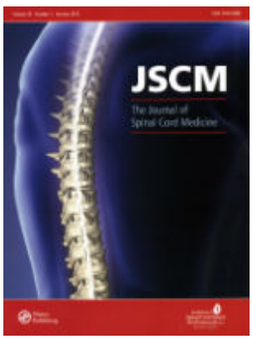

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Research Article

A pilot study to evaluate micro-fragmented adipose tissue injection under ultrasound guidance for the treatment of refractory rotator cuff disease in wheelchair users with spinal cord injury

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Context/Objectives: Wheelchair users with chronic shoulder pain have few options after conservative treatments fail. This pilot study's purpose was to establish safety and treatment effects of micro-fragmented adipose tissue (MFAT) injections under ultrasound guidance for treatment of refractory shoulder pain caused by rotator cuff disease in wheelchair users with spinal cord injury (SCI) to prepare for a larger trial.
Design: Pilot clinical trial.
Setting: Rehabilitation hospital outpatient clinic.
Participants: Ten wheelchair users with chronic SCI who had moderate-to-severe shoulder pain caused by refractory rotator cuff disease (diagnosed via ultrasound) for greater than 6 months.
Interventions: Ultrasound-guided injections of MFAT into the pathologic rotator cuff tendons and other abnormal shoulder structures (e.g. acromioclavicular and glenohumeral joints; subacromial bursa).
Outcome Measures: 6- and 12-month changes in 11-point Numerical Rating Scale (NRS); Wheelchair User's Shoulder Pain Index (WUSPI); Brief Pain Inventory pain interference items (BPI-I7); Patient Global Impression of Change (PGIC); ultrasound and physical exams; and adverse events.
Conclusions: There were no significant adverse events throughout the study period. WUSPI, NRS, and BPI-I7 scores were significantly lower 6 and 12 months post-procedure ($P < .05$). Of those who remained in the trial, clinically meaningful changes (≥30% decrease) in WUSPI, NRS, and BPI-I7 scores were observed in 77.8%, 77.8%, and 66.7% of participants, respectively. All but one participant reported improvement in clinical status. MFAT injection under ultrasound guidance is potentially a safe and efficacious treatment for refractory shoulder pain caused by rotator cuff disease in wheelchair users with SCI. A larger, randomized controlled trial has been initiated.
Trial registration: ClinicalTrials.gov identifier: NCT03167138

Keywords: Spinal cord injuries, Wheelchairs, Shoulder pain, Rotator cuff injuries, Clinical Trials, regenerative medicine, Rehabilitation

Introduction

Wheelchair users with spinal cord injury (SCI) rely on their upper limbs for activities of daily living. Thus, they have a high risk of developing shoulder pain,[1] which is often attributed to pathology of rotator cuff tendons and other shoulder soft-tissue structures.[2] Shoulder pain treatments vary, but generally consist of pharmacological agents, physical therapy, equipment modifications, and education.[1] A limited number of clinical trials have sought to establish efficacy of different shoulder pain treatments, including structured

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exercise programs,[3–6] acupuncture,[7,8] and platelet-rich plasma.[9,10] Recommendations for duration of conservative management vary depending on the situation; however, a 6-month trial is often recommended in the able-bodied population, with conservative treatment failures often referred for surgery.[11] Previous studies have reported favorable post-surgical outcomes in persons with SCI; however, the functional drawbacks are considerable and include hospitalization, switching to a power wheelchair, reliance on others for assistance with upper limb weight-bearing activities during recovery, and/or potential for re-tearing.[12–15] These surgical investigations have not included control groups and thus their validity is limited.

Minimally invasive biological interventions and regenerative treatments have recently emerged as promising treatments for musculotendinous injuries.[16] One such treatment is adipose tissue, which as an endocrine organ harbors a potential source of bioactive and regenerative components for orthopedic conditions, and may provide cushioning.[17] Intratendinous injection of adipose-derived mesenchymal cells for rotator cuff disease has been studied and positive outcomes (pain, function, intratendinous defect volume) were reported.[18] However, in this study the adipose tissue was enzymatically digested, isolated, and cultured prior to injection, which is a process not approved for clinical use by the United States Food and Drug Administration. A recent case series of 18 able-bodied participants reported positive findings after injection with autologous, micro-fragmented adipose tissue injection under ultrasound guidance.[19] Its use in persons with SCI who have shoulder pain, however, has yet to be reported.

