Editorial Commentary: Point-of-Care Harvest and Application of Resident Stem Are Practical and Cost-Effective

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Abstract: Point-of-care harvest and application of residence stem cells are practical and cost-effective. Tissue formerly considered waste contains these biologically potent cells, and use of such tissue may represent a big part of biologics going forward. The practical application of orthobiologics has slowed because of 3 hurdles: the regulatory requirements of stem cell technologies; the energy, time, and money required to develop a clinical evidence base; and the expense that they present to patients and institutions. Orthobiologic technologies that are simple and cheap and that leverage tissues that are already readily available at the point of care (i.e., the surgical procedure) solve many of these challenges. Cell sources could include knee synovium, shoulder subacromial bursa, bone marrow aspirate, and anterior cruciate ligament injury effusion fluid and stump tissue. A current concern is that collagenase processing and culture expansion are steps resulting in regulatory hurdles in the United States.

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The practical application of orthobiologics has slowed because of 3 hurdles: the regulatory requirements of stem cell technologies; the energy, time, and money required to develop a clinical evidence base; and the expense that they present to patients and institutions. It is hard to implement into one's surgery schedule a technique that is expensive and time-consuming and does not have a clear return on investment. When hospitals and surgery centers consider orthobiologics, they often first consider the expense added to procedures already on the schedule. Orthobiologic technologies that are simple and cheap and that leverage tissues that are already readily available at the point of care (i.e., the surgical procedure) are going to be winners sooner and likely in the long run.

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Although a potentially overused phrase, this brings to mind ice hockey legend Wayne Gretsky's quote, "I skate to where the puck is going." The concept still inspires and is currently applicable to the concept of resident stem cells. It is becoming increasingly clear that, for the application of biologics to make strides in everyday orthopaedic practice, it is going to have to become evidence based, practical, and cost appropriate. The concept of using repurposed, locally harvested tissue, formerly considered "waste tissue," is going to be a big part of biologics going forward. Waste tissue has "game."

The article in this issue by Shin, Kim, Park, Min, Yun, Chung, and Min,[1] "Motorized Shaver Harvest Results in Similar Cell Yield and Characteristics Compared to Rongeur Biopsy During Arthroscopic Synovium-Derived Mesenchymal Stem Cell Harvest," helps us take a step forward by answering a practical, real-world question: Is it better to harvest synovium and the fat pad with a shaver or rongeur grasper when we consider the viability of resident stem cells? The shaver produced a more efficient harvest, with 2.5 times more monocytes and 3.7 times more cells when cultured. The authors propose that the shaver is more efficient at harvesting because it accesses a heterogeneous population from both the synovial membrane and

subintimal tissue, a location where pericytes are likely more abundant. The primary strength of this study is that it comprised a homogeneous population and a practical harvest site. One limitation is that although harvest and immediate reapplication are possible, most studies illustrating value based on this technique or similar techniques have involved collagenase processing steps prior to reapplication.[2-5] Collagenase processing and culture expansion are steps that make products high risk in the US regulatory world, a designation that opens a can of worms.[6]

Similar to the authors of this current study, Gus Mazzocca and his colleagues have been developing the harvest of resident stem cells from tissues readily available during rotator cuff surgery.[7-9] They have investigated the subacromial bursal tissue and isolated a significant pluripotent stem cell population from this tissue. Comparing cells harvested from bursal tissue with cells harvested from bone marrow aspirate has determined that cells from the bursa have greater differentiation ability and proliferative potential.[7] When compared with cells harvested from bone marrow aspirate in an animal tendon model, bursal cells have exhibited superior engraftment and survival in tendon, with an increased healing tissue thickness compared with a control.[10] Hats off to Gus and his colleagues as they have developed an evidence base to support the use of repurposed bursal waste tissue during rotator cuff repair surgery.

At our institution, we have investigated resident stem cell harvest in the setting of anterior cruciate ligament (ACL) injury and reconstruction surgery. We first confirmed that both the injury effusion fluid and wasted stump tissue contained a cell population with stem potential.[11] We followed this with a study that confirmed these cells could be harvested and concentrated when mixed with blood in a point-of-care blood processing system, that is, a platelet-rich plasma system.[12] Currently, we are comparing the resident stem cell count of a number of different tissues considered waste during ACL reconstruction when harvested with a suction-activated device designed to capture these tissues. Applying these resident stem cells to augment ACL reconstruction in a practical and cost-effective method is our intended final objective.

The practical harvest as well as reapplication of tissues with resident stem cells is a promising field that will yield results in the near future. Expect to see a number of clinical trials soon. It is an exciting time, and we need to think, at times, like cell biologists; however, we also need to think like practical orthopaedic surgeons.

References

1. Shin D, Kim M, Park D, et al. Motorized shaver harvest results in similar cell yield and characteristics compared to rongeur biopsy during arthroscopic synovium-derived mesenchymal stem cell harvest. *Arthroscopy* 2021;37:2873-2882.
2. Koh YG, Kwon OR, Kim YS, Choi YJ. Comparative outcomes of open-wedge high tibial osteotomy with platelet-rich plasma alone or in combination with mesenchymal stem cell treatment: A prospective study. *Arthroscopy* 2014;30:1453-1460.
3. Koh YG, Kwon OR, Kim YS, Choi YJ, Tak DH. Adipose-derived mesenchymal stem cells with microfracture versus microfracture alone: 2-Year follow-up of a prospective randomized trial. *Arthroscopy* 2016;32:97-109.
4. Koh YG, Choi YJ. Infrapatellar fat pad-derived mesenchymal stem cell therapy for knee osteoarthritis. *Knee* 2012;19:902-907.
5. Koh YG, Jo SB, Kwon OR, et al. Mesenchymal stem cell injections improve symptoms of knee osteoarthritis. *Arthroscopy* 2013;29:748-755.
6. Fang WH, Vangsness CT Jr. Governmental regulations and increasing Food and Drug Administration oversight of regenerative medicine products: What's new in 2020? *Arthroscopy* 2020;36:2765-2770.
7. Morikawa D, Johnson JD, Kia C, et al. Examining the potency of subacromial bursal cells as a potential augmentation for rotator cuff healing: An in vitro study. *Arthroscopy* 2019;35:2978-2988.
8. Morikawa D, Muench LN, Baldino JB, et al. Comparison of preparation techniques for isolating subacromial bursa-derived cells as a potential augment for rotator cuff repair. *Arthroscopy* 2020;36:80-85.
9. Muench LN, Baldino JB, Berthold DP, et al. Subacromial bursa-derived cells demonstrate high proliferation potential regardless of patient demographics and rotator cuff tear characteristics. *Arthroscopy* 2020;36:2794-2802.
10. Dyrna F, Zakko P, Pauzenberger L, McCarthy M, Mazzocca A, Dyment N. Human subacromial bursal cells display superior engraftment versus bone marrow stromal cells in murine tendon repair. *Am J Sports Med* 2018;46:3511-3520.
11. Anz AW, Branch EA, Rodriguez J, et al. Viable stem cells are in the injury effusion fluid and arthroscopic byproducts from knee cruciate ligament surgery: An in vivo analysis. *Arthroscopy* 2017;33:790-797.
12. Branch EA, Matuska AM, Plummer HA, Harrison RM, Anz AW. Platelet-rich plasma devices can be used to isolate stem cells from synovial fluid at the point of care. *Arthroscopy* 2021;37:893-900.