

Low-intensity pulsed ultrasound for chronic patellar tendinopathy: a randomized, double-blind, placebo-controlled trial

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Objective. Patellar tendinopathy (PT) is a common and significant clinical condition for which there are few established interventions. One intervention that is currently being used clinically to manage PT symptoms is the introduction of low-intensity pulsed ultrasound (LIPUS). The aim of this study was to investigate the clinical efficacy of LIPUS in the management of PT symptoms.

Methods. A randomized, double-blind, placebo-controlled study was conducted. Volunteers with clinically and radiologically confirmed PT were randomly allocated to either an active-LIPUS (treatment) or inactive-LIPUS (placebo) group. LIPUS was self-administered by participants for 20 min/day, 7 days/week for 12 weeks. All participants also completed a daily, standardized eccentric exercise programme based on best practice. Primary outcomes were change in pain during the participant's most aggravating activity in the preceding week, measured on 10 cm visual analogue scales for both usual (VAS-U) and worst (VAS-W) tendon pain.

Results. Out of 156 individuals who volunteered, 37 met the eligibility criteria and were randomized to either active-LIPUS ($n=17$) or inactive-LIPUS ($n=20$). Using an intention-to-treat analysis, VAS-U and VAS-W for the entire cohort decreased by 1.6 ± 1.9 cm ($P < 0.01$) and 2.5 ± 2.4 cm ($P < 0.01$), respectively. There were no differences between the active- and inactive-LIPUS groups for change in VAS-U (-0.2 cm; 95% CI, $-1.5, 1.1$ cm) ($P=0.74$) or VAS-W (-0.5 cm; 95% CI, $-2.1, 1.1$ cm) ($P=0.57$). A per-protocol analysis provided similar results.

Conclusions. These findings suggest that LIPUS does not provide any additional benefit over and above placebo in the management of symptoms associated with PT.

KEY WORDS: Anterior knee pain, Jumper's knee, Randomized controlled trial, Sports medicine, Tendinitis, Tendinosis.

Introduction

Patellar tendinopathy (PT) is distinguished by activity-related anterior knee pain, focal patellar tendon tenderness and intra-tendinous imaging changes [1]. It has historically been referred to as 'jumper's knee' or 'patellar tendinitis' as its prevalence is high in individuals participating in jumping sports and the underlying pathology was thought to involve inflammation. However, the condition is found in many who do not partake in jumping sports [2–4] and histopathological studies have consistently shown the underlying pathology to be degenerative (tendinosis) rather than inflammatory (tendinitis) [4–7]. As tendinosis is a distinct histopathological finding that can only be assessed following tissue biopsy, the term tendinopathy (*tendino* = tendon; *pathy* = disease) has been advocated to describe clinically diagnosed overuse conditions of tendons [8].

PT is a common condition with an overall prevalence of 14% in elite athletes [3]. However, its true clinical significance lies in the morbidity that it causes. Disability associated with PT is often prolonged and it causes many to cease their athletic careers [3, 9]. Contributing to this morbidity is a lack of scientific evidence directing the management of the condition. This results from a dearth of randomized controlled trials on clinically implemented

treatments, and has led to the use of varying treatment approaches. Despite this, there is general consensus that initial management of PT should be conservative rather than surgical as both approaches produce equivalent outcomes and courses of recovery [10].

A conservative intervention that is currently being implemented clinically to manage PT symptoms is low-intensity pulsed ultrasound (LIPUS) [11]. LIPUS refers to pulsed-wave ultrasound with a spatial-averaged, temporal-averaged intensity (I_{SATA}) equal to or lower than 100 mW/cm^2 . Such ultrasound has predominantly been used during bone healing where it has been shown by three well-designed clinical studies to reduce fracture healing times by 30–38% [12–14]. There is growing evidence from *in vitro* and animal-based models that LIPUS may also have beneficial effects on non-mineralized tissues, such as ligaments and tendons. For instance, using these models LIPUS has been found to accelerate knee medial collateral ligament healing [15–17], augment tendon repair [18] and modulate tendon cell activity [19]. However, there is currently no evidence regarding the efficacy of LIPUS in the management of PT symptoms. This needs to be investigated in a clinical population as there is currently no published animal model for PT [20].

