

## Clinical Research

**KEYWORDS:** Shoulder pain, regenerative medicine, instability

## USE OF LOCALIZED HUMAN GROWTH HORMONE/TESTOSTERONE INJECTIONS FOR CHRONIC SHOULDER PAIN: A CASE SERIES, WITH 12-MONTH FOLLOW-UP



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**ABSTRACT:**

This case series investigated the feasibility and safety of an injection technique for the treatment of chronic shoulder pain. Injections of recombinant human growth hormone and testosterone were given to the shoulder in individuals with chronic shoulder pain, with proposed capsular pain and/or laxity. Individualized exercise therapy programs were followed. Outcomes were assessed at 12 months with the Shoulder Pain and Disability Index (SPADI), the Shoulder Pain Score (SPS), the Mankowski Pain Sale (MPS), and the patient's self-rated percent improvement. Of the 23 consecutive patients who met the inclusion criteria, 17 (19 shoulders) provided informed consent and 14 (16 shoulders) completed all aspects of the study. Patients completing the study reported a significant decrease in pain ratings ( $p < .0001$ ), a significant improvement in the SPADI scores ( $p < .0001$ ) and SPS ( $p < .0001$ ). Of the patients who withdrew from the study, two underwent surgery and one switched to another intervention.

**INTRODUCTION**

Chronic shoulder pain is a common condition which involves long term pain and disability. Common problems associated with chronic shoulder pain involve tears and fraying of the rotator cuff tendons, the labrum, and involvement of the joint capsule. Most of these conditions are due to degeneration or injury to dense connective tissue, primarily composed of ground substance and collagen. Recent literature indicates that "microinstability" may play a role in the development of glenohumeral pathology including tendinopathy and labral lesions. (Chambers & Altchek, 2013; Mistry & Campbell, 2015; Reinold & Curtis, 2013) An intervention that would lead to intrinsic repair and strengthening of the involved dense connective tissues would be expected to have benefit in regard to pain and an improvement in function.

The Orthobiologic/ Regenerative Medicine revolution is expanding treatment for chronic pain. Chronic musculoskeletal conditions involving joint, tendon, ligament and cartilage are the primary targets. Regenerative medicine involves the use of bioactive cells or factors to stimulate healing and remodeling of pathological tissues. The most commonly studied procedures have been proliferative therapy (Campbell et al., 2015; Dallaudière et al., 2014; DeChellis & Cortazzo, 2011; Franceschi et al., 2014; Pourcho, Smith, Wisniewski, & Sellon, 2014; Topol, Reeves, & Hassanein, 2005), injections with platelet-rich plasma. (Baumgarten et al., 2013a; Campbell et al., 2015;

Dallaudière et al., 2014; Denaro et al., 2010; Franceschi et al., 2014), and increasingly, stem cell injections (Labusca, Zugun-Eloae, & Mashayekhi, 2015) and other tissue engineering interventions. (Meyer, Meyer, Handschel, & Wesmann, 2009)

An emerging area of regenerative medicine is the use of human growth hormone, and other anabolic agents. A few numbers of both animal and human studies have been published, with somewhat mixed results regarding the efficacy of these hormones in facilitating injury repair on musculoskeletal tissues. (Baumgarten et al., 2013b; Dallaudière et al., 2014; Denaro et al., 2010; Gui et al., 2009; Hedner, Linde, & Nilsson, 1996; Lal, Wolf, & Herndon, 2000; Raschke et al., 2007). Demonstrating the ability for the use of potent anabolic agents to improve clinical outcomes in the management of diagnosed chronic musculoskeletal conditions can be a significant advancement in the treatment of these conditions.

In a previously reported study involving the treatment of chronic low back pain, localized injections of recombinant human growth hormone (rhGH) and testosterone were found to lead to an improvement in pain and function. [Dubick, 2014] It was hypothesized that this was due at least in part to an improvement in the integrity and strength of the treated ligaments, tendons, and joint capsules. RhGH and testosterone are both endogenous anabolic hormones that stimulate protein synthesis. (Demling, 2005; Oh & Phillips, 2006) Research describing the mechanism of action of rhGH and testosterone has been previously described. [Dubick, 2014]. It is felt that the localized injection of rhGH and testosterone interact synergistically at the injection site to stimulate protein synthesis, leading to formation of new collagen and ultimately mature connective tissue. In conjunction with the injections, controlled exercise would be expected to positively influence the remodeling of the dense connective tissue, while possibly preventing contractures.

