Intradiscal Leukocyte Rich Platelet Rich Plasma for Degenerative Disc Disease

Gregory E. Lutz, MD

KEYWORDS

• Degenerative disc disease • Chronic low back pain • Intradiscal Leukocyte-rich PRP • Intradiscal PRP

KEY POINTS

- CLBP is an unhealed wound.
- Bacteria play a role in degnerative disc disease.
- Leukocyte-rich PRP is a root cause treatment.

INTRODUCTION

If we could choose a single non-fatal medical condition to find a better solution that would make the greatest impact on global health it would be a solution for degenerative disc disease (DDD) - the number one cause of chronic low back pain (CLBP).

According to the numbers, low back pain is a pandemic; a condition that is prevalent globally, affecting millions of people throughout the world. In 2017 the *Global Burden of Disease* (GBD) study reported that the point prevalence (the number of people in the world at one point in time) of activity-limiting lower back pain about 580 million people worldwide—and chronic, low back pain is now regarded as the number one cause of disability globally.[1] This is the most comprehensive analysis of 354 medical conditions from 195 countries for over nearly three decades from 1990 to 2017. Not only was CLBP the number one cause of Years Lived with Disability (YLDs) recently, it has been the number one cause every year since 1990 and its incidence is only increasing with time.

The numbers reported are staggering in the US: as many as seventy million Americans have chronic lower back pain today. An estimated 80% of all Americans will experience disabling lower back pain at some point in their lifetime. What was thought of as a benign condition, really is not. Many patients have chronic recurrent episodes of LBP that just keep getting worse over time. In one study from 2012, researchers

Hospital for Special Surgery, Weill Medical College of Cornell University, Regenerative SportsCare Institute, 62 East 88th Street, New York, NY 10128, USA
E-mail address: lutzg@regensportscare.com

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published a study in *Physical Medicine and Rehabilitation* that tried to study this issue by surveying thirty different practitioners from a variety of specialties including physical therapists, chiropractors, and surgeons to look at the disease progression of CLBP in 600 new patients.[2] Here's what they found:

35% said their back pain required more than 3 months to improve.
54% reported more than ten episodes of severe, disabling back pain.
20% reported more than fifty episodes of severe, disabling back pain.

An epidemic is a condition that affects a large number of people within a region, and we have been dealing with an opioid epidemic here in the United States (US). Our mismanagement of LBP has only contributed to this problem; in the US, opioids are the most commonly prescribed drug class for patients with LBP and the rates of opioid prescribing is two to three times higher than in most European countries.[3] This is despite evidence that opioids, if they are to be used for managing LBP, should only be used for acute pain and for a short duration of time (a few days at most). There are no studies that support the long-term use of opioids for managing LBP.

Complications of addiction and overdose have risen in parallel with increased prescription rates for LBP. According to the CDC, from 1999 to 2019, nearly 500,000 people have died from opioid overdose involving both illicit and prescription uses.[4] More than 11.5 million Americans reported misusing prescription opioids in 2016.[5] In 2019, more than half of all global overdose deaths occurred in the US.[6] Unfortunately, this trend has only increased; last year overdose deaths from drug overdoses hit an all time high at over 100,000 from both illicit and prescription-based causes. While there are many factors that contributed to these numbers, the liberal prescribing of opioids for patients with CLBP has contributed greatly to this public health crisis. The need for opioid-sparing treatments for patients with CLBP has never been greater.

Having spent a large portion of my professional career at one of the busiest orthopedic hospitals in the world, I have unfortunately seen many patients with complications from spinal surgery. Many of these patients never had taken opioids but were started on them at the time of their surgery to manage their post-operative pain. Failing to achieve adequate pain relief from their surgery, their providers just kept prescribing opioid medications month after month. In a recent meta-analysis of patients after lumbar fusion surgery, investigators found that up to 63% of these patients were on long-term opioids (for > 3 months).[7]

This study also showed that opioid-naive patients were at increased risk for long-term opioids after their fusion surgery. What is equally concerning is, despite these poor outcomes, that the number of these types of lumbar fusions for degenerative conditions has increased according to one study 276% from 2002 to 2014.[8] Think about the millions of people suffering from their CLBP who then become dependent on opioids because we have either mismanaged their treatment with ineffectual nonsurgical treatments or potentially made them worse with surgery.

Drugs and surgery have not been the cure we have been seeking for the majority of patients with CLBP. The economic consequences are not just significant for the individual who fails to get back to gainful employment, but also for our healthcare system as a whole. In 2011 the respected National Academcy of Medicine estimated that just in the US the total direct and indirect costs of managing chronic pain, from all musculoskeletal conditions, to our economy ranges between $560 and $630 billion annually.[9]

Unfortunately, there has been low investment in research to find a cure for CLBP because many are unaware of its severity as most people do not die from it. The US National Institute of Health budget for research on cardiovascular diseases and cancer is dramatically larger than its budget for musculoskeletal conditions ($8.6

Billion combined vs only $754 million in 2018). In 2016 MSK disorders were the largest health expenditures in the US at $380 billion.[10] We spend more money treating MSK conditions than heart disease, diabetes, or cancer, but less than 10% of our research dollars are allocated to finding a cure for them?

The economic consequences of this irrational strategy are significant not just for the US, but for other countries around the world. The increased burden of non-fatal diseases such as CLBP on healthcare systems worldwide is posing considerable challenges to all healthcare systems not equipped to care for such complex and expensive conditions. While healthcare systems have made advancements in the management of fatal diseases, we have not made meaningful advancements in managing "non-fatal" conditions such as CLBP.

