Many practitioners and researchers in the field of orthopedics believe its future will rest in regenerative medicine – and with good reason.

“The regeneration of articular cartilage, acceleration of fracture and tissue healing, and faster incorporation of tendon grafts to bone have long been considered the Holy Grail of Orthopedics,” states Bryan T. Hanypsiak, MD in a recent issue of The American Journal of Orthopedics.¹

While we haven’t hit the Holy Grail yet, orthopedics is moving closer towards it as the scientific evidence around regenerative medicine grows and is very promising. As this emerging form of medicine moves out of the experimental stage and more into the mainstream, it’s an exciting time to be in the field of orthopedics.

Athletes like Kobe Bryant, Tiger Woods and others have put regenerative medicine front-and-center as they take advantage of its power to recover from injuries and return to high-level play. We now receive more questions than ever from patients about how regenerative medicine might help them with their injuries and ability to stay active.

While I agree with many of my colleagues that regenerative medicine holds great promise for orthopedics, it’s important for primary healthcare practitioners to know when it might be a good option for their patients – and when it’s not. For patients, it’s important to have the facts about this promising form of healing and to know how to find a provider who is practicing it correctly.

So, let’s dive right in. In this article, I’d like to share with you:

• The different forms of regenerative medicine
• The scientific evidence to support its use in orthopedics and sports medicine
• What conditions we know it works for and when it’s not the best choice
• Why it matters how regenerative medicine is practiced and its impact on patient outcomes
WHAT IS REGENERATIVE MEDICINE?

When tissue such as muscle, tendon, ligament or cartilage is injured, the body tries to heal the injury through its own repair mechanisms. However, in certain situations (especially in areas where there is lack of blood flow - such as inside and around joints), the body can't heal the injury adequately, if at all. This can lead to ongoing pain, weakness, disability, swelling, catching or locking of a joint. With regenerative medicine, we attempt to augment the natural healing process to heal or even “grow back” the damaged tissue.

Within orthopedics, there are two primary forms of regenerative medicine increasingly being practiced and studied. Each has its place in healing and repairing orthopedic conditions.

**Stem Cells**

Stem cell-based therapies for the repair or regeneration of muscle and tendon represent a promising technology going forward for numerous diseases. A type of stem cell called mesenchymal stem cells (MSCs) have gained the most attention in the field of surgery due to their ability to differentiate into the tissues of interest for the surgeon. These multipotent stem cells in adults originate from mesenchymal tissues such as bone marrow, tendon, adipose (fat) and muscle tissue. In orthopedics, we primarily harvest stem cells from the bone, notably the iliac crest of the pelvis.

We conduct many stem cell procedures right in the clinic – as opposed to in the operating room, where it’s costlier to the patient and often less comfortable. We pre-medicate patients to make them as comfortable as possible. Then the pelvis – where the stem cells will be harvested from – is anesthetized. A special needle called a Jamshidi™ needle is used to harvest the bone marrow.

**Platelet-Rich Plasma Therapy (PRP)**

PRP involves the use of the platelets from blood, which is mainly a liquid composed of plasma, but also contains red cells, white cells and platelets. Platelets contain hundreds of proteins called growth factors, which are very important in healing injuries.

PRP is conducted in the clinic unless it is being used as an addition to a surgical procedure. It begins with a standard blood draw on a patient, where we draw 15 milliliters of blood. PRP is then prepared by separating the platelets from other blood cells and increasing their concentration in a process called centrifugation. This is done in a centrifuge device, and a trained representative from the device company is onsite to prepare the PRP. The PRP with its increased concentration of platelets is combined with the remaining blood and injected via guided ultrasound into the injured tissue. The use of ultrasound is important as it allows us to be very exacting in placing the PRP.

A major advantage of regenerative medicine that is appealing to patients is that it leverages the natural healing process using the body’s own tissue.
BENEFITS TO PATIENTS

Both forms of regenerative medicine are appealing to patients as they are minimally invasive and often performed in the clinic in a relaxed setting with little down time. Both stem cells and PRP can be performed as an adjunct to surgery to enhance its outcome or as a standalone procedure done right in the clinic.