**MATERIALS AND METHODS**

This is a 12-month follow-up case series using a one-group pretest posttest design regarding patients seen in a private pain management clinic. This study is designed to provide preliminary data and determine if a randomized control trial is warranted in the future.

Participants received a standardized shoulder examination by an anesthesiologist/pain management physician. Participants had chronic shoulder pain, with the examination suggesting primarily capsular/tendon or labral involvement with or without associated acromioclavicular joint or rotator cuff involvement in the production of symptoms.

The study was approved by and performed under the auspices of the Institutional Review Board (IRB) of Roper St. Francis Healthcare, Charleston, SC, USA. Data were monitored by a Data Collection Site Monitoring Board and Adverse Experience Reporting Committee. All participants provided informed consent. The outcomes and intervention data used to support the findings of this study are restricted by HIPAA in order to protect patient privacy. Data are available from the primary author for researchers who meet the criteria for access to confidential data and with approval from the IRB of Roper St. Francis Healthcare. No external funding was involved with this case series.

### Participants

Participants were 23 consecutive eligible adult participants, aged 18-85 with chronic shoulder pain, serving as a convenience sample during the interval of June 2009 through June 2011. Inclusion and exclusion criteria are listed in Table 1.

Five-participants had undergone previous shoulder surgery, with one having undergone two previous surgeries. The surgeries included three for rotator cuff repair, two for arthroscopy and debridement including a SLAP lesion repair. Seven of the shoulders had a history of previous dislocations, and two participants had been diagnosed with hypermobility syndrome. The participants had received prior therapies including trigger point injections, subacromial and gleno-humeral joint steroid injections, physical therapy, chiropractic adjustments, and pharmacological pain management. The previous interventions were not consistent across participants. Participant's demographics are in Table 2.

The examination included active/passive range of motion in abduction and flexion, grip strength, Obrien's Active Compression test, glenohumeral external rotation apprehension test, rotator cuff testing for weakness and/or pain, deltoid testing for weakness and/or pain, passive horizontal adduction of the glenohumeral joint for acromioclavicular joint (ACJ) pain, palpation of the coracoid process, ACJ, bicipital groove, greater tuberosity, and bicep and triceps strength testing.

To be included in the cohort, the Obrien's Active Compression test and/or the apprehension test demonstrated reproduction of familiar symptoms or aberrant motion. Local anesthetic injections were performed under fluoroscopic guidance in the region of tenderness and suspected pathology. When the ACJ or rotator cuff findings were positive, injections were performed at the ACJ capsule, coraco-clavicular ligament, or the region of the humeral attachment of the affected rotator cuff muscle. Subjective relief of symptoms by 50% or more and improved strength testing indicated continuation in the study. All patients included met this criteria.

### Intervention

Each participant meeting the inclusion criteria received a series of injections of rhGH/testosterone to the same areas as the local anesthetic was injected. The injections were performed by a board-certified, hospital-affiliated anesthesiologist/pain management physician under fluoroscopic guidance.

The injections consisted of recombinant rhGH (Sandoz International, Holzkirchen, Germany, 3u/10 cc volume), aqueous testosterone (12.5 mg for females, 25 mg for males, per 10 cc volume), 5 cc of 1% preservative-free procaine, and 0.9% NaCl to a total volume of 10 cc. The injections were performed at 3-4 week intervals and averaged 3-4 in number. Approximately 3, 10 cc syringes were administered at each injection visit. The number of injections needed for each participant was determined by improvement noted in Obrien's and apprehension tests, as well as the tissue feel during injections. It is noted by the primary author that healthy and healing ligament and tendon tissue presented with a dense feel to syringe pressure, while degenerative/weakened ligament or tendon tissue has more of a soft feel.

Once able, the participants performed graded resisted exercise as

tolerated and range of motion activities. Individualized exercise programs included the following:

- Pilates exercise with a certified instructor
- Physical therapy for range of motion, motor control and resistance exercise
- Self-administered treatment at a fitness center or home
- Working with a personal trainer at an exercise facility

After completion of the injections, the participants were followed for 12-months.