Pilot studies are an important first step in devising a clinical trial, and there are several reasons why one may be conducted. Namely, to determine effect sizes for sample size calculation, establish safety of the treatment, and evaluate the feasibility of successfully conducting a larger, randomized controlled trial.[20] Therefore, the goals of this study were not to test hypotheses. Instead, they were to (1) evaluate safety of the treatment by cataloguing adverse events; (2) estimate the magnitude of a treatment effect, which could be used to justify the need for a larger trial and sample size; and (3) determine feasibility by examining treatment procedures and outcome measures for appropriateness. Outcome measures of treatment effect included changes in 11-point Numerical Rating Scale (NRS); Wheelchair User's Shoulder Pain Index (WUSPI); Brief Pain Inventory (BPI-I7) pain interference items; and Patient Global Impression of Change (PGIC). Physical and ultrasound examinations were also conducted. Ultimately, the information gained from this pilot study would help to optimize the design of a larger clinical trial.

Methods

Participants

This single-group pilot study received Institutional Review Board approval from the organization's ethical committee and was registered with clinicaltrials.gov (NCT03167138) prior to enrollment. Participants were recruited at an outpatient clinic using flyers and word of mouth between July, 2018 and April, 2020. Upon recruitment, they were screened to determine whether they met the following inclusion criteria:

(1) Male or female, 18–70 years of age, inclusive.
(2) Neurological impairment secondary to SCI that occurred at least twelve (12) months prior to the Screening Visit; neurological level of injury between C6 and L5, inclusive.
(3) Non-ambulatory except for exercise purposes and uses a manual or power wheelchair as his/her primary means of mobility (>40 h/week).
(4) History of chronic shoulder pain due to rotator cuff disease for ≥6 months that was unresponsive to conservative treatment (e.g. physical therapy, pharmacological agents). Average shoulder pain intensity during the week leading up to the Screening Visit of ≥4 out of 10 on an 11-point NRS (0, no pain; 10, maximum pain imaginable). Rotator cuff disease was defined as pain over the anterior shoulder with direct palpation and with provocative tests for rotator cuff disease, and was confirmed by tendinopathic changes visualized with ultrasound imaging (Note: physical exam and ultrasound exam procedures are described in detail below).
(5) Able and willing to comply with the protocol.
(6) Able to and gave voluntarily informed consent prior to the performance of any study-specific procedures.

Participants were excluded if they reported one or more of the following criteria:

(1) Contra-indications to the procedure (e.g. infection, coagulopathy, current use of anti-coagulants).
(2) History of active cancer within 5 years.
(3) History of systemic inflammatory disorders (e.g. diabetes, rheumatoid arthritis).
(4) Prior history of MFAT injection.
(5) Glucocorticoid injection within the past four weeks.
(6) Pregnancy.
(7) Any medical condition, including psychiatric illness, which would interfere with the interpretation of the study results or the conduct of the study.

Physical and ultrasound examinations

Physical examination maneuvers included tenderness during supraspinatus palpation over the greater tuberosity; Jobe's test;[21] painful arc;[22] resisted external rotation; and Neer's,[23] Yocum's,[24] and Hawkins-Kennedy[25] impingement signs. Ultrasound examinations followed the Ultrasound Shoulder Pathology Rating Scale.[26,27] Specific signs included degrees of supraspinatus and biceps tendinopathy; cortical irregularity; glenohumeral joint effusion; bursal thickening; and dynamic tests for supraspinatus and subscapularis impingement. Physical examination was performed at every timepoint, while the ultrasound examination was performed at screening and at 6 and 12 month follow-up visits.

Injection procedure

The intervention consisted of a single percutaneous injection of micro-fragmented adipose tissue (MFAT) into degenerative shoulder lesions identified during screening, with the primary target being pathologic structures noted during the baseline evaluation. This included the supraspinatus tendon in all subjects. Additional structures that were targeted included the acromioclavicular and glenohumeral joints, and biceps, infraspinatus, and subscapularis tendons if significant pathology was identified. If the subject reported bilateral shoulder pain, the more painful shoulder was injected.

