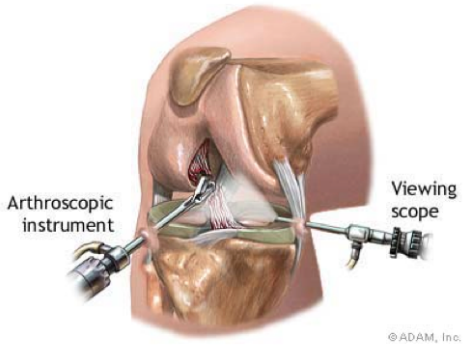
Options for your Arthritis

Overview: The goal of treatment for your arthritis is to reduce pain and restore function to that joint. There are two basic pathways we can take to achieve these goals, these are:

1. Surgical treatments
2. Non-surgical treatments

We will review each option with a brief description of how each treatment works including how it is administered. We will also review the efficacy, safety; amount of time and effort involved (convenience) ; and the expected costs associated with each treatment. We rate each section on a scale of 0-4 + with + indicating more pain, more inconvenience, less safety and less efficacy. A maximum score of 4 ++++ indicates that this procedure has LESS pain, more convenient, better safety and better efficacy. So, in summary, the more + next each segment, the improved rating.

Surgical Treatments



Arthroscopy
What is it?
This is a minimally invasive surgery where a small digital camera is inserted into your knee joint through a small 3-4 mm incision. Another 3-4 mm incision is made so a small tool can be used to remove and or repair tears of the cartilage rings in your knee called a meniscus or to remove small floating pieces of cartilage or loose pieces pealing off your knee. This is all done as an outpatient (meaning you return home the same day).

How does it work?
The arthroscopy is used to treat instability or locking of the knee. Sometimes, the feeling of "giving away", locking or catching to your knee is caused by something that is loose, torn or floating in your knee. This procedure is designed to remove something that is causing a mechanical symptom to your knee. It is not specifically used to treat or cure arthritis of your knee.

Safety of this Procedure: Score: +++
Overall, this is a fairly safe procedure. Complications can occur such as blood clots, infections, pain, skin damage. However, others not mentioned can also occur. In a

recent study entitled "*Complications after arthroscopic knee surgery*"[i] , the authors reviewed 2,623 cases of arthroscopic knee surgery. The overall complication rate was 0.27% (less than 1%) with the most common complication being infection. Another safety review entitled "*Quantifying the excess cost and resource utilization for patients with complications associated with elective knee arthroscopy: a retrospective cohort study*[2] by Bohensky, MA , reviewed 166,700 elective knee arthroscopies and found a total of 976(0.6%) complications, including 573 patients who had a venous thromboembolism (VTE) (0.3%), 227 patients with a joint complication (0.1%) and 141 patients with infections (0.1%). So, we can see that the overall complication rates are normally under 1%.

Efficacy of this Procedure: Score: ++

Knee arthroscopy for degenerative meniscal tears can help to relieve the symptoms of instability and pain associated with this instability. However, it will not relieve the pain associated with arthritis. In a study called "*Is arthroscopic surgery beneficial in treating non-traumatic, degenerative medial meniscus tears? A five year follow-up* [3] the authors designed a prospective, randomized trial comparing exercise alone to knee arthroscopy and exercise. Both groups improved, but the exercise group alone had 1/3rd of the patients still experiencing disabling pain at the end of the study.

Another interesting study entitled *"Arthroscopic debridement compared to intra-articular steroids in treating degenerative meniscal tears"* [4] randomized 120 patients with MRI confirmed medial meniscal tears into treatment with steroid injections vs. arthroscopy. At one year the arthroscopic group still had improvement in 79% of the patients while 61% of the steroid treated patients noted improvement. Thus, we can understand that arthroscopy for a mechanical problem such as a meniscus tear can offer some relief of symptoms associated with a mechanical problem of the knee.

Convenience of this procedure: Score: ++

You will be required to report back to the office for a pre-operative evaluation called a history and physical. Some patients with pre-existing medical conditions such as coronary artery disease may also require an evaluation by their primary care physician or a cardiologist. Sometimes, this means some extra testing such as an EKG or even a cardiac stress test. You will need someone at the surgery center to drive you home and stay with you at least the night of the procedure. You may require assistive aids such as a crutches or a walker for anywhere from 1 day to 2 weeks. You will also need to report back to our office for at least one post-operative visits. Some patients will be prescribed physical therapy, but most can follow a simple home exercise program.

Pain Associated with this procedure: **Score: +++**

Most patients have pain that is well controlled with some prescription medications and most only use these medications for approximately one week after the surgery. However, every patient responds differently to treatment.

Cost: Score: ++

Although most insurance plans cover surgery, there are many plans with deductibles, co-pays, co-insurance and out of network charges. The average charge from a surgical center for a knee arthroscopy in the Detroit area is $11,800 according a survey of surgical centers at: http://www.newchoicehealth.com/procedures/arthroscopic-knee-surgery

Remember, that charge and cost have very little relationship. Charge is what the hospital or surgical center hopes to be paid. Normally, they receive one half to one third of what they charge.

Consumer Reports published the national average cost of simple knee arthroscopy (CPT 29981) to be $3,675 in the *2012 Healthcare Blue Book*. When calculating your expenses, you should also factor in the time lost from work as an opportunity cost. Most patients are off work an average of 7-10 days with an arthroscopy. These expenses **may be** reimbursable through qualified Health Spending Accounts (HSA), Flexible Spending Account (FSA), Medical Savings Account (MSA), or Health Reimbursement Arrangement (HRA). Please contact your plan administrator for details.

Knee or Hip Replacement

What is it?

Joint replacement is really a resurfacing and re-alignment procedure for your arthritic joint. The joint is opened up through an incision and the arthritic portions of the joint are removed with specially designed instruments and tools to place a new surface on either end of the joint.

How does this work?

