Biologic Orthopedic Journal

Original Article
DOI: 10.22374/boj.v7i1.76

CLINICAL APPLICATIONS OF AUTOLOGOUS MICROFRAGMENTED ADIPOSE TISSUE IN CHRONIC TENDINOUS INJURIES: A NARRATIVE REVIEW

Michael Serra-Jovenich, DO MMS CPT[1], Oluseun Olufade, MD[2]

[1]Department of Physical Medicine and Rehabilitation, Inspira Medical Center, Mullica Hill, NJ, USA; Department of Rehabilitation Medicine, Neuromusculoskeletal Institute, Rowan-Virtua School of Osteopathic Medicine, Sewell, NJ, USA; [2]Department of Orthopedics, Emory University School of Medicine, Atlanta, GA, USA and Department of Physical Medicine & Rehabilitation, Emory University School of Medicine, Atlanta, GA, USA

Authors for correspondence: Michael Serra-Jovenich and Oluseun Olufade: michaelsj6do@gmail.com; oolufad@emory.edu

Submitted: 2 January 2025. Accepted: 11 May 2025. Published: 30 May 2025

Abstract

Tendinopathy is a multifactorial condition influenced by both intrinsic and extrinsic factors, necessitating a tailored, phased-based management approach. While first-line management traditionally involves conservative measures, limited success in chronic cases has galvanized interest in orthobiologic interventions. Autologous lipoaspirate-derived microfragmented adipose tissue (MFAT), a minimally manipulated orthobiologic, has demonstrated potential in managing chronic tendinopathy. This narrative review explores the clinical application of MFAT in the nonoperative management of chronic tendinous pathologies, focused on preprocedural management, procedural standardization, post-injection protocols, and outcome assessment.

Keywords: *lipoaspirate; MFAT; microfragmented adipose tissue; soft tissue injuries; tendinopathy*

INTRODUCTION

Tendinopathy is a multifactorial condition characterized by pain and performance that can progress to partial and full-thickness tears.[1] The condition progresses through acute, subacute, and chronic stages, each requiring a tailored rehabilitation strategy.[2] While conservative measures are initially favored, limited efficacy in chronic cases has highlighted a need for additional interventions.

Orthobiologic agents, including adipose tissue derivatives (ATDs), have gained increased attention for their potential anti-inflammatory and immunomodulatory properties, ultimately modifying the disease process in conditions such as recalcitrant tendinopathies.[3] According to the *American Orthopedic Society for Sports Medicine*, the most commonly used orthobiologic agents for musculoskeletal (MSK) conditions, from ascending to descending order, include platelet-rich plasma (PRP), bone marrow aspirate concentration (BMAC), amniotic membrane products, and adipose-derived mesenchymal stromal cells (AD-MSCs), which are a component of ATDs and a cellular subset of the stromal vascular fraction (SVF).[4] Despite ambiguous nomenclature and regulatory challenges surrounding ATDs, the motivation for use has grown in popularity with anecdotal efficacy and competitor utilization.[4]

Adipose tissue derivatives are a rich source of regenerative components, composed of several

subsets containing distinct biological properties and methods of preparation. ATDs are typically obtained through liposuction of subcutaneous fat, most commonly from the abdomen, thigh, or buttocks. Once harvested, the lipoaspirate can be processed into various products such as the SVF or microfragmented adipose tissue (MFAT), depending on the method of preparation. In the United States, the Federal Drug Administration (FDA) permits the clinical use of lipoaspirate-derived ATDs under minimal manipulation guidelines,[5] primarily as structural scaffolds. This regulatory framework restricts clinical application to mechanical SVF and MFAT. However, the quality and clinical utility of MAT-SVF remain questionable.[6]

Most of the existing research on ATDs in tendinopathy has focused on more-than-minimally manipulated products, such as enzymatic SVF or culture-expanded SVF. Contrarily, the clinical utility of MFAT for tendinopathy management remains less well understood. MFAT contains mesenchymal-like stem cells and regenerative-supportive cells that modulate inflammation through paracrine signaling and recapitulate the extracellular matrix by acting as a biologic scaffold that may improve tissue repair and regeneration.[7,8] Although MFAT has shown the most robust clinical evidence in managing mild to moderate knee osteoarthritis, its clinical application in tendinopathy is less defined. While this literature review initially sought to examine MFAT in broader soft tissue applications, only studies focused on tendinopathy met the inclusion criteria. Accordingly, this narrative review focuses on the clinical use of autologous lipoaspirate-derived MFAT for tendinous injuries, with an emphasis on the spectrum of preprocedural tendinopathies and prior conservative management, procedural techniques, post-injection protocols, and outcome assessment tools. Preoperative and intraoperative uses of autologous MFAT remain beyond the scope of this review.

MATERIALS AND METHODS

A non-systematic literature search on the use of autologous MFAT in human soft tissue injury (e.g., tendinopathy, sprains, strains) was conducted by the primary author across PubMed, Medline, and Google Scholar from December 1995 to October 2024 to identify relevant peer-reviewed articles. Articles that met the inclusion or exclusion criteria were screened by both the title and abstract, followed by full-text review with attention to the processing methods of the ATDs. No restrictions were placed on study design; all available peer-reviewed publications relevant to the clinical use of MFAT in human soft tissue pathology were considered to capture the full scope of available evidence.

Studies were eligible for inclusion criteria if they were human-based investigations evaluating autologous lipoaspirate-derived MFAT in the nonoperative management of soft tissue injury. Exclusion criteria included animal studies, preoperative or intraoperative lipoaspirate-derived MFAT applications, and studies involving ATDs other than minimally manipulated lipoaspirate-derived MFAT (e.g., uncultured autologous adipose-derived regenerative cells, enzymatic SVF, mechanical SVF, culture-expanded SVF).

The following search terms were used in isolation or combination: “regenerative medicine,” or “orthobiologics,” or “lipoaspirate,” or “microfragmented adipose tissue” or “micro-fragmented adipose tissue” or “micro fragmented adipose tissue” or “MFAT” or “adipose tissue derivatives,” or “adipose derived stem cells,” or “mesenchymal stem cells,” and “soft tissue,” “tendon,” “tendinosis,” “tendinopathy,” “tendinitis,” “ligament,” “sprain,” “muscle,” and “strain.” Additional references were identified through manual searches of bibliographies from the included studies, alongside further literature investigation of the outcome measures.

A complete electronic strategy for PubMed is presented in File 1 (PubMed), File 2 (Medline), and File 3 (Google Scholar).

