S1 00:17 Our next speaker is actually a local legend. We try to bring in someone from A&M every year. This is a paragon of sports medicine here and they've been trying some really cool stuff here, and he's here to tell you about it, Dr. J.P. Bramhall. [applause]

S2 00:39 Thank you for the opportunity to be here and speak to the Huffines group on the Huffines discussion number four. Our challenge today is to present some very exciting things that are near and dear to our heart in only 15 minutes. In some of my coaching friends' words, when they're trying to get a team prepared fast and they only have a short amount of time to get that team prepared, they have to [sleep pass?]. So as we go through this, I'm going to talk fast and I want you guys to listen fast, all right? We're going to go.

S2 01:09 First of all, what is orthobiologics? What does that mean? Well, basically, orthobiologics is us employing naturally occurring substances in the human body that we already make to affect healing. When we use these in higher concentrations, it can aid in the acceleration of the healing process. A little science first. What does it take to heal an injury? First, we have to lay down extracellular matrix and that's the area where the cells live. As you can see in this slide, the chondrocytes are the little blue dots and they live in that pink stuff called the extracellular matrix and that is what supports the cell. That gives them their nutrition biomechanically and that's where also all of the other cells who are trying to heal that area come to, to gain their nutrition.

S2 01:56 Growth factors. This is going to be the key in the future of orthobiologics in sports medicine and in other fields of medicine. Proteins that are necessary for the cells to work during the healing process, also known as cytokines. The future is, we're going to eventually learn that when we inject orthobiologics or inject a biologic material into the body, we're going to find specific cytokines, specific proteins to inject. If I'm going to inject a ligament, we'll know which cytokine to inject. Right now, we're putting blood products in, and our own body is able to recognize some of those, but we can be more specific and so that's the future of orthobiologics.

S2 02:35 The third thing that occurs when we're healing an injury is stem cells. We have stem cells within us that have the ability to differentiate or change into the area that they are affecting. In our body, when we use plasma or platelet rich plasma, the platelets within us release growth factors, and those growth factors recognize where they are, they know which tissue they're in, and which tissue they need to heal. Some of the cell-based therapies that we have been employing started in the 1980s. One of them is known as autologous chondrocyte implantation, where we would take a piece of cartilage, send it to Boston, they would grow it, fly it back, and we would inject it into an area of cartilage degeneration. That sounds good. That's two surgeries. That's a lot of steps. So what we're trying to do now with cell-based approaches is locally being able to handle injuries to ligament, tendons, cartilage, and meniscal injuries.

S2 03:28 The game changer with orthobiologics - this is the key - cellular tissues. They can migrate, so they can get to the area of injury. Two, they can proliferate. They can form new cells. Third thing is they can differentiate. They can recognize where they are and change into that tissue that they are trying to heal and affect the healing process.

S2 03:48 I'm going to talk about two different orthobiologic treatments that we're currently

using. There's a wide array of them. There's two that we're going to talk about today. First is called platelet rich plasma and another one is called osteochondral allograft implantation. There's a wide array again of orthobiologics, but again, in our 15 minutes, I'm going to touch on two that we're pretty interested in.

S2 04:07

What is platelet rich plasma? Platelet rich plasma is a preparation of a patient's own plasma by removing the red blood cells and the white blood cells from the blood product. You do this by placing a small sample of a patient's own blood into a centrifuge and removing again the white blood cells and the red blood cells. This leaves us with a solution of plasma that is higher concentrated in a patient's platelets and healing cells. It can support regeneration and restoration of the joint or the tissue and basically gives a biological boost to the healing process. PRP can be used to promote healing in many injuries. We can use it in ligaments, tendons, muscle injuries, tendinitis. In laboratory tests, we see a significant increase in cellular proliferation. Again, we see cells grow in the area of the injury once PRP is injected into the area.

S2 05:02

Other things that platelets affect. Platelets decrease inflammation. Platelets decrease pain and they increase hyaluronic acid. As we go through this talk, you'll see in a minute why that's important. But remember that they decrease pain, so when you put it into a joint or an injury, it decreases the pain and it decreases the inflammation which also hurts, but it increases the HA synthesis and the hyaluronic acid is this fluid that our joints normally make for lubrication.

S2 05:28

ACP is another product - also a PRP product or a platelet rich plasma product - that outside of the blood stream, the platelets become activated, and when they become activated, they release these growth hormones or these growth proteins and these growth factors that affect the healing. Possible indications. You can use them in ligament injuries, fractures. You can use it in muscle injuries, hamstring strains, meniscal tears, Achilles tendon injuries, rotator cuff tears, degenerative arthritis, articular cartilage, plantar fasciitis, tendinitis, all these things and [?] it is a big list. But you want to know how do I use it? How do I use ACP? How do we use PRP today in the sports medicine world? How do we use it with our athletes that we encounter? One of our most effective uses of PRP or ACP has been in hamstring injuries. If we confirm on an MRI or an ultrasound a hamstring injury on a high level athlete who has a Grade 1 or a Grade 2 injury, which is not a complete rupture of the hamstring or the muscle, but a strain or a partial tear of the injury, we can inject PRP or ACP into the area of injury and decrease our return to play about half the time normally it would take.

