USE OF AUTOLOGOUS ADIPOSE TISSUE DERIVED STROMAL VASCULAR FRACTION IN TREATMENT OF KNEE OSTEOMARTHRITIS AND CHONDRAL LESIONS

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ABSTRACT: Osteoarthritis is a joint inflammation that results from cartilage degeneration. It can be caused by aging, heredity and injury from trauma or disease. Stromal vascular fraction (SVF), containing large amount of stem cells and other regenerative cells, can be easily obtained from loose connective tissue that is associated with adipose tissue. Here we evaluated safety and clinical efficacy of freshly isolated autologous SVF cells in patients with grade 2-4 degenerative osteoarthritis (OA). A total of 31 patients underwent standard liposuction under local anesthesia and SVF cells were isolated and prepared for application into joints. A total of 61 joints, mainly knee and hip joints, were treated with a single dose of SVF cells. 19 patients were followed for minimum 6 weeks for safety and efficacy. Modified KOOS Clinical Score was used to evaluate clinical effect and was based on pain, non-steroid analgesic usage, limping, extent of joint movement, and stiffness evaluation before and at pre-operative, 1 week post-op, 1 month and 6 weeks after the treatment. No serious side effects, systemic infection or cancer was associated with SVF cell therapy. All patients improved after the treatment. Average KOOS score improved from pre-operative 37.5 to post-operative 6 week average 66.6. All sub scale parameter for pain, symptoms, activity of living & quality of life are also improved. Higher grade of OA were associated with slower healing. In conclusion, here we report a novel and promising treatment approach for patients with degenerative OA that is safe, cost-effective, and relying only on autologous cells, and can be used as one of the minimal invasive treatment modality for osteoarthritis.

INTRODUCTION: Osteoarthritis is a joint inflammation that results from cartilage degeneration. It can be caused by aging, heredity and injury from trauma or disease. Osteoarthritis is the most prevalent form of arthritis in the world, in United States, affecting over 20 million adults. In fact, more than half of all people age 65 and over have evidence of osteoarthritis. The most common symptom of osteoarthritis is pain in the affected joint(s) after repetitive use.(1) There is also evidence that raised systemic inflammatory markers have a role in future joint damage. Higher C-reactive protein (CRP) levels (indicative of inflammation) modestly but significantly predict those whose disease will progress.(2) There is no blood test for the diagnosis of osteoarthritis. The goal of treatment in osteoarthritis is to reduce joint pain while improving and maintaining joint function.(3) The cartilage is a unique avascular, aneural tissue that has limited capacity of self-repair once damaged.(4)
OA of weight-bearing joints is associated with chronic devastating pain, stiffness, decreasing range of motion and joint deformity, being one of the leading causes of decreased quality of life and work limitations in elderly. Despite ongoing research, treatments to manage the disease remain symptomatic. Treatment generally involves a combination of lifestyle modification, analgesics, non-steroidal anti-inflammatories, and joint injections with steroids or hyaluronic acid (lubricant). If pain becomes debilitating, joint replacement surgery may be used to improve the quality of life, e.g. partial joint resurfacing (hip and shoulder), and total joint replacement (hip and knee). Total joint arthroplasty (TJA) is the mainstay of treatment for end-stage OA of the hip or knee. Unfortunately, TJA is relatively frequently associated with serious and life-threatening complications including increased risk of infection, thromboembolism, myocardial infarction, stroke, increased risk of death at 30 and 90 days after surgery, and the life-span of the prosthesis is limited.\(^5,6,7,8\) Recently, it was shown that mesenchymal stromal/stem cells (MSCs) hold a great promise for their healing potential in regenerative medicine.\(^9\) Preclinical animal studies that utilize MSCs demonstrated safety and efficacy in treatment of OA, cartilage defects or other orthopedic conditions.\(^10,11,12,13\) The use of autologous SVF derived from adipose tissue as a treatment option has been rapidly gaining momentum. There are now a significant number of clinical trials listed on clinicaltrials.gov and ongoing IRCM IRB approved studies that support many variations of these therapies.

