

# Joint Distraction May Delay Knee Replacement

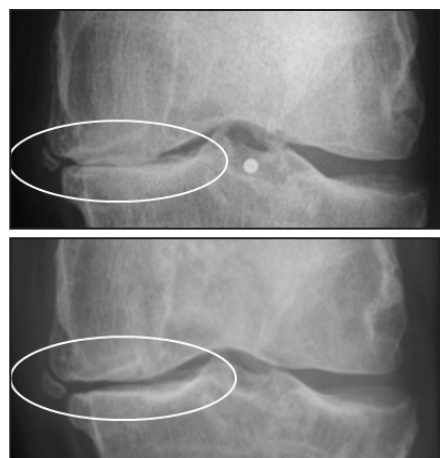
BY M. ALEXANDER OTTO

FROM THE WORLD CONGRESS ON  
OSTEOARTHRITIS

SAN DIEGO – Separating an osteoarthritic knee joint for 2 months – that is, stretching the top of the tibia away from the base of the femur and holding the bones in place with pins set into an external fixation frame – stimulates the joint to produce new cartilage, thereby reducing pain and improving function for at least 2 years, according to findings from a small European pilot study.

The 20 patients in the trial were all facing knee replacement due to osteoarthritis (OA); the technique, known as knee joint distraction, has postponed surgery for 2 years and counting in the subjects. The hope is the patients will never need an artificial knee, according to senior investigator Dr. Floris Lafeber, a professor of experimental rheumatology at the University Medical Center Utrecht (the Netherlands).

Their minimum joint space width increased from a baseline mean of 1.0 mm to 1.8 mm at 2 years. Patients started the trial with, on average, about 22% of their subchondral bone denuded; that dropped to about 8% at 2 years.



IMAGES COURTESY DR. FLORIS LAFEBER

**Three years after a 2-month joint distraction, joint space is larger.**

In short, there was an “astonishing increase in cartilage volume,” Dr. Lafeber said at the congress, which was sponsored by the Osteoarthritis Research Society International.

Meanwhile, total WOMAC (Western Ontario and McMaster Universities) osteoarthritis index scores increased from about 45% at baseline to about 78% at 2 years, with improvements in WOMAC pain, function, and stiffness subscales. Visual Analog Scale pain scores improved from 73 at baseline to 28 at 2 years. The results were statistically significant.

The technique, which had been used in the past for ankle OAs, “looks very promising” for osteoarthritic knees, Dr. Lafeber said. The 1 year results have been previously published (Ann. Rheum. Dis. 2011;70:1441-6;; RHEUMATOLOGY NEWS, August 2011, p. 28)

His team will next pit knee distraction against total knee replacement and osteotomy in two randomized trials. The researchers will keep tracking the original 20 patients as well. “We are now having follow-up of the first patients for more than 4 years, and no prostheses are placed yet,” Dr. Lafeber said.

The researchers plan “more sophisticated MRIs to look at the quality of the cartilage,” although the increased joint space on weight-bearing x-rays suggests mechanical competence. Biomarker analysis also suggests “the quality of the cartilage has a hyaline aspect,” according to Dr. Lafeber.

The 20 patients’ average age was 49 years; 11 were women. All had end-stage, unilateral knee OA with severe pain and cartilage damage. Patients with major problems in both knees were excluded from the study. In a variation of the Ilizarov procedure, a tube with internal coil springs was placed on each side of the patients’ osteoarthritic knees,

bridging the joints. Joints were then distracted to 5 mm over a few days. Full weight bearing was allowed. The tubes and pins were removed after 2 months.

The theory is that temporarily unloading the knee prevents additional wear and tear and allows cartilage to start repairing itself. Pin sites became infected in 17 of the 20 patients, and were treated with local and oral antibiotics. Dr. Lafeber said he and his colleagues hope that technique refinements will reduce the infection rate.

“On the MRI, it looked [as if] the cartilage was regenerated, but it’s unlikely to be truly hyaline articular cartilage.

“It’s much more likely to be fibrocartilage, repair-type cartilage. It’s difficult to know how long [patients] maintain that fibrocartilage” before it’s worn away, said Dr. David Hunter, a rheumatologist, epidemiologist, and professor of medicine at the University of Sydney. “In terms of the clinical applicability of that intervention, I’m not sure it has much utility,” he said, noting that, pending randomized trial results, doubt about the clinical utility of the technique must be maintained.

