Regenexx®

FAT STEM CELLS VS. BONE MARROW STEM CELLS

THE SOURCE OF YOUR STEM CELLS MAKES A BIG DIFFERENCE

Bone marrow aspiration harvests bone marrow stem cells, while liposuction harvests fat stem cells. When considering stem cell procedures in orthopedics, you have to ask these questions: Which stem cells are best supported by the data? Which stem cells are the most effective at repairing and healing bone and cartilage? Which stem cells best treat arthritis? Which procedure is less invasive and safer? Of the stem cell studies being conducted in orthopedics today, 99% are on bone-marrow-derived stem cells, while minimal research has been done on fat stem cells.

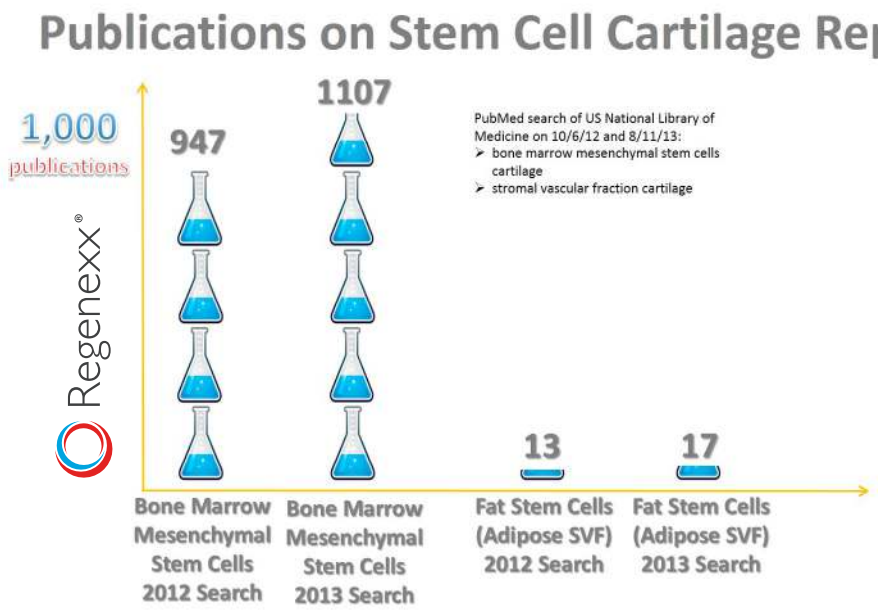
Why is using fat stem cells in orthopedic applications a big deal, and why are bone marrow stem cells the better option? Supporting research data, legal and safety issues, and the effectiveness of the stem cells are some of the big reasons it matters where your stem cells come from.

The Amount of Bone Marrow Stem Cell Data Far Exceeds Fat Stem Cell Data

When Regenexx first started studies using stem cells in 2005, we looked at two possible sources—fat tissue (adipose) and bone marrow aspirate. After a thorough search of the U.S. National Library of Medicine, we learned that there was very little, if anything, published in human or animal models that showed that fat stem cells would be effective for things like healing cartilage. There were, however, hundreds of publications on bone marrow stem cells healing cartilage. At that point there was simply no contest; bone marrow won hands down.

When we first began seeing fat stem cells (also known as stromal vascular fraction, or SVF) being injected into knee and hip joints, we were confused as we knew the literature was pretty clear. With the proliferation of clinics offering fat stem cells for whatever ails you—from arthritis to ALS to antiaging—Regenexx wanted to revisit this topic.

In 2012, I had created an infographic on the different stem cell types used in orthopedic stem cell procedures. Several searches of the U.S. National Library of Medicine were made to give readers an understanding of what was published on cartilage repair. At that point there was a massive amount published on bone marrow stem cells used to treat arthritis and very little published on fat stem cells. Since this was still a question frequently asked by patients and doctors a year later, I downloaded more research on bone marrow versus fat stem cells in 2013. The graph below shows the number of citations listed in the U.S. National Library of Medicine under fat stem cells or bone marrow stem cells for cartilage repair for both the 2012 and the 2013 searches.



During that year, did fat stem cells begin to catch up and close the gap on their huge orthopedic research deficit? No. As the graph above clearly shows, studies on bone marrow stem cells far exceeded those on fat stem cells. In 2013, while there were more than 1,100 research articles published on using bone marrow stem cells in cartilage repair, during the same time frame, there was a paltry 17 on using fat stem cells for the same purpose.

The conclusion? There simply isn't enough research to support using fat stem cells as a primary source to treat arthritis. Ignore the hype, ask the right questions, and choose a well-researched procedure you can trust.