Adipose tissue was harvested and processed into MFAT using the Lipogems System (Lipogems International, SpA, Milan, Italy).[a] Lipogems is a non-enzymatic isolation system that uses mechanical forces to yield a micro-fragmented adipose product, purified of its pro-inflammatory oil and blood residues, in a closed, sterile, and safe manner.[28]

Participants were transferred onto an examination table and placed in a supine position. Assistance during the transfer was provided if needed. Periodic weight-shifts were allowed to minimize risk of pressure injury, and vital signs (blood pressure, heart rate, respiratory rate, and pain) were monitored periodically during the procedure. The skin overlying the abdomen was prepped with a 3.15% chlorhexidine gluconate and 70% isopropyl alcohol solution and draped in the usual sterile fashion. The skin and deeper tissues of the abdomen were then anesthetized with 1% lidocaine using a 27-guage × 1.5 inch needle, and a tumescent solution was prepared by diluting 50.0 mL of 2% Lidocaine and 1.0 mL of 1:1000 epinephrine in 500 mL of normal saline. The tumescent was injected in the fat layer of the abdomen subcutaneously, below Scarpa's fascia, using a 17-guage blunt cannula for local anesthesia. The Lipogems kit was then prepared for lipoaspirate processing. After approximately 15 min, a 13-guage blunt-end cannula was used to aspirate the adipose tissue and injected into the Lipogems device. After processing, the micro-fragmented lipoaspirate was drawn into syringes for injection. Further details of the processing technique have been published previously.[28]

The participant was then placed in a lateral side-lying position, exposing the targeted shoulder for injection. Shoulder structures were scanned with an ultrasound machine (Edge II, FUJIFILM Sonosite, Inc., Bothell, Washington, USA)[b] to identify pathological structures and the appropriate approaches for injection, and the entry locations were marked. The probe and skin was cleansed thoroughly with a chlorhexidine/isopropyl alcohol solution, and the skin and subcutaneous tissues of the entry site were anesthestized with a 1.0% lidocaine solution using a 27-guage × 1.5 inch needle. Sterile ultrasound gel was applied to the probe and injection locations. The targeted structures were then identified and injected with up to a total volume of 8 mLs of MFAT depending on the area previously noted on ultrasound to demonstrate significant pathology (~1–3 mLs into the rotator cuff tendons; 1–2 mLs into the biceps tendon; ~3–4 mLs glenohumeral joint/subacromial bursa; ~0.5–1 mL into the acromioclavicular joint). The injections sites were then cleaned and covered with adhesive bandages.

Post-injection protocol

Participants were kept in a supine position and monitored for complications for 15 min immediately post-injection, and were then raised and transferred into their wheelchair with assistance. They were instructed to avoid the use of aspirin and non-steroidal anti-inflammatory drugs (e.g. ibuprofen, naproxen), but were allowed the use of Ultram, Percocet, or acetaminophen for the pain as needed. They were recommended to ice the harvest site and treatment areas for 15–20 min every hour as needed, and to remove the harvest site dressing after 24 h. Activities were to be reduced during the first four days after the procedure, with return to pre-treatment levels by day seven (as tolerated). Twenty-four hours post-procedure, they were instructed to begin a standardized, four-week stretching program. Muscles targeted for stretching included the pectoralis, biceps, and upper trapezius muscles. After the four weeks, they were instructed to begin a formal strengthening program that targeted the rotator cuff and scapular stabilization muscles. The stretches and

strengthening exercises were based on a randomized controlled trial of an exercise program to alleviate shoulder pain[6]. Participants were recommended to perform stretching and strengthening exercises for both shoulders and to continue performing exercises throughout the duration of the study.

Pain outcome measures

Outcomes were collected at baseline and 1, 2, 3, 6, and 12 months post-procedure. The primary outcome was 6-month change in NRS scores. Secondary outcomes included 6-month changes in WUSPI and BPI-I7 scores, and 12-month changes in WUSPI, BPI-I7, and NRS scores. Patient Global Impression of Change (PGIC), shoulder physical examinations, and clinical ultrasound examinations were evaluated at 6 and 12 months.

