High-energy extracorporeal shock-wave therapy for calcifying tendinitis of the rotator cuff

A RANDOMISED TRIAL

From Rennes University Hospital, Rennes, France

In a prospective randomised trial of calcifying tendinitis of the rotator cuff, we compared the efficacy of dual treatment sessions delivering 2500 extracorporeal shock waves at either high- or low-energy, via an electromagnetic generator under fluoroscopic guidance.Patients were eligible for the study if they had more than a three-month history of calcifying tendinitis of the rotator cuff, with calcification measuring 10 mm or more in maximum dimension. The primary outcome measure was the change in the Constant and Murley Score.

A total of 80 patients were enrolled (40 in each group), and were re-evaluated at a mean of 110 (41 to 255) days after treatment when the increase in Constant and Murley score was significantly greater (t-test, p = 0.026) in the high-energy treatment group than in the low-energy group. The improvement from the baseline level was significant in the high-energy group, with a mean gain of 12.5 (-20.7 to 47.5) points (p < 0.0001). The improvement was not significant in the low-energy group. Total or subtotal resorption of the calcification occurred in six patients (15%) in the high-energy group and in two patients (5%) in the low-energy group.

High-energy shock-wave therapy significantly improves symptoms in refractory calcifying tendinitis of the shoulder after three months of follow-up, but the calcific deposit remains unchanged in size in the majority of patients.

Calcifying tendinitis of the rotator cuff mainly affects the supraspinatus tendon in middle-aged women. Calcific deposits are found in between 2.7% and 7.5% of subjects during routine examination, and in 6.8% of patients presenting with shoulder pain. They are symptomatic in one-third of cases and bilateral in 24% to 66%, predominantly on the right side. The mechanisms underlying the aetiology of intratendinous deposits of carbonated apatite are not fully understood. The natural history and incidence of spontaneous resorption of the calcific deposit is variable. The radiological appearance of the calcific deposit appears to influence the outcome. Gartner reported that resorption occurred over a period of three years after needleling in 85% of patients with fluffy accumulations, but in only 33% of patients with sharply defined calcifications.

Most treatments for calcifying tendinitis are conservative, but their efficacy is poorly documented. They include subacromial steroid injection, oral non-steroidal anti-inflammatory drug therapy, and rehabilitation combined with physiotherapy. When incapacitating symptoms persist beyond a few months, percutaneous needle extraction or bursoscopic excision is generally proposed. Needle extraction has variable efficacy and carries a risk of tendon damage, but bursoscopic excision is successful in between 80% and 90% of cases.

Extracorporeal shock-wave therapy (ESWT) is a non-invasive treatment for calcifying tendinitis of the rotator cuff. Shock waves are acoustic waves associated with a sudden rise in pressure. They may be generated by electro-hydraulic, piezoelectric and electromagnetic devices, but their interactions with tissues are not fully understood. The amount of energy released by the sonic pulse per square area is expressed as energy flux density in mJ/mm². Although there is no universal agreement on the threshold values, low-energy extracorporeal shock waves have an energy flux density below 0.08 mJ/mm², medium-energy shock waves from 0.08 mJ/mm² to 0.28 mJ/mm², and high-energy shock waves from 0.28 mJ/mm² to 0.60 mJ/mm².

All studies published in the last decade have shown a degree of efficacy, but the devices, treatment protocols and end-points differ from
one publication to another. One controlled study showed that, compared to low-energy ESWT, high-energy ESWT had significantly better clinical efficacy than placebo therapy. We therefore conducted a prospective randomised trial comparing high-energy and low-energy ESWT.

**Patients and Methods**

Patients with calcific tendinitis referred by regional rheumatologists and orthopaedic surgeons were considered for inclusion in the study. Prior to ESWT all patients had failed to respond to an oral course of analgesic or non-steroidal anti-inflammatory drug (NSAID), subacromial steroid injection, calcification needling, or physiotherapy.

Patients were eligible for the study if they were between 18 and 75 years of age and had at least a three-month history of shoulder discomfort, with radiological evidence of type A calcification (sharp contours and a homogeneous structure) or type B calcification (sharp contours and a non-homogeneous structure), as defined by Mole and the French Arthroscopy Association, with a largest diameter of calcifications of 10 mm.

The exclusion criteria were pregnancy, clotting disorders, anticoagulant or antiplatelet treatment, cardiac pacemaker, chronic inflammatory joint disease, infections or tumours of the shoulder, adhesive capsulitis, hyperalgia of the shoulder due to resorption of a calcific deposit, and calcification of the shoulder, adhesive capsulitis, hyperalgia of the shoulder. The patients also reported any health disorders that occurred during the follow-up period.