We need to reframe our thinking about the root causes of CLBP, and target our treatments directly at them if we want to truly find a cure. We need simple, safe, cost-effective, scalable treatments that are durable in their effect. Healthcare systems need to shift their approach to musculoskeletal diseases away from volume-based palliative treatments to value-based root cause treatments that create sustained improvements. Intradiscal leukocyte-rich platelet-rich plasma (LR-PRP) has the potential to be a value-based root cause treatment for many patients with symptomatic lumbar disc disease.

Getting to the Root Causes of Degenerative Disc Disease

There is mounting scientific evidence that chronic low back pain is nothing more than an unhealed wound inside the disc that frequently gets infected. When the disc tears it can become infected with a certain type of bacteria that impedes the healing process further called *Cutibacterium Acnes (C. Acnes)*.[11] Proper wound healing requires the migration of cells to the wound. Since the disc is the largest avascular structure in the body, its inherent capacity to heal after injury is poor.

The low blood supply to the disc is also why most medical and surgical treatments for it fail to provide sustained relief. They are not addressing the underlying root causes of DDD.[12] When a disc develops a tear that doesn't heal the wound can continue to propagate causing the disc to bulge. The bulge then begins to protrude if not addressed, the protrusion then can go on to a disc extrusion or even a disc fragment in the spinal canal. By this stage, the disc has degenerated and that segment of the spine can no longer function properly. Loading of that spinal segment begins to shift elsewhere.

The downward spiral can continue to get worse from here, and this is what we refer to as the "degenerative disc cascade" (**Fig. 1**).[13] The degenerative cascade demonstrates the importance of acting early with a regenerative treatment that heals the disc so that this downward spiral can be avoided. As you can see, wound healing is a necessary and dynamic process for restoring the normal architecture and functionality of tissue.

The downward spiral can continue to get worse from here, and this is what we refer to as the "degenerative disc cascade."[14] The degenerative disc cascade demonstrates the importance of acting early with a regenerative treatment that heals the disc so that this downward spiral can potentially be prevented.

The Role Bacteria Play in Degenerative Disc Disease

A microbiome is an environment of trillions of microorganisms also called microbiota or microbes.[15] These can be a collection of thousands of different species of bacteria, fungi, parasites, and/or viruses that live in harmony when you are healthy, but when out of balance can be harmful. This is referred to as "dysbiosis." Scientists are just

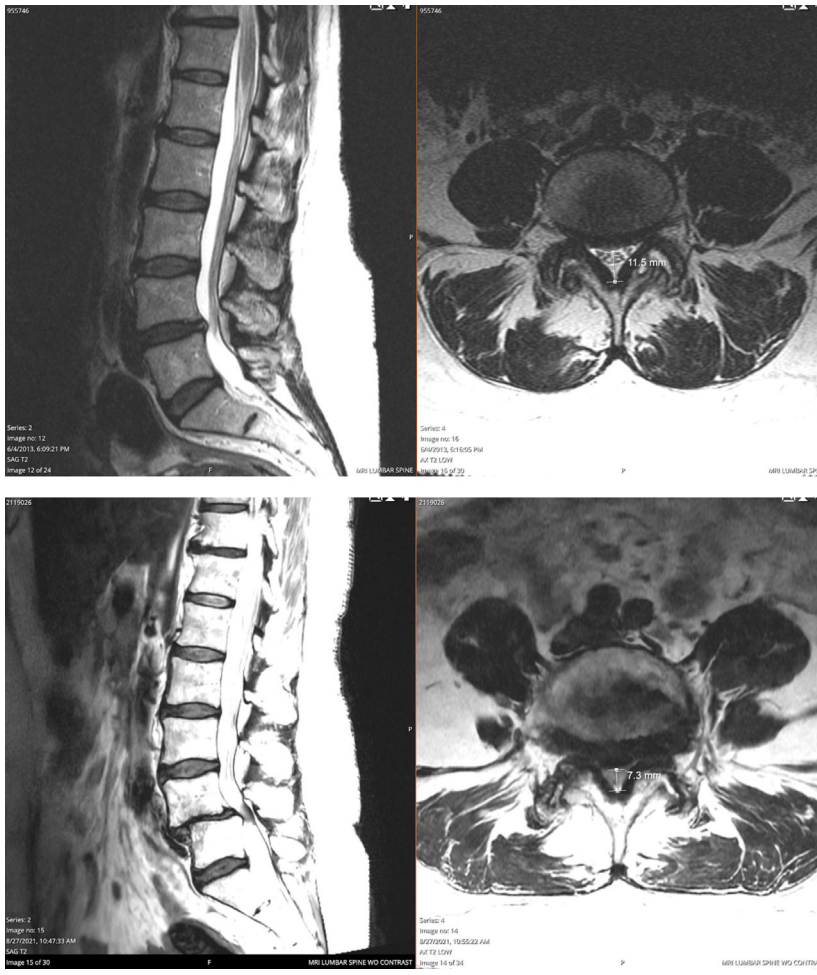

Fig. 1. These are MRI images of a patient of mine demonstraiting the "degenerative cascade." The MRI images on the left are T2- sagittal images of the lumbar spine and on the right are T2-axial images through the L4-5 level. The two MRI images on the top are from 2013. The two MRI images on the bottom are from 2021. Notice how the L4-5 disc has completely degenerated over timecausing progressive narrowing of the spinal canal (spinal stenosis).

realizing the importance of the microbiome not only for your overall health but also with regard to DDD.

A recent study out of Sweden looked at the role the intradiscal microbiome might play in degenerative disc disease.[16] The study examined 162 patients who experienced chronic, low back pain and had particular changes in their MRI (referred to as Modic Type 1 changes (MC1)). In a double-blind randomized controlled study (DB RCT), they separated the patients into two groups and gave one group a 6-month course of oral antibiotics and the other group a placebo. The subset of patients that received the antibiotics improved to a greater degree than the control group. Their findings suggested bacteria may be playing a greater role in the pain caused by degenerative disc disease than we have previously realized.