In humans, the largest collection of culture-expanded bone marrow-derived MSCs used for treatment of 339 patients with OA was recently documented and more than 75% improvement was reported in 41.4% and more than 50% improvement was reported in 63.2% of patients. No severe side effects and no neoplastic complications were detected at any stem cell re-implantation site in a mean follow-up 435 days.\(^14\) We propose that the combined use of autologous SVF, and PRP will deliver significant benefits in the treatment of osteoarthritis.

Stromal vascular fraction (SVF), containing large amount of stem cells and other regenerative cells, can be easily obtained from loose connective tissue that is associated with adipose tissue. Adipose tissue-derived MSCs are more genetically stable in a long term culture, display a lower senescence ratio and higher proliferative capacity.\(^13\) Bone marrow MSCs constitute only about 0.001%-0.01% of all nucleated cells in bone marrow, whereas the amount of adipose tissue-derived MSCs is approximately 1000-fold greater when isolated from equivalent volume of tissue.\(^15,13,16\) Adipose tissue can be easily obtained by standard liposuction under local anesthesia and isolated stromal vascular fraction (SVF) cells contain 1-4% MSCs as well as other cell types involved in tissue regeneration such as vascular endothelial cells, pericytes, fibroblasts, macrophages and regulatory T lymphocytes.\(^17,18,19,13\) SVF cells demonstrated anti-inflammatory and immunomodulatory effects and MSCs have the capacity to differentiate into connective tissue cells including cartilage, tendon and ligament.\(^13,20\)

Here we evaluated safety and clinical efficacy of freshly isolated autologous SVF cells in patients with grade 2-4 degenerative osteoarthritis (OA). Based on previously published results from animal and human studies, we hypothesize that non-manipulated SVF cells freshly isolated from adipose tissue and administered to the close proximity or into the arthritic joint can demonstrate healing potential in patients with degenerative OA. Here we present data from our study that demonstrate how practicing medicine with patient’s own regenerative cells freshly
isolated from a stromal vascular fraction surrounding small blood vessels of the adipose tissue can significantly improve outcome of degenerative OA leading to a better quality of life.

**REVIEW OF LITERATURE:** Preclinical animal studies that utilize MSCs demonstrated safety and efficacy in treatment of OA, cartilage defects or other orthopedic conditions. The use of autologous SVF derived from adipose tissue as a treatment option has been rapidly gaining momentum.

In humans, the largest collection of culture-expanded bone marrow-derived MSCs used for treatment of 339 patients with OA was recently documented and more than 75% improvement was reported in 41.4% and more than 50% improvement was reported in 63.2% of patients. No severe side effects and no neoplastic complications were detected at any stem cell re-implantation site in a mean follow-up 435 days. We propose that the combined use of autologous SVF, and PRP will deliver significant benefits in the treatment of osteoarthritis.

Stromal vascular fraction (SVF), containing large amount of stem cells and other regenerative cells, can be easily obtained from loose connective tissue that is associated with adipose tissue. Adipose tissue-derived MSCs are more genetically stable in a long term culture, display a lower senescence ratio and higher proliferative capacity. Bone marrow MSCs constitute only about 0.001%-0.01% of all nucleated cells in bone marrow, whereas the amount of adipose tissue-derived MSCs is approximately 1000-fold greater when isolated from equivalent volume of tissue. Adipose tissue can be easily obtained by standard liposuction under local anesthesia and isolated stromal vascular fraction (SVF) cells contain 1-4% MSCs as well as other cell types involved in tissue regeneration such as vascular endothelial cells, pericytes, fibroblasts, macrophages and regulatory T lymphocytes. SVF cells demonstrated anti-inflammatory and immunomodulatory effects and MSCs have the capacity to differentiate into connective tissue cells including cartilage, tendon and ligament.

**STATEMENT OF THE PROBLEM:** An experimental study to assess the effectiveness of autologous adipose tissue derived stromal vascular fraction in treatment of knee osteoarthritis and Chondral lesions and the Safety and Effectiveness of Autologous Stromal Vascular Fraction on Pain and Inflammation associated with Osteoarthritis of the Knee.

**OBJECTIVES:**
- To find out the safety & efficacy of the autologous adipose derived stromal vascular fraction in the treatment of osteoarthritis.
- To find out the role of autologous adipose derived stromal vascular fraction in the treatment of osteoarthritis.
- To evaluate the difference in koos score of patients before and after svf treatment.
- To find out the correlation between BMI of the patient and post-operative koos score.