You are admitted to a hospital or surgery center the day or your surgery. Incisions are made over the joint in a manner designed to preserve the normal function of the joint. Special cuts are made on the bones of your joint to allow proper placement of the new joint and to restore normal mechanical alignment of the joint. These joint replacements are made of metal such as titanium and cobalt chrome and they articulate with a high density and durable plastic liner. Most knee replacements are glued to your bones with a special bone cement. Most hip replacements are designed to wedge within your current bone after reaming the bone to a specific geometry. Your own bone grows into this replacement to further stabilize the fixation. Most patients stay in a hospital or

surgery center for 1-2 days, however, a few select patients may leave the day of surgery. You will require constant 24 hr, 7 days a week care for up to 3 weeks after the surgery.

Safety of this Procedure: Score: ++

We take steps to help identify and reduce complications, but there are complications that can occur. Luckily, most of these complications can be treated successfully. In a recent study entitled "*Thirty-day postoperative complications and mortality following total knee arthroplasty: Incidence and risk factors among a national sample of 15, 321 patients"* by Belmont, PJ [5] the author performed a retrospective review of 15, 321 patients revealing that the thirty-day mortality rate was 0.18%, and 5.6% of the patients experienced complications. Patient age and diabetes increased the risk of mortality after primary total unilateral knee arthroplasty. Predictive factors impacting the development of postoperative complications included an ASA classification of ≥3 (what score the anesthesia team assigns you), increased operative time, increased age, and greater body mass.

Another very large study looking at the trends of adverse outcomes after total hip replacement entitled "*Adverse outcomes in hip arthroplasty: Long term trends."* by Brian Wolf [6] found that between 1991 and 2008, 1, 405,379 total hips were performed with a decreasing trend of adverse outcomes from 4% to 3.4%, however, of the 337, 874 revision (re-do) hip replacements, there was a trend towards an increase in adverse outcomes from 7% to 10.9%.

Efficacy of the Treatment Score: ++++

Overall, many patients are vey happy that they had the procedure performed. The knee and hip society reports that most patients have 95% pain relief and that over 80% of these joint replacements will last over 20 yrs. (http://www.aahks.org/care-for-hips-and-knees/do-i-need-a-joint-replacement/total-hip-replacement/) Thus, these procedures are reliable, reproducible and durable. A study entitled " *Patient-level clinically meaningful improvements in activities of daily living and pain after total hip arthroplasty: data from a large US institutional registry"* [7] looked at 6168 total hips from 2 to 5 years after their surgery. Clinically meaningful reduction in pain was reported in 94% of patients with moderate pain and 91% of patients with severe pain. Only 4% of patients with moderate limitations and 17% with severe limitations reported severe limitations on their activities at 2 years after the surgery.

Conveniences of the procedure Score: +

You will have to see your primary care physician for a check up and a letter of medical optimization is requested from your physician for the surgery. Some patients with pre-existing medical issues such as heart or lung disease may need to visit a specialist and undergo special testing. There is a mandatory pre-operative orientation meeting you must attend with the person appointed as your coach. This is a half-day event reviewing the entire procedure. You will have a history and physical exam, informative lectures and a chance to ask questions. You will be admitted to the hospital for 1-3

days with most patients leaving in 24 to 48 hrs. A few select patients will be able to leave the day of surgery. You will have physical therapy starting in your own home for 2 to 3 weeks and transfer over to outpatient physical therapy such as in our therapy department for an additional 4 to 6 weeks. You must have someone who can help you get up from a chair and into your bed or bathroom as well as help you with dressing, bathing and preparing foods for approximately 3 weeks after your surgery. This person (s) must be with you 24 hrs a day, 7 days a week. Some people heal faster than others, and they may be independent in these critical activities of daily living sooner, but count on 3 weeks. Some people can return to a sedentary job within 2- 3 weeks, however it may take up to 3 months for a return to a physically demanding occupation. If you have the procedure performed on your right leg, it is recommended that you not drive for 6 weeks. If you have the procedure on your left leg, this may be reduced to 2 weeks if you are not currently taking narcotics.

Pain associated with the procedure. Score : +

Joint replacement surgery is still a major surgical procedure and may require some sort of pain control for up to 3 months. However, we have made tremendous improvements in pain management that allow easier recovery in a quicker period of time. We use a multi-modal strategy to help relieve pain. This means we use numerous different methods to reduce and/or block your pain with a reduction in some of the complications that can occur with these treatments. This multimodal approach uses a mixture of numbing nerve blocks, combined with lower doses of narcotics, anti-inflammatories, anti-nausea, anti-anxiety, analgesic and cryo-therapy. Most patients are discharged from the hospital with a narcotic medication that is used for 3 to 6 weeks after the surgery.

Costs Score: +

Although most insurance plans cover the cost of a joint replacement, many plans have deductibles, co-insurance, co-pays and other uncovered services. The average charge by a hospital for a joint replacement is approximately $35,000 and the average out of pocket cost for Medicare recipients in Lebanon New Hampshire was $4,275 in a survey conducted in 2011. (http://health.costhelper.com/knee-replacement.html) . The charge and cost are not really related to each other. The charge is what the hospital hopes to receive from an insurance carrier. Normally, they receive one half to one third this charge. Consumers Report published the average fair cost as $19,791 for a total knee replacement (CPT code 27447) with a wide range of payments from $17,800 to $42,750 in their 2012 Healthcare Blue Book. When calculating your expenses, you should also factor in the time lost from work as an opportunity cost. Most patients are off work an average of 2 to 3 weeks for a sedentary job and up to 3 months for a physically demanding job. These expenses **may be** reimbursable through qualified Health Spending Accounts (HSA), Flexible Spending Account (FSA), Medical Savings Account (MSA), or Health Reimbursement Arrangement (HRA). Please contact your plan administrator for details.