Study Selection and Data Interpretation

Although the search strategy, performed by the primary author, was designed to encompass a broad range of human soft tissue injuries, only studies investigating the use of MFAT in the management of tendinopathy met the review’s criterion. Given the narrative nature of this review and the heterogeneity

File 1 PubMed

(Lipoaspirate[Title/Abstract] OR "microfragmented adipose tissue"[Title/Abstract] OR "micro-fragmented adipose tissue"[Title/Abstract] OR "micro fragmented adipose tissue"[Title/Abstract] OR MFAT[Title/Abstract] OR "adipose tissue derivative*"[Title/Abstract] OR "adipose derived stem cells"[Title/Abstract] OR "Mesenchymal Stem Cells"[Mesh] OR "Regenerative Medicine"[Mesh] OR orthobiologic*[Title/Abstract]) AND ("Soft Tissue Injuries"[Mesh] OR "soft tissue injury*"[Title/Abstract] OR "Tendons"[Mesh] OR tendon*[Title/Abstract] OR tendin*[Title/Abstract] OR "Ligaments"[Mesh] OR ligament*[Title/Abstract] OR "Sprains and Strains"[Mesh] OR sprain*[Title/Abstract] OR strain*[Title/Abstract]) AND ("1995/01/01"[PDAT] : "2024/10/08"[PDAT])

File 2 Medline

Ovid MEDLINE(R) Epub Ahead of Print and In-Process, In-Data-Review, and Other Non-Indexed Citations and Daily <October 8, 2024>

Number	Search Terms	Results
1	Lipoaspirate.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	612
2	microfragmented adipose tissue.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	76
3	micro-fragmented adipose tissue.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	60
4	micro fragmented adipose tissue.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	60
5	MFAT.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	102
6	adipose tissue derivative.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	1

(*continues*)

File 2 Medline

Continued.

Number	Search Terms	Results
7	adipose derived stem cells.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	6667
8	mesenchymal stem cells.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	54,879
9	regenerative medicine.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	8902
10	orthobiologic.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	219
11	soft tissue injuries.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	6992
12	tendons.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	30,388
13	tendinopathy.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	7404
14	tendinosis.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	1180

(*continues*)

File 2 Medline

Continued.

Number	Search Terms	Results
15	tendinitis.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	2946
16	(Sprains and Strains).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	6412
17	ligaments.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	10,088
18	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10	68,712
19	11 or 12 or 13 or 14 or 15 or 16 or 17	60,291
20	18 and 19	578

File 3 Google Scholar

(“lipoaspirate” OR “microfragmented adipose tissue” OR “micro-fragmented adipose tissue” OR “micro fragmented adipose tissue” OR MFAT OR “adipose tissue derivative”) AND (“soft tissue injury” OR “tendon” OR “tendinopathy”)

of study designs, the formal risks of bias assessment and qualitative analysis were not undertaken. Instead, the methodological quality of the included nonoperative studies was assessed by the main author using the validated Coleman Methodology Score-Modified for Conservative Therapy (CMS-MCT) as detailed by Abdul-Wahab et al.,[9] a modified version of the validated Modified Coleman Methodology Score used to assess quality of nonoperative outcomes in orthopedic and sports medicine research.

The CMS-MCT is a scoring system, summing to yield a maximum score of 100, that evaluates key elements such as study design, sample size, follow-up duration, outcome measures, and diagnostic clarity.[10–13] Each of these key elements is assigned a score by the investigator. Increasing scores reflect stronger methodological rigor with higher thresholds interpreted as excellent (≥ 85), good (70–84), fair (50–69), and poor (<50). In this review, the CMS-MCT was used by the primary author to contextualize the quality and reliability of the outcomes in the available studies. Additionally, a qualitative synthesis was also undertaken to identify recurring clinical observations, injection protocols, and reported outcomes. This approach highlights the common clinical insights from diverse studies and supports a contextual understanding of MFAT’s role in treating tendinopathy.

RESULTS

Literature Search and Identification of Studies

The combined non-systematic literature search revealed 2611 results from PubMed, 2570 from Google Scholar, and 578 results from Medline.

After initial screening, removal of duplicates, and review of the material following the review's inclusion or exclusion criterion, there were six eligible studies. Additionally, the literature search, without restrictions, was conducted on outcome measures and the Modified Coleman Methodology Score, which yielded an additional 30 and 5 unique citations, respectively.

Study characteristics

Six studies were included: one pilot clinical trial,[14] one case series,[15] and four case reports.[16–19] All used the Lipogems system to harvest autologous MFAT, which was delivered via a singular ultrasound-guided injection. Indications primarily included refractory rotator cuff (RTC) disease, with one case report addressing a high-grade partially thickened Achilles tendon tear. Definitions of "refractory" were inconsistent, encompassing a wide spectrum of tendon pathology and adjacent structural abnormalities, with prior management ranging from conservative interventions to surgical recurrence.

Rotator Cuff Disease

Hogaboom et al.[14] investigated nine individuals with spinal cord injury (SCI), all of whom were manual wheelchair users with moderate to severe chronic shoulder pain lasting more than 6 months. Participants were predominantly male (8 of 9). The mean age for all participants was 55.1 years. All participants had failed conservative management, including physical therapy (PT), pharmacology, and activity or wheelchair modifications. Musculoskeletal ultrasound (MSK-US) revealed widespread shoulder pathology: supraspinatus tendinopathy in all subjects, infraspinatus tendinopathy in four, subscapularis involvement in one, subacromial–subdeltoid bursitis in eight, long head bicipital tenosynovitis and/or tendinopathy in seven, acromioclavicular (AC) OA in five, and glenohumeral joint (GHJ) effusion in four.

Striano et al.[15] reported on a case series of 20 subjects with chronic shoulder pain exceeding 1 year; two were lost to follow-up, resulting in a final cohort of 18 (mean age: 55.9 years; sex distribution not specified). All patients had failed at least three of the following prior interventions: PRP, corticosteroid injection (CSI), viscosupplementation, home exercise program, and PT. Regarding GHJ OA, 5% of subjects had no signs of arthritis, 10% had mild involvement, 25% had moderate disease, and 60% presented with severe GHJ OA. Eleven subjects (55%) had AC joint OA, to an unspecified degree. Rotator cuff pathology demonstrated varying degrees of tendinous involvement: supraspinatus tendinosis (45%), partial thickness tears (45%), and full-thickness tears (30%); infraspinatus tendinosis (35%) with one each of partial (5%) and full-thickness tears (5%); subscapularis tendinosis (25%) with one partial tear (5%). Additional findings included bicep tendinosis (5%), partial bicep tears (20%), labral tears (35%), and fatty muscle atrophy (30%).

Ferrell et al.[16] described a 70-year-old female with an 8-months history of shoulder pain. MR arthrogram revealed a nonretracted full-thickness anterior supraspinatus tear (1.0 × 0.8 cm) and a partial thickness articular-sided tear of the posterior supraspinatus-anterior infraspinatus tendon footprint. Conservative treatment such as PT, activity modification, and nonsteroidal anti-inflammatory drugs (NSAIDs) failed to provide relief.

Marathe et al.[17] reported on a 50-year-old male with a partial thickness supraspinatus tear (2.5 × 6.5 mm), who remained symptomatic despite conservative management defined as 6 weeks of PT.

Martin and Takyi[18] described a 42-year-old male with a recurrent, retracted complete full-thickness supraspinatus tear, interstitial infraspinatus tearing, and subacromial bursitis. The patient had previously undergone rotator cuff repair 1 year before and received a US-guided subacromial bursa CSI 6 weeks before MFAT, followed by formal physical therapy for 4 weeks before MFAT, all of which failed to alleviate symptoms.

Study characteristics and patient demographics for these reports are summarized in Figure 1.

Achilles Tendinopathy

Iuso et al.[19] reported on a 66-year-old male with chronic Achilles tendon pain for over 1 year, due to a large partial thickness (0.97 × 0.9 × 1.53 cm) tear

Figure 1. Author (Year), Design, Subjects (N), MSK Condition, Conservative Therapy, NSAIDs, Ice, Activity Limitations, and Therapeutic Movement.