### Outcome Measures

The primary outcome was determined by the Shoulder Pain and Disability index (SPADI). (Breckenridge & McAuley, 2011a) Secondary outcomes were the Shoulder Pain Score (SPS), (Winters, Sobel, Groenier, Arendzen, & Meyboom-De Jong, 1996b) the patients pain rating from 0-10 using the Mankowski Pain Scale (MPSI), (Douglas, Randleman, DeLane, & Palmer, 2014) and the participants reported overall percent change in presenting symptoms. (Cleland, Gillani, Bienen, & Sadosky, 2011)

The SPADI has been used to measure self-rated function across a number of shoulder diagnoses. (Angst et al., 2007; Christie, Hagen, Mowinckel, & Dagfinrud, 2009; Hill, Lester, Taylor, Shanahan, & Gill, 2011a, 2011b; Tveitå, Ekeberg, Juel, & Bautz-Holter, 2008) The questionnaire is based on a score of 100, with the minimal detectable change (MDC 95%) described as 18 points. (Breckenridge & McAuley, 2011b)

The Shoulder Pain Score assesses the patient's self-rated shoulder pain. This pain score has been found to provide a reliable rating of pain and is useful to follow the improvement in pain from the initial visit to the post treatment interval. (Winters, Sobel, Groenier, Arendzen, & Meyboom-De Jong, 1996a)

The MPSI was used as the pain rating scale. It is a 0-10 pain rating scale that links written descriptors of the intensity of the pain to a numerical value. It has been shown to be a valid and reliable tool for pain measurement, as compared to the Faces Scale, the Visual Analog Scale, and the Numeric Rating Scale. (Douglas et al., 2014) The minimal clinically important difference for the change score has not been determined, but it has been reported for the Numeric Rating Scale as two points. (Michener, Snyder, & Leggin, 2011)

Testosterone levels were measured as total testosterone, and rhGH levels measured as IGF-1 at the beginning of the study in order to determine if baseline blood levels were a positive variable related to the outcome measures.

### Statistical Analysis

All analyses were performed using SAS version 9.4 (Cary, NC). Statistical significance was defined at  $\alpha=0.05$ . Descriptive statistics were used to compare the characteristics of the study sample. Means and standard deviations were calculated to describe continuous data. Frequencies and percentages were calculated to describe categorical data. An intention to treat analysis was used, with the last value carried forward for the patients who did not complete the injections.

The primary outcome measure was change in SPADI scores. Secondary outcome measures were changes in SPS and MPSI scores. Changes in scores from baseline were assessed for normality visually using QQ-plots and statistically using the Shapiro-Wilk test. All three instrument scores were found to be normally-distributed; SPADI ( $p=0.3531$ ), SPS ( $p=0.0880$ ), and MPSI ( $p=0.1243$ ). Changes in scores were tested using paired *Student's t*-tests.

## RESULTS AND DISCUSSION RESULTS

Of the 23 eligible patients, six chose to not enter the treatment program. Figure 1. Of the remaining 17 eligible participants, all

provided informed consent to enter the study. All phases of the study including the 12-month follow-up were completed by 14 participants (16 shoulders). Of the three who did not complete the study, one completed injections but started another injection protocol near the six-month follow-up. The patient did not feel that progression was quick enough. One underwent surgery prior to completing the injections, and one underwent surgery shortly after completing the injections. Both surgical procedures were performed because of continued pain and decrease function, related to the original complaint.

Across the 19 shoulders (17 patients) at the 12-month follow-up, statistically significant mean decreases in Shoulder Pain and Disability Index, Shoulder Pain Score and pain severity (Mankowski Pain Scale) were found. There was also a significant improvement in the participants' report of symptoms with an overall self-improvement of 76%.

The primary outcome measure of change in SPADI was found to significantly change from baseline, with a mean reduction in score of 31.8 points (95% Confidence Interval (CI): 20.7-43.0;  $p < .0001$ ). Figure 2. The SPS also changed from baseline, with a mean reduction in score of 36.7 points (95% CI: 24.0-49.4,  $p < .0001$ ). Figure 3. Finally, the MPSI showed a change from baseline, with a mean change in score of 3.1 points (95% CI: 2.0-4.2,  $p < .0001$ ). Figure 4.

There were no significant correlations between study entry IGF-1 or testosterone levels and changes in the four outcome variables at 12-months. No adverse reactions related to the study were reported during the course of the treatment or at the follow-up sessions.

**DISCUSSION**

The positive outcome scores of the participants reveal a potential for rhGH and testosterone injections in conjunction with an exercise program to play a role in relieving pain and improving function in individuals with chronic shoulder pain due to degenerative disease and potential micro instability. These findings were found in a series of patients whose previous treatments failed to provide long-term benefit. Three participants in the study dropped out.