The Data Show Bone Marrow Stem Cells Are Better for Orthopedic Applications

The issue of fat versus bone marrow stem cells to treat arthritis can be a contentious one that can cause normally stoic doctors to get a bit riled up. For us, we simply let the medical literature do the talking, and anybody that spends any time reading the research knows that bone marrow stem cells to treat arthritis has a huge advantage over fat.

https://www.regenexx.com/stem-cell-type-orthopedic-infographic/

In 2011, I reviewed the medical research in the U.S. Library of Medicine, going back to 2007, on the comparisons of fat versus bone marrow stem cells for cartilage repair. The infographic above on the research paper shows which stem cell type is better, this is a 2015 update to that 2011 data. I found 13 studies showing bone marrow was better than fat and no studies showing the opposite. At the end of the day, there isn't much of a comparison—stem cells from fat pale in comparison to those from bone marrow for cartilage repair by a score of 13 to 0.

There just isn't enough published to support fat (adipose) stem cells as a good source for orthopedic use. On the other hand, there's a massive amount of data showing that bone marrow stem cells are the better choice for orthopedic applications. Let's look at a few of these studies.

Study Shows Bone Marrow Stem Cells are Better for Cartilage Repair

One study shows that bone marrow stem cells are more cartilage producing than fat stem cells. This study also shows bone marrow cells were better than those obtained from periosteum (the covering of a bone), synovium (the lining of a joint), and muscle.

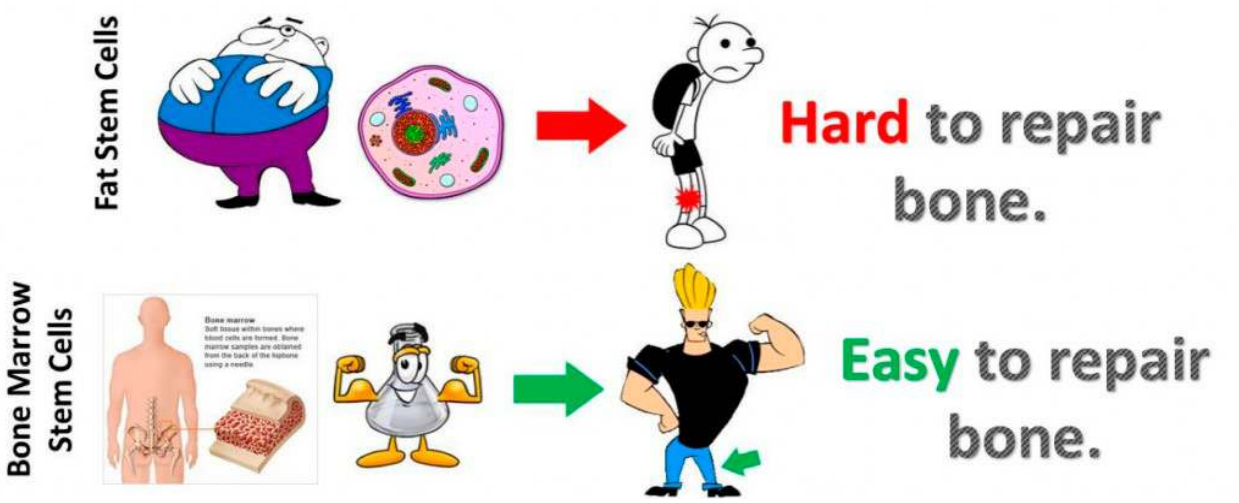
The authors concluded, "The bone-marrow-MSCs produced much more cartilage matrix than that of other groups. Gross and histological grading scale indicates that the defects repaired by MSCs isolated from bone marrow are superior to that repaired by MSCs isolated from periosteum, synovium, adipose tissue, and muscle ($p < 0.05$)."

Fat stem cells don't like to become cartilage, and fat stem cell knee injections are, therefore, not very effective. All stem cells can become other tissue or orchestrate tissue repair. While bone marrow stem cells just need a little nudge to head in the direction of cartilage repair, fat stem cells need a sledgehammer to get there. Case in point is this research paper showing that the researchers had to go through great machinations to get fat stem cells to repair cartilage. In this study the researchers found that stem cells from fat release certain chemicals that can inhibit cartilage formation. Their solution? Use antibodies against the bad chemicals to neutralize them. The obvious question is, why not just use bone marrow stem cells to repair cartilage?

Study Shows Bone Marrow Stem Cells are Better for Bone Repair

Another study shows that bone marrow stem cells are better at repairing bone than fat stem cells. This fits with many other studies showing that bone marrow stem cells are much better at repairing orthopedic tissues than fat stem cells. This, again, makes sense, as why would stem cells from belly fat have any role in repairing bone?

While fat stem cells from your belly or thigh are good at repairing local tissues, like skin, nerves, and blood vessels, fat stem cells are poor at repairing and producing bone.



Fat stem cells have exploded in use the past several years. There are now hundreds of clinics around the United States where you can find these procedures being used to treat arthritis. While fat stem cells have some amazing anti-inflammatory properties that have been shown to be a godsend for patients with chronic neuroinflammatory diseases, like multiple sclerosis (MS), they have been less convincing in their effects on orthopedic problems, like arthritis.

For orthopedic injuries, one of the things that you want fat stem cells to accomplish is healing, or turning into bone tissue. Many severe arthritis patients need bone as well as cartilage, and other diseases like nonhealing fractures and osteonecrosis would benefit greatly from stem cells that could help repair or become bone.

