Informed Consent for this Proposed Cell-based Medicine Procedure

Stem Cell Injections for Arthritis

What is Informed Consent?
Informed consent is a cornerstone of the physician-patient relationship. To be valid, it must involve a partnership, one where patients and doctors make decisions together. Your doctor has a responsibility to disclose the nature of the proposed treatment or procedure, the relevant associated risks and hazards involved, and any other treatment or non-treatment alternatives—along with the attendant risks of those alternatives. Thus, valid informed consent is the patient granting permission for the doctor to proceed with the recommended treatment in the knowledge of the possible consequences.

What are the three (3) elements of Informed Consent?
Jones WJ., McCullough LB., Richman BW, A Comprehensive Primer of Surgical Informed Consent. Surg Clin N Am 87 (2007); 903-918.

1. The *first element* is disclosure by the doctor to the patient of adequate clear information about the patient's diagnosis; the alternatives available to treat the patient's problems, including surgical and non-surgical management; the benefits and risks of each alternative, including nonintervention (i.e., allowing the natural history of the disease to continue); and a frank explanation of those factors about which the medical profession, and the individual doctor in particular, are uncertain and cannot provide guarantees.
2. The *second element* is the patient's understanding of this clinical information. It's not enough for the doctor to simply describe the clinical information, the patient must clearly understand the information. The patient should clearly understand what treatment they are being asked to authorize. The patient needs to grasp the nature of the proposed procedure, its goals, its expected duration, and what can be expected in the near-term and in the long-term. Sequela of the procedure, particularly functional changes that affect job performances, valued activities, and aesthetics such as scar tissue formation, must be understood.
3. The *third element* is the patient's process of decision, based not only what the surgeon has told them, but also on information they have been exposed to from other sources, including: other physicians, family and friends, and perhaps an acquaintance who has had a similar procedure; what they have read by independently researching the problem; and their own emotional response to illness, injury, or medical malady and all that it changes in one's life.

What are your legal and ethical rights as a patient?
1. You have the legal and ethical right to direct what happens to your body.
2. You have the legal and ethical right to be informed about your condition/diagnosis.
3. You have the legal and ethical right to fully understand the recommended surgical, medical, or diagnostic procedure(s), so that you may give or withhold your consent.

To the Patient:
You have the right, as a patient, to be informed about your condition and the recommended surgical, medical, or diagnostic procedure to be used, so that you may make the decision whether or not to undergo the procedure after knowing the risks and hazards involved. This disclosure is not meant to alarm you; it is simply an effort to make you better informed so that you may give or withhold your consent for the procedure.

What is the diagnosis for which treatment has been planned?

Diagnosis (primary): osteoarthritis

Diagnosis (secondary): _____

Diagnosis (secondary): _____

Diagnosis (secondary): _____

Explanation of your primary diagnosis

You have a condition known as osteoarthritis (OA). OA is a disease of joints caused by "wear and tear." It occurs when the cartilage that cushions and protects the end of your joints gradually wears away. OA is often more painful in the joints that bear weight, such as the knee and hip, but it can affect smaller joints too. In many cases, bone growths called "spurs" develop at the edges of osteoarthritic joints. The bone underneath the damaged cartilage can become hard and firm (sclerosis). The joint becomes inflamed, causing pain and swelling. Using the joint hurts.

Treatment options

There is no cure for arthritis, but there are many treatments to help relieve the pain and disability.