Shoulder pain intensity was assessed using an 11-point NRS. Participants were asked to rate their average, worst, and least pain over the past week from 0 ("no pain") to 10 ("worst pain imaginable"). Worst, least, and average pain were averaged for a composite pain score.[29] The NRS in this format is recommended for use in SCI research and clinical trials in general as a primary outcome measure.[30,31]

Functional shoulder pain intensity was measured using the WUSPI, which is a 15-item self-report instrument that measures shoulder pain during various functional activities that may be performed by wheelchair users with SCI.[32] Examples include transfers, propulsion, dressing, bathing, and sleeping. The WUSPI utilizes 10-centimeter visual analog scales, the scores of which are summed to derive a total score between 0 and 150. A score of 0 indicate no pain and 150 indicates maximum pain. It is a valid and reliable measure of shoulder pain in wheelchair users with SCI[33] and has been found to change in response to treatments for shoulder pain.[4,7,8]

The BPI-I7 interference subscale consists of seven items that describe various aspects of life potentially affected by pain.[34] Examples include sleep, mood, general activity, and mobility. Each item is graded between a 0 ("no interference") and 10 ("maximum interference"). Scores are summed and averaged across the scale for a single score between 0 and 10. The BPI-I7 has been used previously to evaluate pain in people with SCI.[35,36] The original scale was modified slightly to fit into the context of wheelchair use; specifically, the item "walking ability" was replace by "ability to get around."

Patient Global Impression of Change was developed as a way to measure changes in overall clinical status in response to an intervention.[37] It is a 7-point Likert scale anchored on one end by "very much improved" and the other by "very much worse." The PGIC scale has been recommended for use in clinical trials involving individuals with SCI because of its extensive use in non-SCI trials, and its sensitivity to change.[31]

Dworkin, *et al*. recommended a 30% reduction in pain scores be considered clinically meaningful as part of clinical trials.[30] This threshold was applied to the NRS, WUSPI, and BPI-I7 scores used in this study to determine the percentage of participants who achieved clinically meaningful decreases in pain and pain interference.

Statistical analysis

All statistical procedures were conducted using SPSS v21 (IBM, Inc., Armonk, New York, USA). Basic descriptive statistics were calculated for all demographic and outcome variables. Primary and secondary outcomes were tested using the Wilcoxon signed-rank test. Dependent variables in each test were baseline and either 6- or 12-month outcomes. All tests were two-sided with alpha level set at 0.05 for statistical significance.

Results

Eleven full-time manual wheelchair users with SCI were screened for the study; ten were ultimately treated. One was disqualified after reporting a NRS score of 2 out of 10. Another received the MFAT treatment, but later received other injections for pain in the contralateral shoulder and thus was excluded. One participant died just prior to 12 month follow-up; however, this death was deemed unrelated to the protocol. Demographic information is presented in Table 1. Treatment notes, including injection locations and injection volumes, are presented in Table 2. The trial was stopped once enough 6-month safety and pain data were collected for the next trial phase.

No adverse events were reported at the harvest or injection sites other than expected pain at the injection site, which resolved within the first week. Significant decreases in 6-month NRS scores, the primary outcome, were observed with an average decrease of 60.1% ($Z = -2.67$, $P < .01$; Fig. 1). Decreases were also observed in 6-month changes in WUSPI scores ($Z = -2.31$, $P < .05$; Fig. 2) and BPI-I7 ($Z = -2.67$, $P < .01$; Fig. 3). Decreases in scores continued to be observed at 12 months in NRS ($Z = -2.37$, $P < .05$), BPI-I7 ($Z = -2.38$, $P < .05$), and WUSPI scores ($Z = -2.03$, $P < .05$). Most participants reported being, "Very Much Improved" (Table 3).

Table 1 Demographic and injury characteristics of all participants screened for entry into the trial.

Study ID	Age (years)	DOI (years)	Level	Sex	Ethnicity/Race	Baseline NRS	Bilateral pain
1	54	10	T10	M	NH/W	7	Yes
2	66	20	T10	F	H/W	4	No
3	49	29	T5	M	H/W	6	No
4	56	18	C6	M	NH/W	8	No
5	54	38	C6	M	NH/W	5	No
6	70	16	T8	M	NH/W	4	Yes
7	57	25.5	T12	M	NH/W	5	Yes
8*	68	39.8	T3	M	NH/W	2	Yes
9	45	25	T12	M	NH/B	5	No
10†	55	27.4	T12	M	NH/W	7	Yes
11	53	8	L3	M	NH/W	5	Yes

Notes. Age, duration of injury (DOI), injury level, sex, ethnicity/race are presented for each subject, including the screen failure. Baseline Numerical Rating Scale (NRS) pain scores and presence of bilateral shoulder pain (yes or no) are also presented.
H/NH = Hispanic/non-Hispanic. W/B = White/Black.
*Excluded due to low pain scores.
†Data were excluded after receiving alternative injections for shoulder pain before the 2-month timepoint.