**Radiological assessment.** The radiological aspects of the calcifications (i.e. type, size and location) were determined by one of the two clinical investigators (JM, J-DA) and subsequently by a single radiologist (FM) who was unaware of the order (pre/post-ESWT) or the allocation (active treatment or control group) of the radiographs. Changes between pre- and post-treatment radiographs were graded as no resorption, partial resorption (slight changes in size or appearance), and total or subtotal resorption (over 80% reduction of calcified surface on anteroposterior view).

**Intervention.** We used a Modulith SLK (Storz Medical AG, Tägerwilen, Switzerland) electromagnetic shock-wave generator with fluoroscopic and sonographic guidance. The patients were scheduled to receive two sessions of 2500 impulses each, 14 days apart. The frequency was 1 Hz (one impulse per second) for the first 200 impulses, then 2 Hz thereafter. In the control group the energy intensity was gradually increased from 0.02 mJ/mm² per impulse to 0.06 mJ/mm² per shock (i.e. 145 mJ/mm² per session). In the active treatment group the aim was to reach the maximum energy level tolerated by the patient, without exceeding 0.45 mJ/mm² per impulse.

Immediately after randomisation the patients were placed in a supine position on a remotely-controlled table and the calcific deposit was identified using fluoroscopy. Ultrasound gel was applied between the skin of the patient and the transducer.
and the water cushion of the shock-wave device. Analgesic premedication was given orally: one 100 mg tablet of ketoprofen and two capsules of a paracetamol-dextropropxyphen combination (400 mg/30 mg per capsule) were given one hour before each session. At this time the patient placed a contact anaesthetic patch with 25 mg of lidocaine and 25 mg of prilocaine (Emla Patch, Astra Zeneca, Switzerland) on the skin, in the field of contact with the shock-wave generator head. After each treatment session the patients were given half a day’s sick leave and were prescribed analgesic and anti-inflammatory drugs in case they experienced severe pain. No restrictions were imposed on the patients regarding their activities after ESWT, except for heavy workers, who were given two days’ sick leave.

Statistical analysis. Data were analysed with SPSS software version 12 for Windows (SPSS Inc., Chicago, Illinois). All

Fig. 1
Flow chart of participants through the trial (ESWT, extracorporeal shockwave therapy).
the results were analysed on an intention-to-treat basis, including all patients who were randomised and who received at least one shock-wave session. Student’s two-sided t-test was used to compare mean variations. The chi-squared test was also used as appropriate. Significance was assumed at p < 0.05. We calculated that, with an α risk of 5%, 40 patients per treatment group would be required to achieve 95% power to detect a difference of at least 15% in the change in Constant and Murley Score between the active treatment and control groups.17,18

Results

A total of 80 patients were enrolled in the study (Fig. 1). The patients were assessed after a mean of 110 days (41 to 255). Only one patient in the control group refused the final visit and was clinically assessed by telephone; the missing data on shoulder strength were considered to be unchanged from the baseline level.

Demographic and clinical data were not different between the active treatment group and the control group at baseline (day zero), except for the number of subacromial injections received before enrolment in the study (Table I). At enrolment and at the first ESWT session every patient had at least a six-month history of shoulder discomfort.

The mean cumulative energy flux density administered was approximately 1210 mJ/mm² (610 to 1700) in the active treatment group and 283 mJ/mm² (17 to 290) in the control group.

Primary outcome measure. The mean change in the Constant and Murley score was significantly greater in the active treatment group than in the control group (+12.5 and +4.5 points respectively; t-test, p = 0.026; 95% confidence interval (CI) 0.9 to 15.1) (Table II).

The mean normalised difference between the two groups (i.e. the difference in gain relative to the pooled standard deviation of the two groups) was 0.51. The proportion of patients who had at least a 15-point improvement in the Constant and Murley score was 50% (20 of 40) in the active treatment group and 20% (8 of 40) in the control group (Chi-squared test, p = 0.005).