- *Medications:* Both over-the-counter NSAIDs like aspirin, ibuprofen, naproxen, etc.; and prescription NSAIDs, like Celebrex, Mobic, Voltaren, etc. can be used to control joint pain and inflammation. Acetaminophen, which is *not* an anti-inflammatory, can be effective in controlling pain. NSAIDs have side-effects and can be unsafe in patients with asthma, liver disease, kidney disease, and ulcers.
- *Steroid injections:* Injections of "cortisone" into the joint may temporarily help to relieve pain and swelling. However, it is important to know that repeated or frequent injections into the same joint can cause damage and undesirable side-effects. Diabetic patients can often see a transient rise in their blood sugar after a steroid injection.
- *Viscosupplementation or injections of hyaluronic acid preparations:* These injections have been approved by the FDA for knee arthritis. They are typically given in a series of 3-5 injections over several weeks. Sometimes they can cause an allergic reaction.
- *Exercise, therapy, and bracing:* Canes, crutches, walkers, or splints may help relieve the pain. Activity modification can also be helpful. Physical therapy can be useful in many cases. Modalities such as ice or heat are other options.
- *PRP (platelet rich plasma injections):* PRP is currently being investigated for its effectiveness in speeding the healing of a variety of musculoskeletal injuries and conditions. PRP is a preparation developed from a patient's own blood. It contains a high concentration of proteins called growth factors that are very important in the healing of injuries. Current research on PRP has produced some very promising results for chronic conditions such as lateral epicondylitis. A few treatment centers across the country are incorporating PRP injections into the non-surgical treatment regimen programs. However, this method is still under investigation and more research is necessary to fully prove PRP's effectiveness. In some cases, PRP may be deployed in conjunction with adult mesenchymal stem cells in the treatment of chronic degenerative conditions, as its growth factors might act synergistically with the regenerative functions of the stem cells.
- *Surgery:* In general, an orthopedic surgeon will perform surgery for arthritis when other methods of nonsurgical treatment have failed. There are many possible procedures that can be considered depending on the severity of the arthritis. For example, arthroscopically removing the diseased or damaged joint lining "cleaning out" the joint. More aggressive procedures include realigning the joint, fusing the joint, or replacing the part or all the joint (total joint replacement). All surgeries have possible risks and complications that are covered by your surgeon before proceeding with the surgical procedure (s). Suffice it to say to any surgery can cause infection, nerve injury, vascular injury, blood clots, pulmonary embolism, and even death. Although surgery is designed to improve an underlying condition, no surgery can be absolutely guaranteed to improve or cure a condition. In some rare cases, surgery can even make your condition worse.
- *Non-intervention (do nothing):* It should be emphasized that doing nothing is an option. Other terms for this include: "just live with it" or "blind neglect." Should you choose this option, you should be aware that the natural history of

osteoarthritis is continued degeneration of the affected area over time. It is impossible for physicians to say with certainty precisely how long your degenerative process will take to progress to the point of worsening symptoms. Often the condition will wax and wane. Eventually, however, if left untreated the condition can cause progressive symptoms such as pain, swelling, loss of joint motion, feelings of instability, and interference with activities of daily living, recreational activities, or work-related activities.

- *Combination treatment:* In most cases, patients with arthritis can continue to perform normal activities of daily living. Exercise programs, NSAIDs, weight reduction, physical therapy, smoking cessation, infrequent steroid injections, bracing, or any combination thereof, can successfully reduce pain and improve function.

- *Stem cell injection:* According to a statement from FDA Commissioner Scott Gottlieb, MD from August 28, 2017, "One of the most promising new fields of science and medicine is the area of cell therapies and their use in regenerative medicine. These new technologies, most of which are in early stages of development, hold significant promise for transformative and potentially curative treatments for some of humanity's most troubling and intractable maladies.

  Recent advances in our basic knowledge of the pathways involved in tissue damage and regeneration have combined with remarkable progress in adult stem cell biology to put us at a genuine inflection point in the history of medicine…"

What you should know about stem cells?
It should be emphasized that the use of mesenchymal stem cells for musculoskeletal conditions is still in the investigative phase. What we know for certain is that our adult stem cell populations decline as we age. We also know that the potency of our stem cells declines with age. Both these factors make us less efficient at repairing injuries to our musculoskeletal systems. Stem cells work in two ways: 1) they can renew themselves and multiply before differentiating into the type of tissue that needs repair; 2) they can secrete biochemicals that help establish a regenerative microenvironment at sites of tissue injury or damage. Thus, the near and long-term goal of the procedure is to establish a regenerative microenvironment using your body's autologous adult mesenchymal stem cells to naturally heal, restore, regenerate, and renew damaged areas. In doing so, it is our hope that your pain will be lessened, and your function and quality of life will be improved. Stem cells have great potential, and there have been clinical studies that show promising results, but more research is necessary.

What you should understand about the proposed procedure (a)
I understand that the following procedure is planned for me: **bone marrow aspiration and injection of the concentrated stem cells (BMAC) into my painful or damaged joint.** I understand that I am being asked to voluntarily consent and to voluntarily authorize the procedure(s) described below. I am being informed that the proposed procedure(s) consists of two elements or phases. The first phase involves the harvesting of my stem cells, and the second phase involves the injection of my stem cells into my painful or damaged joint. The proposed procedure will be described in further detail below.