The majority of participants reported greater than 30% decrease in NRS ($n = 8$, 88.9%), WUSPI ($n = 6$, 66.7%), and BPI-I7 scores ($n = 9$, 100.0%; Table 4) at 6 months. At 12 months, similar observations were noted (NRS: $n = 7$, 87.5%; WUSPI: $n = 6$, 85.7%; BPI-I7: $n = 7$, 87.5%). Improvements were seen across all physical examination maneuvers (Table 5). Four participants exhibited some degree of improvement in ultrasound markers for supraspinatus tendinopathy. Although unable to be tested statistically, no qualitative relationships were observed between ultrasound findings and pain changes.

Table 2 Treatment notes for injection procedure.

Study ID	Injection location, Injectate volume
1	Supraspinatus Tendon, 2.5 mL; Subacromial Bursa, 2.0 mL; ACJ, 1.0mL
2	Supraspinatus Tendon, 3.0 mL; Subscapularis Tendon, 3.0 mL; Infraspinatus Tendon, 3.0 mL; GHJ, 3.0 mL; ACJ, 1.0mL
3	N/A
4	Supraspinatus Tendon, 4.0 mL; Biceps Sheath, 1.0 mL; Subacromial Bursa, 1.5mL
5	Supraspinatus Tendon; 3.0 mL; Infraspinatus Tendon; Subacromial Bursa, 1.0 mL; GHJ, 3.0 mL; ACJ, 1.8mL
6	Supraspinatus Tendon, 3.0 mL; Biceps Tendon, 2.5mL
7	Supraspinatus Tendon, 6.0 mL; Infraspinatus Tendon, 2.0 mL; GHJ, 3.0mL
9	Supraspinatus Tendon, 6.0 mL; Subacromial Bursa, 2.0mL
10	Supraspinatus Tendon, 5.0 mL; Infraspinatus Tendon, 3.0mL
11	Supraspinatus Tendon, 4.0 mL; Subacromial Bursa, 1.0mL

Notes: Treatment notes include location of injection and volumes of injectate. No complications during the procedure were noted. Treatment notes for subject 3 were unavailable.
GHJ = glenohumeral joint. ACJ = Acromioclavicular Joint.

Discussion

Wheelchair users with SCI have a high risk of developing shoulder pain caused by rotator cuff disease, and damage to other shoulder soft-tissues.[2] Conservative treatments are generally considered the first line of treatment. However, these individuals rely on their upper limbs for activities of daily living so conservative treatments may not completely alleviate symptoms. Biologics, such as MFAT, may provide promising alternatives for those who have failed conservative treatment and have no other options to address their shoulder pain other than rotator cuff surgery. This pilot study presents the first clinical trial using MFAT as a treatment for shoulder pain caused by rotator cuff disease in wheelchair users with SCI.

One of the primary objectives of this pilot study was to determine the potential treatment effect of ultrasound-guided injections of MFAT into degenerative lesions of the shoulder. This procedure was found to be safe and well-tolerated in persons with SCI. Various pain outcomes were used, including activity-related pain and pain interference scales and overall impressions of change. Most participants reported clinically meaningful reductions in pain measures after 6 and 12 months, and improvement in overall well-being. Only one participant who completed the trial reported no improvement in pain or function. This subject also had significant, underlying neuropathic pain that may have affected his response to this treatment. A larger study is needed to determine positive and negative factors affecting patient outcomes after this intervention.