The aim of this study was to investigate the clinical efficacy of LIPUS in the management of PT symptoms. The specific hypothesis was that daily active-LIPUS (treatment) for 12-weeks would reduce average and worst pain levels when compared with individuals treated with inactive-LIPUS (placebo). All participants also performed daily, standardized eccentric exercises based on best practice conservative management for PT [21].

Methods

Study design and participants

A randomized, double-blind, placebo-controlled trial was conducted to assess the effect of LIPUS on symptoms associated with PT. Individuals with PT were recruited from advertisements in local media, sporting clubs, university staff and students, and

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sports medicine clinics. After a preliminary phone screen, potential participants underwent clinical and radiological assessments to determine inclusion suitability. Clinical inclusion criteria included: aged ≥ 18 yrs; knee pain on at least one of jumping/landing, running or changing directions; pain on palpation of the patellar tendon [22]; score of < 80 points on the Victorian Institute of Sport Assessment (VISA) scale [23]; and symptoms sufficient to affect exercise and activity for at least 6 months. Radiological inclusion criteria included a confirmed hypoechoic lesion within the patellar tendon on ultrasonography, as previously described [24]. Exclusion criteria included: clinical signs and symptoms of a knee pathology other than PT (including co-existing pathologies); previous patellar tendon surgery; or injection into the knee in the previous 6 months. The study was approved by the Human Research Ethics Committee at the University of Melbourne and all participants provided written informed consent.

Group assignment and blinding

Simple randomization (in blocks of 10) was employed using a computer-generated table of random numbers to allocate participants to an active-LIPUS (treatment) or inactive-LIPUS (placebo) group. This was performed by one investigator who kept the assignment scheme, and provided a blinded investigator with a list of ultrasound unit codes in the predetermined order. Group allocation was concealed from the investigator performing outcome measures and participants at all times during the trial. The participants, examiners, data manager and statistician remained unaware of group allocation, and statistical analyses were performed with maintenance of blinding.

Ultrasound intervention

LIPUS intervention was self-administered by participants for 20 min/day, 7 days/week for 12 weeks. Participants were taught at the initial appointment how to apply LIPUS during sitting with the knee flexed to 90° . Participants with bilateral symptoms had the most symptomatic knee assessed and treated. When symptoms were similar in both knees, the knee to be assessed and treated was randomly allocated. Stationary LIPUS treatment heads were coupled with the skin overlying the patellar tendon using standard ultrasound gel. Participants in the active-LIPUS group received LIPUS consisting of a 2-ms burst of 1.0-MHz sine waves repeating at 100 Hz produced by a modified ultrasound therapy device (Accusonic Lipus Metron Medical Australia, Pty. Ltd, Carrum Downs, Victoria, Australia). The I_{SATA} was set at 100 mW/cm^2 . The units were constrained to these parameters and tested by an investigator other than the outcome assessor at 4-weekly intervals to ensure performance using an ultrasound power meter (UPM-DT-1; Ohmic Instruments Co., Easton, MD, USA). Participants in the inactive-LIPUS group were provided with identical appearing ultrasound units as the active-LIPUS group with the only difference being that the units produced no actual ultrasound output. Participants in both groups were blinded to ultrasound group allocation, with the active-LIPUS producing no sensation.

Exercise intervention

All participants performed daily, standardized eccentric exercises based on best practice conservative management for PT [21]. Participants completed single-legged squats on a decline board (3 sets of 15 repetitions), as previously described [25]. When exercises could be completed without discomfort, load was increased in standard increments using hand weights. A trained physiotherapist taught and supervised the exercise programme, and handouts were provided describing the exercises.