During the initial physical examination, 18 of the 19 shoulders (95%) tested positive during the apprehension test, and 17 of 19 (89%) tested positive for O'Brien's Test/Active Compression Test, indicating possible glenohumeral capsule laxity, apprehension at end range of motion, or superior labral involvement. (Ravin, Cantieri, & Pasquarello, 2008)

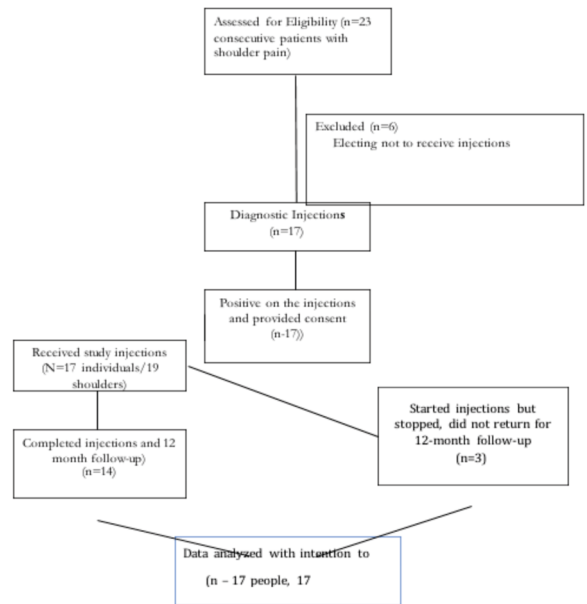
Positive findings during the physical examination with these two tests are, in the primary author's opinion, paramount to the diagnosis of possible capsular or labral involvement versus other shoulder abnormalities. Two subjects revealed mild weakness of a rotator cuff muscle during examination and eight noted discomfort to acromio-clavicular joint testing. The symptomatic rotator cuff attachment on the humerus and/or the acromio-clavicular joint capsule and the coracoclavicular ligament were treated as well. The authors hypothesize that glenohumeral capsular laxity is a common occurrence that is under diagnosed and under treated. A sizeable percentage of chronic shoulder pain that has not responded to conservative treatments, or to arthroscopic surgery, may well have a component of capsular dysfunction, or degeneration of the ligamentous attachment at the enthesis.

Multiple studies found over the last ten years describe a variety of injection procedures for the treatment of musculoskeletal shoulder problems. (Alfredson, Harstad, Haugen, & Öhberg, 2006; Bertrand, Reeves, Bennett, Bicknell, & Cheng, 2016; Bron et al., 2011; Chang et al., 2016; Dimitroulas, Hirsch, Kitas, & Klocke, 2013; Kesikburun, Tan, Yilmaz, Yaşar, & Yazicio lu, 2013; Kwon, Eisenberg, & Zuckerman, 2013; Park, Nam, Lee, Kim, & Park, 2013; Simopoulos, Nagda, & Aner, 2012; Singh, Mahowald, & Noorbaloochi, 2009) With the exception of the studies regarding adhesive capsulitis, the shoulder capsule was not reported as being involved.

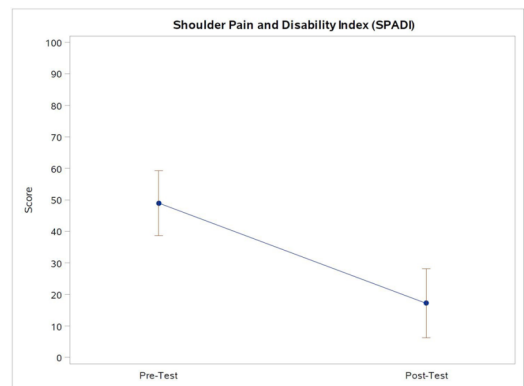
This case series was designed as primarily an injection series. However, any interventional treatment of the shoulder should, in the author's opinion, be followed by rehabilitation therapy or exercise to strengthen the shoulder musculature. If the surrounding musculature is not strengthened, the ligaments may not maintain their integrity. With this in mind, the participants were allowed to utilize any exercise program they wished, whether it be physical therapy, Pilates, individualized exercise, or trainer guided exercise, and agreed to do so following the injections.

The combination of recombinant human growth hormone and testosterone injections for chronic shoulder pain in patients diagnosed with a possible gleno-humeral capsular/labral involvement may hold promise of decreasing pain and restoring normal function in many of these individuals. Concurrent treatment of mild rotator cuff weakness/tendinosis and or acromoclavicular joint involvement was also undertaken, when indicated. Previous treatment options had not resolved the problem. We hypothesized and recent evidence suggests that the injection therapy with rhGH and testosterone stimulates the development of collagen formation that matures into healthy, functional connective tissue, resulting in strengthening of the chronically weakened ligaments and other dense connective tissues. (Hansen et al., 2013; Vestergaard et al., 2012) Limitations to this study include lack of randomization, lack of a control group, no blinding to the treatment group, and the clinician was not blinded. This case series has shown that this line of investigation is safe and accepted by patients. The results support a large-scale randomized controlled trial.

