

## Takes Practice

Ultrasound from page 1

rheumatology experience, including 6 months of training. During training, 36 ultrasound-guided injections were performed.

Ultrasound guidance is easy to learn, according to Dr. Kane.

"A short, focused training period was successful. My approach is to demonstrate injections to the [rheumatology residents], then they do injections. In this study, our injector was competent after 36 injections.

"Most rheumatologists believe ultrasound-guided injections should be part of training," added Dr. Kane, a rheumatologist at the University of Newcastle, Newcastle upon Tyne, England.

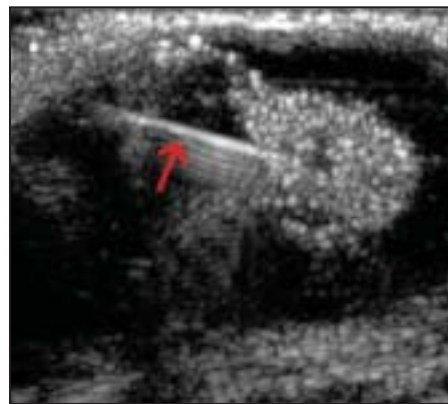
A radiologist blinded to the technique assessed accuracy based on x-rays taken in two planes. The ultrasound-guided injec-



Transverse ultrasound (US) image shows extensor tenosynovitis of the wrist with large tendon sheath effusion.

tions were 83% accurate overall, compared with 66% of the clinical exam-guided injections. This difference was statistically significant.

Anatomic sites injected included the elbow, wrist, knee, ankle, and shoulder. Al-



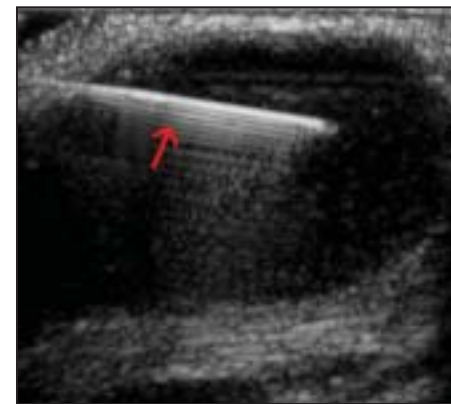
Longitudinal view of needle (arrow) in the tendon sheath effusion on musculo-skeletal US shows the same patient.

though the number of injections was not large enough to reach significance for each joint type, there was a trend toward greater accuracy with ultrasound. For example, 40% of clinical examination-guided injections in shoulder joints were accurate compared with 63% with ultrasound.

"It was clear the shoulder was the area that was the most problematic," Dr. Kane said.

"We might be able to improve [accuracy] with a model of the shoulder prior to clinical experience."

Injections consisted of 40 mg triamcinolone acetonide, 1 mL lignocaine 1%, and Omnipaque contrast so that accuracy



Needle (arrow) injection of hyperechoic corticosteroid into the effusion under US guidance resolved swelling.

of the injection could be checked by x-ray.

In response to a question from an audience member about the volume that is injected into each joint, Dr. Kane noted that there may be a volume effect as well.

"There is a probably a threshold, a small amount of steroids delivered accurately versus a larger amount, where you could get a systemic effect," he said.

He added that at least 5 mL were injected in study participants, compared with up to 2 mL commonly used in clinical practice.

The study is ongoing, Dr. Kane said. "I hope to present outcome data at future meetings." ■

## Repeat Rituximab Treatment As Soon as Symptoms Recur

BY NANCY WALSH  
New York Bureau

BARCELONA — Patients with rheumatoid arthritis who are undergoing repeat courses of treatment with rituximab should begin re-treatment promptly once symptoms begin to recur, Dr. Philip J. Mease said at the annual European Congress of Rheumatology.

This conclusion emerged from analysis of the open-label extension phase of the Randomized Evaluation of Long-Term Efficacy of Rituximab in Rheumatoid Arthritis (REFLEX) trial, a double-blind, placebo-controlled multicenter study in which 298 patients initially received the active drug treatment.

All patients had failed at least one tumor necrosis factor blocker prior to beginning treatment with the B-cell-depleting agent. Those randomized to active treatment received



two doses of rituximab, 1,000 mg, 2 weeks apart, plus stable doses of methotrexate.

Patients who achieved a 20% or greater improvement in swollen and tender joint counts during the 24-week blinded phase of the study were eligible to enter the open-label phase; 168 did so and had adequate follow-up for analysis 24 weeks after the second course of rituximab.

The four components of the 28-joint disease activity score (DAS28)—swollen joint count, tender joint count, erythrocyte sedimentation rate, and patient's global assessment—were assessed before each course of rituximab treatment, and every 4-8 weeks thereafter.

Mean DAS28 was 6.89 before the first course of rituximab and 6.12 before the second course, Dr. Mease wrote in a poster. The second course was administered at a median time of 43 weeks after the first course.

A generalized linear mixed model fit to all visits after the second course was used to evaluate the effects of various variables on DAS28, including pretrial patient and disease characteristics, DAS28 and Health Assessment Questionnaire at various times, and peripheral CD19+ B cell count before courses.

According to the model, DAS28 after the second course of treatment was independently increased by three factors: DAS28 before the second course, DAS28 at trial week 20, and Health Assessment Questionnaire at week 16.

Every 1 point that DAS28 was allowed to worsen before the second course of rituximab resulted in a 0.32-point higher DAS28 after the second course, according to Dr. Mease, who is a rheumatologist in Seattle.

Equally significant in the model but with the opposite effect on DAS28 was the peripheral CD19+ B-cell count before the second course: A count of at least  $80 \times 10^3$ /mL before the second course resulted in a 0.47-point lower DAS28 after the second course.

"The take-home message from this analysis is that in order to achieve the best DAS with a repeat course of rituximab, the preferable time for re-treatment is when the patient is starting to have resurgent symptoms," Dr. Mease commented in an interview.

"On average, patient response lasts 6 months and at that point clinicians should start monitoring more diligently, looking for signs of disease activity. If the patient waits until 8 months for re-treatment, the resulting DAS won't be as good," Dr. Mease added.

REFLEX was supported by Genentech, Biogen, and Roche. Dr. Mease has previously disclosed receiving consulting fees from Genentech and Biogen. ■

**Symptom resurgence usually occurs about 6 months after ending the first course.**

DR. MEASE

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