipose derived or otherwise combined with a DOCA seem like a logical progression to improve clinical outcome, however to date, no clinical investigation for the knee has been undertaken (9,14,15).

The high rate of failure of DOCA may have seemed to shed negative light on the use of this type of implant overall, but that ought not be the case (16). A study of this nature should have been done long ago with similarly available graft materials. While there has been a plethora of investigations that have evaluated fresh OCA demonstrating good long-term outcomes, their use started with frozen OCA that we know had few remaining viable cells at the time of transplantation and it was this direct poor clinical experience that shifted use away from frozen to fresh OCA implants. From this starting point, there are many directions that can be experimentally undertaken to evaluate this platform for possible clinical utility in the future, and implantation with an autologous cellular component seems to be the next logical step, instead of abandonment of this possibly viable platform.

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Footnote

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