**HYPOTHESES:** H1: There is a significant improvement on the pre and post op koos score in patients who underwent Autologous adipose derived stromal vascular fraction injection in the treatment of osteoarthritis at the level p ≤ 0.05.
H2: There is significant correlation between BMI of the patients and their post-operative koos score after Autologous adipose derived stromal vascular fraction injection in the treatment of osteoarthritis.

OPERATIONAL DEFINITIONS: SVF: Stromal vascular fraction derived from autologous adipose tissue extracted from mini-liposuction under tumescent anaesthesia. In the vast majority of scientific publications only the term adipose tissue is used, but the true source of SVF cells is not the adipose part but only the stromal (i.e. loose connective tissue) part of the fat obtained typically by liposuction.

KOOS Score: (Knee Injury & Osteoarthitis Outcome score) scoring system was used to assess the outcome. The KOOS is a knee-specific instrument, developed to assess the patients' opinion about their knee and associated problems. The KOOS evaluates both short-term and long-term consequences of knee injury. It holds 42 items in 5 separately scored subscales; Pain, other Symptoms, Function in daily living (ADL), Function in Sport and Recreation (Sport/Rec), and knee-related Quality of Life (QOL).

MATERIAL & METHODS: A prospective experimental research design is adopted in this study. 31 patients were included in the study who had osteoarthritis. All the patients underwent SVF therapy. Out of which 19 patients were followed for their improvement in their scores of (pain, symptoms, activity of living, quality of life) after 1, 4 and 6 weeks of surgery. Further study will be done with more number of patients with longer follow-up.

SAMPLE SELECTION CRITERIA:
Inclusion Criteria: Patients with indication of Osteoarthritis, grade 2 or more (Kellgren-Lawrence). Can be from degeneration or chronic injury. Patients range from 18-90 years of age. Patients must be able to comply with treatment plan, laboratory tests and periodic interviews. Patients with adequate renal function, Creatinine ≤ 1.5 mg/dl. Patients with adequate cardiac and respiratory function. Patients with adequate blood coagulation activity, PT(INR) < 1.5, APTT. Patients must have adequate immune system function, with no known immunodeficiency disease. Greater than 6 months knee pain on the index side (left or right knee).

Exclusion Criteria: Neoplastic cancer within 5 years prior to screening, except for cutaneous basal cell or squamous cell cancer resolved by excision. Presence of clinically significant acute or unstable cardiovascular and cerebrovascular (stroke). Diagnosis of a transient ischemic attack in the 6 months prior to screening. Patients infected with hepatitis B, C or HIV. Patients with Body Mass Index (BMI) > 40kg/m2. Presence of active infection. Pregnancy & lactation. Any other illness, psychiatric disorder, alcohol or chemical dependence that in the opinion of the investigator would render a patient unsuitable to participate in the study. Conditions/therapies/factors which could confound or interfere with the evaluation of pain/mobility including, but not limited to: Knee instability, any varus/valgus deformity of more than 10º, a deformity requiring osteotomy or complex surgery. Gout or pseudo gout. Treatments with strong opioid drugs in the previous 4...
weeks for other pain rather than knee osteoarthritis. Corticosteroid injection at treatment site within 1 month. Consistent use of NSAIDs within 48 hours of procedure. Health condition (including known allergy to local anesthetic drug) that does not allow to perform liposuction in local anesthesia.

**PATIENT INTAKE:** Prior to scheduling the patient is screened by the doctor. All inclusion and exclusion criteria are considered and patient intake is done at this time. Images are evaluated.

**Protocol:**

1. **Consent:**
   a) Discussion and signing of consent forms: Risks, benefits and alternatives of treatment are discussed. Patient understands that the proposed therapy is not intended to cure any disease. Patient understands that the intended therapy might have no utility at all and is willing to take the risks of no benefit whatsoever.
   b) The patient understands that he/she is consenting to participate in a study and although agreeing to return to the clinic at designated intervals for follow-up visits, and to respond to the questionnaires, there is no obligation on their part to do so and participation is voluntary.