S2 06:45

Just for example, if it's a six weeks injury, we can decrease that return to play, that decreased return to running in about three weeks. Usually, a major hamstring injury or a major muscle injury is a 12 to 16 week recovery. By doing this, with our training room modalities, with our rehabilitation, with all the other things that we use in conjunction to help the healing of an injury, additional PRP can help reduce that recovery time almost in half. For instance, on the right-hand side, you see an MRI of a hamstring injury where there is a large fluid collection. This is a normal hamstring on the right. By pulling the fluid off, injecting the ACP, the cells, again, they proliferate, they migrate, and they differentiate into muscle tissue, and promote healing of that area.

S2 07:38

How else do we use ACP? Ulnar collateral ligament tears in baseball. The elbow, the throwing elbow, is subject to high stress. The ulnar collateral ligament, as you guys may have heard in Tommy John's surgery, is only one third of the strength of a force across the elbow each pitch. So every time a high-level thrower throws a maximum

effort pitch, it's three times the force, which is the strength of the ulnar collateral ligament. So you wonder why you don't see more of them, but we see a lot of ulnar collateral ligament injuries. By injecting ACP or PRP into partial thickness tears in the ulnar collateral ligament-- and we have about 50 plus adolescent or collegiate level athletes who have had PRP injected into a partial tear of an ulnar collateral ligament. At about two years, we were reducing the incidents of going on to surgical reconstruction about 75%. This is a study that we're trying to get worked up through the Huffines Institute, and hopefully, we can get that information out, but these are our preliminary results. We're looking at improving the healing rate and decreasing the incidents of someone having to go onto surgical reconstruction from an injury.

S2 08:47 How else do we use ACP or PRP? Tennis elbow, one of the most difficult things that we see to treat. Very difficult to treat because it involves tendinitis or inflammation in a tendon, which has very poor blood supply and very poor healing potential. By us adding ACP or plasma cells to the area of the injury, again, you can see increased cell proliferation and improvement of the healing. One other way we've been using ACP is in osteoarthritis of the knee, and this decreases pain. Remember, it decreases inflammation in increasing the hyaluronic acid, which is an improvement in the patient's function and symptoms.

S2 09:27 Going on to the second topic, its' very exciting, it's much more invasive treatment, is osteochondral allografts. Cartilage degeneration in the United States is one of our most common conditions or throughout the world that we see causing pain and disability - 250,000-300,000 surgical treatments for symptomatic cartilage injuries in the US. On the research of this, in euros, 25 billion euros per year, 33.2 billion US dollars per year of research on tissue engineered products trying to affect cartilage degeneration. Cartilage has a very limited capability to repair itself. Remember that first cartilage cell where the blood supply is very minimal? Cartilage has a very limited capacity to repair itself once it's damaged. This cartilage has no direct blood supply and the chondrocytes are sequestered in that matrix and that prevents the migrations to the point of injury. This is a slide from a Division 1 softball player who had a full thickness cartilage lesion.

S2 10:29 This is the diagram of the anatomy of the cartilage. The white smooth surface on top, that's what we walk on, and the cells below show that the cartilage cells are very far from the surface and can in a very limited way affect healing. What are some of the surgical treatments we've been employing? Chondroplasty or debridement and that's cleaning it out. Just like on the slide, cleaning it out. What does that do? Makes them feel better. But does that really help them heal? Not a whole lot. 70% of the time in the US, we're doing chondroplasty and debridement, 20% of the time we're doing microfracture trying to stimulate some blood flow from the intramedullary canal. Then, about 10%, we're doing some allograft, autograft, or cartilage replacement therapy.

S2 11:12 Some of the biomaterials for cartilage and joint preservation have given us less than desired clinical outcomes because of the complexity of cartilage. It's very difficult to replicate. So the challenge is to select the technique that offers a significant advantage of the joint, it's cost effective, it's one stage, one surgery, and it's patient friendly. One of the best things we've found is osteochondral allografts. Because, as you can see, they provide that 3D reconstruction and space filling property for medium to large articular surface defects in the joint that we're treating.

S2 11:48 They perform the function of being a scaffold. It maintains that integrity of the joint so that there's no further breakdown and induces that cartilage differentiation again

through a cascade of signalling events. Again, through the regulatory cytokines, through those proteins that are released to heal those osteochondral allografts served as a scaffold, so all that can occur. This sets them apart from other cartilage regenerative or other joint restoration type of surgeries that we perform than the competitors for osteochondral allografts. We have found something that does help and it does provide a good joint restoration procedure. They're designed to be flexible. They take the shape and size of the defect and they mimic the heterogenecity of the articular cartilage. That cartilage is complex, we've got to try to reproduce it.