Outcome measures

Outcomes were assessed at baseline and at the conclusion of the 12-week intervention period by a single blinded examiner. The primary outcome was change in pain during the participant's most aggravating activity in the preceding week, measured on 10-cm visual analogue scales (VAS) for both usual (VAS-U) and worst (VAS-W) tendon pain. Secondary end-points included change on the VISA scale (a validated measure of knee function in individuals with PT [23]) and patient-perceived response to treatment using a 5-point scale (5: markedly worse, 4: moderately worse, 3: same, 2: moderately better, 1: markedly better). Additional secondary end-points included ultrasound and exercise compliance, occurrence of adverse treatment effects and blinding success. Ultrasound and exercise compliance were recorded by participants in a log-book which was checked fortnightly. Participants were asked to report any adverse treatment effects to the outcome assessor at the conclusion of the trial using open probe questioning, while blinding success was determined at the end of the trial by asking participants and the outcome assessor to indicate whether they had been unblinded to their group assignment.

Sample size

An *a priori* power analysis indicated a total sample size of 34 participants (17 participants per group) was required to achieve statistical significance at a 0.05 level with 80% power. This calculation was based on a two-tailed, unpaired *t*-test with an effect size of 2.0 cm for change in VAS-U and VAS-W, and a mean group variance of 2 cm [25]. A change of 2 cm is the minimal clinically important difference required to establish treatment efficacy in chronic anterior knee pain [26].

Statistical analysis

Analyses were performed on an intention-to-treat basis using the Statistical Package for Social Sciences software (SPSS 15.0.1; SPSS Inc., Chicago, IL, USA), with a conservative method to replace missing data. Missing data in the active- and inactive-LIPUS groups were replaced by the inactive- and active-LIPUS group means, respectively. For the global change outcome, all missing data were replaced by a score of 3 ('no change'). In addition, a per-protocol analysis was performed. Baseline comparability and differences between groups following the 12-week intervention period were determined with unpaired *t*-tests, Kruskal-Wallis tests or χ^2 -tests, depending on the measurement scale of the specific variable being compared. Change scores from baseline to the conclusion of the 12-week intervention period were determined and compared between groups using unpaired *t*-tests. Participant-perceived response to treatment was collapsed into two groups (1: markedly or moderately better and 2: markedly worse, moderately worse or the same) and analysed with a χ^2 test. All comparisons were two-tailed with a level of significance set at 0.05.

Results

Out of the 156 individuals who volunteered, 37 met both the clinical and radiological eligibility criteria, and were enrolled into the trial. These participants were randomized to active-LIPUS ($n = 17$) or inactive-LIPUS ($n = 20$), and 27 completed the trial (13 active-LIPUS and 14 inactive-LIPUS). The flow of participants through the trial and reasons for participant withdrawal are shown in Fig. 1. Participants who did not complete the study had similar characteristics at baseline to those who did (all $P > 0.05$). There were no baseline differences between the active- and inactive-LIPUS groups for personal, clinical or imaging characteristics (Table 1), or outcome measures (Table 2).

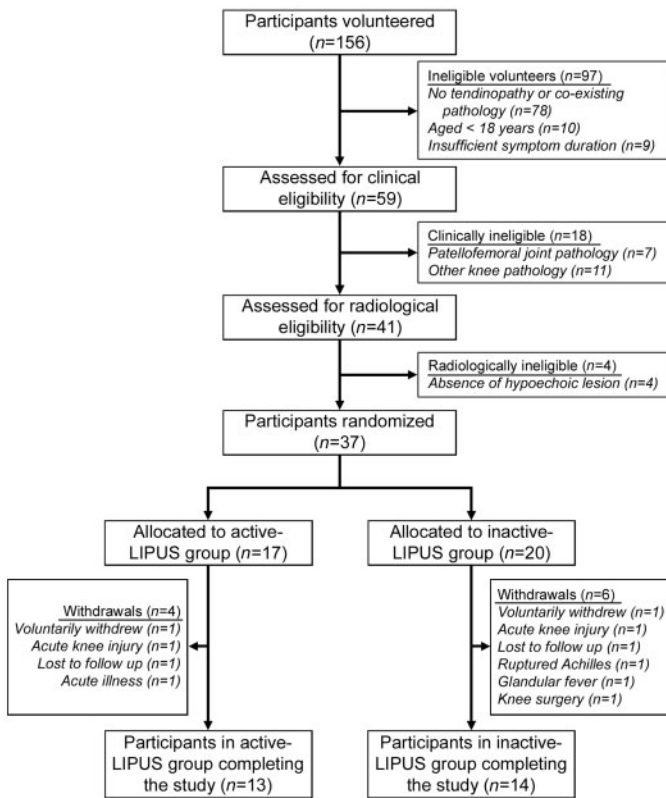


Fig. 1. Flow of participants through the trial and reasons for participant withdrawal.