This issue was also studied in patients having spinal surgery where they harvested disc material, whether from a herniation or degeneration and cultured that material to see if any bacteria would grow. Sure enough, study after study showed that bacteria grew on the disc material and the most common bacteria was *C. Acnes.* At first investigators thought that this was from contamination, but that has later been refuted. The presence of *C. Acnes* infecting extruded and degenerative discs has been unequivocally demonstrated now by more sophisticated testing measures.

In 2016, a group of researchers in China, actually took bacteria (*C. Acnes)* harvested from human disc surgical samples and injected it into rabbit discs to see its effects.[17] When they examined the discs by MRI and under the microscope weeks later, these injected discs demonstrated exactly the same findings you see with degenerative disc disease and MC1.

So why not treat CLBP patients with oral antibiotics? There are a number of valid reasons:

1. The question of whether or not bacteria in the disc represents infection or contamination?
2. Contradictory reports on the efficacy of antibiotics to treat CLBP patients.
3. The potential that widespread use of systemic antibiotics would result in emerging global antimicrobial resistance and the perceived risk of propagating superbugs.
4. Systemic antibiotics can adversely affect your gut's microbiome creating other negative health consequences. Patients in these studies had to take the antibiotic for 100 days.
5. The penetration of oral antibiotics that rely on blood flow to get to the disc is unreliable.

If we view CLBP as an unhealed wound inside the disc that often becomes contaminated with bacteria, you can see how our previous treatments have been off the mark. With LR-PRP we are injecting billions of platelets with thousands of healing growth factors into the disc tissue to stimulate the wound healing process. We are also injecting millions of white blood cells that may also be suppressing the overgrowth of harmful *C. Acnes* or other bacteria that have penetrated those tears.

A Potential Regenerative Medicine Solution for Degenerative Disc Disease

What is regenerative medicine? According to the National Institutes of Health (NIH) it is an emerging area of science that holds great promise for treating and even curing a variety of injuries and diseases by using stem cells and other technologies to repair or replace damaged cells, tissues, or organs. However, it's not just about stem cells. There are many healing cells and proteins in your body that can stimulate your natural healing processes. Regenerative medicine offers not only the hope of a cure for degenerative disc disease, but also a potentially sustainable solution to the most common, most expensive, and most disabling condition globally: DDD. While there are many clinicians investigating a variety of intradiscal biologics, LR-PRP has the most compelling scientific evidence. It has also been the safest and most effective intradiscal biologic we have used in our CLBP patients.

In 2006, researchers at Rush Medical College in Chicago were the first to show that PRP had a beneficial effect on stimulating disc cells.[18] Scientists made PRP from pig's blood and then took their disc cells and cultured them in the lab in a broth of PRP where they measured its effects on cell metabolism. They demonstrated that PRP could stimulate the cells of the disc to turn on and produce collagen. The effect of the PRP was greater on the cells of the annulus fibrosus (AF) than the nucleus pulposus (NP).

At Tapei Medical University in Taiwan,[19] researchers also studied the effects of PRP on human disc cells taken from healthy volunteers. They cultured these cells in PRP and again measured its potential beneficial effects in the lab. Not only were these researchers the first to show the beneficial effects PRP could have on human disc cell metabolism, but they also demonstrated that PRP could decrease the rate of apoptosis. These promising studies showed that PRP caused beneficial effects on cell proliferation (coming to the wound), increased cell metabolism (producing proteins to repair the wound), and decreased cell death (keeping the disc healthy). In addition, researchers also showed that PRP could reduce the number of harmful pro-inflammatory cytokines in the disc that was responsible for pain and degeneration.

Pre-clinical studies like these gave us the support needed to embark on a clinical outcome study. We knew that PRP was not a treatment for every type of CLBP, so we set up very strict inclusion and exclusion criteria for our clinical study. We wanted to specifically study patients suffering from chronic, low back pain as a result of painful annular tears—internal disc disruption (IDD).

Severe disabling back pain that was unresponsive to conservative treatment.

Patients who otherwise would be candidates for a spinal fusion.

Once selected, we performed a discogram to confirm that their disc was the source of their pain and then randomized them into one of two groups: patients who received PRP after the contrast in the discogram and patients who received a placebo, which was just more contrast alone (**Fig. 2**). Then over an initial period of 2 months, we tracked their responses with an independent observer: degree of pain relief, functional improvement, and patient satisfaction. In total, we tracked forty-nine patients. For every two patients who received the PRP one patient was in the control group.

We also added a crossover group, after 2 months if the patient did not see improvement, we unblinded them. If they had received the control and had not improved, we then offered them the intradiscal PRP treatment.[20] In the first 2 months, patients who received the PRP were showing significant improvements in pain and function,

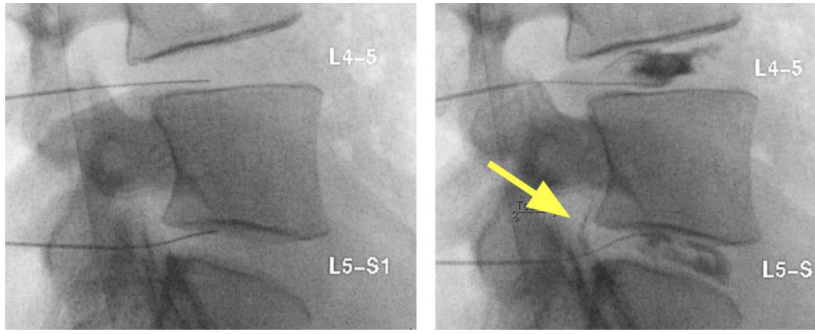

Fig. 2. The fluoroscopic images on the left are the needles placed into the two lower discs(L4-5 and L5-S1) without contrast injection. The images on the right are after contrast injection (black fluid inside the disc).In a normal discogram the contrast should stay in the center of the disc (the nucleus pulposus) and not leak out (L4-5 is normal). If you look closely at the lower disc there is a faint black line of contrast (arrow) outlining the back of the disc that represents a tear of that disc (L5-S1). If the patient experiences similar pain to what they normally have (what is referred to as concordant pain) when we see that tear fill with contrast then that is an abnormal discogram. The discogram helps us confirm the diagnosis of what is referred to as internal disc disruption when the MRI is inconclusive. In our study patients were then randomized to receive either mmore contrast or LR-PRP.