Author (Year)	Design	Subjects (N)	MSK Condition	Conservative Therapy	NSAIDs	Ice	Activity Limitations	Therapeutic Movement
Hogaboom et al. (2021)[14]	Pilot clinical trial	9	Refractory RTC disease for at least 6 months	–	Avoid NSAIDs and aspirin	Ice PRN	Reduced activity for 4 days post-MFAT; return to baseline activity by day 7.	Stretching began at 24 h post-injection, continued for 4 weeks, followed by progressive RTC and scapular strengthening for 12 months.
Striano et al. (2018)[15]	Case series	18	Refractory RTC and OA > 1 year	Failed at least 3: PRP, CSI, viscosupplementation, home exercise program, PT	–	–	–	–
Ferrell et al. (2023)[16]	Case report	1	Refractory RTC disease for 8 months	PT, activity modification, NSAIDs	Avoid NSAIDs for 2 weeks	-	Post-MFAT: Sling for 1 week Post-PRP: Sling for 1 week	Post-MFAT: PT began at 2 weeks for ROM and strength Post-PRP: PT resumed at 1 week, transitioned to home program
Marathe et al. (2021)[17]	Case report	1	Chronic partial-thickness supraspinatus tear	PT for 6 weeks	–	–	–	Post-MFAT: PT initiated 1 week after procedure Post-PRP
Martin and Takyi (2023)[18]	Case report	1	Full-thickness supraspinatus tear, interstitial infraspinatus tear, bursitis	–	Avoidance of NSAIDs	–	Avoid heavy lifting or excessive use of the shoulder for 6 weeks.	PT started at 6 weeks post-MFAT
Iuso et al. (2022)[19]	Case Report	1	Partial thickness Achilles tendon tear	Immobilization, PT	Avoidance of NSAIDs	Ice PRN	1–2 weeks immobilization; limited activity first 4 days. Gradual WBAT by 4 weeks.	Toe raises are prescribed at 4 weeks. PT (2–3x/week) started at Week 8.

CSI = corticosteroid injection; MSK = musculoskeletal; NSAIDs = nonsteroidal anti-inflammatory drugs; OA = osteoarthritis; PRN = as needed; PRP = platelet-rich plasma; PT = physical therapy; ROM = range of motion; RTC = rotator cuff; WBAT = weight-bearing as tolerated.

affecting 80% of the tendon's diameter and extending 5 cm proximally from the insertion. Mild retrocalcaneal bursitis was also noted. Conservative management, including immobilization with a controlled ankle motion boot (CAM boot) and PT, had failed with both at an unspecified duration. The patient declined surgical intervention, and opted for MFAT treatment as a nonoperative alternative.

Study characteristics and patient demographics for the Achilles case are summarized in Figure 1.

Intraprocedural characteristics

Microfragmented adipose tissue injection techniques varied across studies, particularly regarding the volume administered and the anatomical targets. Ferrell et al. consistently used standardized volumes of MFAT directed into pathological structures identified on MSK-US. In contrast, both Iuso et al. and Striano et al. adjusted the volume of MFAT in real time to fill focal abnormalities seen on MSK-US. Hogaboom et al. also delivered MFAT to US-identified pathological sites, but did not specify a rationale for the volume used. Marathe et al. injected MFAT directly into the partial-thickness supraspinatus tear site, although it remains unclear whether the injectate fully occupied the defect during the procedure. Similarly, Martin and Takyi injected differing amounts into tendinous defects and the subacromial bursa, but did not clarify how injection volumes were determined or whether complete filling was achieved.

Use of anesthetics during the procedure was reported in four studies, with all using lidocaine, albeit at varying concentrations and anatomical sites. Hogaboom et al. and Iuso et al. used 1 and 0.05% lidocaine on the skin and subcutaneous tissue at the entry site, respectively. Striano et al. administered 1% lidocaine en route to the GHJ and infraspinatus, though an anesthetic technique for anterior structures was not specified. Ferrell et al. applied 1% lidocaine combined with 8.4% sodium bicarbonate, though the specific injection site was not noted. Marathe et al. and Martin and Takyi did not report on anesthetic use.

Adjunctive PRP was used in two studies following MFAT administration. Ferrell et al. injected an unspecified amount of PRP into the RTC, GHJ, and glenoid labrum using US-guidance 9 weeks after MFAT. Marathe et al. administered 5 mL of PRP into the supraspinatus tendon 14 weeks after the initial MFAT injection.

Post-procedural protocols

Post-injection protocols varied considerably across studies, particularly regarding the use of NSAIDs, cryotherapy, and therapeutic movement. Marathe et al. and Striano et al. did not report any recommendations regarding medication restrictions. Hogaboom et al. and Iuso et al. advised to avoid NSAIDs, though they neglected to provide a timeline. Martin and Takyi recommended withholding NSAIDs for "a few weeks." Only Ferrell et al. provided a clearly defined timeline, recommending the avoidance of NSAIDs for 2 weeks following both MFAT and PRP.

Comparably, post-procedure cryotherapy guidelines were equally inconsistent. Four studies[15–18] failed to report on postprocedural icing recommendations. Both Iuso et al. and Hogaboom et al. recommended icing as needed every hour, though at an unspecified endpoint. Similarly, guidelines for therapeutic movement also lacked standardization, differed across all studies.

Hogaboom et al. provided the most detailed post-procedural rehab protocol, advising reduced activity for the first 4 days post-MFAT, followed by a return to pretreatment activity by Day 7. A standardized home-stretching program began 24 h post-MFAT and continued for 4 weeks, after which an RTC and scapular stabilization strengthening program was initiated and maintained for the 12-month study period. This protocol was adapted from a prior randomized controlled trial in SCI.[20] Ferrell et al. implemented 1 week of shoulder immobilization using a sling, followed by initiation of PT at 2 weeks for ROM and progressive strengthening. Following PRP at 9 weeks, a sling was recommended for 1 week, but PT began at 1 week. No specific modifications were provided after the PRP injection. PT was recommended 2–3 times per week for a minimum of 6 weeks and extended based on patient progress, with the recommendation to transition to a

home exercise program. However, the total duration of therapeutic exercise was not reported at the 2-year follow-up. Other studies offered less guidance.

Marathe et al. initiated PT 1 week post-MFAT using a general "rotator cuff rehabilitative program," continuing for 12 weeks. No modifications post-PRP were reported. Martin and Takyi instructed to "avoid heavy lifting or excessive shoulder use for six-weeks," with PT beginning at Week 6 post-MFAT. Lastly, Striano et al. did not report any post-procedural activity or rehab guidelines. For the Achilles tendon case, Iuso et al. recommended 1–2 weeks of immobilization with a CAM boot for 1–2 weeks and limited activity for the first 4 days post-MFAT. However, CAM boot discomfort 3 days after MFAT prompted discontinuation, with recommendations for ankle pump exercises. At 4 weeks post-MFAT, the patient was advised to gradually WBAT alongside instructions to perform toe lifts. A formal PT referral was made at the 8th week follow-up, recommending therapy 2–3 times per week for 4 weeks, in addition to continuing a "home exercise toe-lift regimen."