TABLE 1. Baseline demographics of the active-LIPUS (n=17) and inactive-LIPUS (n=20) groups

	Intervention group ^a		Group differences	
	Active-LIPUS	Inactive-LIPUS	Mean (95% CI)	P-value
Personal characteristics				
Age (yr)	27 (7)	27 (7)	0 (-5, 4)	0.90
Height (m)	1.79 (0.10)	1.80 (0.09)	0.01 (-0.07, 0.05)	0.79
Mass (kg)	81 (13)	82 (15)	1 (-10, 9)	0.87
Physical activity (h/wk)	5 (5)	5 (4)	1 (-3, 3)	0.74
Gender (men : women)	12:5	18:2	-	0.13
Clinical characteristics				
Duration of symptoms (yr)	3.4 (3.1)	4.1 (3.8)	1 (-3, 2)	0.55
Unilateral : bilateral symptoms	10:7	7:9	-	0.81
Dominant:non-dominant leg symptoms	9:8	13:7	-	0.46
Currently taking NSAIDs (yes : no)	4:13	6:14	-	0.66
Previous corticosteroid injection (yes : no)	2:16	1:19	-	0.27
Radiological (ultrasonography) characteristics				
Lesion cross-sectional area (mm ²)	8 (4)	9 (6)	-1 (-5, 2)	0.57
Lesion length (mm)	5 (2)	4 (3)	1 (-1, 3)	0.34
Lesion width (mm)	14 (7)	15 (8)	0 (-6, 5)	0.90
Vascularity present (yes : no)	13:4	13:7	-	0.24

^aValues indicate mean (S.D.), except for frequencies.

Primary outcome measures

VAS-U and VAS-W for the entire cohort decreased by 1.6 ± 1.9 cm (28 ± 40%) (P < 0.01) and 2.5 ± 2.4 cm (35 ± 31%) (P < 0.01) over the study period, respectively. There were no differences between the active-LIPUS and inactive-LIPUS groups

TABLE 2. Effect of active-LIPUS (n=17) and inactive-LIPUS (n=20) on pain and function outcomes

	Active-LIPUS Mean (s.d.)	Inactive-LIPUS Mean (s.d.)	Group differences	
			Mean (95% CI)	P-value
Baseline				
VAS-U	5.2 (2.5)	5.6 (2.4)	-0.4 (-2.0, 1.3)	0.65
VAS-W	6.8 (2.4)	6.8 (2.3)	0 (-1.5, 1.6)	0.98
VISA	58.1 (15.9)	56.6 (18.5)	1.5 (-10.1, 13.2)	0.79
Final				
VAS-U	3.8 (2.3)	3.9 (2.2)	-0.2 (-1.7, 1.3)	0.82
VAS-W	4.1 (2.5)	4.5 (2.6)	-0.4 (-2.1, 1.3)	0.65
VISA	69.8 (14.5)	69.2 (17.9)	0.7 (-10.3, 11.7)	0.90
Change (final-baseline)				
VAS-U	-1.8 (2.0)	-1.6 (2.0)	-0.2 (-1.5, 1.1)	0.74
VAS-W	-2.7 (2.4)	-2.3 (2.4)	-0.5 (-2.1, 1.1)	0.57
VISA	11.9 (14.3)	12.6 (17.8)	-0.7 (-11.6, 10.3)	0.90

for VAS-U (P = 0.82) or VAS-W (P = 0.65) at the completion of the intervention period, or for change in VAS-U (P = 0.74) or VAS-W (P = 0.57) over the time course of the study (Table 2).