whereas the control group was not. Further, our patients who had been in the control group and then unblinded also saw significant improvement when they crossed over into the treatment group and received the PRP. We then followed the treated patients for years and surprisingly the majority of patients continued to do well from a single intradiscal injection of their PRP.[21,22]

We frequently analyze the MRIs of patients that we have treated. In many of the PRP-treated patients the tears improved significantly or disappeared within months of treatment (**Figs. 3** and **4**). Out of the 49 patients enrolled in the study, only six went on to a spinal fusion. So intradiscal LR-PRP effectively decreased the fusion rate by roughly 80% in this group of patients.

Since our initial DB RCT study in 2016, it has been encouraging to witness other investigators from around the world publishing similar encouraging results.[23–25] Akeda and colleagues recently published another DB RCT comparing intradiscal platelet release to corticosteroid injections in patients with degenerative disc disease. While there are several limitations to this study (no control, only 16 patients, corticosteroid injected with 2 mL saline, not an LR-PRP, no statistical difference in outcome), they found that over a 60-week period the PRP group did experience a greater degree of pain relief and functional improvement. This makes intradiscal PRP the only orthobiologic treatment option with two supportive DB RCT studies.

There was, however, a very recent single-blind randomized controlled study of intradiscal PRP that did not show a significant difference between the treatment group and the control group. If wecritically analyze this study, there were some serious flaws in their methodology that I believe confounded their conclusion that intradiscal PRP was no better than their control: they used a leukocyte- poor PRP, they injected only a small amount (1 cc) of a low platelet concentration PRP, they did not quantify what they injected, they did not use contrast to demonstrate flow into the annular tears, they used saline and antibiotics as the control, and they excluded a very important subset of patients (Modic 1 changes) from their study.

In our experience, it is exactly that subset of patients that have responded the best to intradiscal LR-PRP. In addition, using saline and antibiotics really are not a negative control. These agents have an antibacterial effect that may have improved some of the patients in the control group thereby confounding their results. The type of PRP used to treat degenerative disc disease really does matter. There continues to be a need for more rigorous research on intradiscal PRP for patients with degenerative disc disease.

While overall, the results we were achieving with intradiscal LR-PRP were impressive, there were still a fair number of patients that did not improve—roughly 40%.

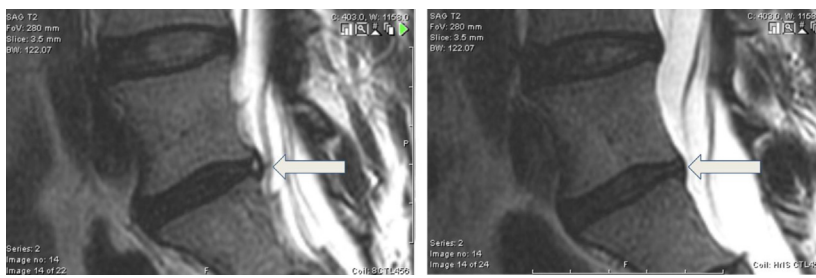

Fig. 3. These are magnified MRI images of lumbar spine from a side view (T2-sagittal images). The image on the left is before PRP treatment and shows a white line in the back of the disc (called a high-intensity zone (HIZ)). The HIZ on the MIR represents a tear inside the disc. The image on the right shows the HIZ healed 3 months after PRP treatment.

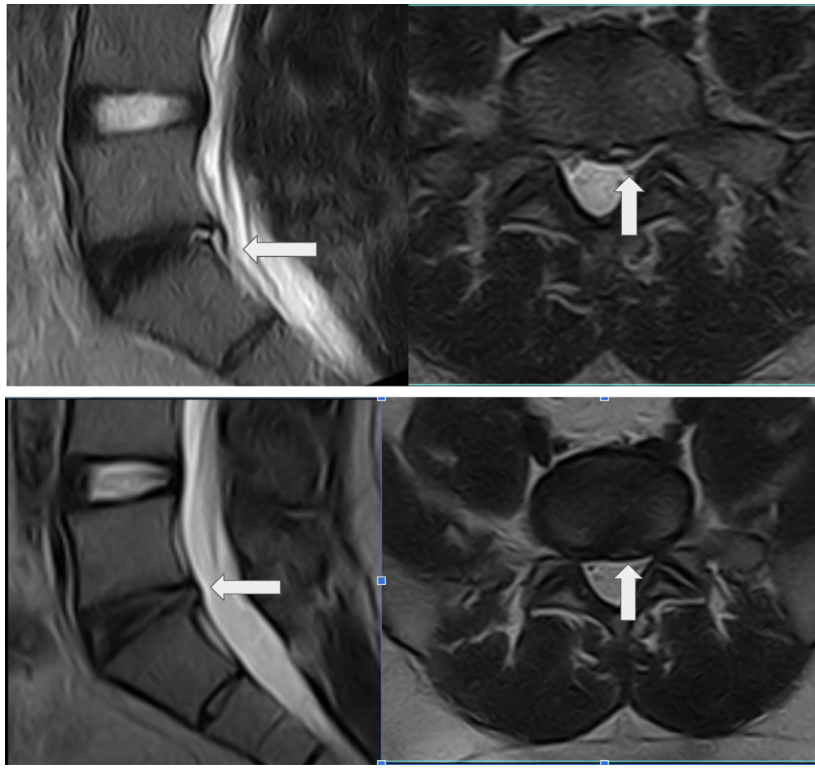

Fig. 4. These are magnified T2 sagittal and axial MRI images of lumbar spine from a patient who received intradiscal LR-PRP treatment. The images on top are before treatment and the images on the bottom are from 3 months after LR-PRP treatment. The images reveal structural improvement in the large annular fissure and a reduction in the size of the left-sided protrusion