Dr. Lafeber and Dr. Hunter each reported having no disclosures. The work was supported by the Dutch Arthritis Association. ■

**Live Vaccines** Live vaccines should not be given concurrently with HUMIRA [see Warnings and Precautions].  
**USE IN SPECIFIC POPULATIONS**

**Pregnancy** Pregnancy Category B - There are no adequate and well-controlled studies in pregnant women. Because animal reproduction and developmental studies are not always predictive of human response, HUMIRA should be used during pregnancy only if clearly needed.

**Pregnancy Registry:** To monitor outcomes of pregnant women exposed to HUMIRA, a pregnancy registry has been established. Physicians are encouraged to register patients by calling 1-877-311-8972.

**Nursing Mothers** It is not known whether adalimumab is excreted in human milk or absorbed systemically after ingestion. Because many drugs and immunoglobulins are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from HUMIRA, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

**Pediatric Use** Safety and efficacy of HUMIRA in pediatric patients for uses other than juvenile idiopathic arthritis (JIA) have not been established.

**Juvenile Idiopathic Arthritis** In the JIA trial, HUMIRA was shown to reduce signs and symptoms of active polyarticular JIA in patients 4 to 17 years of age. HUMIRA has not been studied in children less than 4 years of age, and there are limited data on HUMIRA treatment in children with weight <15 kg.

The safety of HUMIRA in pediatric patients in the JIA trial was generally similar to that observed in adults with certain exceptions [see Adverse Reactions].

Post-marketing cases of malignancies, some fatal, have been reported among children, adolescents, and young adults who received treatment with TNF-blockers including HUMIRA [see Warnings and Precautions].

**Geriatric Use** A total of 519 rheumatoid arthritis patients 65 years of age and older, including 107 patients 75 years of age and older, received HUMIRA in clinical studies RA-I through IV. No overall difference in effectiveness was observed between these subjects and younger subjects. The frequency of serious infection

and malignancy among HUMIRA treated subjects over 65 years of age was higher than for those under 65 years of age. Because there is a higher incidence of infections and malignancies in the elderly population in general, caution should be used when treating the elderly.

#### OVERDOSAGE

Doses up to 10 mg/kg have been administered to patients in clinical trials without evidence of dose-limiting toxicities. In case of overdosage, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions or effects and appropriate symptomatic treatment instituted immediately.

#### NONCLINICAL TOXICOLOGY

**Carcinogenesis, Mutagenesis, Impairment of Fertility** Long-term animal studies of HUMIRA have not been conducted to evaluate the carcinogenic potential or its effect on fertility. No clastogenic or mutagenic effects of HUMIRA were observed in the *in vivo* mouse micronucleus test or the *Salmonella-Escherichia coli* (Ames) assay, respectively.

#### PATIENT COUNSELING INFORMATION

Patients or their caregivers should be provided the HUMIRA “Medication Guide” and provided an opportunity to read it and ask questions prior to initiation of therapy. The healthcare provider should ask the patient questions to determine any risk factors for treatment. Patients developing signs and symptoms of infection should seek medical evaluation immediately.

**Patient Counseling** Patients should be advised of the potential benefits and risks of HUMIRA. Physicians should instruct their patients to read the Medication Guide before starting HUMIRA therapy and to reread each time the prescription is renewed.

• **Infections** Inform patients that HUMIRA may lower the ability of their immune system to fight infections. Instruct patients of the importance of contacting their doctor if they develop any symptoms of infection, including tuberculosis, invasive fungal infections, and reactivation of hepatitis B virus infections.

• **Malignancies** Patients should be counseled about the risk of malignancies while receiving HUMIRA.

• **Allergic Reactions** Patients should be advised to seek immediate medical attention if they experience any symptoms of severe allergic reactions. Advise latex-sensitive patients that the needle cap of the prefilled syringe contains latex.

• **Other Medical Conditions** Advise patients to report any signs of new or worsening medical conditions such as congestive heart failure, neurological disease, autoimmune disorders, or cytopenias. Advise patients to report any symptoms suggestive of a cytopenia such as bruising, bleeding, or persistent fever.

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