aid tendon repair [Peerbooms JC et al. *Am J Sports Med* 2010], and the injection technique has been reported to be augmented by ultrasound guidance [Chiavaras MM, Jacobson JA *Semin Musculoskelet Radiol* 2013].

Prof. Le Goux and colleagues conducted this prospective, double-blind, placebo-controlled randomized trial from 2011 to 2012. Patients with epicondylitis lasting 3 months or fewer were enrolled. Other potential causes of pain were ruled out, and features of epicondylitis were confirmed by magnetic resonance imaging, ultrasound, or both. Patients with previous corticosteroid infiltration were excluded.

Patients received 2 ultrasound-guided injections of either PRP or saline solution at 4-week intervals and were monitored by an independent clinical evaluator, who was blinded to the treatment, at baseline and 1-, 3-, 6-, and 12-month time points. PRP was obtained from each patient, treated by centrifugation only to concentrate the material, and reinjected into the injured joint of the same patient. Injections were done in a blinded and identical manner for both treatments by using a dual-chamber syringe that penetrated 3 layers into the tendon to target the lesion without entering it.

Each treatment group comprised 25 patients following randomization; however, 3 patients in each arm withdrew from the study within 6 months, due to reasons unrelated to treatment. Patients were evaluated at 6 months for the decrease in pain score from baseline (primary evaluation criteria) using a visual analog scale (VAS; range, 0 to 10). At 6 months, pain scores were reduced by 54.7% with PRP versus 63.6% with saline (p=0.24).

Secondary endpoints included assessment of pain (yes/no) during isometric contraction of the extensor carpi radialis brevis and the extensor digitorum communis and measurement of the degree of pain using the Roles and Maudsley score (range, 1 to 4). Mean baseline Roles and Maudsley scores were 6.8 (±0.8) in the PRP group and 7 (±1) in the saline group; a mean reduction of 1.5 points was observed in both groups at 12 months.

No significant differences between treatment groups were observed at 6 or 12 months in either primary or secondary criteria.

However, significant patient benefit was observed; both groups showed a 50% reduction of pain scores within 3 to 6 months. At 6 and 12 months, respectively, 34% and 66% of all patients were asymptomatic, defined as VAS scores of 1 or less. The proportion of patients with persistent pain at 12 months was equivalent at 23.8% in both groups. No adverse events were reported.

Prof. Le Goux attributed the pain reduction observed with both treatments to the stimulating role of ultrasound-guided intratendinous injections, or prolotherapy, on the process of tendon repair. He further commented that the study was limited by not including a group of patients with epicondylitis who received no treatment so that the pain reduction observed over time with natural healing could be compared with the PRP and saline results.

Denosumab May Warrant Further Testing in Patients Receiving Long-Term GC Therapy

Written by Lynne Lederman

Although glucocorticoids (GCs) are a backbone of the treatment of rheumatic diseases, they are the major cause of secondary osteoporosis and are associated with increased fracture rate and decreased bone quality. The American College of Rheumatology guidelines for glucocorticoid-induced osteoporosis recommend bisphosphonate (BSP) treatment for most patients receiving high-dose or long-term GC therapy [Grossman JM et al. *Arthritis Care Res* 2010]. Drawbacks of BSPs include adverse events (AEs), poor adherence, and treatment failures, resulting in a need for other agents to prevent and treat osteoporosis. Denosumab is a fully humanized monoclonal antibody against the receptor activator of nuclear factor-κB ligand (RANKL), which is essential for the formation, function, and survival of osteoclasts. Denosumab inhibits osteoclast activity and has been shown to reduce the incidence of hip and spine fractures and to increase hip and spine bone mineral density (BMD) in postmenopausal women [Bone HG et al. *J Clin Endocrinol Metab* 2013; Cummings SR et al. *N Engl J Med* 2009]. A subgroup analysis of patients with rheumatoid arthritis (RA) receiving GCs suggested that denosumab increases spine and hip BMD and reduces bone turnover [Dore RK et al. *Ann Rheum Dis* 2010].

Chi Chiu Mok, MD, Tuen Mun Hospital, Hong Kong, China, reported outcomes from Denosumab in Current Users of Bisphosphonates for Glucocorticoid-Induced Osteoporosis [NCT01465568]. This 12-month, open-label, randomized trial conducted at 1 site in China assessed the effects of denosumab on BMD in adults with systemic lupus erythematosus and RA who required long-term prednisolone therapy and who had suboptimal responses to 2 years or more of BSPs. Patients had received long-term prednisolone or equivalent, defined as more than 2.5 mg daily, within 3 months of trial entry. Suboptimal response to BSP was

defined as lumbar spine or hip BMD failing to increase by 2% or more, BMD remaining osteoporotic with a *t* score less than –2.5 or z-score less than –2.0, or development of new fragility vertebral or nonvertebral fractures during BSP treatment. Patients were randomly assigned to subcutaneous denosumab 60 mg every 6 months instead of BSPs or to continuation of BSPs; 21 patients were assigned to each treatment group, and 20 in each completed 12 months of therapy. There were no significant differences in clinical characteristics between treatment groups.