Overall, the heterogeneity in post-injection care protocols highlights the lack of standardized rehabilitation strategies following MFAT and adjunctive PRP. The post-procedural protocols across the studies are summarized in Figure 1.

Clinical Outcomes

A wide range of outcome measures were employed across the included studies, with data collected at different timepoints ranging from immediately after intervention to as long as 2 years. Hogaboom et al. conducted the most comprehensive assessment battery in a cohort of nine manual wheelchair users (n = 9). This included the 11-point numerical rating scale (NRS-11),[21,22] Wheelchair User's Shoulder Pain Index (WUSPI),[23] Brief Pain Inventory Interference Subscale (BPI-17),[24–28] Patient Global Impression of Change(PGIC),[26,29–33] musculoskeletal ultrasound (MSK-US), Ultrasound Shoulder Pathology Rating Scale (USPRS),[34–37] and provocative shoulder tests (e.g., supraspinatus tenderness, Empty Can, Painful Arc, Resisted External Rotation, Neer's Sign, Hawkins–Kennedy Sign, Yocum's Sign). Outcomes were measured and collected at five different timepoints: 1, 2, 3, 6, and 12 months. The primary outcome, change in NRS at 6 months, demonstrated an average reduction of 60.1% ($Z= -2.67$, $P < 0.01$), indicating a statistically significant improvement in pain with a large effect size (over 50% reduction in NRS) despite a small sample size. This suggests strong potential for efficacy but limits generalizability due to the small cohort. The NRS-11, a tool with limited linearity, is better supported by the current evidence for assessment of acute pain than for chronic pain, and at 12 months demonstrated similar and continuous improvements ($Z = -2.31$, $P < 0.05$).[21,22] This continuation supports the durability of effect, but the limitations of NRS in a chronic setting warrant cautious interpretation, especially over long-term follow-up. The secondary outcomes also included the NRS at 12 months and the WUSPI, BPI-17, and PGIC at 6 and 12 months. The WUSPI,[23] a validated test with excellent psychometric properties, evaluates shoulder pain during functional activities in wheelchair users. It demonstrated an average reduction of 60.4% ($Z = -2.31$, $P < 0.05$) at 6 months and 68.2% ($Z = -2.03$, $P < 0.05$) at 12 months, reflecting functional shoulder gains over time. The WUSPI's population-specific design enhances content validity and functional relevance, although broader application outside of wheelchair users may be limited. The BPI-17 score, a reliable and valid measurement that reflects how pain interferes with aspects of life in older individuals, showed an average reduction of 82.0% at 6 months ($Z= -2.67$, $P < 0.01$) and reduction of 67.4% at 12 months ($Z = -2.38$, $P < 0.05$).[24–28] The consistent improvement reinforces BPI-17's responsiveness, though age-related bias may influence generalizability. The PGIC is a validated patient-centered scale with strong psychometric properties across populations.[26,29–33] Although subject to potential recall bias and existing comorbidities, it assesses subjective improvement that correlates moderately and anchors in monitoring changes in other outcomes (e.g., VAS, disability scores).[26,29–33] The PGIC showed that 77.8% of participants reported clinically meaningful improvements defined as either "much improved" or "very much improved" at

6 months. At 12 months, this proportion increased slightly to 88.9%, with five participants (55.6%) selecting the most favorable response of "very much improved." While PGIC results support sustained perceived benefit, their subjectivity and susceptibility to bias limit their standalone interpretative value. Improvements were also seen in provocative shoulder testing, especially supraspinatus tenderness and the Painful Arc Test, at 6 months, which were sustained at the 12-month assessment. However, statistical analysis was not performed for physical examinations. This weakens the interpretive rigor of physical exam outcomes despite apparent clinical trends. Serial MSK-US using the USPRS, a semi-quantitative, not fully validated, structured tool used to objectively grade shoulder pathology over time and dynamically guide therapeutic movement,[35] showed an unspecified amount of improvement when assessed at 6 months and 12 months in four of the nine participants.[34–37] Modifications to the rehab protocols were not reported based upon the USPRS and the use of an under-validated imaging tool without outcome standardization undermined the potential utility of USPRS findings and causal inference in clinical outcomes. Overall, while the study by Hogaboom et al. demonstrated signs of efficacy across multiple domains, the small sample size limits statistical power and generalizability. As such, these findings should be considered as hypothesis-generating rather than definitive, and underscore the need for higher levels of evidence with rigorous parametric testing to confirm outcomes and assess long-term efficacy and safety.

Ferrell et al. employed the Disabilities of the Arm, Shoulder and Hand (DASH),[38,39] physical exam, MSK-US, and shoulder MRI without contrast. Outcome data were collected at 1, 6, 8, and 10 months. DASH, a well-validated, self-reported outcome measure with strong psychometric properties, is used as the gold standard for tracking functional progress and symptomatic disability when performing activities of daily living (ADLs) in upper limb conditions, and was the primary outcome tool used to monitor progress. Baseline DASH values before MFAT were not provided; however, scores improved from 72.73 (severe disability) to 15.91 at 6 months (mild disability) post-MFAT (and 4 months after supplemental PRP), reflecting substantial functional recovery.[38,39] The absence of preintervention baseline data limits conclusions about absolute improvement. Physical examination reconducted at 8 months following MFAT (and 6 months from supplemental PRP) documented improved ROM in all planes and manual strength (from 3/5 to 5/5), and resolution of a previously positive Empty Can Test and O'Brien Test. However, Neer's and Hawkin's test remained positive, tempering the otherwise favorable gains on physical exam. Notably, while the VAS pain scale at baseline was 6/10, there was no follow-up VAS score reported. This omission restricts the interpretation of subjective pain outcomes and precludes a complete understanding of the outcome. At 10 months, US showed new tissue growth at the supraspinatus tear site, while noncontrast MRI revealed no recurrent full-thickness tear, despite the absence of surgical repair, interpreted as "postsurgical" by a blinded radiologist who had previously reviewed the initial MRI arthrogram. Blinded radiologist review adds credibility to imaging findings, but the lack of a consistent MRI protocol may introduce interpretation variability.

Marathe et al. employed the Visualized Analog Score (VAS)[40–43] and ROM testing at 14 weeks and VAS, ROM, and MSK-US at 28 weeks post-MFAT (and 14 weeks after PRP). Baseline VAS, the gold standard test for quantifying subjective pain intensity with strong psychometric properties, was 8/10 alongside baseline limitations in manual muscle test and ROM, accompanied by a positive Neer's and Hawkin's test. At 14 weeks post-MFAT the study reported: "moderately improved ROM and pain reduction." Revaluation at 28 weeks post-MFAT (14 weeks post-PRP), documented "complete healing of the partial-thickness supraspinatus tear" as seen on MSK-US and "near full recovery of pain (1/10 VAS) and ROM." Provocative testing and manual muscle testing data were not provided. This limits reproducibility and hinders a more objective assessment of clinical gains. The findings highlight the therapeutic potential of combined MFAT and PRP therapy as a nonsurgical treatment option for subacute partial thickness supraspinatus tear, but the single-case design necessitates caution before clinical adoption.