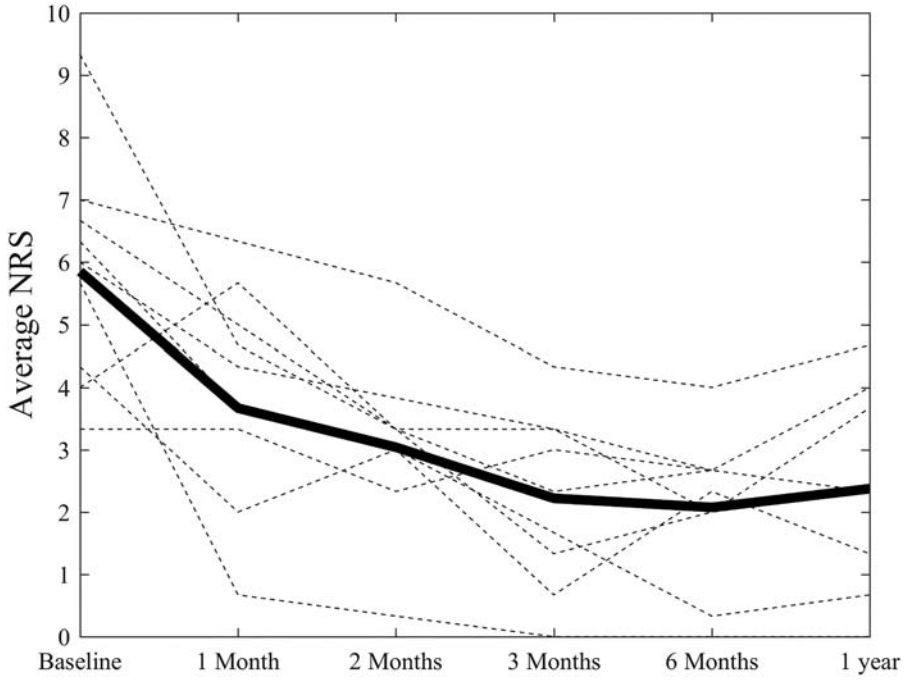

Figure 1 Change in numerical pain rating scale (NRS) scores at each timepoint over the 24-week course of the trial. Scores declined steadily over the first 3 months, with minimal observed changes between 3 and 12 months. Dotted lines indicate individual scores. The solid black line indicates mean scores.

Dropout and missing data in a clinical trial are considerable problems and can introduce bias when analyzing and interpreting outcomes. There are several methods of accounting for missing data during analysis, but none can replace designing a study to minimize attrition.[38] Retention rates were high for this pilot trial, with only one participant dropping out of the trial at the 2-month mark. This individual had

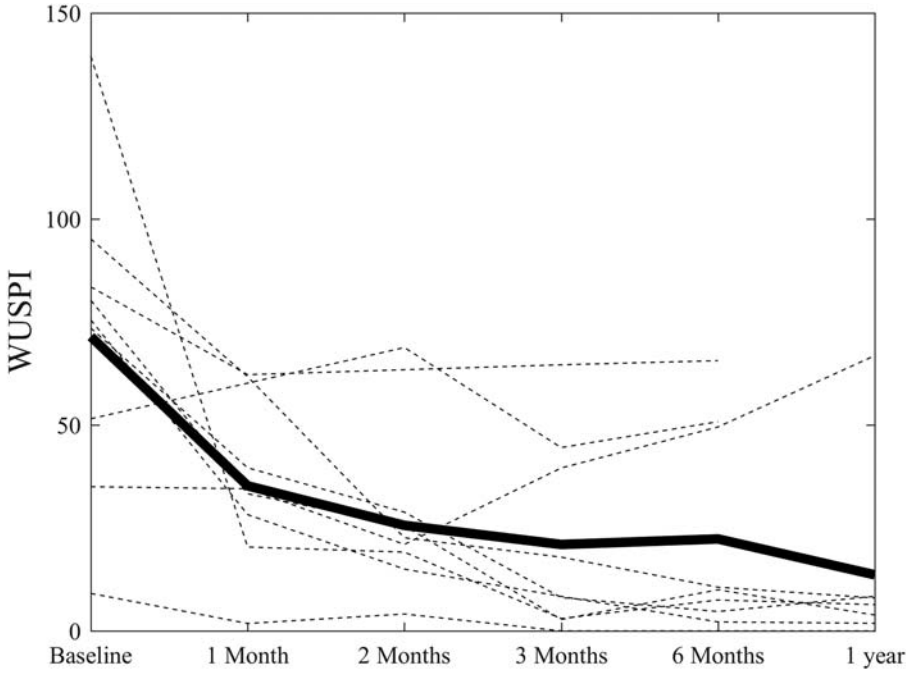

Figure 2 Change in Wheelchair User's Shoulder Pain Index (WUSPI) scores at each timepoint over the 12-month course of the trial. Scores declined steadily over the first 3 months, with minimal observed changes between 3 and 12 months. Dotted lines indicate individual scores. The solid black line indicates mean scores.