Secondary outcome measures

VISA score for the entire cohort improved by 12.3 ± 16.1 (30 ± 44%) (P < 0.01) over the study period. There were no differences between the active-LIPUS and inactive-LIPUS groups for VISA score at the completion of the intervention period (P = 0.90) or for change in VISA score (P = 0.90) (Table 2). The patient-perceived response to treatment revealed that 11/13 participants in the active-LIPUS group and 9/14 participants in the inactive-LIPUS group felt that they had improved after the treatment. There was no significant difference in patient-perceived response between the treatment groups (χ² = 1.45, P = 0.23).

Per-protocol analysis

The outcomes were re-analysed using data only from those who completed the trial. VAS-U and VAS-W for the entire cohort decreased by 1.3 ± 2.2 cm (P < 0.01) and 1.7 ± 2.6 cm (P < 0.01), respectively. There were no differences between groups for VAS-U (P = 0.92) or VAS-W (P = 0.88) at intervention completion, or for change in VAS-U (P = 0.33) or VAS-W (P = 0.76). The VISA score for the entire cohort improved by 9.4 ± 14.0 (P < 0.01) and there were no differences between the groups for VISA score at the completion of the intervention period (P = 0.78) or for change in VISA score (P = 0.71).

Compliance, adverse events and co-interventions

Participants were compliant during the intervention period with 82 and 91% of ultrasound treatments, and 60 and 65% of exercise sessions completed in the active- and inactive-LIPUS groups, respectively. There were no differences in compliance between groups (all P > 0.05). No adverse events were reported during the intervention period. Medication use was similar between the active- and inactive-LIPUS groups (45 and 50%, respectively). One participant in the active-LIPUS group and three participants in the inactive-LIPUS group sought alternative treatments during the trial.

Success of blinding

Neither the outcome assessor nor any of the participants were unblinded during the trial.

Discussion

This randomized, double-blind, placebo-controlled study found LIPUS to provide no benefit over and above placebo treatment in the management of pain associated with PT. Average and worst

pain in both the active- and inactive-LIPUS-treated groups decreased significantly over the 12-week study period; however, there were no differences between the groups. These findings suggest that LIPUS is not efficacious in the management of PT symptoms.

There are a number of putative explanations for the absence of a beneficial LIPUS effect in the current study. One explanation is the relatively short intervention period. The intervention period in the current study (12 weeks) was relatively short in comparison with the extended duration (≥ 6 months) and recalcitrant nature of PT symptoms. It is possible that a longer intervention period may have enabled the elucidation of a LIPUS effect. However, it was impractical to extend the intervention period due to the patient time commitment required for daily LIPUS treatment. Furthermore, the clinical utility of an intervention that requires longer than 12 weeks to generate a treatment effect is questionable. We believe that the intervention period was of sufficient duration to allow a LIPUS effect to be detected if one existed. Intervention periods of equivalent or shorter duration have previously been used to elicit treatment effects for alternate therapies in other randomized controlled trials on PT [27–29]. Similarly, in the current study, there were significant reductions in pain in the entire cohort over the intervention period suggesting that its length was sufficient to see at least a trend towards a beneficial LIPUS effect if one existed. Such a trend is not visibly evident.

Our results do not exclude the possibility of a tissue-level effect of LIPUS on the underlying pathology associated with PT. The ability of LIPUS to change pain was chosen as the primary outcome measure as pain is the most frequent clinical complaint associated with PT [1]. Meanwhile, change on the VISA scale was chosen as an indicator of the ability of LIPUS to change function as this scale provides a validated measure of knee function in individuals with PT [23]. As neither pain nor function differed between the active- and inactive-LIPUS groups, this study found that LIPUS does not substantially alter the clinical features of PT. However, it is possible that LIPUS influenced the underlying pathology and resultant radiological features associated with PT. We did not radiologically assess tendon morphology at the completion of the study; however, this is not a limitation as tendon morphology assessed via imaging is not predictive of PT symptoms on clinical measures [24, 30–33] and imaging cannot distinguish outcome after intervention for PT [30, 34]. Also, an intervention that benefits the radiological features of PT without influencing its clinical features would be of limited clinical utility.