Non-operative treatments

This group of treatments focuses on an ancient concept of ***homeostasis***. This is a concept where damage to your joint is reduced to equal the reparative processes constantly going on in your body. We attempt to reduce the damage through a comprehensive approach including goal setting, weight control, nutrition, shoe wear modification, bracing, medications, supplements and constant encouragement and monitoring. These steps can be found and followed using our *10 Steps to Healthy Joints* handout. However, we can also improve your outcome by encouraging your body to up-regulate your reparative process. We will review some of the more common options.

Steroid Injections

What are they?
Corticosteroids have been used since the 1940's to help reduce an interrupt the process of inflammation in your joint. The type of steroids we use for joint pain works mainly within the joint they are injected. However, there is always some systemic effect of injected steroids that can also help reduce inflammation in other areas. The reduction in inflammatory chemicals in your joint help reduce pain.

How does this work?
A dose of the steroid is mixed with a local anesthetic such as lidocaine. After your joint is cleansed to prevent infection, the cocktail is injected directly into the joint. There is immediate relief of pain within 3-5 minutes in most patients due to the injection of the anesthetic. However, this will wear off in approximately 30 to 60 minutes. The steroid portion of the injection requires anywhere from 48 hrs to one week to take effect. These steroids work on the chemicals producing inflammation in your joint and help reduce their activity. The result is a temporary reduction of pain, and an increase in your activity levels. The peak effect of the steroids is normally in the first 2 weeks and most patients notice a relief of pain for an average of 6-8 weeks. Although there are no hard set rules on the number and interval of repeat injections, a generally accepted rule is one injection every 3 months.

Safety of this Procedure: Score: +++
Steroid injections are normally safe. The risk of complications such as infections is very low. However, other side effects such as an increase in your blood sugar for 1 to 5 days, vision changes, heart palpitations, insomnia, hyperactivity and skin color changes can occur. Despite what you may have been told, repetitive steroid injections into a joint does not lead to further progression of the arthritic disease as found in the study conducted by Raynauld JP named "*Safety and efficacy of long-term intra-articular steroid injections in osteoarthritis of the knee: A randomized double-blinded, placebo-controlled trial*."[8] The chance of systemic effects on your bone density, weight gain and facial changes have not been reported with the proper use of joint injections.

Efficacy of this Procedure: Score: ++
Approximately 80% of patients will report reduction of their joint pain with this treatment. This will last anywhere from 2 weeks to 2 months with most receiving pain relief for 6 weeks. A review of all the current evidence of use for corticosteroids for arthritis is found in an article entitled "*Corticosteroid injections for osteoarthritis of the knee: meta-analysis*" by Arrol, B et al. [9] concluded: "*Evidence supports short term (up to two weeks) improvement in symptoms of osteoarthritis of the knee after intra-articular corticosteroid injection.*" Improvement was also shown in some studies addressing longer-term response (16-24 weeks). So, in conclusion, steroid injections can provide some short-term pain relief for arthritis.

Convenience of this Procedure: Score: ++++
There is very little inconvenience for steroid injections. This is normally done during your normal physician visit. Normally, patients are asked to rest and ice the joint for the first 24 hrs. You can resume normal activities the next day.

Pain of this Procedure: Score: +++
Most joint injections are not extremely painful. The area of the injection is sprayed with a cooling spray called ethyl chloride. This reduces the pain and distracts your pain fibers. The injection is over in 10 to 15 seconds. We normally use a numbing type of medication in the injection called lidocaine. This helps reduce the pain of the injection. Most patients come back frequently and request these injections indicating that the temporary pain associated with this injection is minimal compared to the relief they receive.

Cost: Score: ++++
Most insurance plans cover the cost of steroid injections. However, many plans have deductibles, co-pays, co-insurance and other un-covered services. The average cost for a steroid injection is between $120-140. These expenses may be reimbursable through qualified Health Spending Accounts (HSA), Flexible Spending Account (FSA), Medical Savings Account (MSA), or Health Reimbursement Arrangement (HRA). Please contact your plan administrator for details.

Hyaluronic Injections

What are they?
Hyaluronic acid is a normal, natural component of collagen in your body. It is also a natural component of the fluid in your joint called synovial fluid. As you age, your body slowly loses this vital component. The result is a failure of these structures. For example, when you lose hyaluronic acid in the collagen found in your face, wrinkles will start to form. When you lose this in your eyes, cataracts occur, and when you lose this in your joints, arthritis happens. This is not the only cause of your arthritis, it is just one of the many biochemical processes which begin to fail. Hyaluronic acid is found in numerous components of your joint including the synovial fluid, the menisci and the articular cartilage. Luckily, we can replace this hyaluronic acid with a substitute found most readily in the combs of roosters. The trade name Supartz is one such type.

How Does this Work?
You are given a series of 3 or 5 injections about one week apart into the joint. The hyaluronic acid in these injections attaches to the lining of your joint called the synovium. The receptors of this lining are stimulated to actually produce more of your natural hyaluronic acid. This can increase the viscosity (thickness) of your joint fluid. This increase in viscosity helps the native cartilage cells metabolize and function similar to a healthier joint. The end result is a reduction in pain and an increase in function.

Safety of this Procedure: Score: +++
These injections have a good safety record. Some patients with allergies to poultry or feathers may have swelling and pain with these injections. Thus, it is important to make us aware of these allergies. We can easily use a non-avian (non bird) formula. Infections and persistent joint pain or swelling is extremely rare with these injections. A review of multiple studies using hyaluronic acid revealed that the only adverse effects of significance are transient local reactions in the injected joint observed at a rate of 2% to 4% [10]