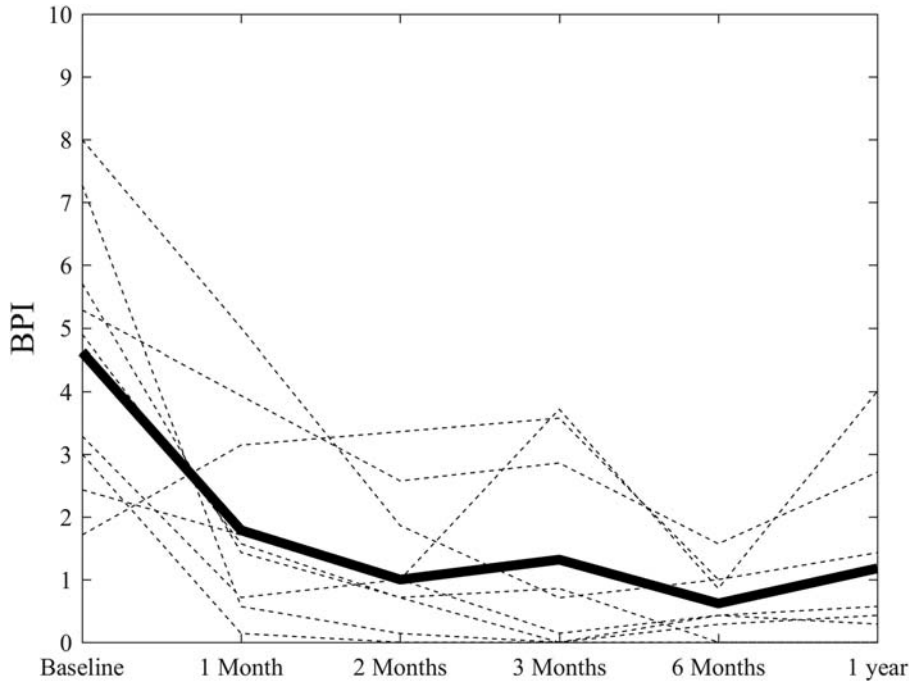

Figure 3 Changes in Brief Pain Inventory pain interference (BPI-I7) scores at each timepoint over the 12-month course of the trial. Scores declined steadily over the entire year. Dotted lines indicate individual scores. The solid black line indicates mean scores.

significant bilateral shoulder pain; however, the protocol limited the injection to one shoulder. The individual continued to have significant shoulder pain in the opposite shoulder and elected to withdraw from the study to pursue outside treatment (platelet-rich plasm injection). Otherwise, only two post-treatment data points were missed out of the potential 45 (excluding the aforementioned subject who dropped out of the trial). Overall, this retention rate was considered a success and efforts should be maintained in a larger trial to maximize participation.

Pain-related outcome measures were primarily self-report, which is a vital component of any chronic pain clinical trial.[30] Future trials would benefit from additional objective measures of tendon health to further evaluate treatment effect. Physical examination maneuvers and clinical ultrasounds were conducted in an effort to include more objective measures. However, physical examination maneuvers have limited clinical utility for diagnosing rotator cuff disease.[39] The ultrasound measure used translated subjective interpretations of tendon health into an ordinal

Table 3 Subject-specific changes in outcome measures at 6- and 12-months post-procedure.

	ΔNRS (%)		ΔWUSPI (%)		ΔBPI-I7 (%)		
Study ID	6M	12M	6M	12M	6M	12M	PGIC (12M)
1	−100.0	−100.0	−100.0	−100.0	−100.0	−100.0	Very much improved
2	−100.0	−69.2	−87.6	−95.2	−94.1	−89.3	Very much improved
3	−100.0	−45.0	−88.8	−91.6	−87.5	−82.1	Very much improved
4	−77.8	−75.0	−94.6	−95.47	−94.1	−92.2	Very much improved
5	−100.0	−89.5	−97.1	−97.5	−100.0	−100.0	Very much improved
6*	−50.0	NA	−21.4	NA	−41.5	NA	NA
7	0.0	20.0	41.4	90.9	−64.6	64.6	Minimally worse
9†	−42.9	−33.3	−1.4	NA	−70.3	−48.8	Much improved
11	−50.0	−41.7	−93.6	−88.6	−86.9	−91.2	Very much improved

Notes. Subject-specific changes in primary and secondary outcomes at 6 and 12 months (M) are presented, expressed as a percentage change with respect to baseline.
*Subject 6 died at 12 months so data were unavailable.
†In-person data collection was canceled for subject 9 due to COVID-19, so WUSPI scores could not be collected.
NRS = Numerical Rating Scale. WUSPI = Wheelchair User's Shoulder Pain Index. BPI-I7 = Brief Pain Inventory. PGIC = Patient Global Impression of Change.