During our first clinical study, we concentrated the platelets in our PRP preparation to approximately five times the normal baseline concentration. It seemed logical that more platelets would translate into a higher delivery of healing growth factors, but we needed to test that hypothesis: Could patients with more severe disc disease just require a greater degree of growth factors to obtain pain relief?

We found that we could achieve platelet concentrations of greater than ten times the patients' baseline—sometimes even higher—on a consistent basis by simply lowering the volume of plasma.[26] We then looked retrospectively at the number of patients we had treated over the past few years with this higher concentration PRP and found about forty-five patients who were over a year out. We were able to get data on thirty-seven of those patients, which is an acceptable follow-up rate of over 80%. Then we compared their results—pain relief, functional improvement, and patient satisfaction—to our historic DB RCT results to see if they were equal, worse, or potentially better. Not only did we see greater degrees of pain relief and functional improvement, but our patient satisfaction rates now reached over 80%.[27]

Unfortunately one of the patients in the study had a complication of a spinal infection.[28] She was infected with the same bacteria that you have already learned about - *C. Acnes.* In our attempt to concentrate the platelets to higher levels some patients received a leukocyte-poor PRP, and this is what happened in that patient. She had

to be treated with a prolonged course of intravenous antibiotics to recover and the infection destroyed that disc. So her case prompted us to go even further in our research to see what type of PRP is the safest.

Leukocyte-Rich PRP: Are We Killing Two Birds with One Stone?

We wanted to see what more we could do to reduce the risk so that the potential benefits of this promising new procedure would significantly outweigh the potential risks. We already knew from the literature and our own personal experience that *C. Acnes* was the culprit in many of the infections associated with intradiscal biologic procedures.[29] So we went back to the lab and cultured the *C. Acnes* bacteria in different types of PRP - leukocyte rich versus leukocyte poor. We cultured the bacteria for up to 48 hours and found that indeed the LR-PRP created greater kill rates than the LP-PRP (**Fig. 5**).[28] Now we have more evidence for what we believe to be not only the most effective type of PRP for degenerative disc disease but also potentially the safest. Our clinical experience reflects this finding. In more than 1000 disc injection procedures, we have not had any infections thus far using an LR-PRP inside the disc.

I believe we may actually be killing two birds with one stone with our intradiscal LR-PRP. Not only are we igniting the body's natural healing response in the disc, but the high levels of white blood cells in the PRP may also be suppressing the overgrowth of certain types of bacteria associated with disc degeneration.

A 32-year-old woman who presented to my office with severe LBP that had not responded to traditional treatments. What was unusual about her history was that she couldn't attribute the onset of her pain to any specific event. She rated the pain as an 8 out of 10. She had a 2-year-old daughter that she was having a difficult time caring for because she couldn't lift her. So we obtained an MRI of her lumbar spine to see what was going on. It revealed two degenerative discs with significant Modic Type I changes (MC1).

She had already failed oral medications, chiropractic care, acupuncture, and an epidural steroid injection gave only short-term pain relief. Spinal surgery she said

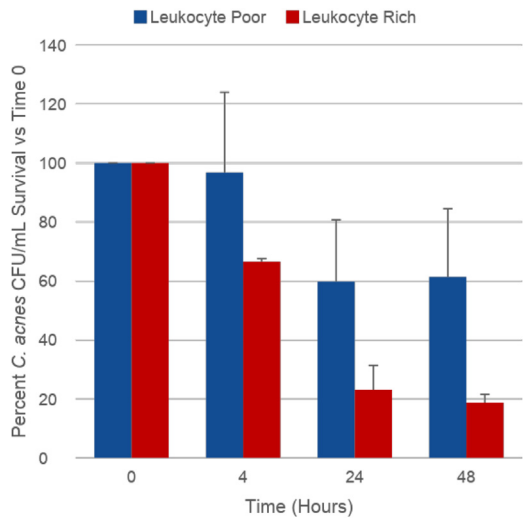

Fig. 5. Graph representing the change in C. Acnes survival over time in LR-PRP vs LP-PRP. LR-PRP creating a greater degree of suppression of C. Acnes growth in-vitro.

was a last resort. So we discussed the pros and cons of intradiscal LR-PRP in her case and she agreed to the procedure.

Working with an industry partner we have been able to develop a new PRP system that is now able to concentrate the platelets and white blood cells to higher levels than the best available commercial PRP system on the market. So to give you an idea of the powerful cocktail we are injecting, we injected over 5 billion platelets and 100 million white blood cells (WBCs) into each of her discs. Think about the 1000s of healing proteins in the platelets and the antibacterial power of the WBCs exactly where they are needed. Finally, a root cause treatment for so many patients with CLBP looking for a better alternative than spinal fusion surgery (**Fig. 6**).

At first, her pain was worse from the pressure of the injection into a painful structure and the inflammatory response these cells cause in the first few days, but within weeks she started to improve. When we repeated the MRI 3 months later and not only was the majority of her pain gone, so were those MC1 changes (**Fig. 7**).