Table I. Characteristics of the patients at enrolment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Active treatment group (n = 40)</th>
<th>Control group (n = 40)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age in yrs (range)</td>
<td>46.6 (31 to 64)</td>
<td>47.5 (32 to 69)</td>
<td>NS</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female:male</td>
<td>31:9</td>
<td>30:10</td>
<td>NS</td>
</tr>
<tr>
<td>Mean duration of symptoms in mths (range)</td>
<td>41.2 (6 to 120)</td>
<td>36.4 (7 to 160)</td>
<td>NS</td>
</tr>
<tr>
<td>Affected side (right:left)</td>
<td>30:10</td>
<td>25:15</td>
<td>NS</td>
</tr>
<tr>
<td>Location of the main calcific deposit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supraspinatus tendon</td>
<td>36</td>
<td>33</td>
<td>NS</td>
</tr>
<tr>
<td>Infraspinatus tendon</td>
<td>4</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Number of calcific deposits</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>30</td>
<td>33</td>
<td>NS</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Mean number of subacromial injections (range)</td>
<td>1 (1 to 3)</td>
<td>1.9 (0 to 5)</td>
<td>0.002</td>
</tr>
<tr>
<td>Number of patients with at least one subacromial injection</td>
<td>26</td>
<td>31</td>
<td>NS</td>
</tr>
<tr>
<td>Number of patients with physiotherapy</td>
<td>20</td>
<td>18</td>
<td>NS</td>
</tr>
<tr>
<td>Number of patients with needling of calcification</td>
<td>3</td>
<td>5</td>
<td>NS</td>
</tr>
<tr>
<td>Mean Constant and Murley Score (range)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (100 points)</td>
<td>50.7 (33.2 to 70.2)</td>
<td>50.3 (28.2 to 83.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Pain (15 points)</td>
<td>5.9 (2.5 to 12)</td>
<td>5.8 (1.0 to 11.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Activities of daily living (20 points)</td>
<td>10.6 (5 to 15)</td>
<td>10.3 (5.0 to 16.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Range of movement (40 points)</td>
<td>25.6 (12.0 to 38.0)</td>
<td>25.7 (10.0 to 40.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Power (25 points)</td>
<td>8.6 (0 to 25.0)</td>
<td>8.5 (3.0 to 20.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Mean VAS† score for pain (10) (10 points)</td>
<td>5.6 (0.4 to 9.7)</td>
<td>5.6 (1.2 to 9.4)</td>
<td>NS</td>
</tr>
</tbody>
</table>

† VAS, visual analogue scale

* NS, not significant

Table I. Characteristics of the patients at enrolment
At the follow-up visit the Constant and Murley score was significantly higher than at the baseline level in the active treatment group but not in the control group (Table III). In addition, the mean relative improvement in the Constant and Murley score at three months was significantly higher in the active treatment group than in the control group (27.3% and 11.1% respectively, \( t \)-test, \( p = 0.048; 95\% \text{ CI} 0.16\% \text{ to } 32.1\% \)).

**Secondary outcome measures.** Pain relief as assessed by the mean VAS score was more marked in the active treatment group than in the control group (-2.3 (-8.3 to 4.9) and -1.1 (-7.3 to 3.8) respectively; \( t \)-test, \( p = 0.069; 95\% \text{ CI} -2.4 \text{ to } +0.9 \)). This was in keeping with the mean change in the pain component of the Constant and Murley score (+3.2 and +1.1 respectively; \( t \)-test, \( p = 0.069; 95\% \text{ CI} -2.4 \text{ to } +0.9 \)). The mean activities of daily living component of the Constant and Murley score also improved significantly in the active treatment group compared with the control group (+3.2 and +1.1 respectively, \( t \)-test, \( p = 0.037; 95\% \text{ CI} 0.1 \text{ to } 4.1 \)) (Table II).

The cumulative proportions of patients who considered the treatment very effective, effective or moderately effective were 67.5% (27) in the active treatment group and 27.5% (11) in the control group (chi-squared test, \( p = 0.001 \)).

**Radiological outcome.** Total or subtotal resorption of the calcific deposits occurred in six patients (15%) in the active treatment group and in two patients (5%) in the control group, and partial resorption occurred in three patients (7.5%) in the active treatment group and in five patients (12.5%) in the control group.

All the treatment sessions were completed as planned, with the exception of one session that had to be interrupted after 400 impulses because the patient, from the low energy group, had a panic attack. One patient in the active treatment group received only one treatment because of complete resolution of symptoms and resorption of the calcific deposit by the second visit. All but three of the patients in the active treatment group reached a dose of at least 0.30 mJ/mm\(^2\), generally after 1000 to 1500 impulses. A total of 17 and 21 patients tolerated an energy of 0.40 mJ/mm\(^2\) to 0.45 mJ/mm\(^2\) during the first and second sessions, respectively. During both treatment sessions, toleration was better in the control group than in the active treatment group (Table IV).