I. Primary proposed procedure: bone marrow aspiration (Phase1)
As the patient, you should understand that the primary proposed procedure is to remove autologous bone marrow containing mesenchymal stem cells (MSCs) from the back of the iliac crest (hip area) using sterile technique. You will be positioned on a cushioned radio-lucent table in the prone (face-down) position or the lateral (side-up) position for the procedure.

Your surgeon will use a state-of-the art fluoroscopy C-arm to image your pelvic bone. This is done to make certain the bone marrow is extracted safely from the proper spot. The C-arm will be used throughout the procedure to guide the surgeon in real-time. Once properly positioned, the surgical site will be sterilely prepped-and-draped. After anesthetizing the area with local anesthetic, your surgeon will make a small incision, then insert an aspiration

device that resembles a hollow needle into the bone marrow cavity (this will be done under fluoroscopic guidance).

Using a syringe, your surgeon will withdraw a sample of the liquid portion of the bone marrow. You may fell a brief sharp pain or stinging. The aspiration takes only a few minutes. Several samples may be taken from different areas to increase the number of stem cells. Once the sample is taken, your surgeon will apply pressure over the site until any bleeding stops. Small strips of specialized surgery tape will be placed over the incision to bring the skin edges together.

In some instances, your surgeon may elect to suture the incision. Once the incision is closed, sterile dressings will be applied. The bone marrow aspirate will be taken to our on-site processing center for centrifugation. You can comfortably rest during this phase of the procedure.

II. Primary proposed procedure: BMAC stem cell injection (Phase 2)

Once the stem cells have been concentrated by centrifugation, the second phase of the procedure will begin. The target area will be sterilely prepped and draped using sterile technique. Local anesthetic will be used to anesthetize the injection site. The stem cell concentrate will then be injected into the target area using ultrasonic guidance, fluoroscopic guidance, needle-scope arthroscopic guidance, or any combination of these injection guidance tools.

Your surgeon may elect to inject the stem cells into several different locations depending on your diagnosis. Most of the time, this can all be done with a single injection. If more than one injection is required, the process will be repeated for each injection site. In some cases, your surgeon may advise the use of other products, such platelet rich plasma (PRP) or growth factors from other sources, that are designed to improve your outcome.

Use of these ancillary products may require separate and distinct informed consent forms to be signed.

III. Duration of procedure: including Phases 1 and 2)

Phase 1 of the procedure, where the stem cells are harvested from the bone marrow, should take about 20 minutes. This includes positioning, initial imaging, prepping and draping, anesthetizing the area, aspiration of the stem cells, applying pressure to the site to stop bleeding, cleaning and closing the incision, and applying sterile dressings.

There will be an approximate 20-minute break between Phase 1 and Phase 2, as the bone marrow aspirate undergoes centrifugation. Phase 2 of the procedure, where the concentrated stem cells are injected into the target site, should take about 20 minutes, depending on the number of sites to be injected.

This includes using ultrasound or C-arm to inspect target site. Prepping and draping the area. Anesthetizing the target injection sites. Injecting the stem cells. Applying sterile dressings and elastic bandages (in some cases).

IV. Near and long-term goals of procedure

The near-term goals of the procedure are to allow the stem cells the opportunity to begin the process of renewal and regeneration. Your surgeon will provide you with very specific post-procedure instructions that should be followed. The long-term goals are to decrease pain and improve function. This, however, is not a guarantee or warranty that the procedure will serve its intended purpose.

V. Investigational procedure acknowledgement:

This medical procedure is still considered experimental and investigative. This means it has not yet met the standard of care in the medical community. While your surgeon believes that this procedure holds promise, there are no large research studies that have shown it to be conclusively effective.

The American Academy of Orthopedic Surgeons issued a position statement on the “Use of Emerging Biologic Therapies” in December 2017 that states:

“The increasing shift to therapeutic biologic products for restoring structure and function presents new questions of safety and effectiveness. No longer reserved for treating trauma and soft tissue injuries, biologic therapies are now explored as options for osteoarthritis. As we note in the statement ‘Innovation and New Technologies in Orthopedic Surgery.’ surgeons must be aware of the scientific basis for different treatment

options offered to patients, including the benefits and risks. The varying regulatory pathways by which biologic therapies come to market require additional burden for surgeons to become familiar with, the Food and Drug Administration's current thinking with respect to the source, retrieval and/or manufacturing methods, processing, storage, and use of these products, whether alone or as part of combination products. Emerging biologic therapies may lack the demonstrated safety and effectiveness profiles of many traditional orthopedic treatments. Patient education is needed for informed consent…"