We have treated many patients with Modic 1 changes. I do believe we may be killing two birds with one stone and that is why an intradiscal injection of an LR-PRP is the potential solution we have been searching for to treat DDD. So now that we've identified what we believe to be the safest, most effective intradiscal biologic - how else can we potentially improve patient outcomes?

Precision Cell Delivery

One of the things I have learned over the past three decades of performing interventional spinal procedures is that you need to deliver the therapeutic agent as close to the problem as possible to create the greatest benefit. Even with an epidural steroid injection, the best effects are when it is placed precisely between the inflamed disc and nerve root.

The problem when we perform an intradiscal injection is that we are placing a straight needle into a round structure. When we think about where most of the painful tears are, they are in the periphery of the disc. So we are often unable to get a straight needle into that area consistently. Most of the time the needle is placed in the middle of the disc and then we inject and hope that the LR-PRP flows into these tears. Hope is not a strategy we like in medicine. We prefer to have a reliable means of precisely placing the cells as closely into the tears as possible so with an industry partner we developed the first intradiscal curved catheter (**Fig. 8**).

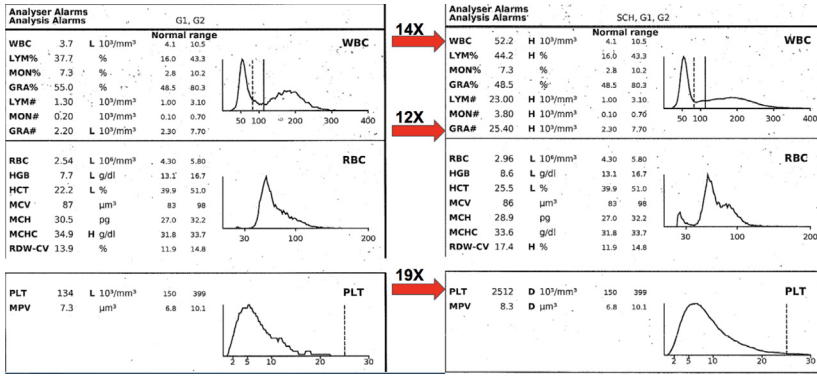

Fig. 6. Hemocytometer measurements of baseline peripheral blood and final LR-PRP concentrations.

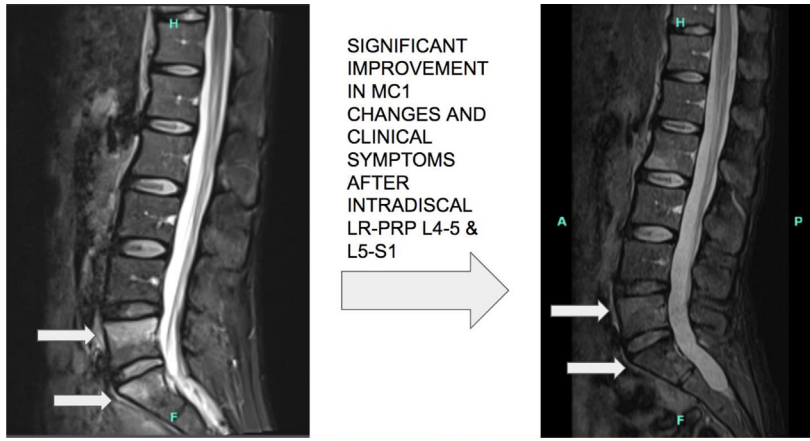

Fig. 7. T2 sagittal MRI images pre and postintradiscal LR-PRP demonstrating improvement in the Modic 1 changes

In our first in-human test, we used it on a 62-year-old gentleman with an 8 year history of low back pain in his right leg who failed conservative treatments. His MRI from 2013 revealed a right foraminal HIZ at L4-5 which was unchanged in his most recent MRI from 2022 (Fig. 9). Three months posttreatment not only were his symptoms completely resolved, but there were documented structural changes in his MRI that showed the resolution of the HIZ (Fig. 10). What was so interesting about this case were the almost immediate annular changes that occurred within 4 weeks of the intradiscal injection (Fig. 11).

A Promising Future

Chronic back pain is usually nothing more than an unhealed wound that can be colonized with a certain types of bacteria that can further contribute to degeneration of the disc. Intradiscal LR-PRP is one of our first treatment options that actually targets directly the root causes of CLBP for many. Treatments that just relieve pain and do not create healing structural changes are only palliative, not curative. This is a complete paradigm shift in how we are managing CLBP patients in our clinical practice.

There are many different types of autologous orthobiologics clinicians are injecting into the disc. There is bone marrow aspirate, bone marrow concentrate, leukocyte

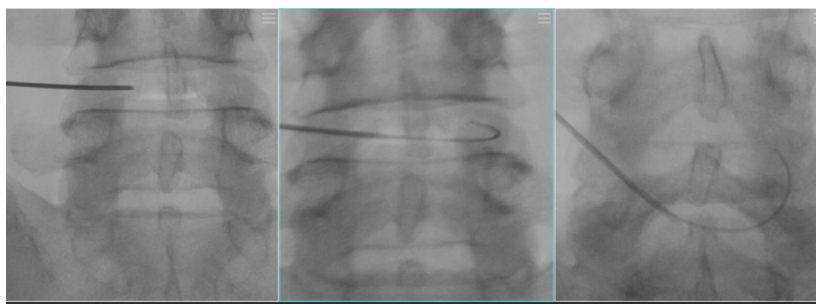

Fig. 8. Fluoroscopic images of the intradiscal insertion of a curved catheter to precisely deliver LR-PRP into the right posterolateral corner of the L4-5 disc.

