

## ULTRASOUND THERAPY FOR CALCIFIC TENDINITIS OF THE SHOULDER

GEROLD R. EBENBICHLER, M.D., CELAL B. ERDOGMUS, M.D., KARL L. RESCH, M.D., MARTIN A. FUNOVICS, M.D.,  
FRANZ KAINBERGER, M.D., GEORG BARISANI, M.D., MARTIN ARINGER, M.D., PETER NICOLAKIS, M.D.,  
GÜNTHER F. WIESINGER, M.D., MEHRDAD BAGHESTANIAN, M.D., ELISABETH PREISINGER, M.D.,  
AND VERONIKA FIALKA-MOSER, M.D.

**ABSTRACT**

**Background and Methods** Although ultrasound therapy is used to treat calcific tendinitis of the shoulder, its efficacy has not been rigorously evaluated. We conducted a randomized, double-blind comparison of ultrasonography and sham insonation in patients with symptomatic calcific tendinitis verified by radiography. Patients were assigned to receive 24 15-minute sessions of either pulsed ultrasound (frequency, 0.89 MHz; intensity, 2.5 W per square centimeter; pulsed mode, 1:4) or an indistinguishable sham treatment to the area over the calcification. The first 15 treatments were given daily (five times per week), and the remainder were given three times a week for three weeks. Randomization was conducted according to shoulders rather than patients, so a patient with bilateral tendinitis might receive either or both therapies.

**Results** We enrolled 63 consecutive patients (70 shoulders). Fifty-four patients (61 shoulders) completed the study. There were 32 shoulders in the ultrasound-treatment group and 29 in the sham-treatment group. After six weeks of treatment, calcium deposits had resolved in six shoulders (19 percent) in the ultrasound-treatment group and decreased by at least 50 percent in nine shoulders (28 percent), as compared with respective values of zero and three (10 percent) in the sham-treatment group ( $P=0.003$ ). At the nine-month follow-up visit, calcium deposits had resolved in 13 shoulders (42 percent) in the ultrasound-treatment group and improved in 7 shoulders (23 percent), as compared with respective values of 2 (8 percent) and 3 (12 percent) in the sham-treatment group ( $P=0.002$ ). At the end of treatment, patients who had received ultrasound treatment had greater decreases in pain and greater improvements in the quality of life than those who had received sham treatment; at nine months, the differences between the groups were no longer significant.

**Conclusions** In patients with symptomatic calcific tendinitis of the shoulder, ultrasound treatment helps resolve calcifications and is associated with short-term clinical improvement. (N Engl J Med 1999;340:1533-8.)

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**C**ALCIFIC tendinitis of the shoulder is characterized by a reactive calcification that affects the rotator-cuff tendons.<sup>1</sup> Frequently, such calcifications are incidental radiographic findings in asymptomatic patients. In most cases, they are located 1 to 2 cm from the insertion of the supraspinatus tendon on the greater tuberosity. Approximately 50 percent of patients with calcific tendinitis have shoulder pain,<sup>2,3</sup> with acute or chronic painful restrictions of the range of motion of the shoulders and thus limitation of the activities of daily living.

Treatments directed toward the calcium deposits, such as surgery and percutaneous needle aspiration, seem to reduce pain and restore shoulder function in some, but not all, patients.<sup>3-6</sup> Promising results have been reported for shock-wave therapy.<sup>7,8</sup> Ultrasound therapy with an intensity ranging from 0.5 to 2.0 W per square centimeter of body-surface area is widely used for the treatment of painful musculoskeletal disorders.<sup>9</sup> However, the clinical efficacy of this approach for most such applications has not been confirmed.<sup>10,11</sup> Thus, the use of therapeutic ultrasonography is predominantly empirical, based on reported biophysical effects within tissue<sup>12,13</sup> and on anecdotal experience in clinical practice.