The pathophysiology of PT may have contributed to the absence of a beneficial LIPUS effect. LIPUS was introduced based on its demonstrated benefits on injured bone [12–14] and preliminary evidence from pre-clinical studies suggesting LIPUS benefits on the healing of acute soft-tissue injuries [15–18]. However, the pathology and pathological processes underlying PT substantially differ from the acute reparative processes present in previous LIPUS applications. PT is a recalcitrant condition characterized histologically by tissue degeneration (tendinosis) with a failed reparative response, as is evident by atypical fibroblast hypercellularity and extensive neovascularization [4–7]. A recent study suggests that the neovascularization and the nerves that accompany the neovessels are involved in the pain mechanism associated with tendinopathy [35]. Supporting this, sclerosing the area containing neovessels in PT results in clinical and radiological improvement [27]. In contrast, one of the proposed mechanisms of action of LIPUS during healing following acute tissue injury is the stimulation of angiogenesis and blood flow [36, 37]. This does not appear warranted in the

management of PT given the pre-existence of pathological neovascularization.

Statistical power needs to be explored in any intervention study that fails to detect a significant treatment effect. The current study was powered *a priori* to detect a LIPUS treatment effect size on pain of 2.0 cm, which is the minimal clinically important difference required to establish treatment efficacy in chronic anterior knee pain [26]. *Post hoc* analyses using the acquired data indicated that we could ultimately detect group differences of 2.0 and 2.4 cm for change in VAS-U and -W, respectively. Thus, the current study was powered adequately to detect the *a priori* treatment effect size and the findings indicate a true absence of a clinically relevant LIPUS effect at the dose and mode administered. Supporting this, we would require in excess of 1500 and 500 participants per group in order for our observed group differences for change in VAS-U and -W to become statistically significant, respectively.

In addition to having sufficient statistical power, other strengths of the current study include the extent of blinding, and similar results obtained from both the intention-to-treat and per-protocol analyses. The participants, examiners, data manager and statistician remained unaware of group allocation, and statistical analyses were performed with maintenance of blinding. This level of blinding ensured that results were not consciously or unconsciously biased by any party involved in the study. Also, we avoided bias related to the withdrawal of participants by using a conservative method to allocate values for missing data in our intention-to-treat analysis. This was supplemented by a per-protocol analysis to ensure that the absence of a beneficial LIPUS was independent of participant withdrawal. As both statistical approaches independently provided very similar results, a beneficial clinical effect of LIPUS on PT symptoms is unlikely even when it has been administered in compliance with the study protocol.

In summary, our findings suggest that LIPUS does not have a beneficial effect on the clinical features of PT over and above that generated by a standardized eccentric exercise programme. These findings are supported by those of D'Vaz *et al.* [38] who found LIPUS to have no benefit over placebo in the treatment of tendinopathy of the common extensor origin at the elbow ('tennis elbow'). Based on the combined results of the current and this previous study, it is possible that LIPUS simply does not influence the pathology associated with tendinopathy. This requires further investigation as the results of the current study do not conclusively indicate that LIPUS use should be ceased in the management of PT as no detrimental effects were elicited and an effect smaller than that which could be detected with sufficient statistical power may be present. The latter requires establishment by way of a larger randomized controlled trial and the clinical benefits of such a small improvement in clinical symptoms should be debated.

Rheumatology key messages

- LIPUS has proven clinical efficacy in managing acute bone injuries.
- We have demonstrated that similar ultrasound provides no benefit beyond that of placebo in the management of patellar tendinopathy symptoms.