Patients receiving denosumab had a significant increase in lumbar spinal BMD, the primary endpoint, compared with the BSP group at 6 months (3.07% vs 0.56%; p=0.047) and at 12 months (3.39% vs 1.48%; p=0.026); these results were adjusted for baseline BMD, duration of disease and calcium and vitamin D use, osteoporosis risk factors, and cumulative dose of prednisolone. There were no significant differences in the secondary end point of changes in hip and femoral neck BMD at 6 and 12 months between treatment groups. No new fractures developed in any patients during the trial. Bone turnover marker assays are ongoing. Denosumab was well tolerated but was associated with increased infections. AEs are summarized in Table 1.

Table 1. Adverse Events

	Denosumab (n=21)	BSP (n=21)	p Value
Any AEs	18 (86%)	5 (24%)	<0.001
Fever after injection	1 (5%)	0 (0%)	>0.99
Infective episodes (eg, URI)	7 (33%)	1 (5%)	0.045
Dyspepsia, reflux	3 (14%)	0 (0%)	0.23
Dizziness/vertigo	2 (9.5%)	0 (0%)	0.49
High blood pressure	1 (5%)	1 (5%)	>0.99
Arthralgia	1 (5%)	1 (5%)	>0.99
Skin rash	1 (5%)	1 (5%)	>0.99
Alopecia	1 (5%)	0 (0%)	>0.99
Menorrhagia	0 (0%)	1 (5%)	>0.99
Keratitis	1 (5%)	0 (0%)	>0.99

No cases of hypocalcemia or cellulitis occurred; there were no withdrawals due to AEs.
AE=adverse events; BSP=bisphosphonate; URI=upper respiratory infection.

Although 12 months of therapy with denosumab was associated with increased lumbar spine BMD in patients receiving long-term GCs who did not respond to BSP therapy, there were no increases in hip or femoral neck BMD with denosumab. These results should be confirmed in a larger study.

Ultrasound Detects Early Involvement and Correlates With Other Techniques in SSc

Written by Lynne Lederman

Systemic sclerosis (SSc) is characterized by increased dermal thickness (DT); the severity and extent of skin involvement are used to establish the diagnosis and subclassify the disease. The modified Rodnan skin score (mRSS) is a validated method to evaluate skin involvement in SSc, and it is based on manual palpation of 17 areas of the skin. Alberto Sulli, MD, University of Genova, Genoa, Italy, discussed detection of subclinical diffuse dermal involvement by high-frequency ultrasound (US) in patients with limited cutaneous SSc (lcSSc) and presented a poster on the correlation among 3 different methods: mRSS, high-frequency ultrasound (US; a 18-MHz probe), and a plicometer skin test (plicometry) to evaluate skin involvement in patients with SSc [Ruaro B et al. EULAR 2014 (poster SAT0304)].

In patients with lcSSc, areas of skin that were normal according to mRSS were evaluated by high-frequency US. The aim of the study of mRSS, high-frequency US, and plicometry in patients with SSc was to identify possible correlations among these techniques to evaluate DT.

Prof. Sulli presented the results of a study in which 50 patients with lcSSc diagnosed by mRSS (a 5-year median duration of disease) were compared with 50 healthy subjects. DT was evaluated in the 17 standard skin areas (cheeks, fingers, dorsum of hands, forearms, arms, chest, abdomen, thighs, legs, and feet) in patients and healthy control subjects by both mRSS and high-frequency US. He then highlighted a comparative technique study by Ruaro and colleagues [EULAR 2014 (poster SAT0304)], in which the DT of 70 patients with SSc was compared with that of 63 healthy subjects using mRSS, high-frequency US, and plicometry on the standard 17 skin areas. The 3 techniques were performed on the same day for each subject and repeated by 2 blind operators to evaluate interobserver and intraobserver variability.

In patients with lcSSc, DT measured by high-frequency US was significantly higher than DT in healthy subjects for all skin areas (p<0.0001) except the thighs. DT was significantly higher in patients with lcSSc than in healthy subjects in 4 out of 6 skin areas (the arms, chest,