2. **Lipo aspiration (Performed by surgeon on staff):**
   a) Patient prepped in a sterile manner.
   b) Pre-procedural antibiotics, anxiolytic and/or opiate pain medication administration if necessary.
   c) Stab incisions are made for cannula entry with #11 blade after local infiltration with 1% Lidocaine with epinephrine 1:100,000.
   d) Areas to be treated are then infiltrated with the tumescent anesthesia fluid with the following concentration of Lidocaine and epinephrine using the infiltration cannula. (40 ml of Lidocaine 2% without epinephrine plus 1 ml of epinephrine 1% are added to a 1000 ml bag of 0.9% Normal Saline.)
   e) 300 - 450cc adipose tissue is aspirated into a sterile container containing sterile 0.9% Normal Saline and sodium bicarbonate.

3. **ACRU (Autologous Adipose tissue Cell Recovery Unit):**
   a) Take patients adipose (fat) that was harvested to lab area.
   b) Turn Class II Bio Hood on.
   c) Wipe down surface in hood with 70% alcohol.
   d) Take sample and divide into 50ml tubes.
   e) The fat is processed in ACRU. Ultrasonic cavitation is used to separate fat and stromal vascular fraction.
   f) Then 50ml tubes are centrifuged.
   g) You will see a pellet at the bottom of the tube. You will need to remove the top layer until you reach 5ml. Do your best not to disturb the pellet.
4. **Intra-articular injections:**
   a) If the patient has osteoarthritis in both knees then both knees will be injected, with the worst knee identified as the Index knee, which will be reported on.
   b) Area is prepared for injection with Chlorhexidine.
   c) Local anesthetic (Lidocaine 1%) given to skin and deep tissue as needed.
   d) SVF are injected ultrasound guided to improve the accuracy of procedure.

5. **Follow Up:**
   a) Patient is discharged when stable after observation and all post procedure instructions have been discussed.
   b) Patient is asked to report any side effects such as fever, pain and others.
   c) Patient is seen for follow up next day or within one week.
   d) Patients are interviewed by phone, email, or in person and asked to complete the KOOS questionnaires prior to initial treatment, at 1 week, 1 month and at 6 weeks.

**DATA ANALYSIS AND INTERPRETATION:** All patients underwent treatment with SVF cells as scheduled and no complications related to adipose tissue processing and SVF cells preparations were noticed. There were no serious side effects associated with SVF cell therapy. Other side effects related to the procedure consisted of local pain and swelling at the site of injection, fever, and mild headache.

At this point, we should also clarify the terminology regarding the source of SVF cells. In the vast majority of scientific publications only the term adipose tissue is used, but the true source of SVF cells is not the adipose part but only the stromal (i.e. loose connective tissue) part of the fat obtained typically by liposuction. We can demonstrate indirectly the healing potential of SVF cell therapy in OA using clinical examinations and symptom scoring as well as objective visualization of damaged joints by MRI and X-ray imaging. Since imaging was not the primary aim of this case control study, the follow-up X-ray and/or MRI examination was not performed in all patients. Since it is a short-term follow-up study Thus, we are not able to draw any conclusion on the correlation between clinical improvement and imaging studies.

We have given SVF injection to 31 patients from May 2015 to July 2015, in 62 joints. Most of the patients were in age group 41-60 yrs. i.e. 19 out of 31 (Range 26yrs to 78 yrs.). As per sex distribution there was 23 female and 8 male in study. We studied 19 patients 38 joints were injected with SVF with minimal follow-up of 6wks in detail and we are able to demonstrate safety with no serious side effects reported in 6 week of follow-up and clinical improvement in a vast majority of patients. Some patient’s experienced local pain and swelling at the injection site, but those symptoms were lasting shortly and were well controlled with common analgesics.

BMI ranges from 21.5 to 37 in 19 patients. 5 patients (26.3 %) had associated cardiovascular disease, 1 patient (5.3%) had migraine and one patient (5.3%) had undergone
unicompartment knee arthroplasty but majority 12 patients (63.2%) patients had no associated disease. One Patient had grade II, 12 patients had grade III & 6 patients had grade IV osteoarthritis (as per Kellgren-Lawrence classification).

Koos (Knee Injury & Osteoarthitis Outcome score) scoring system was used to assess the outcome. The KOOS is a knee-specific instrument, developed to assess the patients' opinion about their knee and associated problems. The KOOS evaluates both short-term and long-term consequences of knee injury. It holds 42 items in 5 separately scored subscales; Pain, other Symptoms, Function in daily living (ADL), Function in Sport and Rec- reaction (Sport/Rec), and knee-related Quality of Life (QOL).\(\text{[21]}\)

Frequency and percentage is used to describe the demographic variables of the study samples.