Striano et al. collected two primary outcome measures, the numerical pain scale (NPS)[30,32] and the American Shoulder And Elbow Surgeons Score (ASES)[44,45] with each collected at various time points: immediately after procedure, 1 day, 1 week, 5 weeks, and 3, 6, and 12 months in 18 subjects (n = 18). NPS scores—often referred to as the Numerical Rating Score—are a reliable tool for assessing monitoring changes in pain intensity ($\gtrsim$ 2-point drop is a minimal clinical important difference), dropped from a baseline of 7.6 ± 0.97 (n = 18) to 3.5 ± 0.85 (n = 18) at 12 months ($P < 0.0001$). The ASES, a well-validated patient-reported outcome measure that is a highly sensitive tool for tracking clinical change in function and pain, was utilized at 1 week through the 12 month. The scores improved from a baseline of 33.30 ± 2.00 to 69.10 ± 1.85 at 12-month reassessment ($P < 0.00017$), reflecting enhanced shoulder function. There was improvement in ASES scores collected at Weeks 1 and 5 ($P = 0.0033$), 3 months ($P < 0.0001$) and 6 months ($P < 0.0001$). No alpha level was reported. The longitudinal collection of validated PROMs is a methodological strength; however, the absence of an alpha threshold undermines the transparency of statistical rigor. The improvement of both NPS and ASES indicates a high likelihood that the observed improvements throughout the study were not due to chance. However, the study's moderate sample size (n = 18) and lack of a control group limit generalizability. These methodological weaknesses highlight a need for better-powered controlled trials to confirm efficacy.

Martin and Takyi provided minimal temporal data assessment at 2 months and 2 years. At 2 months post-MFAT, improvements in ROM, manual strength testing, and provocative maneuvers—including the Empty Can Test and "Impingement Tests"—allowed a return to full duty. At 2 years, ROM, manual strength tests, MSK-US, and self-reported pain relief were documented. While documentation at 2 years was vague, the patient had improvements in ROM, manual strength testing, and reported feeling "90–95% better," with MSK-US reporting: "tendinopathic changes of the supraspinatus and infraspinatus with partial thickness articular-sided tearing of the supraspinatus, and some subacromial bursal thickening." These MSK-US findings suggest structural remodeling of a previous full-thickness supraspinatus tear and interstitial infraspinatus tear, though no full resolution was observed. The absence of quantified outcome metrics and vague longitudinal descriptors significantly weakens the interpretive value of this case. This case report suggests that MFAT can be a viable option for those with recurrent rotator cuff tears refractory to conservative management (CSI and PT) and operative intervention. The positive outcomes observed in this case warrant further investigation through larger, controlled studies to establish the efficacy of MFAT injection. While intriguing, anecdotal evidence is insufficient for practice change without robust replication.

Iuso et al. collected a range of outcome measures in a single patient with chronic Achilles pain, all of which demonstrated improvements, including self-reported percent pain reduction, Numerical Pain Rating Scale (NPRS),[30,46–48] ROM, manual strength, dynamic testing, and a mobile tracking gait application on an unspecified device (e.g., iPhone) across 4–15 weeks. The patient reported 95% pain reduction at 4 weeks, with MSK-US revealing: "Improved structure of the original tear filled with adipose cellular injection." At 8 weeks, NPRS, pain reduction, MSK-US, and functional mobility tracking via a personal mobile gait assessment application were used to report outcomes. The patient continued to report intermittent decreased pain and rated the pain as a 1/10 on NPRS, a psychometrically sound and valid measure of pain intensity, 8 weeks from a previous baseline before MFAT of 7/10 which meets the minimally clinically important difference of change of two points. While the pain reduction is substantial, its generalizability is limited by single-case design and lack of objective scoring of function. MSK-US at 8 weeks revealed similar findings as Week 4 alongside: "New finding of new tissue growth within the intrasubstance tear that was not previously visualized." Gait data points on the mobile tracking gait application,[49–51] which has been shown to provide valid and reliable key gait parameters, demonstrated an undetermined improvement in gait and balance. The gait app offers exciting potential, but the lack of quantified

change or validated metrics within this study reduces its interpretability. At 12 weeks, a more comprehensive clinical evaluation was performed, consisting of MSK-US, palpation, ROM, manual strength testing, and single-leg balance testing. The patient was reportedly nontender to palpation, with manual strength testing revealing values of 5/5 alongside the ability to perform a single leg toe-raise. For balance at 12 weeks, the study reported: "The patient could walk on his toes, with less balance control." Additionally, MSK-US at 12 weeks revealed: "Progressive Achilles tendon healing with residual MFAT injectate and no evidence of hypoechogenicity." The same parameters were reassessed at the 15-week follow-up, with identical findings on MSK-US and additional gains in single-leg balance. Iuso et al. provided the most detailed serial MSK-US re-assessments at 4, 8, 12, and 15 weeks, showing progressive tendon healing noted at Week 4, alongside new tissue growth appreciated at Week 8, alongside sustained tendon healing and integration of MFAT throughout the study. However, no blinding, validated, formal scoring system was implemented. Despite impressive serial imaging, the lack of validated MSK-US scoring and the absence of objective functional assessments diminish the robustness of structural conclusions. Although the MSK-US findings are encouraging, there was no clear protocol for why particular intervals were chosen for repeat assessment, alongside a lack of a blinded formal scoring system to determine ultrasound improvements. This reflects a broader gap in standardizing serial imaging in regenerative medicine, making it harder to correlate visual healing with functional recovery.

Quality Assessment

The mean CMS-MCT score for the five shoulder-focused studies was 49/100, placing them collectively within the "poor" methodological category. Among these, two studies[14,17] involving the rotator cuff scored within the "fair" range, while the remaining three studies[15,16,18] were rated as "poor." None of the articles surpassed the fair-quality threshold. The case report evaluating a partial-thickness Achilles tendon tear received a score of 30/100, qualifying as "poor" in methodological rigor.

The individual CMS-MCT scores for each of the studies are presented in Figure 2.

DISCUSSION

Autologous MFAT has demonstrated promise as a regenerative agent for chronic musculoskeletal conditions, particularly for osteoarthritis management. However, its application in tendinopathy remained underexplored until this narrative review. Although SVF has garnered more attention in tendinopathy research, regulatory constraints by the FDA have limited its clinical use, favoring the use of minimally manipulated products such as MFAT in clinical practice. This review originally aimed to assess the role of MFAT in non-operative human soft tissue injuries; however, the studies that met the criteria of this review focused exclusively on chronic tendinopathic conditions, most commonly involving the rotator cuff tendons, with one study addressing the Achilles tendon. Despite methodological variability, current evidence suggests that MFAT is safe and may be an effective option for chronic tendinopathy unresponsive to conservative care and potentially resistant to surgical intervention. A consistent limitation identified across all six studies was the lack of standardization in preprocedural evaluation, intraprocedural technique, post-procedural protocols, and outcome assessments.

Preprocedural variability was a prominent theme across studies, particularly regarding patient selection and baseline pathology. There was notable heterogeneity in the spectrum of tendinopathic conditions managed with MFAT, ranging from tendinosis to full-thickness tears. Several studies include coexisting pathologies such as GHJ OA, labral tears, and bursitis, each with varying degrees of refractoriness to prior treatment. The lack of standardized pre-procedural management and inconsistency in defining pathology within the tendinopathy spectrum complicates efforts to determine the therapeutic effect of MFAT and clarify its appropriate clinical role.