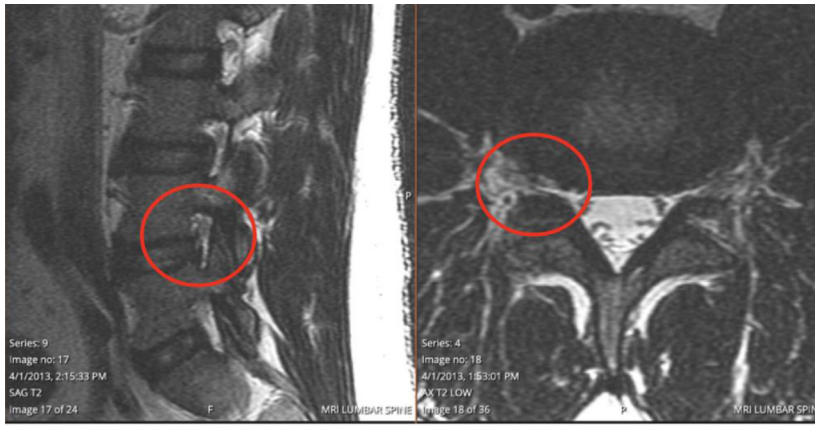

Fig. 9. T2 sagittal and axial MRI images from 2013 revealing an HIZ and a small protrusion effacing the right L4 nerve root.

poor PRP, platelet lysate, etc….I believe based on over a decade of clinical experience performing these procedures, that the infection risk is the least with LR-PRP. LR-PRP is also the only orthobiologic option that has DB RCT support and long-term outcomes data. We have used intradiscal bone marrow concentrate in the past, but have concerns regarding an increased rate of spondylodiscitis for reasons we do not fully understand.[30]

For intradiscal LR-PRP to become the standard of care for patients we will now need multi-center studies demonstrating its efficacy for specific subsets of patients with DDD.[25] We will also need a quality control system that can provide a range of consistency with the LR-PRP preparation method. PRP is relatively easy to quantify quickly on-site when compared to other types of cell therapies. With the use of a hemocytometer one can easily calculate the delivered dose of platelets, white blood

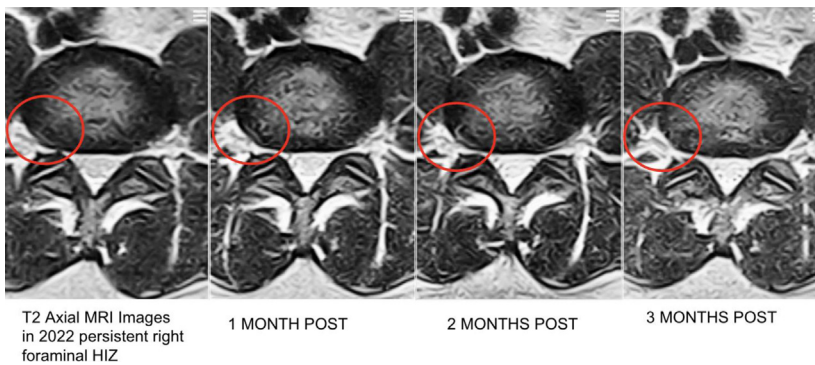

Fig. 10. Serial T2 axial MRI images over time demonstrating structural changes of the right-sided annular fissure and protrusion post-intradiscal LR-PRP precisely delivered with a curved catheter.

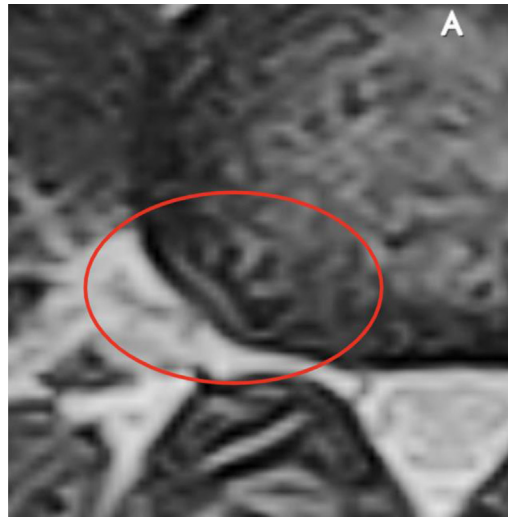

Fig. 11. Magnified T2 Axial MRI image of right foraminal HIZ demonstrating structural changes 1-month postintradiscal LR-PRP delivered precisely into the region with acurved intradiscal catheter.

cells, etc… by simply taking small aliquots of the baseline peripheral blood and the PRP.[25] This is important to also establish a dosing range that can ultimately be linked to clinical outcomes for optimization. What gets measured gets managed.

The power of regenerative medicine is real, and we are in the early stages of a paradigm shift in how we can better manage this global condition. It's going to take time, but this shift is already beginning to happen. We do not yet know for sure if our regenerative treatments halt the progression of degeneration, but it is my belief based on the patients we have treated that it certainly has the potential. Time will tell. Wouldn't that be remarkable if these treatments not only provide substantial pain relief - but also halt or even reverse disc degeneration (**Fig. 12**).

No single drug can come close to mimicking what your body already does so well. The healing process is not a solo, it's a symphony of cells and proteins that are distinctly yours. Our capacity to heal is so much greater than we ever imagined. Our cells are "naturally intelligent" and are perfectly designed to heal each of us.

However, for this paradigm shift to really gain momentum, it is going to be so important for physicians to collaborate not only with the patient, but also with each other, with researchers, with the FDA, hospitals, insurance payors, politicians, and industry to better improve the safety and clinical outcomes of these regenerative procedures.

These procedures need to be democratized so that anyone suffering from CLBP can have this treatment option before crossing the rubicon into the surgical maze. We will need to overcome the reimbursement challenges and provide payors with convincing data on the potential benefit of intradiscal LR-PRP over the current standards of care.