**Frequency and Percentage Distribution of Socio-demographic Variables:**

| AGE OF PATIENTS | F | % |
|-----------------|---|---|
| 48              | 1 | 5.3 |
| 50              | 2 | 10.5 |
| 52              | 1 | 5.3 |
| 58              | 2 | 10.5 |
| 59              | 3 | 15.8 |
| 60              | 1 | 5.3 |
| 62              | 1 | 5.3 |
| 63              | 1 | 5.3 |
| 66              | 1 | 5.3 |
| 67              | 2 | 10.5 |
| 68              | 1 | 5.3 |
| 71              | 1 | 5.3 |
| 73              | 1 | 5.3 |
| 74              | 1 | 5.3 |
| **TOTAL**       | 19| 100|

**TABLE 1**

| GENDER | F | % |
|--------|---|---|
| **FEMALE** | 16| 84.2 |
| **MALE**   | 3 | 15.8 |
| **TOTAL**  | 19| 100|

**TABLE 2**
### DIAGNOSIS

| DIAGNOSIS | F  | %   |
|-----------|----|-----|
| OA        | 18 | 94.7|
| RA        |  1 |  5.3|
| TOTAL     | 19 | 100 |

**TABLE 3**

### BMI OF PATIENTS

| BMI | F | %  |
|-----|---|----|
| 20  | 2 | 10.5|
| 21  | 1 |  5.3|
| 24  | 2 | 10.5|
| 25  | 1 |  5.3|
| 26  | 1 |  5.3|
| 27  | 5 | 26.3|
| 28  | 2 | 10.5|
| 30  | 1 |  5.3|
| 31  | 3 | 15.8|
| 37  | 1 |  5.3|
| TOTAL| 19| 100 |

**TABLE 4**

### GRADE OF OSTEOARTHRITIS

| GRADE | F  | %   |
|-------|----|-----|
| 1     |  0 |  0  |
| 2     |  1 |  5.3|
| 3     | 12 | 63.2|
| 4     |  6 | 31.6|

**TABLE 5**

### AGE OF PATIENTS

![Bar chart showing age distribution](chart.png)
DATA ANALYSIS AND INTERPRETATION: Parametric test is used to find the difference in KOOS scores of 19 patients for various subscale, prior to the surgery, one week after the surgery and 6 weeks after the surgery.

Paired t test was used to find out the difference in pre and post score of patients who underwent SVF therapy, before the treatment one week after the treatment and 6 weeks after the treatment.

Paired sample t test was used to find the difference between pre score and score after one week of SVF therapy, pre score and score after 6 weeks of therapy and score of one weeks and score of 6 weeks after SVF therapy.

A statistical significance is assessed for difference in the scores were found between the scores of Pain, Symptoms, Activity of Living (AoL), Quality of Life (QoL), average score, before surgery and after one and 6 weeks of surgery. Karl Pearson correlation is used to test the correlation between BMI, grade of Osteoarthritis and different scores of patients after 6 weeks of surgery.

P ≤0.05 significance was used throughout the study. SPSS version 20 was used to do the statistical analysis of the study.