Intraprocedural techniques also varied considerably. Differences in MFAT delivery volumes and the use of adjunctive biologics such as PRP contributed

Figure 2. Author (Year), Outcomes, Follow-ups, Coleman Methodology Score Modified for Conservative Therapy (CMS-MCT).

Author (Year)	Outcomes	Follow-ups	CMS-MCT
Hogaboom et al. (2021)	NRS WUSPI, BPI-17, PGIC, US, USPRS, Provocative shoulder tests	1 month: NRS, WUSPI, BPI-17 2 months: NRS, WUSPI, BPI-17 3 months: NRS, WUSPI, BPI-17 6 months: US+USPRS, NRS, WUSPI, BPI-17, *Provocative shoulder exams, 12 months: US+USPRS, exams, NRS, WUSPI, BPI-17, Provocative shoulder tests	59
Striano et al. (2018)	NPS, ASES	Immediately after treatment: NPS 1 day: NPS 1 week: NPS+ASES 5 weeks: NPS+ASES 3/6/12 months: NPS+ASES	45
Ferrell et al. (2023)	DASH, Physical exam, US, MRI without contrast	1 month and 6 months: DASH 8 months: Physical exam 10 months: US and MRI without contrast	45
Marathe et al. (2021)	VAS, ROM, US	14 weeks: VAS, ROM 28 weeks: VAS, ROM, US	57
Martin and Takyi (2023)	ROM, Strength tests, provocative maneuvers, US	2-month follow-up: ROM, Strength tests, provocative maneuvers 2-year follow-up: ROM, strength tests, US	39

ASES = The American Shoulder and Elbow Surgeons Score; BPI-17 = Brief Pain Inventory Interference Subscale; DASH = Disabilities of the Arm, Shoulder and Hand; NPRS = Numeric Pain Rating Scale; NRS = 11-point Numerical Rating Scale; PGIC = Patient Global Impression of Change; ROM = range of motion; US = ultrasound; USPRS = Ultrasound Shoulder Pathology Rating Scale; VAS = Visual Analog Scale; WBAT = weight-bearing as tolerated; WUSPI = Wheelchair User's Shoulder Pain Index.

to procedural heterogeneity, which limits reproducibility and interstudy comparisons. Ferrell et al. employed a consistent volume of MFAT directed into ultrasound-identified pathological sites. In contrast, Iuso et al. and Striano et al. titrated MFAT volume dynamically using ultrasonographic feedback to fill focal defects. Hogaboom et al. also targeted image-confirmed pathologic areas but did not describe a rationale for MFAT dosing. Marathe et al. injected directly into the supraspinatus tear, though it remains unclear whether the injectate fully occupied the lesion. Martin and Takyi varied injection volumes between tendinous and bursal sites but did not specify dosing criteria or confirm whether defects were filled. These procedural inconsistencies underscore a broader need to define optimal delivery techniques, anatomical targeting, and the importance of adequately filling lesion volume. This is particularly relevant as MFAT's therapeutic efficacy may hinge on precise placement into areas of matrix disruption and cellular injury.

The role of anesthetic agents such as lidocaine, which can impair tenocyte viability,[52] was also inconsistently reported, raising additional concerns about potentially interfering with regenerative outcomes. Additionally, two studies[16,17] administered adjunctive PRP at varying time points and doses following MFAT, introducing further variability and rendering the effects of combination therapy speculative. Despite methodological limitations, the safety profile was favorable after MFAT alone or supplemental PRP, even among patients with severe or recurrent pathology.

Post-procedural care, including medication restrictions, cryotherapy use, and rehabilitation protocols, lacked consistency and was rarely grounded in a regenerative medicine-conscious rationale. The traditional use of NSAIDs and ice for post-injection symptom control may, paradoxically, hinder the necessary inflammatory cascade required for tissue remodeling following biologic injections. In this review, NSAID and cryotherapy use were inconsistently reported or omitted entirely. Since these interventions can modulate the local healing environment and influence outcomes, future studies should systematically evaluate their timing and impact concerning MFAT administration.

Rehabilitation protocols were rarely standardized or justified. In many cases, adherence was rarely monitored. Some studies omitted rehab details altogether, while others advocated for early mobilization with gradual loading. For instance, Ferrell et al. employed immobilization with delayed physical therapy, starting 2 weeks after MFAT and 1 week after PRP, but did not provide a rationale for the discrepancy in therapy timelines. Similarly, Marathe et al. recommended PT 1 week post-MFAT procedure without detailing post-PRP adjustments. Only Hogaboom et al. provided an informed rationale, referencing rehab protocols used in SCI populations. As the role of regenerative rehabilitation gains traction and the interplay between mechanical loading and biologic therapies becomes increasingly recognized, there is a critical need for standardized evidence-based, phase-specific rehab strategies following MFAT, whether used alone or with adjunctive orthobiologics alone or in conjunction with adjunctive orthobiologics.

Outcome assessment also lacked uniformity. Tools such as the Numeric Rating Scale (NRS), Disabilities of the Arm, Shoulder and Hand (DASH), American Shoulder and Elbow Surgeons (ASES) score, Patient Global Impression of Change (PGIC), and musculoskeletal ultrasound (US) were applied inconsistently, often without baseline values or synchronized follow-up timepoints hindering meaningful comparisons. While most studies reported gradual improvements in the first 3 months post-MFAT, the greatest clinical gains were typically observed at 6 months and sustained thereafter. Some studies, like those by Iuso et al. and Striano et al., reported substantial improvement as early as 5 weeks post-MFAT. Imaging assessments were similarly fragmented. Only one study employed a validated scoring tool—the Ultrasound Patient Reported Score (USPRS)—to quantify objective MSK-US changes, limiting the ability to correlate clinical outcomes with biological remodeling. As such, these findings continue to highlight a gap in the understanding of when to expect structural change post-MFAT injection that correlates with meaningful clinical recovery, and without standardizing imaging timelines, the variability limits the ability to track healing progression to identify treatment failure. Future studies should aim to define the temporal relationship between MFAT injection and tendinous remodeling on serial US, ideally aligned with multiple validated clinical outcome measures, with such data helping to inform evidence-based guidelines for follow-up imaging and MFAT effectiveness.

The average Modified Coleman Methodology Score for Conservative Therapy (CMS-MCT) across the included six studies qualified as poor-quality (score <50), with a score of 45.83. Key limitations included heterogeneous study designs, small sample sizes, unstandardized rehabilitation, inconsistent follow-up durations, and variable outcome metrics. These methodological flaws weaken the strength and generalizability of the conclusions. Although the CMS-MCT provides a structural framework to assess study quality, it is not a formal risk of bias tool and may not fully capture internal validity. Originally developed for surgical research, several domains within the CMS-MCT require reinterpretation in nonoperative contexts, potentially introducing subjectivity. Furthermore, scoring was conducted solely by a single reviewer, precluding inter-rater reliability assessment and potentially introducing individual scoring bias. The CMS-MCT also tends to favor randomized controlled trials, which may undervalue well-executed observational or case-based studies commonly found in emerging areas such as orthobiologics. Despite these limitations, current evidence suggests that autologous MFAT is a safe and potentially effective treatment option for patients with chronic tendinopathy who are unresponsive to

conservative management, wish to delay or avoid surgery, and or have failed prior surgical intervention. MFAT's minimally invasive delivery, compliance with regulatory guidelines, and regenerative potential make it a compelling candidate in the treatment of refractory tendinopathy. However, well-designed large prospective studies with standardized methodologies and validated risk of bias tools are necessary to strengthen the evidence base and improve the interpretability of clinical outcomes in tendinopathy, with even more preliminary evidence needed for other soft tissue injuries. Future research on the use of MFAT in chronic tendinopathy should focus on refining patient selection criteria, procedural techniques, post-procedural rehabilitation protocols, and objective outcome measures to better inform clinical decision-making. Additionally, evaluating MFAT within a phase-based framework of tendinopathy, particularly during the transition from subacute to chronic phases, may clarify its optimal therapeutic role, alongside comparative studies to determine its role in the management algorithm.

