

The Effect of Micro Fragmented Adipose Tissue (MFAT) on Knee Osteoarthritis

Study Protocol

NCT03467919

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1) Name of study

Micro Fragmented Fat Tissue on Knee Osteoarthritis

2) PI and other key investigators or key study personnel

Co-PI: Eugene Y. Roh, MD and Seth Sherman, MD

Research coordinator: Jessica Nguyen, CRCA

3) Specific source of institutional funding (account number)

Internal funding from Charity

4) List of sources from whom you are seeking funds (or have sought funding) for this project

AMSSM funding

Stanford internal funding

PM&R foundation

Charity from donors

5) Specific aims and basic hypothesis including an explicit primary hypothesis or goal

Microfragmented Adipose Tissue (MFAT) may be beneficial to patients with OA because they may differentiate into chondrocytes, promote endogenous tissue repair, and have potent anti-inflammatory properties.

We aim to determine whether MFAT injection as an alternative therapy in patients with degenerative arthritis will result in improved clinical outcomes and structural improvement compared to conventional therapy.

Hypothesis:

Intraarticular injection of Microfragmented Adipose Tissue (MFAT) into the knee of patients with symptomatic moderate osteoarthritis will improve patient-reported outcomes of pain and function better compared to a conventional intra articular steroid injection.

6) General background (2 page maximum including published preclinical and animal data supporting basic hypothesis, if relevant)

Preliminary studies of Mesenchymal stem cell (MSC) therapy in osteoarthritic patients have generally shown positive results, albeit in uncontrolled studies. Jo et al injected ADSCs into osteoarthritic knees, finding the procedure to be safe and effective at 6-month follow-up in 18 patients; no adverse reactions were noted while WOMAC scores and cartilage volume increased.

A large study by Michalek et al in 1128 patients also showed no adverse events with ADSC injection into knee and hip joints with at least 50% score improvement in 91% of patients at 12-month follow-up. (Michalek 2015)

Koh et al treated 30 patients with knee OA (age > 65) by injecting ADSCs obtained using liposuction techniques. Eighty-four percent (84%) had no worsening of radiographic OA at 2 years following ADSC injection, and 88% of patients that consented to a second-look arthroscopic procedure improved or maintained their cartilage status at least 2 years following ADSC injection. (Koh 2015)

7) Preliminary unpublished data (1 page maximum)

N/A

8) Experimental design and data analysis, including inclusion and exclusion criteria, statistical basis for the number of subjects to be enrolled, the statistical plan for analyzing at least the primary hypothesis, matrix showing procedure plan for each study visit, data safety monitoring plan (4 pages maximum)

design

Randomized double blinded study.

Data analysis

-t test

Inclusion Criteria

- Age between 25 and 75 years-old
- Diagnosis of pre-existing osteoarthritis of the joint by Kellgren-Lawrence Grade 2 or 3.
- Working understanding of the English language and able to fully understand the procedure
- Capable of providing informed consent
- Able to complete online, in-person or phone surveys for the purposes of follow-up
- Capable of understanding pre- and post-procedure care instructions
- Ambulatory at baseline
- Previous trial and failure of conservative therapy consisting of a minimum of 6 weeks of physical therapy and trial of anti-inflammatory medications if not contraindicated, with or without concomitant bracing and/or injections.

data safety monitoring

Redcap will be used as a secure database in which to compile and capture all data.

All data will be entered directly to the Redcap database. Data will be de-identified and coded through Redcap prior to exportation to spreadsheet form for data analysis.

procedure plan

Time of Visit	Knee Exam	Questionnaires	X-Ray	MRI
Baseline	Standard care	Study	Standard care	Standard care
Injection	Study	Study	N/A	N/A
1 month ($\pm 1w$)	Standard care	Standard care	N/A	N/A
6 weeks ($\pm 1w$)	N/A	N/A	N/A	Study
3months ($\pm 4w$)	Standard care	Standard care	N/A	N/A
6 months ($\pm 4w$)	Standard care	Standard care	N/A	N/A
12 months ($\pm 2mos.$)	Standard care	Standard care	N/A	Study
24 months ($\pm 2mos.$)	Standard care	Standard care	N/A	N/A

Exclusion Criteria

- Age < 25 or > 75 years old
- Radiographs demonstrating either no, little or severe osteoarthritis (Kellgren-Lawrence Grade 0, 1)
- Prior total or partial joint replacement surgery or a surgery involving cartilage regeneration (microfracture, ACI, etc)
- Previous cortisone and/or Hyaluronic acid or PRP(Platelet rich plasma) intra-articular injection within the last 3 months
- Co-morbiditiy with rheumatologic condition, inflammatory arthritis
- Currently undergoing immunomodulatory therapy
- Uncontrolled endocrine disorder
- BMI >35
- Current diagnosis of osteomyelitis, human immunodeficiency virus (HIV-1, -2) and/or hepatitis C (HCV), infection and poorly controlled diabetes (HgA1C >7.0)
- Pregnancy or planned pregnancy
- previous stem cell injection into treatment joint
- Patient scheduled to undergo any concomitant surgical procedures.
- Coagulopathy or anticoagulant treatment
- Chronic pain involving multiple body parts or opioid medication management

9) Significance

Osteoarthritis (OA) is a leading cause of morbidity in the United States, causing pain and impaired physical function at an individual level, along with significant economic burden of

disease at a population level. Regenerative medicine, specifically through the use of mesenchymal stem cells (MSCs), presents novel and promising therapies to aid in treating this ubiquitous disease. However, it should be pointed out that there is no strong evidence of stem cell treatment of knee OA treatment. Early studies investigating the effects of MSCs in the setting of OA have noted a dual benefit to stem cell therapy, which includes both tissue restoration and inflammation-reduction. MSCs have shown some promise to directly restore cartilage defects in animal models. Early clinical trials of adipose-derived stem cells (ADSCs), an easily harvested source of MSCs, have shown encouraging results but no randomized controlled trials have been published. This study aims to evaluate the efficacy of MFAT therapy, in conjunction with growth factors from platelet-rich plasma, on osteoarthritis compared to conventional treatment in a randomized controlled trial.

10) Key References

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