We recently found that calcifications of the shoulder resolved after ultrasound therapy,<sup>14</sup> thus confirming the findings in earlier reports.<sup>15,16</sup> In general, however, evidence of the effectiveness of this approach is inconclusive, possibly because previous trials have been small, or their methods have been flawed.<sup>11</sup> Therefore, we assessed the efficacy of pulsed ultrasound as a treatment for idiopathic calcific tendinitis in a controlled trial.

**METHODS****Patients**

Between October 1994 and April 1997, patients with radiographically verified calcific tendinitis who were seen at various de-

From the Departments of Physical Medicine and Rehabilitation (G.R.E., C.B.E., P.N., G.F.W., E.P., V.F.-M.), Osteoradiology (M.A.F., F.K.), Traumatic Surgery (G.B.), Rheumatology (M.A.), and Angiology (M.B.), University Hospital of Vienna, Vienna, Austria; and the Forschungsinstitut für Balneologie und Kurortwissenschaft, Bad Elster, Germany (K.L.R.). Address reprint requests to Dr. Ebenbichler at the Department of Physical Medicine and Rehabilitation, University Hospital of Vienna, Währinger Gürtel 18-20, 1090 Vienna, Austria, or at gerold.ebenbichler@akh-wien.ac.at.

Reinhard Weinstabl, M.D., Department of Traumatic Surgery, University Hospital of Vienna, Vienna, Austria, was also an author.

partments and outpatient clinics in participating hospitals and by specialists in private practice in Vienna, Austria, were invited to take part in a randomized, double-blind comparison of ultrasound therapy and sham insonation. Those interested were referred to the outpatient clinic of the Department of Physical Medicine and Rehabilitation of the University Hospital of Vienna.

The diagnosis of calcific tendinitis was established by analysis of standard radiographs and ultrasonograms of the shoulder. To be eligible for the study, patients had to have idiopathic calcific tendinitis type 1 (i.e., clearly circumscribed and dense appearance on radiography) or type 2 (i.e., dense or clearly circumscribed appearance) according to the classification of Gärtner and Heyer.<sup>17</sup> Patients with idiopathic calcific tendinitis type 3 (i.e., translucent or cloudy appearance without clear circumscription) were excluded, because this type has a strong tendency to resolve spontaneously.<sup>2,17</sup> The diameter of calcification had to exceed 5.0 mm. To be eligible, patients had to have either mild-to-moderate pain that had been present for more than four weeks or a restricted range of motion of the affected shoulder or shoulders.

Patients were excluded if they had systemic diseases associated with an increased risk of calcification (such as gout, hypercalcemia of any cause, and various rheumatic diseases) as indicated by predefined pathological findings; had previously undergone surgery for calcifications or percutaneous needle aspiration, ultrasonography, or shock-wave therapy for calcific tendinitis; had received injections of glucocorticoids in the shoulder within the three months preceding the study; or regularly took analgesic or anti-inflammatory drugs for relief of tendinitis.

All participants provided written, informed consent. The study protocol was approved by the ethics committee of the University of Vienna.

### Ultrasound Therapy

Ultrasound therapy was administered for 15 minutes per session to the area over the calcification at a frequency of 0.89 MHz and an intensity of 2.5 W per square centimeter. The pulsed mode was 1:4, the transducer was 5 cm<sup>2</sup> (Sonodyn, Siemens), and an aquasonic gel was used as the couplant. To optimize treatment of the affected areas in the supraspinatus and infraspinatus muscles and tendons, the transducer was moved slowly in circles distal to the lateral acromion and the acromial part of the clavicle while the patient flexed his or her upper arm and internally rotated the forearm. Treatment of calcium deposits in the subscapularis muscle was performed with the patient's upper arm in an abducted and externally rotated position. The sham therapy was administered in the same way except that the ultrasonic generator was not turned on.

The device was standardized initially, and output was monitored regularly by means of a simple underwater radiation balance. An on-off key introduced into the transducer circuit allowed normal ultrasonic output as well as mock insonation (sham treatment). The first 15 of the 24 treatments were given daily (five times per week) for three weeks, and the remaining 9 were given three times a week for three weeks.