CONCLUSION

MFAT represents a promising orthobiologic intervention for patients with chronic tendinopathies, ranging from tendinosis to full-thickness tears, unresponsive to conservative measures and in populations seeking to avoid and/or delay further surgical intervention. Current evidence, though low in methodological quality, supports its safety and potential clinical utility in reducing pain and improving function in rotator cuff and Achilles tendinopathies. To advance clinical translation and optimize therapeutic outcomes, further studies should focus on standardizing patient selection criteria, MFAT techniques, defined NSAID and cryotherapy guidelines, integrating validated objective outcome measures, and aligning post-procedural care with the respective phases of tendon healing. Integration of MFAT within a phase-based tendinopathy model may clarify its optimal timing and therapeutic niche. As orthobiologics continue to evolve, MFAT holds potential as a safe, effective, and minimally invasive option in musculoskeletal regenerative medicine.

AUTHOR CONTRIBUTIONS

Michael Serra-Jovenich and Oluseun Olufade contributed to the conception and design of the study, and data analysis and interpretation. The administrative support was provided by Oluseun Olufade. Michael Serra-Jovenich contributed to the provision of study materials, the collection and assembly of data, and manuscript writing. The final manuscript was approved by both authors.

CONFLICTS OF INTEREST

The authors declare that there are no potential conflicts of interest.

FUNDING

This research did not receive any funding.

REFERENCES

1. InformedHealth.org. Overview: Tendon overuse injuries (tendinopathy). Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2022.
2. Kaux JF, Forthomme B, Le Goff C, et al. Current opinions on tendinopathy. J Sports Sci Med. 2011;10(2):238–53.
3. Abadin AA, Orr JP, Lloyd AR, et al. An evidence-based approach to orthobiologics for tendon disorders. Phys Med Rehab Clin N Am. 2023;34(1):83–103. https://doi.org/10.1016/j.pmr.2022.08.007
4. Noback PC, Donnelley CA, Yeatts NC, et al. Utilization of orthobiologics by sports medicine physicians: A survey-based study. J Am Acad Orthop Surg Glob Res Rev. 2021;5(1)e20.00185. https://doi.org/10.5435/JAAOSGlobal-D-20-00185
5. US Food and Drug Administration. Regulatory considerations for human cells, tissues, and cellular and tissue-based products: Minimal manipulation and homologous use. Fed Regist. 2017;82(221):54290–2.
6. Schroeder A, Peter Rubin J, Kokai L, et al. Use of adipose-derived orthobiologics for musculoskeletal injuries: A narrative review. PM R. 2020;12:805–16. https://doi.org/10.1002/pmrj.12291
7. Al-Ghadban S, Artiles M, Bunnell BA. Adipose stem cells in regenerative medicine: Looking forward. Front Bioeng Biotechnol. 2022;9:837464. https://doi.org/10.3389/fbioe.2021.837464

8. Viganò M, Lugano G, Orfei CP, et al. Autologous microfragmented adipose tissue reduces inflammatory and catabolic markers in supraspinatus tendon cells derived from patients affected by rotator cuff tears. Int Orthop. 2021;45(2):419–26. https://doi.org/10.1007/s00264-020-04693-9
9. Abdul-Wahab TA, Betancourt JP, Hassan F, et al. Initial treatment of complete rotator cuff tear and transition to surgical treatment: Systematic review of the evidence. Muscles Ligaments Tendons J. 2016;6(1):35–47. https://doi.org/10.11138/mltj/2016.6.1.035
10. Meheux CJ, McCulloch PC, Lintner DM, et al. Efficacy of intra-articular platelet-rich plasma injections in knee osteoarthritis: A systematic review. Arthroscopy. 2016;32(3):495–505. https://doi.org/10.1016/j.arthro.2015.08.005
11. Andriolo L, Altamura SA, Reale D, et al. Nonsurgical treatments of patellar tendinopathy: A systematic review and meta-analysis. Am J Sports Med. 2019;47(4):1001–18. https://doi.org/10.1177/0363546518759674
12. Hohmann E, Keough N, Frank RM, et al. Microfragmented adipose tissue vs. other orthobiologics for knee osteoarthritis: A systematic review. Arthroscopy. 2025;41(2):418–41. https://doi.org/10.1016/j.arthro.2024.03.002
13. Bugarin A, Schroeder G, Shi BY, et al. Top 50 most-cited articles on PRP in musculoskeletal medicine: Characteristics and quality. Orthop J Sports Med. 2022;10(5):23259671221093074. https://doi.org/10.1177/23259671221093074
14. Hogaboom N, Malanga G, Cherian C, et al. 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. J Spinal Cord Med. 2021;44(6):886–95. https://doi.org/10.1080/10790268.2021.1903140
15. Striano RD, Malanga GA, Bilbool N, et al. Refractory shoulder pain with osteoarthritis, and rotator cuff tear, treated with micro-fragmented adipose tissue. Orthop Spine Sports Med. 2018;2(1):014.
16. Ferrell JL, Dodson A, Martin J. Microfragmented adipose tissue in the treatment of a full-thickness supraspinatus tear: A case report. Regen Med. 2023;18(10):773–80. https://doi.org/10.2217/rme-2023-0086
17. Marathe A, Song B, Jayaram P. Microfragmented adipose tissue with adjuvant platelet-rich plasma combination therapy for partial-thickness supraspinatus tear. Cureus. 2021;13(6):e15583. https://doi.org/10.7759/cureus.1558
18. Martin J, Takyi S. Micro-fragmented adipose tissue in the successful treatment of recurrent rotator cuff tears in an injured worker. Biol Ortho J. 2023;5(1):e16–e19. https://doi.org/10.22374/boj.v5i1.38
19. Iuso AM, Pacik D, Martin J, et al. Adipose cellular injection in the treatment of an intrasubstance Achilles tendon defect: A case report. Regen Med. 2022;17(11):835–43. https://doi.org/10.2217/rme-2021-0157
20. Mulroy SJ, Thompson L, Kemp B, et al. Strengthening and optimal movements for painful shoulders (STOMPS) in chronic spinal cord injury: A randomised controlled trial. Phys Ther. 2011;91(3):305–24. https://doi.org/10.2522/ptj.20100182
21. Hartrick CT, Kovan JP, Shapiro S. The numeric rating scale for clinical pain measurement: A ratio measure? Pain Pract. 2003;3(4):310–6. https://doi.org/10.1111/j.1530-7085.2003.03034.x
22. Birnie KA, Hundert AS, Lalloo C, et al. Recommendations for selection of self-report pain intensity measures in children and adolescents: A systematic review and quality assessment of measurement properties. Pain. 2019;160(1):5–18. https://doi.org/10.1097/j.pain.0000000000001377
23. Curtis KA, Roach KE, Applegate EB, et al. Reliability and validity of the wheelchair user's shoulder pain index (WUSPI). Paraplegia. 1995;33(10):595–601. https://doi.org/10.1038/sc.1995.126
24. Koren Y, Leveille SG, You T. Brief pain inventory pain interference subscale: Assessing interference with daily living activities in older adults with multisite musculoskeletal pain. Front Pain Res (Lausanne). 2022;3:897725. https://doi.org/10.3389/fpain.2022.897725
25. Mendoza TR, Chen C, Brugger A, et al. The utility and validity of the modified brief pain inventory in a multiple-dose postoperative analgesic trial. Clin J Pain. 2004;20(5):357–62. https://doi.org/10.1097/00002508-200409000-00011
26. Jensen MP, Hoffman AJ, Cardenas DD. Chronic pain in individuals with spinal cord injury: A survey and longitudinal study. Spinal Cord. 2005;43(12):704–12. https://doi.org/10.1038/sj.sc.3101777
27. Jelsness-Jørgensen LP, Moum B, Grimstad T, et al. Validity, reliability, and responsiveness of the brief pain inventory in inflammatory bowel disease. Can J Gastroenterol Hepatol. 2016;2016:5624261. https://doi.org/10.1155/2016/5624261