**Figure 1. Consort diagram for study procedures**

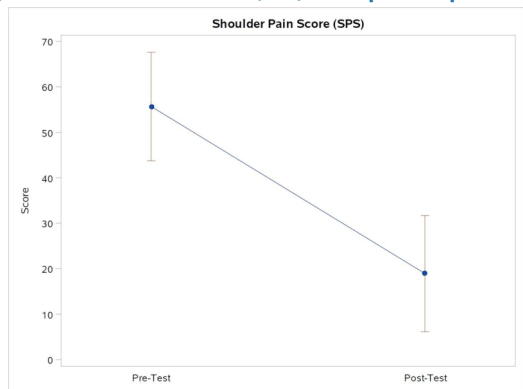


**Figure 2. Shoulder Pain and Disability Index (SPADI) scores pre- and post-test.**



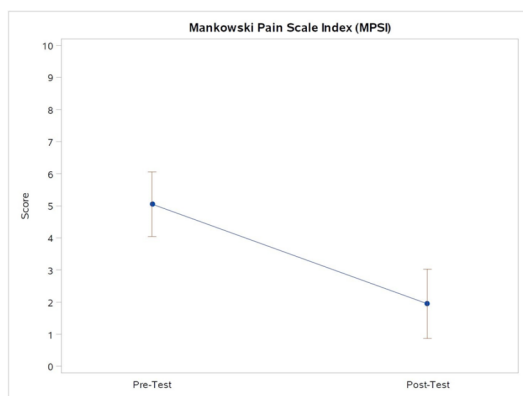
**Figure 2.** Shown above are the point estimates for the mean scores and 95% confidence limits for the SPADI scores, which shows a mean reduction of 31.8 points (95% CI: 20.7-43.0,  $p < .0001$ ). The minimal detectable change is 18.1 points, with a minimal clinically-important difference of 13.2 points (Schmitt & Di Fabio, 2004).

**Figure 3. Shoulder Pain Scores (SPS) scores pre- and post-test.**



**Figure 3.** The point estimates for the mean scores and 95% confidence limits for the SPS scores, which shows a mean reduction of 36.7 points (95% CI: 24.0-49.4,  $p < .0001$ ).

**Figure 4. Mankowski Pain Scale Index (MPSI) scores pre- and post-test.**



**Figure 4.** The point estimates for the mean scores and 95% confidence limits for the MPSI scores, which shows a mean reduction of 3.1 points (95% CI: 2.0-4.2,  $p < .0001$ ).

**Table 1 Inclusion and exclusion criteria**

**Inclusion**

- 18 years or older
- Shoulder pain without neurological deficits
- Symptoms subjectively relieved by 75% or greater with fluoroscopically guided diagnostic local anesthetic injections
- Willingness and ability to self-pay for the injections
- Symptoms of 4 months or greater duration
- Positive finding during examination of the Active Compression/O'Brien's Test, Seated Drawer Test, Apprehension Test

**Exclusion**

- Adhesive capsulitis
- Objective neurological deficits
- Failure to demonstrate significant relief with diagnostic injections
- Active or recurrent carcinoma
- History of prostate cancer
- Pregnancy
- Rheumatic disease
- Severe debilitating disease

**Table 2. Demographics for participants completing study.**

Age	Mean 49.9, range 29-85
Females	3
BMI	Mean 25.95, range 18.8 – 32.8
Duration of symptoms per shoulder	6 > 6 months, < 1 year
Financial per participant	16 self-pay
	2 insurance (one with bilateral shoulder pain)
Occupation	5 retired
	3 law enforcement
	1 electrical engineer
	1 welder
	1 aesthetician
	1 technician
	1 military
	1 sales
	1 tour guide
	1 college professor
	1 dock builder
Previous dislocation	7
Inciting incidents	6 none
	4 heavy weight lifting
	2 systemic hypermobility
	2 accident (MVA, Fall)
	2 sports (softball, tennis)
	3 repetitive work history