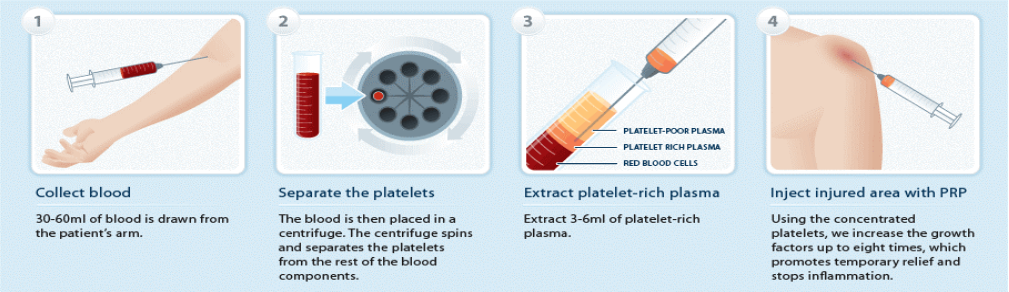
Efficacy of this treatment Score: ++
A double blinded, placebo controlled study of 495 patients in which 56% of patients receiving Hyaluronate had pain relief for 6 months & improved function with less side effects (2% vs. 9%) as compared to Naprosyn.[11] Another study by Wadell presented at the American Academy of Orthopedic Surgeons convention 2005 showed that they were able to delay the need for a knee replacement. They injected 11187 patients and over 75% of patients with severe arthritic changes had not undergone a knee replacement at 3.8 yrs.

Convenience of this Procedure: **Score: +++**
There are 3 to 5 injections at about one week apart meaning you would come in to the office 3 to 5 times. The maximum effect of the injections is at about 3 months and thus, you may have to be patient. You can drive yourself home. There is no need for a driver. Normally patients are asked to rest for the first 24 hrs after each injection.

Pain of the Procedure: Score +++
We numb the skin with a cooling spray to reduce any pain. Occasionally, some patients will have pain during the injection which may last for anywhere from 5 minutes to an hour. Resting and icing the knee will help.

Cost: Score: +++
Most health insurance plans cover hyaluronic injections to the knee but not any other joint (i.e. hips or ankles). Many plans have deductibles, co-pays, co-insurance and un-covered services. The average cost of a hyaluronic acid injection is approximately $325 each (5 injections = $1625 3 = $975). These expenses **may be** reimbursable through qualified Health Spending Accounts (HSA), Flexible Spending Account (FSA), Medical Savings Account (MSA), or Health Reimbursement Arrangement (HRA). Please contact your plan administrator for details.

Platelet Rich Plasma (PRP) Injections



What are They?
This is a therapy based on your own cells and thus is in a class called ***Cell Based Therapies.*** When you have a cut or scratch, the scab that forms is filled with platelets. These are special cells of your blood that causes the blood to clot. This clot helps heal an injury by releasing special growth factors (insulin-like growth factor, transforming growth factor b-I, platelet derived growth factor). In addition, the platelets can also help reduce some harmful chemicals released by a trauma (Matrix Metalloproteinase). Your joint or injured tissue can benefit by the release of these growth factors in a concentrated form.

How Does this Work?
A small amount of your own blood (anywhere from 10 to 40cc) is drawn and then centrifuged (spun at a very high speed) to separate out your blood cells from your

plasma and platelets. A concentration of anywhere from 3 to 9 times your normal amount of platelets is than formed into a solution called platelet rich plasma. This is rich in some growth factors as well as cytokines, chemokines, arachidonic acid metabolites, extracellular matrix proteins, nucleotides, and even ascorbic acid which help heal damaged tissue. This is all done in our office setting within 20 to 30 minutes. There are different protocols for these injections, but we normally recommend one injection. Some patients require more, but most respond to one injection lasting anywhere from 3 months to 2 years. Most people start to notice improvement in approximately 2 weeks.

Safety of This Procedure: Score: ++++

In clinical studies to date, PRP is safe, with no serious complications reported. Minor adverse events associated with repeated injections have been moderate pain, swelling and mild effusion that lasted a few days. In a double blinded randomized study conducted by Sanchez[12] of PRP vs. Hyaluronic Acid injections, found a 14.1% improvement in the reduction of pain in the PRP group with a report of adverse events that were mild and evenly distributed between the groups. In another study entitled "*Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: a prospective, double-blind, randomized trial.*" [13] the authors evaluated the use of a single PRP injection vs. two injections of PRP vs. a simple saline injection. The result revealed similar improvements of pain relief of one injection and two PRP injections over saline injections and there were very transient, brief experiences of dizziness, and nausea noted in the treatment groups. However, in a study conducted by Sampson et al in the American Journal of Physical Medicine and Rehabilitation in 2010 there were no adverse reactions reported. [14]

Efficacy of the Treatment: Score: +++

There have been numerous studies evaluating the positive effects of this treatment for arthritis of the knee. A few worth reviewing include "*Platelet-rich plasma: intra-articular knee injections produced favorable results on degenerative cartilage lesions*." by Kon and colleagues[15] They looked at 115 patients treated with 3 PRP injections and followed up at 6 and 12 months. A statistically significant improvement of all clinical scores was obtained from the base line evaluation to the end of the therapy and at 6-12 months follow-up ($P < 0.0005$). They concluded *" The preliminary results indicate that the treatment with PRP injections is safe and has the potential to reduce pain and improve knee function and quality of live in younger patients with low degree of articular degeneration.*" One other study by Filardo [16] was a retrospective study of 90 patients treated with three injections of PRP into arthritic knees at 24 month follow up. All of the parameters at the 24-month period improved including the IKDC subjective and objective parameters for a median length of improvement for over 9 months. If we compare PRP to hyaluronic injections (ie Supartz), PRP patients tend to have better pain and function scores. A great review article entitled "*The effects of platelet rich plasma in the treatment of large-joint osteoarthritis: a systemic review.*"[17] compared 13 studies of hyaluronic acid to PRP. Most (12) were for knee arthritis. All of the studies revealed

that PRP had statistically significant benefit in knee osteoarthritis compared to hyaluronic acid. Although most of these studies utilized 3 separate PRP injections, a few have shown that one injection is effective. One study conducted by Torreo in 2012 found that one injection of PRP was effective in reducing pain. [18]

Convenience of this procedure: Score: ++++
This is all done in one simple 30 minute or less office visit. The blood is drawn and processed within 15 minutes and injected into the affected area. You can resume your normal activities the day of the injections within reason. Nobody is needed to drive you home or stay with you during this treatment.