For occasional pain relief, patients could take an analgesic drug (usually tramadol). Nonsteroidal or steroidal antiinflammatory drugs were not allowed.

### Randomization

A spreadsheet program (Lotus Symphony, Lotus) was used to generate a list of random numbers. Since patients could have calcific tendinitis in one or both shoulders, randomization was conducted according to shoulders rather than patients. Thus, a patient could receive sham treatment for one shoulder and ultrasound treatment for the other. A therapist who was not involved in treatment handed out the treatment assignments, which were in sealed, opaque envelopes. Thus, the patients, the therapists applying the therapy, and the evaluator were all unaware of the treatment assignments.

The therapist who made the treatment assignments also switched the ultrasonic generator to either active or sham mode. Since the

intensity of ultrasound therapy was usually below the threshold of sensitivity, patients were theoretically unable to distinguish between genuine and sham ultrasonography.

### Outcome Measures

The primary outcome measure was changes from base line in the calcium deposits on radiography at the end of treatment and at the nine-month follow-up visit. Radiography was performed at each follow-up visit, and the results were assessed independently by two radiologists who were unaware of the patients' treatment assignments. The three-point scale of Gärtner and Heyer<sup>17</sup> was used, in which a score of 1 indicates no change or a worsening of the condition, a score of 2 a decrease of at least 50 percent in the area and density of the calcification, and a score of 3 complete resolution of the calcification.

Radiographs were obtained under standardized conditions: a predefined posteroanterior position was used, and the same machine was used at each site, with the same exposure settings and radiographic settings. With the patient sitting and the arm placed parallel to the trunk in a standardized position, one exposure was obtained during external rotation, one while in a neutral position, and one during internal rotation. At base line, ultrasonography was used to pinpoint the location of the calcium deposits and to see whether there was a tear in the rotator cuff or inflammatory reactions within the bursae.

Secondary outcomes included subjective and objective measures. The 100-point Constant score<sup>18</sup> was used to provide an overall clinical assessment of the shoulder with respect to the degree of pain, the patient's ability to perform normal tasks of daily living (maximal score, 35), and the active range of motion and power of the shoulder, or torque (maximal score, 65). On this scale, the worst possible score is 0, indicating that a patient has the most severe pain and is unable to perform any activities of daily living involving the impaired shoulder. The best possible score is 100, indicating that a patient is free from pain and able to perform all activities of daily living. We also used the pain score of Binder et al.,<sup>19</sup> which focuses exclusively on subjective symptoms including pain, pain on resisted movement, and pain on active abduction, to assess the level of pain. On this scale, the best possible score is 0 and the worst possible score is 52. The severity of pain at night and during the day, both on movement and at rest, is assessed by means of a visual-analogue scale that ranges from 0 (no pain) to 10 (severe pain). The pain induced by resisted abduction in the neutral position and external and internal rotation of the shoulder is assessed on a four-point scale in which a score of 0 indicates the absence of pain; a score of 1 slight pain, but full power; a score of 2 moderate pain and reduced power; and a score of 3 severe pain with no power against even minimal resistance. The presence of pain on active abduction is also assessed on a four-point scale in which a score of 0 indicates the absence of pain, a score of 1 pain at only one point in the arc, a score of 2 pain throughout the arc, and a score of 3 pain so severe as to prohibit completion of the arc. The patients also assessed their quality of life on a 10-cm visual-analogue scale on which 0 cm indicated an excellent quality of life and 10 cm indicated the worst imaginable.

Radiography and clinical examinations were performed immediately before the first treatment session and after the last session (an interval of about six weeks). Patients were asked to return for a follow-up visit nine months after the base-line evaluation, at which time the code was broken and patients were either no longer followed or offered individualized further treatment.

### Statistical Analysis

A two-tailed Fisher's exact test was used to assess the primary outcome measure (changes in radiographic findings),<sup>20</sup> and the Cochran-Mantel-Haenszel test was used to control for the two types of calcifications.<sup>21</sup> For secondary outcome measures, we used two-tailed t-tests<sup>22</sup> for independent samples to compare mean changes between the groups at the end of treatment and at the nine-month follow-up visit.