**REFERENCES**

1. Alfredson, H., Harstad, H., Haugen, S., & Öhberg, L. (2006). Sclerosing polidocanol injections to treat chronic painful shoulder impingement syndrome-results of a two-centre collaborative pilot study. *Knee Surgery, Sports Traumatology, Arthroscopy*, 14(12), 1321-1326. doi:10.1007/s00167-006-0205-8
2. Angst, F., Goldhahn, J., Pap, G., Mannion, A. F., Roach, K. E., Siebertz, D., ... Simmen, B. R. (2007). Cross-cultural adaptation, reliability and validity of the German shoulder pain and disability index (SPADI). *Rheumatology*, 46(1), 87-92. doi:10.1093/rheumatology/kei040
3. Baumgarten, K. M., Oliver, H. A., Foley, J., Chen, D. G., Autenried, P., Duan, S., & Heiser, P. (2013a). Human growth hormone may be detrimental when used to accelerate recovery from acute tendon-bone interface injuries. *Journal of Bone and Joint Surgery - Series A*, 95(9), 783-789. doi:10.2106/JBJS.L00222
4. Baumgarten, K. M., Oliver, H. A., Foley, J., Chen, D. G., Autenried, P., Duan, S., & Heiser, P. (2013b). Human growth hormone may be detrimental when used to accelerate recovery from acute tendon-bone interface injuries. In (Vol. 95 <p>, pp. 789 <p>).
5. Bertrand, H., Reeves, K. D., Bennett, C. J., Bicknell, S., & Cheng, A. L. (2016). Dextrose prolotherapy versus control injections in painful rotator cuff tendinopathy. *Archives of Physical Medicine and Rehabilitation*, 97(1), 17-25. doi:10.1016/j.apmr.2015.08.412
6. Breckenridge, J. D., & McAuley, J. H. (2011a). Shoulder Pain and Disability Index (SPADI). *Journal of Physiotherapy*, 57(3), 197. doi:10.1016/S1836-9553(11)70045-5
7. Breckenridge, J. D., & McAuley, J. H. (2011b). Shoulder Pain and Disability Index (SPADI). *Journal of Physiotherapy* <p>, 57 <p>(3), 197 <p>. doi:10.1016/S1836-9553(11)70045-5 <p>
8. Bron, C., De Gast, A., Dommerholt, J., Stegenga, B., Wensing, M., & Oostendorp, R. A. B. (2011). Treatment of myofascial trigger points in patients with chronic shoulder pain: A randomized, controlled trial. *BMC Medicine*, 9. doi:10.1186/1741-7015-9-8
9. Campbell, K. A., Saltzman, B. M., Mascarenhas, R., Khair, M. M., Verma, N. N., Bach, B. R. J., & Cole, B. J. (2015). Does Intra-articular Platelet-Rich Plasma Injection Provide Clinically Superior Outcomes Compared With Other Therapies in the Treatment of Knee Osteoarthritis? A Systematic Review of Overlapping Meta-analyses. *Arthroscopy: the journal of arthroscopic & related surgery: official publication of the Arthroscopy Association of North America and the International Arthroscopy Association* <p>, 31 <p>(1), 2221 <p>. doi:10.1016/j.arthro.2015.03.041 <p>
10. Chambers, L., & Altchek, D. W. (2013). Microinstability and internal impingement in overhead athletes. *Clinics in Sports Medicine*, 32(4), 697-707. doi:10.1016/j.csm.2013.07.006
11. Chang, K. V., Hung, C. Y., Wu, W. T., Han, D. S., Yang, R. S., & Lin, C. P. (2016). Comparison of the Effectiveness of Suprascapular Nerve Block With Physical Therapy, Placebo, and Intra-Articular Injection in Management of Chronic Shoulder Pain: A Meta-Analysis of Randomized Controlled Trials. *Archives of Physical Medicine and Rehabilitation*, 97(8), 1366-1380. doi:10.1016/j.apmr.2015.11.009
12. Christie, A., Hagen, K. B., Mowinckel, P., & Dagfinrud, H. (2009). Methodological properties of six shoulder disability measures in patients with rheumatic diseases referred for shoulder surgery. *Journal of Shoulder and Elbow Surgery*, 18(1), 89-95. doi:10.1016/j.jse.2008.07.008
13. Cleland, J., Gillani, R., Bienen, E. J., & Sadosky, A. (2011). Assessing Dimensionality and Responsiveness of Outcomes Measures for Patients with Low Back Pain. *Pain Practice*, 11(1), 57-69. doi:10.1111/j.1533-2500.2010.00390.x
14. Dallaudière, B., Pesquer, L., Meyer, P., Silvestre, A., Perozziello, A., Peuchant, A., ... Serfaty, J. M. (2014). Intratendinous injection of platelet-rich plasma under US guidance to treat tendinopathy: A long-term pilot study. *Journal of Vascular and Interventional Radiology*, 25(5), 717-723. doi:10.1016/j.jvir.2014.01.026
15. DeChellis, D. M., & Cortazzo, M. H. (2011). Regenerative medicine in the field of pain medicine: Prolotherapy, platelet-rich plasma therapy, and stem cell therapy-Theory and evidence. *Techniques in Regional Anesthesia and Pain Management*, 15(2), 74-