Pain Associated with this Procedure: Score : +++
Sometimes you can experience some pain with the drawing of the blood but not usually more than another other blood draw. The injection into the joint is not any more painful than other injections and if pain occurs, it is normally for just a few minutes.

Cost: Score: +++
Most insurance plans do not cover these injections and the cost for these on a national average is between $600 and $1000 per injection. Advanced Orthopedic Specialists offer these at $500/injection. These expenses may be reimbursable through qualified Health Spending Accounts (HSA), Flexible Spending Account (FSA), Medical Savings Account (MSA), or Health Reimbursement Arrangement (HRA). Please contact your plan administrator for details.

Bone Marrow Concentrate Injections
What are they?
Our body stores specific cells required for repair within specific areas of our body. One such area is within your bone marrow. This is the space within the middle of your bone rich in cells used to regenerate damaged cells. Some of the cells found in this space are progenitor cell which are cells used to repair damaged tissue, but they are further along in their differentiation than stem cells. A small percentage of mesenchymal stem cells are also found in this area. However, these stem cells are considered superior in their ability to develop cartilage tissue than other stem cells found in other parts of the body. Some of the same growth factors found in platelet rich plasma as well as some additional cells called pericytes important in the paracrine cell to cell communication are also included within this bone marrow. These cells are easily obtained, filtered and concentrated for use in certain degenerative conditions such as arthritis.

How Does this Work?
You will have the area over the front or back of your pelvis numbed with a local anesthetic. A specially designed needle is than used to enter into the middle of your pelvic bone to remove the bone marrow concentrate. This concentrate is than processed in a sterile manner to further concentrate the progenitor, stem and pericyte cells as well as the platelet rich plasma into a fibrin material that is injected directly into the area of concern. These regenerative cells work on numerous biochemical pathways in your joint to help reduce inflammation, pain and to increase cell-to-cell communication resulting in improved function of this organ.

Safety of this procedure: **Score: ++++**
This procedure has been used for many years with a very good safety record. An interesting uncontrolled, retrospective study conducted by Mendoca [19] injecting Bone Marrow Concentrate (BMC) into 14 patients with spinal cord injury. All subjects displayed variable improvements in tactile sensitivity, and eight subjects developed lower limbs motor functional gains, principally in the hip flexors. Seven subjects presented sacral sparing and improved American spinal injury association impairment scale (AIS) grades to B or C - incomplete injury. Nine subjects had improvements in urologic function. Statistically significant correlations between the improvements in neurological function and both injury size and level were found. Most importantly, *no adverse events occurred in this sensitive procedure.* In another meta-analysis (a review of numerous studies) of 78 studies using bone marrow derived stem cell therapy for cirrhosis of the liver concluded that there were no adverse events or complications. [20]

Efficacy of Treatment: **Score: +++**
Overall, most of the studies evaluating the use of this treatment have been encouraging but not conclusive. One such study is the use of bone marrow concentrate (BMC) injection compared to an orthopedic surgery used to grow cartilage cells in a culture and re-implant these into a surgically created pouch in the damaged joint called Autologous Chondrocyte Implantation (ACI) . The ACI procedure requires two invasive surgical treatments and prolonged rehabilitation. On the other hand the bone marrow concentrate only required the simple injection to the knee without any significant pain or rehabilitation. Seventy two (72) patients were in each group and both groups improved in all parameters. Interesting enough, only patients younger than the age of 45 improved with the ACI surgery. However, age did not alter results in patients receiving the bone marrow concentration. [21] Another study evaluating the use of bone marrow concentrate in combination with a procedure that straightens the knee (called a high tibial osteotomy or HTO) revealed some encouraging results. Seventy six (76) patients were split into two groups. The first group received the standard joint straightening procedure (HTO) along with a micro-fracture technique (holes placed in the bone to stimulate cartilage-like formation) to help repair the damaged cartilage. The second group had the same HTO procedure but they added culture expanded bone

marrow cells to the knee. They were followed for 2 years and had a follow up MRI. The bone marrow group had statistically significant improvements in all the measurement scores including improvements of the cartilage as seen on the MRI scans.[22] Another orthopedic surgeon in Colorado has used a technique of culture expanded bone marrow cells (meaning these were grown in a lab) and than re-injected into the knee. In a single case study report, the researcher was able to show an improvement in clinical outcome with improvements seen on follow up MRI of the knee. [23] Further *in-vitro* studies (Latin for "in glass") which is studying cells outside their environment revealed that bone marrow cells can differentiate into cartilage cells better than adipose derived cells. [24]

Convenience of this Procedure: Score: ++++

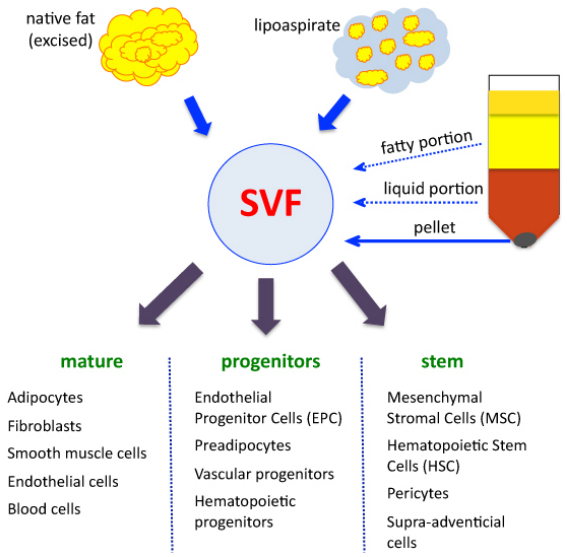
This procedure is done in the office setting within 30 minutes. You may require someone to drive you home if you choose to use an oral sedative for the procedure. You can resume all your normal activities within reason the day of the procedure. There is no need for time off work and there are limited follow up visits. To help the cells proliferate, we do provide an additional platelet rich plasma injection about 2-3 weeks after your initial BMC injection at no additional cost. We do ask most patients to perform simple home exercises to help heal the joint. Other patients are encouraged to use a brace for 3 months. Finally, we offer the option of using an antibiotic called doxycycline to help prevent damage to the growing cells and the use of hyaluronic acid injections prior to the procedure to help preserve and cross-link some of the cells. The pain relief from this procedure may not occur until 3 months, so immediate pain relief is not a benefit. However, most patients receiving a PRP injection to their knee will start to notice a difference at 2 weeks.