| PAIRED t TEST TO COMPARE THE DIFFERENCE IN KOOS SCORE | t   | df | sig  |
|------------------------------------------------------|-----|----|------|
| Pair 1 Pre-op AVG - Post-op AVG 1 week               | -11.232 | 18 | .000 |
| Pair 2 Pre-op AVG - Post-op AVG 6 weeks              | -11.742 | 18 | .000 |
| Pair 3 Pre-op Pain - Post-op Pain                    | -10.948 | 18 | .000 |
| Pair 4 Pre-op Pain - Post-op pain                    | -9.569 | 18 | .000 |
| Pair 5 Pre-op Symptom - Post-op Symptom              | -5.427 | 18 | .000 |
| Pair 6 Pre-op Symptom - Post-op Symptom              | -4.308 | 18 | .000 |
| Pair 7 Pre-op AOL - Post-op AOL                      | -11.149 | 18 | .000 |
| Pair 8 Pre-op AOL - Post-op AOL                      | -14.409 | 18 | .000 |
| Pair 9 Pre-op Qol - Post-op Qol                      | -6.485 | 18 | .000 |
| Pair 10 Pre-op Qol - Post-op Qol                     | -6.191 | 18 | .000 |
The above table signifies that t test shows extremely significant improvement in KOOS score for Pain (t=-10.926), symptom (t=-5.418), AoL (t=-11.195), QoL (t=-6.633) and average (t=-11.323) when pre-operative & 1 week scores were compared at the level of p ≤ 0.05 (df=18). There is also extremely significant improvement in KOOS scores for Pain (t=-9.545), symptom (t=-4.313), AoL (t=-14.457), QoL (t=-6.274) and average (t=-11.799). When pre-operative & 6 week scores were compared at the level of p ≤ 0.05 (df=18). When scores of 1 week post-op are compared with 6 week post-op there was no significance difference was found in average koos, koos pain, koos symptom & koos QOL but there was significant improvement in KOOS AOL (t=), P <0.05.

A positive correlation was found in BMI and average KOOS (r=0.411), Koos Pain (r=0.492), koos symptom (r=0.133), koos AoL (r=0.319) and koos qol (0.164) in patients who underwent SVF therapy. A negative correlation was seen between grade of OA and KOOS score improvement in patients who underwent SVF therapy.

**DISCUSSION:** Knee osteoarthritis is a common chronic orthopedic disease that significantly reduces the patient’s quality of life. In recent years, stem cell application to osteoarthritis has rapidly developed, with promising results in pre-clinical and clinical trials. This clinical study showed that SVF injection brought about some good outcomes for patients with osteoarthritis. We have seen significant improvement in pain & symptom score as early as in first week that shows strong anti-inflammatory and analgesic effect of stromal vascular fraction derived from autologous adipose tissue obtained by liposuction. The anti-inflammatory and pain reduction effects are also contributed by soluble factors secreted from the SVF or ADSCs. ADSCs secrete many important soluble factors, such as HGF, VEGF, NGF, EGF, FGF, and TGF. Unlike PRP, growth factors from ADSCs are continuously produced after injection of these cells into the joint (22, 23, 24).

Clinical case reports provides clear MRI evidence of apparent bone regeneration in osteonecrosis of femoral heads and meniscus cartilage regeneration in osteoarthritis of human knees. Along with MRI evidence, the measured physical therapy outcomes, subjective pain, and functional status all improved.(25) In a level IV study, all 21 patients showed improved joint function after 8.5 months. The pain score decreased from 7.6±0.5 before injection to 3.5±0.7 at 3 months and
1.5±0.5 at 6 months after injection. The Lysholm score increased from 61±11 before injection to 82±8.1 after injection. Significant improvements were noted in MRI findings, with increased thickness of the cartilage layer. Moreover, there were no side effects or complications related to microorganism infection, graft rejection, or tumorigenesis. These results provide a new opportunity for osteoarthritis treatment.\(^{(17)}\)

The patients will be further monitored and longer follow-up data will help to answer question about durability and long-term safety of SVF cell therapy. Although in a clinical study, with single injection of SVF 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 years, 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.\(^{(19)}\)

Another limitation of our study is no randomization and no placebo control. There were two reasons for designing that case control study: 1) ethical aspect and 2) economical aspect. We believe it would be rather unethical to ask placebo group of patients to undergo liposuction and placebo administration to the joint with OA. Since this study was designed as autologous cell therapy, there is strong previously documented clinical evidence of safety of autologous non-manipulated or minimally manipulated cell therapies.\(^{(26)}\)

On the other hand, this study is well designed and strong evidence for minimal risks based on previous studies exists, can lead to a cost-effective, safe, ethical and objective evaluation of a novel treatment.

CONCLUSION: To summarize, autologous SVF injection is a safe and efficient method for treating osteoarthritis. The efficiency of transplantation clearly improved after 6 months. Overall, 100% of patients were pleased with this method. Pain was strongly reduced after therapy, and the quality of life was significantly improved. Although further studies with control subjects and more patients need to be performed to confirm the above results, this study suggests that our treatment is a promising minimally invasive therapy for osteoarthritis patients.

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