A major advantage of regenerative medicine that is appealing to patients is that it leverages the natural healing process using the body’s own tissue. Additionally, the ease of preparation and administration; relative safety; and cost-effectiveness, as compared with surgical options, are attractive to patients.

3 EVIDENCE-BASED USES FOR REGENERATIVE MEDICINE IN ORTHOPEDICS

There are three primary areas where the research and outcomes support the use of regenerative medicine in orthopedics. In alignment with the research, I consistently see great results in these areas in both the clinic and surgical settings when using stem cell therapy and PRP to treat these conditions.

Osteoarthritis

Research indicates promising results for the use of PRP for treatment of osteoarthritis. In one meta-analyses – a study combining data from multiple studies to identify a common effect – the use of PRP over standard treatment led to significant improvements in patient outcomes at six months after injection. The improvements were seen starting at the two-month mark and were maintained for up to 12 months.

In another study, both PRP and hyaluronic acid injections (a more traditional therapy for osteoarthritis) demonstrated decreased joint catabolism, or breakdown. However, PRP also resulted in a significant reduction of MMP-13 gene expression, an increase in HAS-2 expression in synoviocytes and an increase in cartilage synthetic activity compared with hyaluronic acid injections. What does this all mean? It indicates that PRP acts to stimulate the body’s own internal hyaluronic acid production, which helps to cushion and lubricate the joints, and decrease cartilage breakdown.

These studies, along with my clinical experience, demonstrate that PRP can be an effective treatment for osteoarthritis. Notably, I have found it to be a great option for patients who do not respond to more traditional treatments such as hyaluronic acid injections.

In a recent review of randomized controlled trials (RCTs) conducted for stem cell injection for knee osteoarthritis, researchers found that all RCTs reviewed reported superior efficacy for patient-reported outcomes. While more research is needed in this emerging area of stem cell usage, early results show good initial outcomes and strong promise for stem cell use to treat osteoarthritis.

Tendinopathy

When it comes to regenerative medicine and tendon injuries, the first thing we do is get an MRI to gain a clear understanding of the injury. PRP and stem cells can be used with positive results for low-grade partial, intrasubstance tendon tears; whereas, PRP would not be indicated for medium to large tears.

In one randomized controlled trial, 23 patients with patellar tendinopathy (an injury affecting the knee) were broken into two groups: 13 received ultrasound-guided dry needling alone with exercise; 10 received ultrasound-guided leukocyte-rich PRP injection with dry needling. The results showed an accelerated recovery from patellar tendinopathy within the PRP group.

In another study looking at chronic lateral epicondylitis – better known as tennis elbow – 100 patients were divided into a PRP group (51 patients) and a group that received the more standard treatment of corticosteroid injections (49 patients). Treatment for patients in the PRP group showed a reduction in pain and a significant increase in function over the corticosteroid injection group.

In a systematic review and meta-analysis of 18 PRP tendinopathy studies, good evidence supports the use of a single injection of leukocyte-rich PRP under guided-ultrasound in tendinopathy. However, it’s important to note that the preparation and injection technique appear to be of great clinical significance in outcomes using PRP for tendinopathy.
Rotator Cuff Repair

The use of stem cells as a complement to rotator cuff surgery to enhance its outcomes is demonstrating great potential. A study to evaluate the effectiveness of biologic augmentation of cuff repair using iliac crest bone marrow-derived mesenchymal stem cells (MSCs) measured results of patients in control and experimental groups. Forty-five patients received concentrated bone marrow-derived MSCs as an adjunct to rotator cuff repair at the time of arthroscopic surgery and 45 patients did not receive MSCs.10

Those in the experimental group who received MSC injection during surgery enhanced the healing rate and improved the quality of the repaired surface – as determined by ultrasound and MRI. In fact, 100 percent of the MSC patients had healed by six months versus 30 (67 percent) of the repairs done without MSC treatment at the six-month mark. Furthermore, bone marrow concentrate (MBC) injection prevented further ruptures during the next ten years, with intact rotator cuffs for 39 of the 45 patients in the MSC-treated group and just 20 of the 45 patients in the non-MSC treated control group.

This is a powerful study in that it demonstrates a decreased risk of rotator cuff retear over time and an increased heal rate of a surgically repaired rotator cuff using stems cells during the procedure.