In one study, the investigators took both bone marrow and fat stem cells and gave them a stimulus to turn into bone. While they got bone progenitor cells and bone formation out of bone marrow stem cells, they were unable to get the same thing to happen with the fat stem cells. In essence, they couldn't get the fat stem cells to produce bone without some very heavy-handed tricks.

All of this is consistent with many other studies out there. In the world of cell therapy, the tail wagging the dog happens when physicians experienced in liposuction use fat stem cells to treat orthopedic tissues because that's the weekend course they took, not because they are the best cells for the job!

Study Shows Bone Marrow is Better for Bone and Cartilage Repair

In another study, out of China, there is more data showing that bone marrow stem cells outperform fat stem cells for both bone and cartilage repair.

The study set up a direct head-to-head comparison of the biological characteristics of adipose and bone marrow mesenchymal stem cells (MSCs) to evaluate their potential for regenerative-medicine applications. After evaluating many different characteristics for use in cell therapy, their findings demonstrated that the two different types of stem cells had very different differentiation potential. Adipose MSCs grew more easily and had better immune-system potential. Each source contained different but equal growth factors. Bone marrow MSCs had a much greater biological advantage in osteogenic (bone making) and chondrogenic (cartilage making) differentiation characteristics. They concluded that the different characteristics should be considered when selecting the tissue source of MSCs for different regenerative-medicine applications.

The general bone marrow versus fat stem cell debate makes sense in that MSCs are plentiful in both tissue sources. It's when that debate narrows to specific applications that it loses steam. Specific types of stem cells simply do different things, and while there are more MSCs in fat than bone marrow as a percentage of nucleated cells, there are many fewer nucleated cells in fat—meaning both have similar stem cell content.

The conclusion? The research is clear and points in one direction for orthopedic applications—bone marrow stem cells. We now have 13 studies showing that bone marrow stem cells are better for orthopedic purposes than fat stem cells. We've tested both adipose and bone marrow stem cells extensively in the lab and have used both in treatment. We found the use of, or addition of, adipose stem cells provided no benefit over bone marrow stem cells. If you're told that fat stem cells are the way to treat your knee, know that the published data doesn't support that claim; however, there is a massive amount of data published showing that bone marrow stem cells are the way to go.

Liposuction vs. Bone Marrow Aspiration

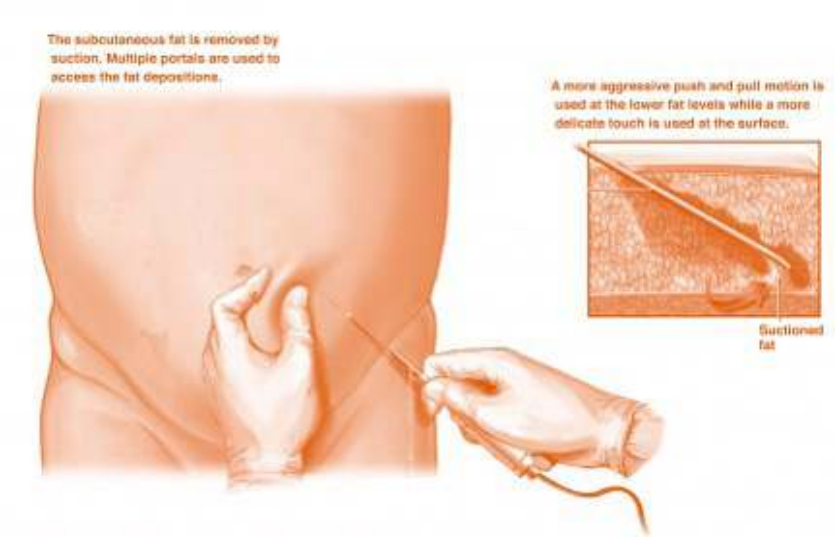
We know the data support bone marrow stem cells for orthopedic applications, but what about the harvesting techniques? Liposuction is used to harvest fat stem cells, while bone marrow aspiration (BMA) is used to harvest bone marrow stem cells, and there are numerous research articles and websites suggesting that a BMA has a high complication rate when compared to liposuction. But is this true?

While we use fat for structural grafts in our Regenexx-AD procedure, we have never considered liposuction safer or more comfortable than a BMA procedure. We have studied the discomfort of properly anesthetized patients undergoing a BMA to obtain stem cells, and found it to be very comfortable for the vast majority of people. We feel the discomfort during liposuction is similar.

On the complications side, while we've seen very few issues with both procedures, they have different levels of invasiveness. Since liposuction involves placing a larger needle or probe into the fatty area under the skin and moving that probe about to break up the fatty tissue (which can potentially harm arteries, nerves, and other structures), we consider liposuction more invasive than a BMA. This is because a BMA involves placing a needle through the skin in a direct route into the bone (more like a complex blood draw). However, what does the research say about the safety of these two procedures?