80. doi:10.1053/j.trap.2011.05.002
16. Demling, R. H. (2005). The role of anabolic hormones for wound healing in catabolic states. *Journal of burns and wounds*, 4.
17. Denaro, V., Ruzzini, L., Longo, U. G., Franceschi, F., de Paola, B., Cittadini, A., . . . Sgambato, A. (2010). Effect of dihydrotestosterone on cultured human tenocytes from intact supraspinatus tendon. *Knee Surgery, Sports Traumatology, Arthroscopy*, 18(7), 976-981. doi:10.1007/s00167-009-0953-3
18. Dimitroulas, T., Hirsch, G., Kitas, G. D., & Klocke, R. (2013). Clinical outcome of ultrasound-guided steroid injections for chronic shoulder pain. *International Journal of Rheumatic Diseases*, 16(4), 398-402. doi:10.1111/1756-185x.12023
19. Douglas, M. E., Randleman, M. L., DeLane, A. M., & Palmer, G. A. (2014). Determining pain scale preference in a veteran population experiencing chronic pain. *Pain Management Nursing*, 15(3), 625-631. doi:10.1016/j.pmn.2013.06.003
20. Franceschi, F., Papalia, R., Franceschetti, E., Paciotti, M., Maffulli, N., & Denaro, V. (2014). Platelet-rich plasma injections for chronic plantar fasciopathy: A systematic review. *British Medical Bulletin*, 112(1), 83-95. doi:10.1093/bmb/ldu025
21. Gui, T. T., Pagkalos, J., Tsiroidis, E., Narvani, A. A., Heliotis, M., & Mantalaris, A. (2009). Growth hormone: Does it have a therapeutic role in fracture healing? *Expert Opinion on Investigational Drugs*, 18(7), 887-911. doi:10.1517/13543780902893069
22. Hansen, M., Boesen, A., Holm, L., Flyvbjerg, A., Langberg, H., & Kjaer, M. (2013). Local administration of insulin-like growth factor-I (IGF-I) stimulates tendon collagen synthesis in humans. *Scandinavian Journal of Medicine and Science in Sports*, 23(5), 614-619. doi:10.1111/j.1600-0838.2011.01431.x
23. Hedner, E., Linde, A., & Nilsson, A. (1996). Systemically and locally administered growth hormone stimulates bone healing in combination with osteopromotive membranes: An experimental study in rats. *Journal of Bone and Mineral Research*, 11(12), 1952-1960.
24. Hill, C. L., Lester, S., Taylor, A. W., Shanahan, M. E., & Gill, T. K. (2011a). Factor structure and validity of the shoulder pain and disability index in a population-based study of people with shoulder symptoms. *BMC Musculoskeletal Disorders*, 12. doi:10.1186/1471-2474-12-8
25. Hill, C. L., Lester, S., Taylor, A. W., Shanahan, M. E., & Gill, T. K. (2011b). Factor structure and validity of the shoulder pain and disability index in a population-based study of people with shoulder symptoms. *BMC Musculoskeletal Disorders*, 12. doi:10.1186/1471-2474-12-8
26. Kesikburun, S., Tan, A. K., Yilmaz, B., Yaşar, E., & Yazicio lu, K. (2013). Platelet-rich plasma injections in the treatment of chronic rotator cuff tendinopathy: A randomized controlled trial with 1-year follow-up. *American Journal of Sports Medicine*, 41(11), 2609-2615. doi:10.1177/0363546513496542
27. Kwon, Y. W., Eisenberg, G., & Zuckerman, J. D. (2013). Sodium hyaluronate for the treatment of chronic shoulder pain associated with glenohumeral osteoarthritis: A multicenter, randomized, double-blind, placebo-controlled trial. *Journal of Shoulder and Elbow Surgery*, 22(5), 584-594. doi:10.1016/j.jse.2012.10.040
28. Labusca, L., Zugun-Eloae, F., & Mashayekhi, K. (2015). Stem cells for the treatment of musculoskeletal pain. *World J Stem Cells*, 7(1), 96-105. doi:10.4252/wjsc.v7.i1.96
29. Lal, S. O., Wolf, S. E., & Herndon, D. N. (2000). Growth hormone, burns and tissue healing. *Growth Hormone and IGF Research*, 10(SUPPL. B), S39-S43.