S2 12:40 What we're trying to do also is to reproduce the area that's effective. When you say a medium to large area, well, in someone who's very small, a 10 or 15 mm lesion which doesn't seem very big is a large relative surface area of that person's knee or that person's joint. Whereas in a much larger person, we may be able to perform a lesser invasive procedure. So we have to, number one, make good decisions for our patients, and if we're going to do a major invasive surgery, we have to make sure, is the postoperative state worthy of the preoperative condition?

S2 13:14 When we get allografts from someone else, they are usually obtained within 24 hours of asystole or within 24 hours of death. They are not sterilized, but they are aseptically procured. They undergo all the bacteriologic testing and they're available for implant at 14 days, and we usually like to implant them by 28 days. They are usually available for up to 42 days, but the recommendation is that the cartilage cells remain their viability for 28 days.

S2 13:43 What are the indications for OATS or osteochondral allograft transfer? Medium to large surface defects, osteochondritis dissecans, avascular necrosis, posttraumatic lesions, or failed primary treatment, meaning they've already had some other treatments and that's usually our indication. This is the treatment of that softball player that we had a while ago that we had put in an osteochondral allograft, and you can see how well it conformed, gave her a 3D reconstruction of her cartilage lesion. When we're looking at cartilage lesions, the conditions are usually not surface, they usually go deeper up into the marrow cavity with inflammation, pain, and edema up into the bone. That's why we put in a bone cartilage transfer to completely reconnect that whole area to expose it to the appropriate healing matrix, migration of cells, and then the differentiation into normal cartilage. You insert the grafts up to 18 to 35 mm, but most are about 18 to 20 mm. If you have a long oval lesion, you can snowman, you can put multiple grafts in. Something about the snowman thing. You know people say, "Oh, that looks kind of like a cobblestone road." Well, look in Europe, they've been putting cobblestone roads that have lasted hundreds of years, so those things work.

S2 14:59 This is a really good case that we had recently. A 21-year-old female collegiate basketball player, D1 basketball player, who was three years post anterior cruciate ligament reconstruction for insufficiency of her ACL. She had had two previous arthroscopic surgeries at a small town where they took out part of her meniscus but didn't address her ACL. As you can see, in her knee, she has marked deterioration of her medial compartment. You can see on her MRI how her deterioration also included the subchondral bone with pain, edema, and inflammation up into the bone. This is her arthroscopic photo where the cartilage is actually showing significant deterioration and degeneration. This is the open part of her surgery where you can actually see Grade 3-4 degenerative changes of her condyle. As we prepare the socket, we place an osteochondral allograft into the area of the injury. You can see the conformity, the reproduction, the regeneration, and the restoration of her joint.

	The before and the after shows a well-restored joint with an osteochondral allograft. These can be performed through small arthrotomies or arthroscopically, and this is often the most versatile and predictable treatment option for young active athletic patients with articular cartilage disease.
S2 16:30	These are two really exciting things. We are just scraping the surface on what the future holds in orthobiologics, but these are two of the things that we are currently using, clinically applying, and hopefully improving the quality of patient's lives. Thank you. [applause]
S1 16:51	Thank you Dr. Bramhall. We've got a couple questions here for you. If I can get my phone to turn around. This is from Ben F. at A&M. How much blood is required to obtain enough platelets for treatment of something such as a hamstring tear?
S2 17:04	We take 15 cc of a patient's blood from a simple stick. When we spin it down, the resulting ACP layer is about 4 cc of plasma. So injecting that into the area of injury is pretty simple.
S1 17:20	Cool. This is from [Mehwish B.?] Any negative side effects of ACP or the excess growth hormones being released? Can it cause any hormonal imbalances?
S2 17:30	We have not run into any hormonal imbalances or any significant complications with ACP because basically we're taking a patient's own blood product and returning it right back to them. We have to do it of course sterilely and aseptically, but we have had very few side effects, very few long-term problems, and no complications.
S1 17:51	Cool. This is from Reagan M. Is it possible that you could see an increase in injuries or re-injuries with PRP injections due to the faster healing?
S2 18:04	Pain is what drives this wagon. Probably, what we're going to see with platelet rich plasma injections is that someone is able to return to play, someone is able to get back on the field, they will know whether or not they can perform at a higher level or not. So they probably will not allow themselves to be injured unless it's just the fact that their injury was not completely healed.
S1 18:26	You chatted a little bit earlier about what more research needs to be done before this is done everywhere by everyone.
S2 18:32	Well, we need to make sure that we are understanding exactly what the long-term outcomes are, if we are having actually improvement of outcomes or if we're actually having just a short-term improvement with long-term deterioration. We also need to do further research on, again, what specific proteins, what specific cytokines need to go to the specific areas that we're treating.
S1 18:56	Super. Thank you, Dr. Bramhall. Please join me in thanking Dr. Bramhall. [applause]
S2 19:01	Thank you so much.