Our analysis of papers published in the U.S. National Library of Medicine on both techniques revealed that the complication rate of a bone marrow aspiration is far less than liposuction. Depending on the study, liposuction is approximately 4–100 times more risky in terms of reported complications than a bone marrow aspirate. While serious complications like death, skin necrosis, permanent scarring, and blood clots are reported for liposuction, none are reported for bone marrow aspiration (BMA). To be completely fair, the type of limited liposuction performed for an orthopedic procedure is much less invasive than the types reported in many of the studies below. However, the statement that a bone marrow aspirate used to obtain stem cells is more invasive than liposuction is not at all supported by the medical research. Let's review the procedures a bit more in depth.

To get fat through a mini-liposuction, you need to first use a scalpel to open a small incision in the skin. This isn't at all required for a BMA as the needle is just inserted into the skin like any other needle. In the liposuction, the whole goal is to disrupt large amounts of normal tissue. In fact, the stem cells live around the blood vessels, so you have to chew up as many blood vessels in the fat as possible to get a good stem cell yield. This involves placing a small wand-like device under the skin and into the fat and moving it back and forth (through much resistance) to break apart large swaths of tissue with suction, sucking the broken tissue and blood vessels into a syringe.



In comparison, the bone marrow aspiration simply involves directing the needle under X-ray to the desired area of bone. The needle is then turned back and forth a few times to enter the bone (which is like hard plastic). Then the doctor simply draws the BMA (which looks like blood) into the syringe, like a common blood draw.

The complication rates (revealed in the next section) for these two procedures tell the rest of the story.

The conclusion? At the end of the day, rooting for one type of stem cell because that's all the doctor knows how to harvest is like rooting for only one stem cell sports team and not recognizing that all stem cell teams have their positives and negatives. For example, stem cells derived from fat are much better for cosmetic work and structural fat grafts than stem cells derived from bone marrow. Likewise, stem cells derived from bone marrow are much better for bone, cartilage, and other orthopedic purposes. Use the stem cell source that fits the job!

Complication Rates of Liposuction vs. BMA

In a study of 700 patients undergoing BMA, no complications were reported. In another study, 49 patients were studied who underwent large-volume bone marrow aspiration (>1,000 ml versus the 70 ml we usually harvest), and there were no complications. In one United Kingdom study, out of 20,323 bone marrow aspirations, only 15 adverse events were reported (complication rate of less 0.01% or less than 1 in 1,000). These aspirates were much more aggressive than we would perform for a stem cell harvest.

Out of 2,398 superficial liposuction cases, overall complication rate was 8.6% (208 patients). There were 4 cases of skin necrosis (the skin died off) and 2 infections. The safety of tumescent local anesthesia liposuction in 3,240 patients was studied and complications were found to occur in 9 patients, or 1 in 360. In another study of 609

consecutive patients undergoing ultrasound-assisted liposuction the complication rate was 1.36%. There were 2 cases of low blood pressure and 7 local complications (3 fluid collections—seroma, 3 cases of dermatitis, 1 case of excessive bleeding). There are various single-case reports found including death, blindness, severe scarring, and serious blood clots due to liposuction.

The conclusion? Liposuction is not a safer procedure than bone marrow aspiration, and fat stem cells are not easier to access. A liposuction to obtain fat stem cells is about one thousand times more dangerous than a bone marrow aspiration, so don't believe fat-stem-cell advocates when they claim that a bone marrow aspiration procedure is so invasive.

Are Stem Cell Yields Higher in Fat?

You may also find fat-stem-cell advocates claiming liposuction yields far more stem cells than a bone marrow aspiration, and while there are more mesenchymal stem cells (MSCs) in fat than bone marrow as a percentage of nucleated cells, there are many fewer nucleated cells in fat. This claim is based on flaws by the fat-stem-cell industry in calculating simple mathematics.

I've seen claims as high as 2,000 times more MSCs in fat than in bone marrow. These inflated numbers can also happen when less-sophisticated flow cytometry devices run by scientists who should know better erroneously count a fat or oil droplet as a stem cell. Confusion is also abundant in how best to count stem cells in the first place. For example, do you count them using a simple culture technique called CFU analysis or with a more sophisticated machine called a flow cytometer? Each has its strengths and weaknesses. One of the problems with comparing fat and bone marrow stem cell counts is that since the stem cells from each source grow at different rates, using a culture-based method where you grow cells (the CFU method) is fraught with apples-to-oranges error issues. Hence, for this discussion we will use flow cytometry to discover the real differences between fat and bone marrow stem cell content. This is a complex machine that counts the markers on the stem cells, one by one, but very quickly.