Additional studies confirm the value of PRP and stem cells for arthroscopic repair of medium to large rotator cuff tears.11, 12, 13 Experience in my own practice bears these findings to be true, as surgeries I have performed using PRP and stem cells for rotator cuff repair have been met with positive outcomes. It’s important to note that not everyone is a candidate for PRP and stem cells for rotator cuff repair. Adding it into the surgical process is often indicated for those over 65, as heal rates tend to decrease with age, as well as for those who have previously had one or more failed rotator cuff surgeries.

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**STEAMS CELLS & ROTATOR CUFF REPAIR ARTHROSCOPIC SURGERY**

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<th>STUDY GROUP</th>
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| **Experimental Group:** | • 100 percent of the MSC patients had healed by six months.  
• Bone marrow concentrate (MBC) injection prevented further ruptures during the next ten years, with intact rotator cuffs for 39 patients in the MSC-treated group. |
| **Control Group:** | • 30 (67 percent) of the patients without MSC treatment had healed at the six-month mark versus 100% in the experimental group receiving MSC.  
• Just 20 of the 45 patients in the non-MSC group had intact rotator cuffs at the 10-year mark versus 39 in the experimental MSC group. |

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WHAT HEALTHCARE PROVIDERS & PATIENTS NEED TO KNOW

Not all regenerative medicine is created equal. Since this emerging form of medicine is not yet FDA-regulated, it's a bit of the wild west in terms of how it's being practiced. This makes it incredibly important to ensure that a healthcare practitioner is using it wisely and only for conditions where the medical research supports its effectiveness.

For both stem cell therapy and PRP, the preparation is critical. A healthcare provider should be working with a reputable centrifuge device and company, who will be onsite to prepare the PRP and stem cell preparations for the patient on an as needed basis. If a patient discovers that a provider is preparing their own centrifuge device that is not associated with a reputable vendor, this should be a red flag.

Another key factor in PRP and stem cells is in how it's administered. The use of guided ultrasound greatly enhances the ability to accurately insert it into the affected area. The use of ultrasound is a more recent advancement, but providers who are offering regenerative medicine should be using it, as it will increase the likelihood of a successful treatment outcome.

Patients should not shy away from regenerative medicine, as it can be very effective. Healthcare providers should not avoid recommending to their patients either. However, it's important to have the facts and know what the medical research supports its use for and when other treatment approaches would be more beneficial.

TRACKING THE OUTCOMES & CONTRIBUTING TO THE SCIENCE

At our practice, we participate in a large-scale regenerative medicine outcomes tracking program called Surgical Outcomes Systems (SOS). SOS uses standard medical scoring protocols to track patient results. Patients are measured before a regenerative medical treatment and at key intervals post-treatment up to two years later.

This program allows us to carefully track our patient population's outcomes. It also enables us to access a larger database of patient outcomes from SOS-participating providers and be part of contributing to the research and evidence base for regenerative medicine.
About Brian Gruber, MD, MBA & Integrated Orthopedics

Dr. Gruber is board certified by the American Board of Orthopedic Surgeons. His expertise is in arthroscopic surgery of the shoulder and knee, with specific interests in rotator cuff disease and anterior cruciate ligament injury to the knee.

As an early adopter and leader in the emerging field of regenerative medicine, Dr. Gruber uses both stem cell and platelet-rich plasma therapy (PRP) in his practice with outstanding results in the areas of arthritis, tendon injuries and rotator cuff repair.

In 2015, after several years of practicing in the Valley, he founded Integrated Orthopedics – an orthopedic and sports medicine practice and physical therapy clinic that serves patients statewide. Dr. Gruber and the entire team at Integrated Orthopedics are committed to providing the most innovative and comprehensive orthopedic care to every patient they serve.

Dr. Gruber graduated with honors and Alpha Omega Alpha recognition from the University of Illinois, Chicago. He completed an orthopedic surgery residency at the University of Michigan Hospital and Health System in Ann Arbor, Michigan, and completed his orthopedic and sports medicine training at Washington University. In addition to his medical training, Dr. Gruber holds a master of business administration from the University of Southern California.

REFERENCES