RESULTS

Base-Line Evaluation

A total of 63 consecutive patients (70 shoulders) were enrolled. Nine patients (nine shoulders, 13 percent) did not complete treatment: seven (seven shoulders; three in the ultrasound-treatment group and four in the sham-treatment group) dropped out soon after the first session, and two patients (two shoulders) in the sham-treatment group withdrew because of excessive pain. The characteristics of these patients did not differ significantly from the characteristics of those who completed the study. A total of 54 patients (61 shoulders: 32 in the ultrasound-treatment group and 29 in the sham-treatment group) completed the treatment. Of the seven patients who received bilateral treatment, five received ultrasound treatment for one shoulder and sham treatment for the other, one received bilateral ultrasound treatment, and one received bilateral sham treatment. Of these, 50 patients (56 shoulders: 31 in the ultrasound-treatment group and 25 in the sham-treatment group) also completed the nine-month follow-up. Base-line characteristics were similar in the two groups (Table 1).

The treatment period lasted a mean ( $\pm$ SD) of  $44 \pm 8$  days in the ultrasound-treatment group and  $44 \pm 8$  days in the sham-treatment group. The mean lengths of follow-up in the two groups were  $237 \pm 32$  days and  $240 \pm 38$  days, respectively.

Radiologic Assessment

All the radiologic assessments of the two independent radiologists were in agreement except for two shoulders evaluated at the end of the treatment period; for evaluation in these two cases, the more conservative ratings were used. In the ultrasound-treatment group, the calcium deposits had resolved in six shoulders (19 percent) and decreased by at least 50 percent in nine shoulders (28 percent) at the end of treatment (Table 2). In contrast, the respective values in the sham-treatment group were zero and three (10 percent) ( $P=0.003$ ). At the nine-month follow-up visit, calcium deposits had resolved in 13 shoulders in the ultrasound-treatment group (42 percent) and improved in 7 (23 percent), as compared with values of 2 (8 percent) and 3 (12 percent), respectively, in the sham-treatment group ( $P=0.002$ ). The findings were similar when only the left or the right shoulders of the patients who had both shoulders treated were analyzed (data not shown). Analysis of the results according to the type of calcifications (type 1 or 2) also revealed significant differences between the groups at the end of therapy ( $P<0.001$ ) and at the nine-month follow-up visit ( $P<0.001$ ).

Clinical Assessment

At the end of therapy, patients who had received ultrasound treatment had greater decreases in pain and

TABLE 1. BASE-LINE CHARACTERISTICS OF THE 61 SHOULDERS STUDIED IN 54 PATIENTS.\*

CHARACTERISTIC	ULTRASOUND TREATMENT (N=32)	SHAM TREATMENT (N=29)
Age (yr)	49 $\pm$ 11	54 $\pm$ 10
Body-mass index†	25.2 $\pm$ 3.7	25.3 $\pm$ 3.3
Shoulder affected (no.)		
Left	13	15
Right	19	14
Location (no.)		
Supraspinatus muscle	24	24
Infraspinatus muscle	6	4
Subscapularis muscle	2	1
Diameter of calcification (mm)	14.0 $\pm$ 6.4	12.4 $\pm$ 6.0
Type of calcification (no.)‡		
Type 1	27	20
Type 2	5	9
Bursitis (no.)	7	5
Severity of pain (no.)		
Mild	8	9
Moderate	21	16
Severe	3	4
Duration of pain (wk)		
Median	8	8
Interquartile range	4–20	4–19
Pain due to trauma (no.)	7	7
Impaired range of motion (no.)	20	17
Duration of impaired range of motion (wk)		
Median	8	6
Interquartile range	2–20	1.5–20
Previous drug therapy (no.)	11	15
Degree of pain on abduction (no.)		
None	2	5
Slight	14	6
Moderate	14	15
Severe	2	3
Pain on external rotation (no.)		
None	2	6
Slight	8	9
Moderate	20	14
Severe	2	0
Pain on internal rotation (no.)		
None	13	9
Slight	15	13
Moderate	4	7
Severe	0	0
Pain on active abduction (no.)		
None	1	2
Only at 1 point	6	2
Throughout the arc	21	16
Too severe to complete the arc	4	9

\*Plus-minus values are means  $\pm$ SD. There were 31 patients in the ultrasound-treatment group, and 28 patients in the sham-treatment group. Five patients were in both groups.