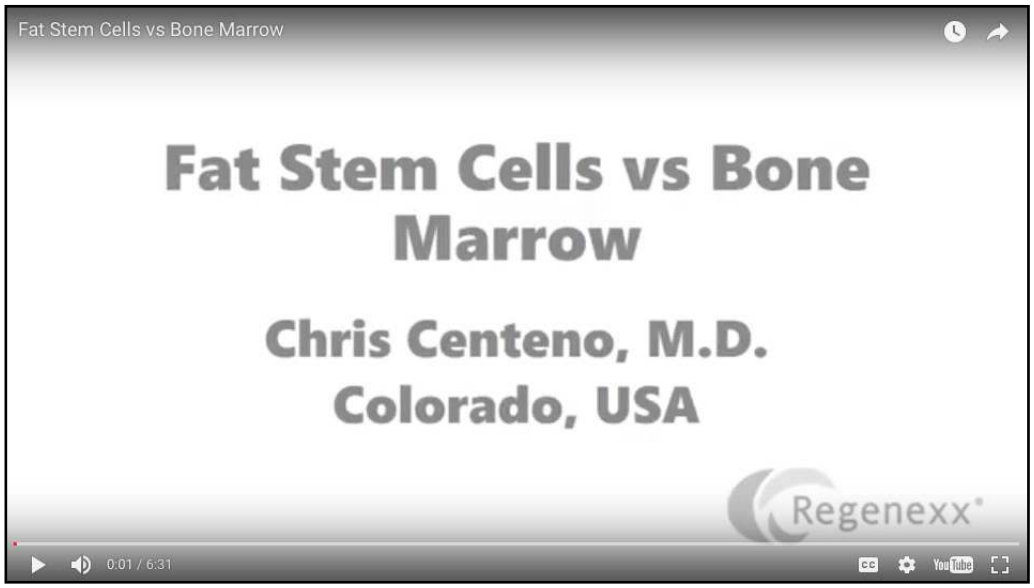
First, let's just look at MSC content. MSCs represent about 1–5% of the total nucleated cells in fat versus 0.1–0.5% for bone marrow. This has not only been published, but it is also consistent with what we see in our lab when we look at the MSC content of both tissues. That is 10X more MSCs in fat than bone marrow. However, we have to be careful with that number, as there are many more nucleated cells in bone marrow. How many more? In one study, each ml of bone marrow had about 100 times more nucleated cells per mg (roughly a ml) of fat. In fact, it's this huge disparity in the total number of cells in each tissue that causes the erroneous comparison numbers discussed above. For example, if you try to look at the percentage of stem cells out of bone marrow that form colonies in culture (the CFU number), it's going to be minuscule compared to fat. However, this is expressed as a percentage of total cells, which are 100 times greater in bone marrow! Even the flow cytometry data above is expressed as a percentage of the total cells being counted, with

there being many more cells per ml in bone marrow. The numeric advantage of a higher percentage of MSCs relative to the total cells in fat is washed away by the fact that there are far fewer total cells in fat. Now let's look at the other stem cells found in bone marrow that aren't present in fat.

Bone marrow contains not only MSCs, but also hematopoietic stem cells (HSCs), which are quite good at muscle repair. These are not found in fat in any significant quantity. How many of these HSCs are there in bone marrow? They represent about 1%+ of the total nucleated cells. For our proprietary method of isolating stem cells from bone marrow, on average we get around 150 million total cells per ml of isolate injected (that's only from one of the fractions in bone marrow that we isolate). That's 1.5 million HSCs per ml injected. Bone marrow also has endothelial progenitor cells (EPCs), which are key in creating new blood supply, which is often critical for chronic orthopedic injuries, many of which don't heal because they happen in areas of poor blood supply. Finally, bone marrow also contains the newly discovered OCR cell which is specific for orthopedic tissue repair.

Does fat really have 2,000 times more stem cells than bone marrow? Nope. Does it have 500 times or even 10 times more? Nope. In fact, if you adjust for the fact that there are 100 more cells per unit volume in bone marrow than fat and that bone marrow has many more other useful stem cells than adipose tissue, the concept that fat has any more stem cells than bone marrow seems like a weak argument. In addition, once you add in the fact that bone marrow has three stem cell types critical for orthopedic tissue repair that aren't present in abundance in fat, the "fat has more stem cells" argument gets even weaker. The HSCs in bone marrow alone (without the EPCs and OCR cells) shows that bone marrow has more orthopedic-injury-relevant stem cells than fat. If you then look at studies showing that bone marrow MSCs outperform fat MSCs for things like cartilage repair, the case for using fat stem cells to treat orthopedic injuries becomes extremely weak.

Watch my video below to learn more about these stem cell counts.



Stem cell counts in fat can also be negatively affected by anesthetics. This study concluded that the most common local anesthetics (used by 99% of all physicians who use fat stem cells) used in liposuction kill stem cells. Healing can't happen if your stem cells are DOA.

The conclusion? The myth that fat has dramatically more stem cells than bone marrow seems to have been perpetuated by adipose stem cell advocates who began to compare the percentage of MSCs in fat to bone marrow using the proportion of MSCs to total cells found in the tissue. These proponents left out a critical number—that bone marrow has 1,000 times more cells per unit volume than fat. They also left out the fact that there are other relevant stem cells in bone marrow that aren't in fat and that anesthetics used in most liposuction procedures are rendering many of these fat stem cells DOA. In the end, when you look at the comparison critically, there are just as many if not more stem cells in bone marrow than fat!