In the active treatment group, 14 and 15 patients developed superficial skin lesions (petechiae or small bruises) during the first and second treatment sessions, respectively. All the lesions disappeared within 48 hours. All but one of the lesions occurred at a positive energy density flow of at least 0.35 mJ/mm\(^2\), generally after 1000 to 1500 impulses. A total of 17 and 21 patients tolerated an energy of 0.40 mJ/mm\(^2\) to 0.45 mJ/mm\(^2\) during the first and second sessions, respectively. During both treatment sessions, toleration was better in the control group than in the active treatment group (Table IV).

The treatment was well accepted in both groups; 35 and 27 patients in the active treatment and control groups, respectively, said they would be prepared to have the same treatment again (chi-squared test, \( p = 0.08 \)).

### Table II. Change in the mean Constant and Murley score (range) from the baseline to a mean of three months after intervention

<table>
<thead>
<tr>
<th></th>
<th>Active treatment group (n = 40)</th>
<th>Control group (n = 40)</th>
<th>Difference</th>
<th>Mean (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total score</td>
<td>12.5 (-20.7 to 47.5)</td>
<td>4.5 (-24.4 to 39.3)</td>
<td>8.0</td>
<td>(0.9 to 15.1)</td>
<td>0.026</td>
</tr>
<tr>
<td>Pain</td>
<td>3.2 (-4.7 to 12.0)</td>
<td>1.6 (-5.0 to 10.0)</td>
<td>1.6</td>
<td>(-0.2 to 3.4)</td>
<td>0.085</td>
</tr>
<tr>
<td>Activities of daily living</td>
<td>3.2 (-6.0 to 15.0)</td>
<td>1.1 (-9.0 to 11.0)</td>
<td>2.1</td>
<td>(0.1 to 4.1)</td>
<td>0.037</td>
</tr>
<tr>
<td>Range of movement</td>
<td>3.8 (-10.0 to 22.0)</td>
<td>0.8 (-14.0 to 24.0)</td>
<td>3.0</td>
<td>(-0.36 to 6.4)</td>
<td>0.079</td>
</tr>
<tr>
<td>Power</td>
<td>2.3 (-6.2 to 16.1)</td>
<td>1.0 (-6.5 to 12.3)</td>
<td>1.3</td>
<td>(-0.45 to 3.1)</td>
<td>0.142</td>
</tr>
</tbody>
</table>

* CI, confidence interval

### Table III. Constant and Murley Score (CMS) at baseline (day 0) and a mean of three months after intervention

<table>
<thead>
<tr>
<th></th>
<th>Day zero</th>
<th>Three months</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean total CMS score (range)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active treatment group</td>
<td>50.7 (33.2 to 70.2)</td>
<td>63.2 (23.8 to 90.0)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Control group</td>
<td>50.3 (28.2 to 83.8)</td>
<td>54.8 (19.9 to 86.8)</td>
<td>0.061</td>
</tr>
</tbody>
</table>

### Table IV. Toleration of treatment

<table>
<thead>
<tr>
<th>Visual analogue score for pain</th>
<th>Active treatment group</th>
<th>Control group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>During first treatment</td>
<td>6.5 (0.0 to 9.8)</td>
<td>4.4 (0.2 to 9.0)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>During second treatment</td>
<td>5.8 (0.0 to 8.2)</td>
<td>4.3 (0.4 to 8.5)</td>
<td>0.061</td>
</tr>
</tbody>
</table>
Discussion
This study shows that high-dose extracorporeal shock-wave therapy (a mean of 1210 mJ/mm² was delivered in two sessions) is significantly more effective than low-dose shock-wave therapy (a mean of 283 mJ/mm² was delivered in two sessions) in the treatment of calcifying tendinitis of the shoulder, as measured by the change in the Constant and Murley score at a mean of three months. The mean improvement in the Constant and Murley score was moderate in both groups (12.5 in the active treatment and 4.5 in the control group, from a total score of 100), but a large range demonstrates a wide range of individual responses. The minimum effect size of the Constant and Murley score is not known. If a 15-point increase in the Constant and Murley score is considered a clinically significant response, then 50% in the active treatment group achieved this change and 20% in the control group (chi-squared test, p = 0.005). Moreover, the mean normalised difference between the two groups (0.51) can be considered as a clinically relevant effect size.15