†The body-mass index is calculated as the weight in kilograms divided by the square of the height in meters.

‡The classification of Gärtner and Heyer<sup>17</sup> was used.

**TABLE 2. RADIOLOGIC OUTCOMES OF TREATMENT.**

TIME OF ASSESSMENT	RADIOLOGIC FINDINGS			P VALUE*
	UNCHANGED OR WORSE	IMPROVEMENT	RESOLUTION	
	no. of shoulders (%)			
End of treatment				0.003
Ultrasound treatment (n=32)	17 (53)	9 (28)	6 (19)	
Sham treatment (n=29)	26 (90)	3 (10)	0	
Follow-up visit at 9 mo				0.002
Ultrasound treatment (n=31)	11 (35)	7 (23)	13 (42)	
Sham treatment (n=25)	20 (80)	3 (12)	2 (8)	

\*P values were calculated with the use of the two-tailed Fisher's exact test.

**TABLE 3. EFFECTS OF TREATMENT ON THE SEVERITY OF PAIN AND QUALITY OF LIFE.\***

VARIABLE	BASE-LINE SCORE	MEAN CHANGE IN SCORE AT END OF TREATMENT (95% CI)	P VALUE	MEAN CHANGE IN SCORE AT 9-MO FOLLOW-UP VISIT (95% CI)	P VALUE
Constant score†			0.002		0.52
Total (maximum, 100 points)					
Ultrasound treatment	74.5±18.0	17.8 (12.0 to 23.8)		15.7 (8.5 to 22.9)	
Sham treatment	71.7±21.5	3.7 (-3.3 to 10.7)		12.4 (4.8 to 19.9)	
Pain (maximum, 15 points)			<0.001		0.23
Ultrasound treatment	5.6±3.0	6.4 (5.1 to 7.7)		5.7 (4.0 to 7.3)	
Sham treatment	6.9±3.6	1.6 (0.01 to 3.1)		4.0 (1.8 to 6.2)	
Activities of daily living (maximum, 20 points)			0.01		0.84
Ultrasound treatment	15.0±2.9	3.6 (2.6 to 4.5)		2.7 (1.2 to 4.1)	
Sham treatment	14.6±3.7	1.4 (-0.1 to 2.9)		2.9 (1.5 to 4.3)	
Range of motion (maximum, 40 points)			0.05		0.57
Ultrasound treatment	33.4±7.5	4.3 (1.9 to 6.7)		3.7 (0.9 to 6.4)	
Sham treatment	31.9±8.3	0.4 (-2.8 to 3.6)		2.5 (-0.5 to 5.6)	
Torque (maximum, 25 points)			0.10		0.97
Ultrasound treatment	20.8±7.8	3.7 (1.0 to 6.4)		3.1 (0.2 to 6.0)	
Sham treatment	18.4±9.0	0.8 (-1.6 to 3.1)		3.0 (-0.2 to 5.8)	
Binder's pain score (minimum, 0 points)‡			0.001		0.48
Ultrasound treatment	21.8±8.9	-14.9 (-18.4 to -11.3)		-13.7 (-18.3 to -9.1)	
Sham treatment	20.7±10.6	-6.3 (-10.0 to -2.7)		-11.3 (-16.6 to -6.0)	
Quality of life (minimum, 0 points)§			0.002		0.52
Ultrasound treatment	6.1±2.6	2.6 (1.7 to 3.6)		2.4 (1.2 to 3.5)	
Sham treatment	6.6±2.0	0.4 (0.6 to 1.4)		1.9 (0.8 to 2.9)	

\*Plus-minus values are means ±SD. A total of 32 shoulders in the ultrasound-treatment group and 29 shoulders in the sham-treatment group were analyzed at the end of treatment, and 31 and 25, respectively, were analyzed at the nine-month follow-up visit. CI denotes confidence interval.