Other Flaws in the Fat-Stem-Cell Industry

While performing PubMed (website for the U.S. National Library of Medicine) searches to provide input to the Regenexx Prometheus Project, I discovered three papers on fat stem cells that, in summary, stated that many of the notions on which the nascent fat-stem-cell industry is based may be seriously flawed.

Fat stem cells have a very seductive business plan. Most Americans have extra pounds they carry, and we'd all love to get rid of it the easy way, via liposuction. There are stem cells in that fat, so why not bank or use those stem cells elsewhere? Makes sense at face value, but the science behind the proposition is weak.

The first paper I found showed that the large-scale liposuction that surgeons perform to suck out fat doesn't produce good fat stem cells. This is a huge issue, as most fat stem cell biobanks rely on surgeons who collect fat during common liposuction to provide fat for stem cell isolation and banking. The researchers found that the common liposuction surgery produced cells that were less viable and less functional than a mini-liposuction designed to harvest stem cells.

The second paper showed that fat stem cells obtained from obese patients were less capable of tissue repair than fat stem cells obtained from normal weight patients. This is a showstopper, as most of the patients seeking fat stem cell treatment for their arthritis are heavier patients. The authors believe the problem is metabolic, meaning heavier patients usually have a metabolic syndrome that involves insulin resistance, which likely causes their stem cells to be less capable of repair.

This leads us to the third paper. In this research the authors found that patients with diabetes (which is the logical successor to a metabolic syndrome) have fat stem cells that are less capable of healing tissue.

The conclusion? The industrial-strength liposuction that's used to feed fat stem cell biobanks doesn't produce good fat stem cells. Heavier patients who might want to undergo liposuction and who have more arthritis have cells that are less capable of healing tissue. Finally, heavier patients with diabetes also take another hit to the repair abilities of their cells. To be fair, heavier patients with metabolic syndrome also have less bone marrow stem cell activity. Having said that, the adipose tissue in humans is a reservoir of bad chemicals where many of the fat soluble industrial pollutants live and where many pro-inflammatory cytokines take residence.

The Right Stem Cell for the Right Job

We are not wed to one stem cell source but try to match the source of stem cells to the patient's problem. For example, we've noted that adipose tissue is great for a structural graft that happens to contain stem cells (for example to buttress a failing knee meniscus). Bone marrow stem cells are best to help joints heal or to use in areas where you need to establish new blood supply.

Since there are different stem cell tissue sources being offered for orthopedic treatments, the important thing is to make sure the source of the stem cells matches the tissue you're trying to repair. Certain sources produce stem cells more capable of repairing certain tissues while stem cells from other sources are less capable. The general rule of thumb is, the closer the stem cells are to the structure in need of repair, the better they are at repairing that area. This makes sense at face value, as these resident stem cells in all of our tissues have a role in maintaining and repairing that local organ or tissue.

In addition, watch out for the stem cell research shuffle, which can be found on many clinics' websites. When patients and physicians hear the term "stem cell," they have some sense of what that means. However, what many may not know is that there are many different stem cell types and mixes. In fact, some of these may have little in common with each other. Many fat stem cell clinics, are seemingly oblivious to these facts, insert research on their websites that has little to do with the procedures they offer.