VI. Possible risks or complications of the procedure(s):

Bone marrow aspirations and BMAC stem cell injections are generally safe procedures. Complications are rare but can include:

1. Excessive bleeding, particularly in people with low numbers of platelets.
2. Infection, especially in people with weakened immune systems.
3. Long-lasting discomfort at the aspiration site.
4. Numbness or tingling.
5. Blood clots in veins and lung.
6. Hemorrhage, allergic reactions, or even death.
7. Local pain.
8. Bruising.
9. Cellulitis.
10. Increased pain.
11. Hypertrophic scar formation or keloid.
12. Injury to bone, muscle, or nerve.
13. Drop in blood pressure.
14. Loss of consciousness.
15. Abnormal heart beat.
16. Vaso-vagal reaction with vomiting and possible aspiration.
17. Increased cancer risk.
18. Kidney failure.
19. Structural failure of the treatment site.
20. Bony fractures related to instability.
21. Bone infection.
22. The above risks and complications are not the only possible side effects.

VII. Contraindications to stem cell injections

Contraindications to this procedure include:
1) Acute or Chronic infections; 2) Skin diseases (SLE, porphyria, contact dermatitis); 3) Cancer; 4) Chemotherapy; 5) Severe metabolic and systemic disorders; 6) Abnormal platelet function (blood disorders, hemodynamic instability; hypofibrinogenemia, critical thrombocytopenia); 7) Chronic liver disease; 8) Anti-coagulation therapy; 9) Underlying sepsis; 10) Systemic use of corticosteroids within two weeks of the procedure.

We encourage you to discuss the informed consent with family members, friends, physicians, and other trusted sources.

VIII. Insurance coverage for this procedure

By signing this form, you understand that there is no insurance coverage for the stem cell procedure. This means that the costs for the stem cell procedure (that have been quoted to you by our office) will not be reimbursed by a health insurer. You are responsible for these costs.

That said, while a health insurer will not reimburse for the stem cell aspiration or injection, there may be ancillary elements of the procedure that might be reimbursable by a health insurer. These would include the following:

a. Your initial orthopedic consultation.
b. Any diagnostic studies performed as part of your initial evaluation, including x-rays or ultrasound diagnostic studies.
c. Use of the mi-eye 2™ diagnostic arthroscopic needle scope.

Our staff will provide you with ICD-10 codes, CPT codes, consultation reports, ultrasound reports, x-ray reports, and diagnostic arthroscopic surgery reports to assist you in obtaining reimbursement from your insurance company should these procedures be covered under your policy.

By signing this form, you attest that you have been given the opportunity to ask questions about your diagnosis/condition, alternative forms of treatment, risks of non-treatment, the procedure(s) to be used, and the risks and hazards involved. By signing this form, you attest that you have been made aware that the use of adult mesenchymal stem cells is currently considered investigational. By signing this form, you attest that you have been given sufficient information to give this informed consent. Your physician has answered all your questions to your satisfaction.

I understand that I am free to refuse consent for any procedure.

Giving Consent
By signing below, I confirm that I have read: **What is Informed Consent?** (page 1)

By signing below, I confirm that I have read: **Informed Consent stem cell aspiration and BMAC injection into target site** (pages 1-5).

By signing below, I confirm that I have had: 1) each item explained to me; 2) a chance to ask questions; and 3) all my questions have been answered to my satisfaction.

Full name of procedure(s):	Bone Marrow aspiration and bone marrow aspiration concentrate (BMAC) injection into target site:		
Healthcare Professional performing procedure:	Patrick N. Bays DO		
Patient Signature	Print Name	Date	Time
Witness Signature	Print Name	Date	Time
Interpreter Signature	Print Name	Date	Time

Healthcare Professional's Statement
I explained the treatment/procedure(s) stated on this form, including the possible risks, complications, alternative treatments (including non-treatment) and anticipated results to the patient and/or his/her representative before the patient and/or his/her representative consented. If only the patient has signed this form, in my clinical opinion, the patient is capable of making his/her health care decisions. If in my clinical opinion, the adult patient has questionable ability to make his/her own health care decisions, I discussed the above with the patient and with the patient's legally authorized representative.

Healthcare Provider Signature	Print Name	Date	Time