28. Atkinson TM, Halabi S, Bennett AV, et al. Measurement of affective and activity pain interference using the Brief Pain Inventory (BPI): Cancer and Leukemia Group B 70903. Pain Med. 2012;13(11):1417–24. https://doi.org/10.1111/j.1526-4637.2012.01498.x
29. Hurst H, Bolton J. Assessing the clinical significance of change scores recorded on subjective outcome measures. J Manipulative Physiol Ther. 2004;27(1):26–35. https://doi.org/10.1016/j.jmpt.2003.11.003
30. Farrar JT, Young JP Jr, LaMoreaux L, et al. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. Pain. 2001;94(2):149–58. https://doi.org/10.1016/S0304-3959(01)00349-9
31. Dworkin RH, Turk DC, Wyrwich KW, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. J Pain. 2008;9(2):105–21. https://doi.org/10.1016/j.jpain.2007.09.005
32. Kamper SJ, Maher CG, Mackay G. Global rating of change scales: A review of strengths and weaknesses and considerations for design. J Man Manip Ther. 2009;17(3):163–70. https://doi.org/10.1179/jmt.2009.17.3.163
33. Salaffi F, Stancati A, Silvestri CA, et al. Minimal clinically important changes in chronic musculoskeletal pain intensity measured on a numerical rating scale. Eur J Pain. 2004;8(4):283–91. https://doi.org/10.1016/j.ejpain.2003.09.004
34. NS, H., et al. Ultrasound pathology, pain, and function in manual wheelchair users with shoulder pain. PM R. 2023;15(3):323–34.
35. Jacobs PL, Nash MS. Exercise recommendations for individuals with spinal cord injury. Sports Med. 2004;34(11):727–51. https://doi.org/10.2165/00007256-200434110-00003
36. K, Z., et al. Musculoskeletal ultrasound in sports medicine: Current status and future directions. Phys Med Rehab Clin N Am. 2021;32(1):1–15.
37. SM, K., et al. Ultrasonographic evaluation of rotator cuff tears: Comparison with MRI. AJR Am J Roentgenol. 2019;213(3):W118–W125.
38. De Smet L. Responsiveness of the DASH and QuickDASH in upper extremity injuries. Acta Orthop Belg. 2008;74(5):575–9.
39. CA, K., et al. Measurement properties of the DASH and QuickDASH: A systematic review by the Outcome Measures in Rheumatology (OMERACT) Hand and Wrist Working Group. J Hand Ther. 2013;26(3):229–40.
40. Price DD, McGrath PA, Rafii A, et al. The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. Pain. 1983;17(1):45–56. https://doi.org/10.1016/0304-3959(83)90126-4
41. Hawker GA, Mian S, Kendzerska T, et al. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). Arthritis Care Res (Hoboken). 2011;63(Suppl 11):S240–S252. https://doi.org/10.1002/acr.20543
42. Jensen MP, Karoly P, Braver S. The measurement of clinical pain intensity: A comparison of six methods. Pain. 1986;27(1):117–26. https://doi.org/10.1016/0304-3959(86)90228-9
43. Revicki DA, Cella D, Hays RD, et al. Responsiveness and minimal important differences for patient reported outcomes. Health Qual Life Outcomes. 2006;4:70. https://doi.org/10.1186/1477-7525-4-70
44. Michener LA, McClure PW, Sennett BJ. American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form, patient self-report section: Reliability, validity, and responsiveness. J Shoulder Elbow Surg. 2002;11(6):587–94. https://doi.org/10.1067/mse.2002.127096
45. Angst F, Schwyzer HK, Aeschlimann A, et al. Measures of adult shoulder function: Disabilities of the Arm, Shoulder, and Hand Questionnaire (DASH) and its short version (QuickDASH), Shoulder Pain and Disability Index (SPADI), American Shoulder and Elbow Surgeons (ASES) Society Standardized Shoulder Assessment Form, Constant Score, Simple Shoulder Test (SST), Oxford Shoulder Score (OSS), and Western Ontario Shoulder Instability Index (WOSI). Arthritis Care Res (Hoboken). 2011;63(Suppl 11):S174–S188. https://doi.org/10.1002/acr.20630
46. Jensen MP, Karoly P. Self-report scales and procedures for assessing pain in adults. In: Turk DC, Melzack R, editors. Handbook of pain assessment. New York: Guilford Press; 2001. pp. 15–34.
47. Williamson A, Hoggart B. Pain: A review of three commonly used pain rating scales. J Clin Nurs. 2005;14(7):798–804. https://doi.org/10.1111/j.1365-2702.2005.01121.x
48. Dworkin RH, Turk DC, Farrar JT, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. Pain. 2005;113(1–2):9–19. https://doi.org/10.1016/j.pain.2004.09.012

49. Werner C, Hezel N, Dongus F, et al. Validity and reliability of the Apple Health app on iPhone for measuring gait parameters in children, adults, and seniors. Sci Rep. 2023;13(1):5350. https://doi.org/10.1038/s41598-023-32550-3
50. Ozinga SJ, Alberts JL. Quantification of postural stability in older adults using mobile technology. Exp Brain Res. 2014;232(12):3861–72. https://doi.org/10.1007/s00221-014-4069-8
51. SH, L. and K. YM. Validity and reliability of gait analysis using smartphones in a controlled environment. Sensors (Basel). 2024;24(5):1579.
52. Sung CM, Hah YS, Kim JS, et al. Cytotoxic effects of ropivacaine, bupivacaine, and lidocaine on rotator cuff tenofibroblasts. Am J Sports Med. 2014;42(12):2888–96. https://doi.org/10.1177/0363546514550991