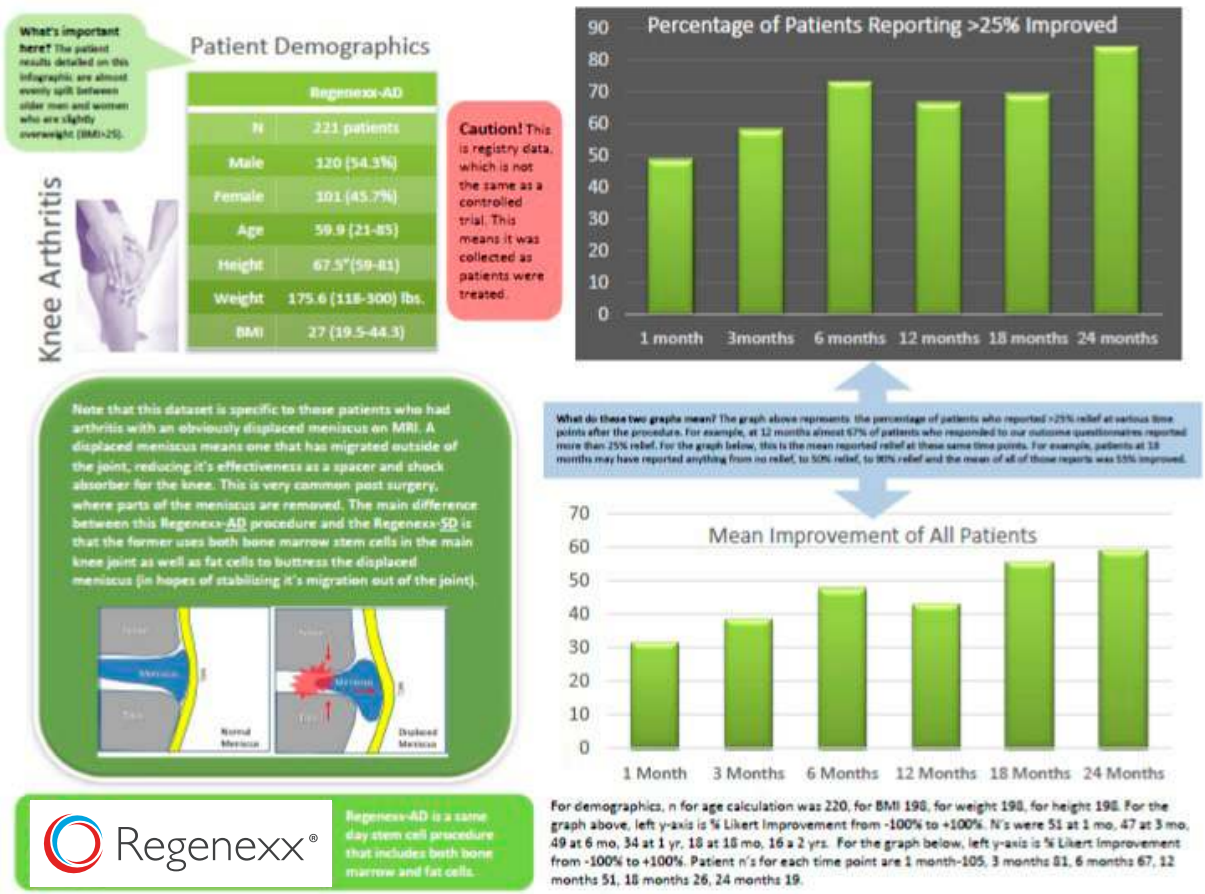
While the use of bone marrow concentrate (BMC) to treat orthopedic conditions is well established via animal models and patient data, the use of fat cells to treat a panoply of diseases is poorly established, or even nonexistent, in most instances. Hence, fat stem cell clinics offering to treat a wide variety of diseases often, knowingly or unknowingly, "shuffle" the research, showing studies for stem cell types that don't relate to what they are actually using. Don't let this fool you; make sure the research listed relates to what is being done.

Adding to the fat versus bone marrow stem cells research issue, it is important to make sure the data in the study compares apples to apples. It's always interesting to see the back and forth on bone marrow versus fat as a source for stem cells. Given that the FDA has long declared the same-day fat stem cell procedure that breaks down the tissue in which stem cells are imprisoned (SVF) as an illegal and unapproved drug, you would

think this would be a moot point. However, it still comes up, and now a paper published in 2016 purports to reverse the findings of many other papers (remember those 13 studies discussed earlier) that show fat is inferior to bone marrow for orthopedic uses.

It's important to delve deeply into this publication to see how it came up with its unusual findings, especially since it contradicts so many that came before it. Reviewing the paper, I quickly discovered serious issues in its comparisons of bone marrow and fat stem cells. Some of these are obvious; some we'll never know how the authors got contrary results. In the meantime, I'm sure we'll see many fat stem cell advocates use this paper as proof of the superiority of these cells, but, in fact, it's just a poorly constructed experiment with outlier results.

The conclusion? In cartilage repair and bone repair, bone marrow stem cells do the best job because they are closest to the area needing repair. Don't be fooled by the stem cell research shuffle many clinics use, and make sure you explore the validity of the research you're reviewing.



Combining Fat Stem Cells with Bone Marrow Stem Cells: Regenexx-AD

The infographic above covers knee outcome data for the Regenexx-AD procedure. The procedure is only performed on patients who have a displaced meniscus with moderate to severe arthritis, so this is a select group of >200 patients we tracked who aren't included in the last group of >500 SD knee patients. The procedure adds both bone marrow stem cells and fat stem cells to the joint to buttress the meniscus. With over 80% of the respondents reporting >25% improvement at 24 months post procedure, the numbers look good in this difficult-to-treat population. They are similar but slightly less robust than the SD data. This makes sense, as these patients have lost the ability to use the meniscus as a shock absorber and have bigger biomechanical problems, usually due to a prior meniscus surgery.

What's also interesting is what these numbers don't say. There are many advocates for fat stem cells. There are doctors processing fat at the bedside to enrich the stem cells, doctors injecting just the fat itself into joints, and new bedside machines that will minimally process the fat and bone marrow for reinjection. All of these techniques lay claim to the miracle of fat stem cells—there are many more of them, they are magic, they can help the crippled walk.

Regrettably, this data doesn't show a huge advantage to adding fat into the knee joint and in a head-to-head comparison with adding just bone marrow stem cells. Having said that, it certainly looks like this procedure accomplishes what it needs to for many of these patients, all of whom were either knee-replacement candidates at the time of the procedure or would soon be.

The conclusion? In the 2013 Regenexx-AD data, it looks like the procedure is accomplishing its goal in a difficult-to-treat population. But what it doesn't show is that adding fat stem cells to knee joints produces magical additional effects.