The percentage of patients who found the treatment effective was significantly higher in the active treatment group (chi-squared test p = 0.0001). Pain relief, measured with a VAS was more marked in the active treatment group, but did not reach statistical significance (t-test, p = 0.085). The improvement in the Constant and Murley score three months after treatment in the active treatment group was smaller than reported elsewhere.13,20,21 However, an improvement has been described occurring between months three and six.22

In contrast to previous studies, we did not observe a significant clinical improvement after low-energy ESWT. Both Loew et al15 and Rompe et al20 reported improvement in the Constant and Murley score 12 weeks after low-energy ESWT treatment, although it was inferior to the improvement observed in their high-energy treatment group. More recently, Sabeti-Aschraf et al23 reported a significant increase in the Constant and Murley score 12 weeks after three low-energy ESWT sessions. Cacchio et al24 and Magosch, Lichtenberg and Habermann25 also reported good clinical and radiological results of low-energy treatment with a non-focused radial shock-wave device. Technical issues, such as the number of sessions, energy-flux density threshold, and shock-wave device could explain the discrepancy between these results and ours.

The calcific deposits disappeared from the radiographs at three months in only 15% and 5% of patients in the active treatment and control groups, respectively. These rates are far lower than those observed in other studies, which showed complete calcification resorption rates ranging from 31% at one month23 to 47% and 86% at 12 months follow-up.22,26 The resorption rate may increase between 6 and 24 weeks,20 and between 6 and 12 months after treatment.22

High-energy shock-waves were significantly more painful than low-energy waves in our study, but the pain was short-lived and bearable for the vast majority of patients, even though we did not use regional anaesthesia or intravenous analgesia. This confirms the findings of Peters et al.27

No serious adverse events occurred in this study, thus confirming the safety of this procedure.28 Two cases of humeral head osteonecrosis have been reported in the literature.29,30 In the first case the relationship with ESWT was questionable.29 In the second case the patient suffered from a rotator cuff tear, which is usually considered a contra-indication for ESWT, and the energy flux density was far above what is usually recommended.30

This study has a number of limitations. Low-energy treatment was preferred to the use of a sham procedure, which is generally expected in a randomised controlled trial because it would have been ethically and psychologically difficult to obtain informed consent to enter a placebo-controlled study from patients presenting with chronic pain. Also, alternatives were available (calcification needing, arthroscopic calcification removal) and a positive effect of low-energy ESWT on symptoms has previously been observed, although of less magnitude than high-energy ESWT, giving a rational basis for a 'less active similar therapy'-controlled study.13,20 Strict patient blinding seems impossible to maintain unless local or regional anaesthesia is given because the technique is reputedly painful. In addition, the study did not have a double-blind design. The three-month follow-up assessment was undertaken by a clinician (J-DA) involved in the treatment.

The divergence between the global Constant and Murley score and the visual analogue pain rating scale could be because the latter is inappropriate for evaluating pain in this setting (the pain is often intermittent and experienced only during certain gestures or in certain positions). Furthermore, the high-energy ESWT protocol used here may have been inadequate; better results have been obtained with higher energies.26,27 Also, the three-month follow-up period may have been too short to observe radiological resorption of the calcific deposits. This end-point was chosen because of concerns over loss to follow-up over a longer period.

The mechanism of action of shock waves delivered at the energies used in clinical practice is uncertain,31 and despite some correlation between clinical and radiological outcome,32 the procedure appears to be associated with a mid-term symptomatic effect that is independent of any lithotriptic action. The divergence between clinical and radiological outcomes raises the possibility that the improvement in symptoms is independent of the physical presence of the calcific deposit.33

In summary, the results of this study support the use of high-energy extracorporeal shock-wave therapy in patients with chronic calcifying tendinitis of the rotator cuff of the shoulder. This out-patient treatment is well tolerated. One problem is the availability of shock-wave delivery devices with very different modes of action and guidance methods. Therapeutic protocols therefore need to be standardised,
particularly with respect to the dose delivered to the target tendon and neighbouring tissues.

This work was supported by a grant from the Clinical Research Commission of Rennes University Hospital. The electronic dynamometer was kindly provided by Smith-Nephew France (ZI Tournes-Cliron BP 119, Tournes, France). The funding source had no involvement in the study design; in the collection, analysis and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

The authors wish to thank Pr. B. Lobel, head of the Department of Urology of Rennes University Hospital, and Dr. M. Cugia from the Department of Medical Information of Rennes University Hospital for their support.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References