Pain of this Procedure: Score: ++

There is minimal pain associated with this procedure. Some people may have some soreness around their pelvis along with some bruising for up to a week. There is minimal if any swelling or pain to the joint injected.

Cost: Score: ++

No insurance plans currently cover this procedure. The current complete cost of this procedure is $2,850 for one joint and $4,800 for two. Comparison to other centers throughout the country reveals that price varies between $2,000 to $4,500 for a single joint and $5,000 to $6,000 for two joints. *Our procedure includes an additional PRP injection about 2-3 weeks after the initial BMC injection to help with cell growth. This is provided at no extra cost.* These expenses **may be** reimbursable through qualified Health Spending Accounts (HSA), Flexible Spending Account (FSA), Medical Savings Account (MSA), or Health Reimbursement Arrangement (HRA). Please contact your plan administrator for details. Deferred payment plans are available is you are interested. Our surgical scheduler can provide you with the details of this simple plan.



Adipose Derived Stem Cell Injections.

What are they?
Adipose cells are your fat cells. These cells have small blood vessels that feed the cells and keep them alive. Within these vessels is a very rich supply of mesenchymal stem cells. These blood vessel cells can be concentrated into a small pellet called the stromal vascular fraction. This pellet not only contains the valuable stem cells, it also contains pericytes that help cells talk to each other and act like a normal functioning organ.

How does this work?
Currently, patients report to an outpatient surgical center to ensure optimal sterility and quality control. Registered nurses and technicians using highly regulated standard operating procedures ensure that you will have the safest procedure possible.

Most patients will not generally require the supervision of an anesthesiologist since the procedure is done through a simple local anesthetic fluid. Some patients will be administered oral Ativan or Valium (muscle relaxer) if necessary within an hour of the procedure. There is no need to start an IV or antibiotics since these will be given by mouth about an hour prior to the procedure. The patient will be taken into an OR suite. A small incision will be made on either side of the abdomen for entry of the local anesthetic. The abdominal area is numbed with a specially prepared fluid called tumescent fluid. A small liposuction tool called a Mercedes cannula is inserted. The liposuction is carefully performed in a fan wise motion on one side of the umbilicus removing only 30 to 60 cc of fatty tissue form each side of the abdomen to ensure even sculpting. However, the procedure is not designed to provide any aesthetic effect (it is not designed to make you look good). During this procedure, four to eight 10cc tubes of blood are taken for preparation of the platelet rich plasma.

The fat cells are processed in a strict and regulated manner. A registered perfusionist, with training in this procedure, processes the adipose tissue and blood. She will follow

the strict lab protocol washing the fat cells and spinning these down to produce the stromal vascular fraction (SVF) layer containing the stem cells. During this process, the platelet rich plasma is also prepared yielding between 4-5 cc of the growth factor rich fluid. Think of the PRP as fertilizer and the stem cells as seeds. The two work with each other to provide a higher yield. The two are mixed together for the final process. The entire process is completed in one setting using a sterile hood; strict sterile technique and a Current Good Manufacturing Process (cGMP). We can also sample the final product and perform cell count and viability studies with the use of a video microscope. The patient can be brought into the pre or post surgical area and injected with the properly labeled mixture into the corresponding joint. Patients are required to have someone drive them home because some patients may still feel tired from the muscle relaxant. The entire process will take between 2-3 hours. Most patients take it easy with no heavy lifting for about 1 week to protect the abdomen but the joint can be used normally in 24 hrs.

Safety of this Procedure: Score: ++++

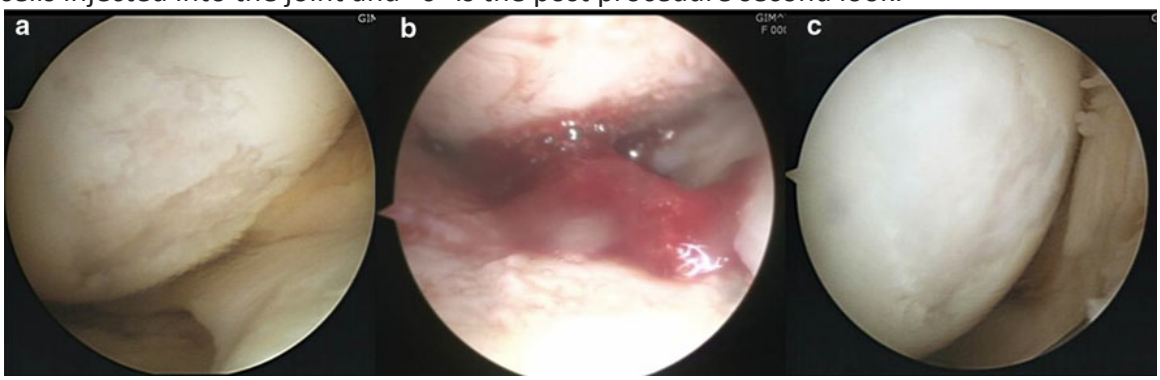
One of the best papers on the safety of this procedure comes from Pak, J in their paper entitled " *Safety reporting on implantation of autologous adipose tissue-derived stem cells with platelet-rich plasma into human articular joints*." [25] The authors concluded : " *Using both MRI tracking and telephone follow ups in 100 joints in 91 patients treated, no neoplastic complications were detected at any ADSC implantation sites. Based on our longitudinal cohort, the autologous and uncultured ADSCs/PRP therapy in the form of SVF could be considered to be safe when used as percutaneous local injections*." Another, more in-depth review surveying 100 private plastic surgical clinics, 68 plastic surgery departments at general and university hospitals, and 5 biotechnology companies by telephone. They found " *No toxicity resulting from residual collagenase or tumorigenicity associated with the ADSCs was observed*." [26]

Is Adipose Derived Stem Cell Therapy Effective? Score: +++

The purpose of this discussion is not to claim that this treatment cures or treats a specific condition, but to rather report the results of some previous studies.