Conclusion

The general debate over fat versus bone marrow stem cells makes sense as mesenchymal stem cells (MSCs) are plentiful in both tissue sources; however, when that debate narrows to specific applications, it loses steam. Despite all the hype, fat stem cells are great for some things and not for others. The same is true for bone marrow stem cells. What's important is that we are using the right type of stem cells for the right thing. While there are more MSCs in fat than bone marrow as a percentage of nucleated cells, there are many fewer nucleated cells in fat—meaning that both have similar stem cell content.

While we use fat stem cells from time to time, we always make sure that the more potent bone marrow stem cells (if possible) are used in conjunction with these cells. The research data, while abundant and supportive of bone marrow stem cells, is scarce on the use of fat stem cells alone to treat orthopedic issues. In addition, the harvesting of bone marrow stem cells is safer and less invasive than that of fat stem cells, and bone marrow stem cells have been shown time and time again to be more effective at healing and repairing cartilage and bone and treating arthritis.

Like any medical procedure, all Regenexx procedures have a success and failure rate.

Regenexx® is VERY Different - Why Regenexx Stem Cell Treatments are Superior to Other Solutions

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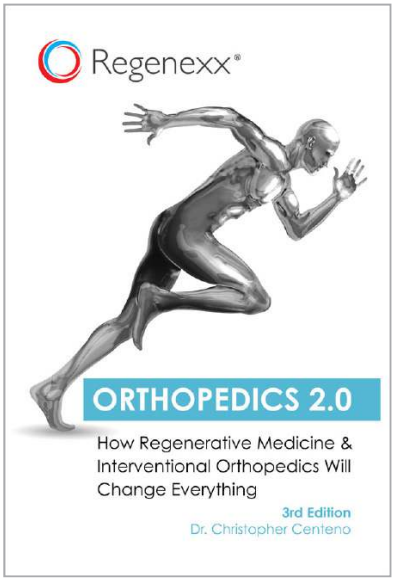
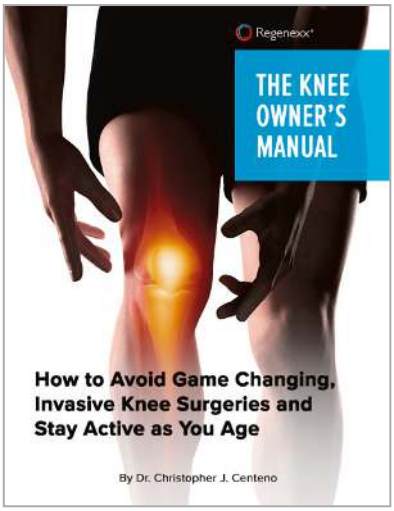
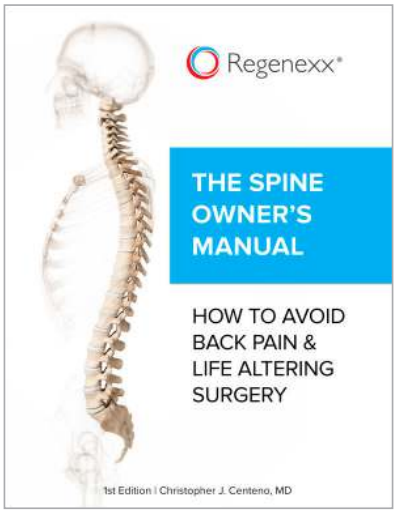


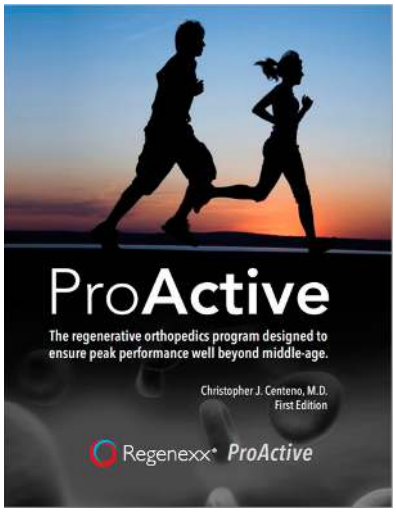
The Knee Owner's Manual Book



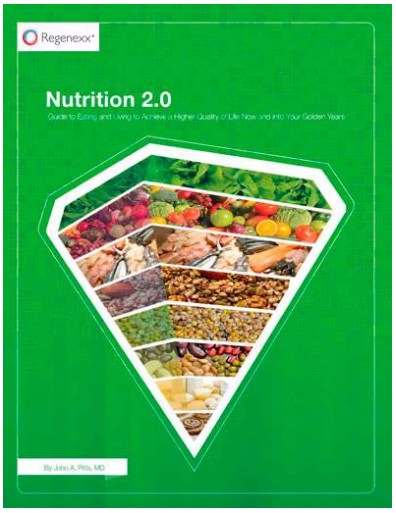
The Spine Owner's Manual



ProActive Book



Nutrition 2.0



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