†On the Constant score, the worst possible score is 0, indicating that a patient has the most severe pain and is unable to perform any activities involving the impaired shoulder, and the best possible score is 100, indicating that a patient is free from pain and able to perform all tasks of daily living.

‡Binder's score assesses the severity of pain at night and during the day, both on movement and at rest, by means of a visual-analogue scale that ranges from 0 (no pain) to 10 (severe pain). The pain induced by resisted abduction, external rotation, and internal rotation of the shoulder is assessed on a four-point scale in which 0 indicates the absence of pain; 1 slight pain, but full power; 2 moderate pain and reduced power; and 3 severe pain with no power against even minimal resistance. The presence of pain on active abduction is also assessed on a four-point scale in which 0 indicates the absence of pain, 1 pain at only one point in the arc, 2 pain throughout the arc, and 3 pain so severe as to prohibit completion of the arc.

§Quality of life was measured on a 10-cm visual-analogue scale on which 0 cm indicated an excellent quality of life and 10 cm indicated the worst imaginable.

greater improvements in the quality of life than patients who had received sham treatment (Table 3). At the nine-month follow-up visit, however, although further improvements were noted in both groups, the differences between groups were no longer significant. At the end of therapy the total Constant score was within the normal range (i.e.,  $\geq 90$ ) for 24 shoulders in the ultrasound-treatment group (75 percent) and 10 shoulders in the sham-treatment group (34 percent,  $P=0.002$  by two-tailed Fisher's exact test). At the nine-month follow-up visit, the respective values were 19 (61 percent) and 12 (48 percent,  $P=0.20$  by two-tailed Fisher's exact test).

#### Other Measurements

At the end of treatment, clinical improvement was significantly more common in the ultrasound-treatment group than in the sham-treatment group (29 [91 percent] vs. 15 [52 percent],  $P=0.002$  by two-tailed Fisher's exact test). At the nine-month follow-up visit, the outcome was unsatisfactory for 7 shoulders in the ultrasound-treatment group and 11 shoulders in the sham-treatment group ( $P=0.15$  by two-tailed Fisher's exact test), and further treatment was offered. Three shoulders in the ultrasound-treatment group and four in the sham-treatment group were injected with local anesthetics and glucocorticoids. Surgery was not considered for any patient.

The rate of use of analgesics and the number of days lost from work during treatment and follow-up were moderate. Ten patients occasionally took analgesics (four in the ultrasound-treatment group and six in the sham-treatment group), and nine patients missed work (four and five, respectively). There were no reported side effects of ultrasound therapy.

### DISCUSSION

In 20 to 30 percent of patients with calcific tendinitis of the shoulder, both shoulders are involved.<sup>2,3</sup> Since ultrasound therapy may produce only localized effects, we included patients with bilateral calcific tendinitis in our study, and in these patients each shoulder underwent randomization. Bias resulting from flaws in blinding was unlikely for two reasons. First, ultrasound therapy was administered in a pulsed mode at an intensity (2.5 W per square centimeter) that is usually below the threshold of sensitivity and therefore not distinguishable from sham insonation. Second, the therapist who was in charge of randomization was also the one who switched the ultrasound generator from sham treatment to real treatment, depending on a patient's treatment assignment. Thus, no one directly involved in treatment knew the treatment assignments.