Recent peer reviewed published studies also have some promising results. Yong-Gon Koh and his colleagues in S. Korea published an article entitled: "*Clinical results and second-look arthroscopic findings after treatment with adipose-derived stem cells for knee osteoarthritis*"[27] Dr. Koh treated thirty elderly patients, suffering from osteoarthritis of the knee with the same ADSC procedure and followed them closely for 2 years. He also took a second look of the knee through an arthroscopy in 16 of these patients. His published findings were the following: *"Almost all patients showed significant improvement in all clinical outcomes at the final follow-up examination. All clinical results significantly improved at 2-year follow-up compared to 12-month follow-up (**P** 0.05). Among elderly patients aged **(**65 year)s, only five patients demonstrated worsening of Kellgren–Lawrence grade. On second-look arthroscopy, 87.5 % of elderly patients (14/16) improved or maintained cartilage status at least 2 years*

postoperatively. Moreover, none of the patients underwent total knee arthroplasty during this 2-year period. " In plain English this means that almost all the people in the study reduced their knee pain and increased their overall physical function over a 2 year period. A very interesting finding is the continued improvement over time. Patients improved from year 0 to year 1 but they continued to improve further from year 1 to year two showing continued improvement in almost all parameters. Best of all, none of the participants had their knee replaced. A sample picture of one patient in this study is included below. Picture "a" is the pre-procedure, "b" is the picture of the stem cells injected into the joint and "c" is the post procedure second look.



A controlled study comparing mesenchymal stem cells injections after an arthroscopy (common surgery used to treat cartilage tears of the knee) to a standard arthroscopy alone was published in 2010 by Dr. Varma in the *Journal of the Indian Medical Assoc*.[28] In this study, 50 patients with mild to moderate osteo-arthritis knee were selected and divided in two groups (group A and group B). Group A received arthroscopic debridement alone and group B received buffy coat (mesenchymal stem cell concentrate) injection along with the arthroscopic debridement of the knee. On follow-up, patients were assessed on the basis of visual analogue scale (VAS) score and osteo-arthritis outcome score, to compare results in both groups against each other to determine the efficacy of arthroscopic injection of buffy coat in the management of osteo-arthritis. The results suggest that the technique used in the study considerably improved the overall osteo-arthritis outcome score, especially the quality of life within the studied follow-up period and at the end of the follow-up. This study has some flaws in the reporting of the standardized testing, but does reveal that stem cells are superior to a common treatment for degenerative arthritis.

Another study published in the prestigious *Journal of Bone and Joint Surgery (JBJS*) , by C. Thomas Vangsness Jr, MD entitiled "*Adult Human Mesenchymall Stem Cells Delivered via Intra- Articular Injection to the Knee Following Partial Medial Meniscectomy*"[29] introduced some interesting findings. This was a nicely designed double blinded, placebo controlled, randomized trial of the use of manufactured product of stem cells taken from someone else and injected into knees after a surgery was performed to remove a portion of the patients meniscus (which is a cartilage ring in the knee). The placebo group received a sodium hyaluronate (i.e. Supartz) injection and the

intervention groups received different doses of the stem cells along with the sodium hyaluronate. Everyone was followed up with magnetic resonance images (MRI) and exams at six weeks, six months, one and two years. The MRI's of the stem cell treatment groups revealed both an increase in the volume of regenerated meniscus tissue as well as a reduction of pain as compared to just the Supartz (hyluronate) injection over a two-year period without any adverse side effects. Although, this is a different technique, this study does reveal that stem cell injections can increase tissue growth of the meniscus and reduce pain in arthritis of the knee better than a common injection used by many orthopedic surgeons for arthritis.

A recent study published in the *Stem Cells, May 2014* by researchers out of South Korea tried to determine the optimal dosing of adipose derived stem cells by injecting three different concentrations.[30] Eighteen patients with osteoarthritis of the knee were injected ADSCs into the knee. The phase I study consists of three different doses; the low-dose (1.0 × 10(7) cells), mid-dose (5.0 × 10(7)), and high-dose (1.0 × 10(8)) group with three patients each. The phase II included nine patients receiving the high-dose. The primary outcomes were the safety and the Western Ontario and McMaster Universities Osteoarthritis index (WOMAC) at 6 months (a standard score used to evaluate the function of patients with arthritis) . Secondary outcomes included clinical, radiological, arthroscopic, and histological evaluations. There was no treatment-related adverse event. The WOMAC score improved at 6 months after injection in the high-dose group. The size of cartilage defect decreased while the volume of cartilage increased in the medial femoral and tibial condyles of the high-dose group. Arthroscopy (looking into the knee with a fiber optic camera) showed that the size of cartilage defect decreased in the medial femoral and medial tibial condyles of the high-dose group. Histology (looking at the tissue under a microscope) demonstrated thick, hyaline-like cartilage regeneration. These results showed that intra-articular injection of 1.0 × 10(8) ADSCs into the osteoarthritic knee improved function and pain of the knee joint without causing adverse events, and reduced cartilage defects by regeneration of hyaline-like articular cartilage. In summary, this study revealed that patients with a higher dose, single injection of ADSC had improved function, decreased size of the cartilage defect and better looking cells.