Our healthcare system has over-complicated the CLBP problem and mismanaged patients for decades. It has placed patients at unnecessary risk with poorly conceived, ineffectual treatments that have wasted precious healthcare resources. Drugs and surgery have a very limited role in the management of CLBP. It's been rare to see in my 30 years of practice a patient totally cured from these types of therapeutics. While

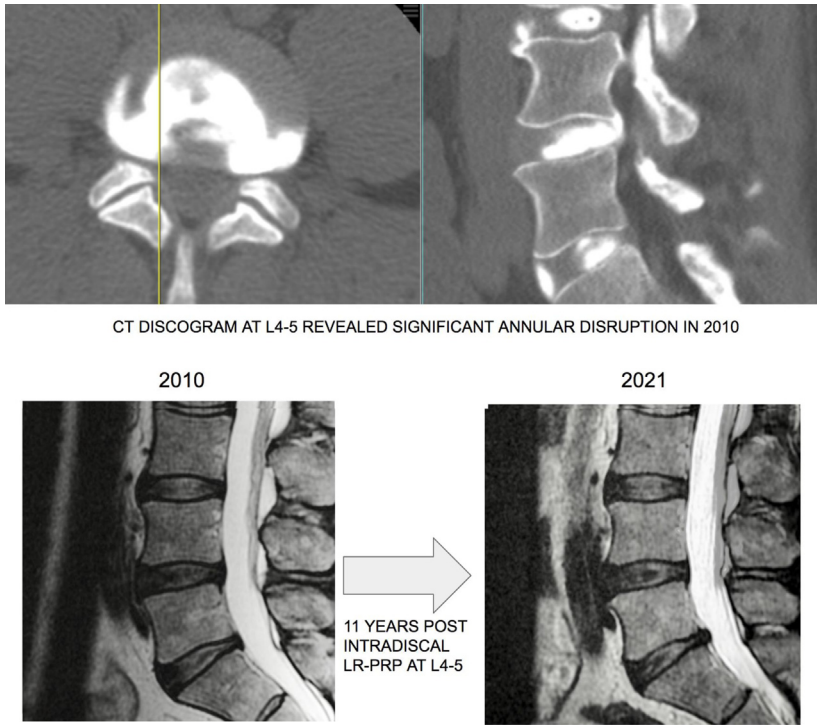

Fig. 12. Images on top are CT-discogram axial and sagittal images of the first patient I ever treated with intradiscal LR-PRP revealing significant annular disruption of the L4-5 disc. Images below are T2 sagittal MRI images from the same patient treated from before and 11 years after treatment showing no signs of disc degeneration at the treated L4-5 level.

the opposite is now true with the patients we've treated with intradiscal LR-PRP. Many of these patients have had no further treatments, and their MRIs have demonstrated healing of their degenerated discs for years. Further studies are necessary to analyze structural changes in the MRIs of patients treated with intradiscal LR-PRP.

My prediction is that regenerative medicine is going to change how we manage patients with CLBP in the years to come for the better. Think about the millions of lives improved and the billions of healthcare dollars saved when a simple outpatient injection of your own cells replaces many of those costly hospital-based spinal surgeries. Spinal surgery will still be needed for some patients with more severe later stage degenerative disc disease that has associated spinal deformity, but nowhere near how many are currently being performed. Think about how intradiscal LR-PRP kills two birds with one stone, finally offering patients an opioid-sparing treatment option that is readily available and scalable. This is value-based musculoskeletal care.

Low back pain should be nothing more than a hiccup in life, rather than the wrecking ball it is for so many. Unfortunately, our traditional treatments have failed to "fix" low back pain. Mainly because only recently have we really begun to understand the underlying mechanisms that stop a disc from healing. Our understanding of why LBP becomes chronic has been rudimentary at best. So it's exciting to finally identify new and potentially reversible factors contributing to degenerative disc disease that we can

target with regenerative medicine. If there is a cure for LBP, it lies within this realm of regenerative medicine.

The Regenerative Medicine Revolution is already underway and it is better for patients if we all collaborate to make these treatments as simple, safe, and effective as we can. While many companies are searching for proprietary cell preparations or pharmaceuticals to stimulate disc healing, it will be difficult to mimic what the body has evolved to do so well on its own over thousands of years. In the time of personalized and precision medicine, what could be more personalized and precise than the use of your own cells to heal your disc?

When you look at the risk/reward comparison with our historical surgical treatments, there really is no comparison. These treatments in the skilled hands of an interventional spine specialist are extremely safe and effective. While there are numerous promising regenerative strategies in development LR-PRP is FDA compliant and available for our patients now. As molecular therapies, biomaterials-based tissue engineering, and other cell therapies evolve - these novel therapies will have to demonstrate better results than what we have already shown with LR-PRP to gain adoption by key opinion leaders.

Finally, we need to think of the disc as the "heart" of the spine. It should not be cut out or fused, it should be healed and preserved. Maybe if we begin to treat it as such, we will have a chance to preserve the spine and end back pain for many. We are on the cusp of an exciting new era in regenerative medicine that will change the way we manage LBP so that it doesn't have to become chronic. Intradiscal LR-PRP is a promising initial regenerative treatment choice to start this paradigm shift. It is currently the safest orthobiologic intradiscal choice with the most supportive pre-clinical and clinical data.

CLIONICS CARE POINTS

- Intradiscal orthobiologics are a promising new treatment for degenerative disc disease.Intradiscal LR-PRP is our preferred orthobiologic because of its safety, efficacy, and pre-clinical support.Further research is needed to optimize cell concentrations and delivery to improve clinical outcomes.

DISCLOSURE

The Authors have nothing to disclose.

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