The cause and pathogenesis of calcifications of the rotator cuff are unclear.<sup>23-26</sup> Relative ischemia as a result of hypovascularization in the so-called critical zone of the rotator cuff,<sup>23</sup> degeneration of the ten-

ons,<sup>24</sup> and metabolic disturbances<sup>25</sup> have been suggested as possible causes. According to Uthoff and colleagues,<sup>1,26</sup> fibrocartilaginous transformation of the tendon tissue leads to calcium deposits. The course of the disease may be cyclic, with spontaneous resorption and reconstitution of the tendon.<sup>1,26</sup> The factor that triggers metaplasia has not yet been determined, although tissue hypoxia is thought to be the primary factor.<sup>25</sup>

In the acute phase of calcific tendinitis, spontaneous resorption may occur within a period of two to three weeks.<sup>3,27</sup> This course may be typical for calcium deposits that appear translucent or cloudy and are not clearly circumscribed on radiography.<sup>2,17</sup> However, it is not uncommon for the disease to become chronic, accompanied by pain at rest and kinesiologia. In patients with chronic calcific tendinitis, calcifications are still present in more than 90 percent after three years.<sup>2,17</sup> In our study, we included only patients with homogeneous and clearly circumscribed calcium deposits, for which spontaneous resolution is thought to be uncommon.<sup>1,17</sup>

Surgery to remove shoulder calcifications has a relatively high rate of success but carries a risk of operative complications.<sup>3</sup> Arthroscopic procedures fail about half the time.<sup>4,5</sup> In uncontrolled studies, shock-wave therapy reportedly disintegrated calcium deposits partially or completely in almost two thirds of patients, and three quarters had clinical improvement.<sup>7,8</sup> Percutaneous needle aspiration alleviates symptoms in up to 60 percent of patients<sup>3</sup> and resolves the deposits in 40 to 60 percent.<sup>3,6</sup>

Our finding that ultrasound treatment is beneficial in patients with calcific tendinitis of the shoulder confirms preliminary data.<sup>14-16</sup> Ultrasound therapy alleviated symptoms in the short term. In the long term, the symptoms of calcific tendinitis may be self-limiting and improve independently from the resolution of the calcium deposit. We did not compare ultrasound therapy with the current standard treatment for symptomatic calcific tendinitis — nonsteroidal antiinflammatory drugs. Therefore, we cannot comment on the relative effectiveness of ultrasound therapy with respect to standard treatment. Although not seen in this study, a few patients with calcific tendinitis and minimal shoulder pain may experience a transient increase in shoulder pain shortly after the onset of ultrasound treatment. This effect usually subsides after further treatment. Patients should therefore be informed of this possibility before they start treatment.

A recent study found no difference between no treatment and treatment with acetic acid iontophoresis followed immediately by nine sessions of ultrasound therapy in a constant mode (0.8 W per square centimeter at a frequency of 1 MHz for five minutes) over a period of three weeks.<sup>28</sup> Our treatment protocol involved 24 sessions of pulsed ultrasound administered over a period of six weeks. Although our

dropout rate was low, such a treatment schedule is time consuming and was the main reason for non-compliance. Ultrasound treatment is relatively inexpensive. We estimate that in Austria, 24 15-minute sessions would cost \$360.

The way in which ultrasound stimulates resorption of calcium deposits has not been established. It may stimulate the accumulation of peripheral-blood mononuclear cells by activating endothelial cells. It may also act indirectly by increasing the intracellular calcium levels.<sup>29</sup> Since activated endothelial cells express and release a variety of chemoattractant substances such as chemokines (monocyte chemoattractant protein, interleukin-8, and regulated upon activation normal T-cell expressed and secreted [RANTES]) and cytokines (interleukin-2 and stem-cell factor),<sup>30-32</sup> migrating macrophages might be involved in the phagocytosis of calcified particles. At higher intensities, ultrasound may trigger or accelerate the disruption of apatite-like microcrystals. The appearance of these smaller calcium crystals may then stimulate macrophages to remove calcifications by phagocytosis.<sup>33,34</sup> Finally, the increases in the temperature of tissue exposed to ultrasound may increase blood flow (i.e., induce hyperemia) and metabolism, thus facilitating the disintegration of calcium deposits.

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