Another study published by *Biomedical Research and Therapy,* by Khanh Hong-Thien Bui and colleagues [31] at Ho Chi Minh University (obviously in Vietnam) injected 21 patients with ADSC along with PRP and evaluated the patients pain and return of activities of living through questionnaires called the Visual Analog Scale (they rate their pain on a scale of 0-10) and the Lysholm score (asking how much pain, swelling, and instability they have as well as ability to climb stairs, squat and climb stairs). All of the 21 patients improved at 6 months. The VAS pain score reduced on average from 7.6 to 1.5 and the Lysholm Score increased from 61 to 82. Furthermore pre and post MRI's were reviewed and revealed that the cartilage layers were partially regenerated. There were no adverse reactions or side effects and 100% of the participants were happy with the treatment results. This study also has some flaws, but still continues to provide some

further evidence of efficacy in the short term.

These studies have small numbers and some are not controlled, blinded, or randomized, but they do show a common pattern of:

- Reduction of pain.
- Restoration of function.
- High rate of patient satisfaction.
- Improved MRI or physical findings (microscopic or arthroscopic).
- Safe use with little or no side effects or adverse events.

Convenience of this Procedure: Score: +++

Because this procedure is performed in a certified surgical center, you must come in to our office for a history and physical visit about one week prior. You will also be asked to complete a series of hyaluronic injections to help the cells grow and survive. In addition, we ask that you start on a medication called doxycycline to help reduce enzymes that might injure the new cells. You will arrive about 1 hr prior to the start of your procedure at the surgical center and will be prepped for liposuction. You can eat a light meal prior to your procedure. The entire liposuction, processing and injection will take about 4 hours. Someone will drive you home if you take the relaxing medication. There is no need for formal physical therapy, but we do ask that you complete some simple exercises daily. Some patients are requested to use a brace for 2 months after the procedure. You can resume all your normal activities with the exception of abdominal exercises in 48 hrs and resume all sporting activities in 3 months. Most patients do not notice any significant relief of symptoms for 3 months, so immediate pain relief, is not a benefit of this procedure.

Pain of the Procedure: Score: +++

Overall, there has been very little or mild pain reported by patients undergoing this procedure. Most of the discomfort is mild and relates to some bruising of the abdomen from the liposuction. Most patients do not take the pain medications given to them. There is some spasm-like pain reported by patients during the injection into the joint. This resolves within 4-5 minutes.

Cost: Score: ++

At the current time, this procedure is not covered by any known insurance in the United States. Thus, we have been very sensitive to the cost of this procedure, but want to also ensure the highest quality service with the safest possible environment. This includes:

- Evaluation by a board certified and fellowship trained orthopedic surgeon.
- History and physical by a licensed and certified physician assistant.
- Review of your medical condition by a registered nurse.
- Procedure completed at a state licensed and Joint Commission approved surgical center.
- Procedure performed in a sterile, licensed and regulated operating room.

- Procedure performed by a board certified orthopedic surgeon.
- Preparation of the adipose derived stem cell injection along with platelet rich plasma by a certified and credentialed perfusionist.
- Sampling of the stromal vascular fraction for cell viability and count verification.
- Sterile injection of the properly prepared and labeled cell mixture.
- Follow up calls by the surgical center to answer any questions or concerns.

With the above quality control process, there is a monetary cost and we try to keep these costs to a minimum. With that being said, the current charge for this service is $4,850 for one joint. Because many of these quality control costs are not increased significantly for an injection to another joint, the cost for two joints at the same time is $7,275. These expenses **may be** reimbursable through qualified Health Spending Accounts (HSA), Flexible Spending Account (FSA), Medical Savings Account (MSA), or Health Reimbursement Arrangement (HRA). Please contact your plan administrator for details. Deferred payment plans are available is you are interested. Our surgical scheduler can provide you with the details of this simple plan.

To help you make your decision, we have put together two simple charts. Chart 1 compares all the components discussed above. Chart 2 compares some of the most common concerns of patients such as number of office visits, recovery time, need for therapy. pain and cost. We rate each section on a scale of 0-4 + with + indicating more pain, more inconvenience, less safety and less efficacy. A maximum score of 4 ++++ indicates that this procedure has LESS pain, more convenient, better safety and better efficacy. So, in summary, the more + next each segment, the improved rating.

Treatment	Safety	Efficacy	Convenience	Pain	Cost
Arthroscopy	+++	++	++	+++	++
Joint Replacement	++	++++	+	+	++
Steroid Injections	+++	++	++++	+++	++++
Hyaluronic Injections	+++	++	+++	+++	+++
PRP Injections	++++	+++	++++	+++	+++
Bone Marrow Concentrate	+++	+++	+++	+++	++
Adipose Derived Stem Cell Injection	+++	++++	++	+++	++

Treatment	Office visits	Recovery	Therapy	Pain	Cost
Arthroscopy	3 visits	7-10 days	Home Exercise	Narcotics 3-7 days	$3,675 *
Joint Replacement	8 visits, 3 pre-op , 5 post op	3 wks to 3 mo	6 – 8 weeks (12 to 24 visits)	Narcotics 3 - 6 weeks	$35,000 *
Steroid Injections	1	1 day	None	None needed	$120-140*
Hyaluronic Injections	3 to 5	1 day	None	None needed	$100 to $325/ea*
PRP Injections	1	1 day	None	None needed	$500 **
Bone Marrow Concentrate	2 (excludes HA injections)	1 day	Home exercise	OTC or mild narcotics 1-2 days	$2,850 **
Adipose Derived Stem Cell Injection	2 (excludes HA injections)	1 day	Home exercise	OTC or mild narcotics 1-2 days	$4,850**

*- Means that this a normally covered benefit in most insurance plans. However, this does not include co-payments, co-insurance, deductibles, and other services not covered, but provided with the procedure such as medications, anesthesia, and durable medical equipment.

-Means -These expenses **may be reimbursable through qualified Health Spending Accounts (HSA), Flexible Spending Account (FSA), Medical Savings Account (MSA), or Health Reimbursement Arrangement (HRA). Please contact your plan administrator for

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