30. Meyer, U., Meyer, T., Handschel, J., & Wesmann, H. P. (2009). *Fundamentals of Tissue Engineering and Regenerative Medicine*: Springer-Verlag.
31. Michener, L. A., Snyder, A. R., & Leggin, B. G. (2011). Responsiveness of the Numeric pain rating scale in patients with shoulder pain and the effect of surgical status. *Journal of Sport Rehabilitation*, 20(1), 115-128.
32. Mistry, A., & Campbell, R. S. D. (2015). Microinstability and internal impingement of the shoulder. *Seminars in Musculoskeletal Radiology*, 19(3), 277-283. doi:10.1055/s-0035-1549321
33. Oh, D. M., & Phillips, T. J. (2006). Sex hormones and wound healing. *Wounds*, 18(1), 8-18.
34. Park, K. D., Nam, H. S., Lee, J. K., Kim, Y. J., & Park, Y. (2013). Treatment effects of ultrasound-guided capsular distension with hyaluronic acid in adhesive capsulitis of the shoulder. *Archives of Physical Medicine and Rehabilitation*, 94(2), 270-275. doi:10.1016/j.apmr.2012.10.002
35. Pourcho, A. M., Smith, J., Wisniewski, S. J., & Sellon, J. L. (2014). Intraarticular platelet-rich plasma injection in the treatment of knee osteoarthritis: Review and recommendations. *American Journal of Physical Medicine and Rehabilitation*, 93(11), S108-S121. doi:10.1097/PHM.0000000000000115
36. Raschke, M., Højby Rasmussen, M., Govender, S., Segal, D., Suntum, M., & Christiansen, J. S. (2007). Effects of growth hormone in patients with tibial fracture: A randomised, double-blind, placebo-controlled clinical trial. *European Journal of Endocrinology*, 156(3), 341-351. doi:10.1530/EJE-06-0598
37. Ravin, T., Cantieri, M., & Pasquarello, G. (2008). *Principles of prolotherapy*. Denver, CO: American Academy of Musculoskeletal Medicine.
38. Reinold, M. M., & Curtis, A. S. (2013). Microinstability of the shoulder in the overhead athlete. *Scandinavian Journal of Sports Medicine*, 8(5), 601-616.
39. Simopoulos, T. T., Nagda, J., & Aner, M. M. (2012). Percutaneous radiofrequency lesioning of the suprascapular nerve for the management of chronic shoulder pain: A case series. *Journal of Pain Research*, 5, 91-97. doi:10.2147/JPR.S29864
40. Singh, J. A., Mahowald, M. L., & Noorbaloochi, S. (2009). Intra-articular botulinum toxin A for refractory shoulder pain: a randomized, double-blinded, placebo-controlled trial. *Translational Research*, 153(5), 205-216. doi:10.1016/j.trsl.2009.02.004
41. Topol, G. A., Reeves, K. D., & Hassanein, K. M. (2005). Efficacy of dextrose prolotherapy in elite male kicking-sport athletes with chronic groin pain. *Archives of Physical Medicine and Rehabilitation*, 86(4), 697-702. doi:10.1016/j.apmr.2004.10.007
42. Tveit, E. K., Ekeberg, O. M., Juel, N. G., & Bautz-Holter, E. (2008). Range of shoulder motion in patients with adhesive capsulitis: Intra-tester reproducibility is acceptable for group comparisons. *BMC Musculoskeletal Disorders*, 9. doi:10.1186/1471-2474-9-49
43. Vestergaard, P., Jørgensen, J. O., Olesen, J. L., Bosnjak, E., Holm, L., Frystyk, J., . . . Hansen, M. (2012). Local administration of growth hormone stimulates tendon collagen synthesis in elderly men. *Journal of Endocrinology*, 173(2), 143-150. doi:10.1038/ejcn.2011.11
44. Winters, J. C., Sobel, J. S., Groenier, K. H., Arendzen, J. H., & Meyboom-De Jong, B. (1996a). A shoulder pain score: A comprehensive questionnaire for assessing pain in patients with shoulder complaints. *Scandinavian Journal of Rehabilitation Medicine*, 28(3), 163-167.
45. Winters, J. C., Sobel, J. S., Groenier, K. H., Arendzen, J. H., & Meyboom-De Jong, B. (1996b). A shoulder pain score: A comprehensive questionnaire for assessing pain in