Table 4 Average changes across the sample in pain outcome measures at 6- and 12-months post-treatment.

	Mean (SD)	Δ (SD)	Δ% (SD)
NRS			
Baseline	5.9 (1.8)		
6 Months	2.1 (1.2)	−3.8 (2.3)	−60.1 (27.5)
12 Months	2.4 (1.7)	−3.5 (2.5)	−54.2 (38.1)
BPI-I7			
Baseline	4.5 (2.2)		
6 Months	0.6 (0.5)	−3.9 (2.2)	−82.0 (19.5)
12 Months	1.2 (1.5)	−3.7 (2.7)	−67.4 (55.8)
WUSPI			
Baseline	71.4 (37.2)		
6 Months	22.3 (25.4)	−49.1 (48.1)	−60.4 (52.6)
12 Months	13.6 (23.7)	−59.0 (54.1)	−68.2 (70.3)

Notes. Data are presented as means, absolute change (Δ), and percentage change (Δ%) with standard deviations of each. $N = 9$ for all baseline and 6-month variables. $N = 8$ for 12-month NRS and BPI-I7, and 7 for 12-month WUSPI. NRS = Numerical Rating Scale; BPI-I7 = Brief Pain Inventory; WUSPI = Wheelchair User's Shoulder Pain Index.

scale whose psychometric properties have not been established. Repeated measurements with both exams may also be biased due to error and lack of blinding. Additional measures, such as quantitative ultrasound or MRI, may be fruitful in evaluating changes in tendon health after the intervention if proven reliable and conducted without bias.[40,41] The relationship between clinical and imaging findings is somewhat controversial,[42] so it is important to view treatment holistically.

Limitations

The study consisted of a convenience sample of mostly white males, so was limited with respected to its diversity in race and sex. Changes in wheelchair seating or set-up or changes in types/levels of activity, all of which are factors that could have impacted changes in shoulder pain over the duration of the study[1] were also not measured. Future studies should aim to recruit a more diverse study sample and to collect wheelchair seating/set-up and activity level data. Recruitment of a larger sample would also potentially allow for subgroup analyses based on injury level, age, sex, race/ethnicity, and treatment volumes and locations.

Table 5 Positive physical examination tests at baseline and after 12 months post-treatment.

Physical Exam Test	Baseline	6 Months	12 Months
Supraspinatus Tenderness	5 (55.6)	0 (0.0)	0 (0.0)
Empty Can	7 (77.8)	1 (11.1)	1 (11.1)
Painful Arc	6 (66.7)	1 (11.1)	1 (11.1)
Resisted ER	5 (55.6)	0 (0.0)	0 (0.0)
Neer's Sign	4 (44.4)	0 (0.0)	0 (0.0)
Hawkins-Kennedy Sign	7 (77.8)	0 (0.0)	0 (0.0)
Yocum's Sign	5 (55.6)	1 (11.1)	1 (11.1)

Notes. The absolute number of positive signs for the treated arm are presented alongside percentages in parentheses.

Conclusions

Results of this pilot study indicate that ultrasound-guided injection of MFAT into degenerative shoulder structures is a safe and potentially efficacious treatment for refractory shoulder pain, when paired with a standardized exercise program. Significant improvements in pain and function were noted in outcome measures through 6 and 12 months. Overall the pilot was considered a success, with high retention rates and minimal missing data. Continued efforts to maximize retention and data collection rates, recruit a more diverse sample, and include more objective measures of tissue healing, would yield a highly successful randomized, controlled trial. A randomized controlled study with a larger number of subjects has now been initiated in this patient population, facilitated by the results of this pilot study.

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Conflicts of interest The authors declare no other conflicts of interest.

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