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References

- 1 Warden SJ, Brukner P. Patellar tendinopathy. *Clin Sports Med* 2003;22:743–59.
- 2 Cook JL, Khan KM, Harcourt PR, Grant M, Young DA, Bonar SF. A cross sectional study of 100 athletes with jumper's knee managed conservatively and surgically. The Victorian Institute of Sport Tendon Study Group. *Br J Sports Med* 1997;31:332–6.
- 3 Lian ØB, Engebretsen L, Bahr R. Prevalence of jumper's knee among elite athletes from different sports: a cross-sectional study. *Am J Sports Med* 2005;33:561–7.
- 4 Khan KM, Bonar F, Desmond PM *et al*. Patellar tendinosis (jumper's knee): findings at histopathologic examination, US, and MR imaging. *Victorian Institute of Sport Tendon Study Group. Radiology* 1996;200:821–7.
- 5 Fu SC, Wang W, Pau HM, Wong YP, Chan KM, Rolf CG. Increased expression of transforming growth factor-beta1 in patellar tendinosis. *Clin Orthop* 2002;400:174–83.
- 6 Maffulli N, Testa V, Capasso G *et al*. Similar histopathological picture in males with Achilles and patellar tendinopathy. *Med Sci Sports Exerc* 2004;36:1470–5.
- 7 Yu JS, Popp JE, Kaeding CC, Lucas J. Correlation of MR imaging and pathologic findings in athletes undergoing surgery for chronic patellar tendinitis. *AJR Am J Roentgenol* 1995;165:115–8.
- 8 Maffulli N, Khan KM, Puddu G. Overuse tendon conditions: time to change a confusing terminology. *Arthroscopy* 1998;14:840–3.
- 9 Kettunen JA, Kvist M, Alanen E, Kujala UM. Long-term prognosis for jumper's knee in male athletes. A prospective follow-up study. *Am J Sports Med* 2002;30:689–92.
- 10 Bahr R, Fossan B, Loken S, Engebretsen L. Surgical treatment compared with eccentric training for patellar tendinopathy (jumper's knee). A randomized, controlled trial. *J Bone Joint Surg* 2006;88A:1689–98.
- 11 Warden SJ. A new direction for ultrasound therapy in sports medicine. *Sports Med* 2003;33:95–107.
- 12 Heckman JD, Ryaby JP, McCabe J, Frey JJ, Kilcoyne RF. Acceleration of tibial fracture-healing by non-invasive, low-intensity pulsed ultrasound. *J Bone Joint Surg* 1994;76A:26–34.
- 13 Kristiansen TK, Ryaby JP, McCabe J, Frey JJ, Roe LR. Accelerated healing of distal radius fractures with the use of specific, low-intensity ultrasound. *J Bone Joint Surg* 1997;79A:961–73.
- 14 Mayr E, Rutzki MM, Rutzki M, Borchardt B, Hausser H, Rüter A. Does low intensity, pulsed ultrasound speed healing of scaphoid fractures? *Handchir Mikrochir Plast Chir* 2000;32:115–22.
- 15 Sparrow KJ, Finucane SD, Owen JR, Wayne JS. The effects of low-intensity ultrasound on medial collateral ligament healing in the rabbit model. *Am J Sports Med* 2005;33:1048–56.
- 16 Takakura Y, Matsui N, Yoshiya S *et al*. Low-intensity pulsed ultrasound enhances early healing of medial collateral ligament injuries in rats. *J Ultrasound Med* 2002;21:283–8.
- 17 Warden SJ, Avin KG, Beck EM, Dewolf ME, Hagemeyer MA, Martin KM. Low-intensity pulsed ultrasound accelerates and a nonsteroidal anti-inflammatory drug delays knee ligament healing. *Am J Sports Med* 2006;34:1094–102.
- 18 Asahi S, Yamamoto K, Masaoka T, Sormachi T. Effect of low-intensity ultrasound stimulation on the repair process after Achilles tendon injury. *J Tokyo Med Univ* 2005;63:144–53.
- 19 Chujo T, Akeda K, Miyamoto K *et al*. The effect of pulsed low-intensity ultrasound on matrix metabolism by bovine tendon cells cultured in alginate beads. *Trans Orthop Res Soc* 2005;30:750.
- 20 Warden SJ. Animal models for the study of tendinopathy. *Br J Sports Med* 2007;41:232–40.
- 21 Curwin S, Stanish WD. *Tendinitis, its etiology and treatment*. Lexington, MA: Collamore Press, 1984.
- 22 Cook JL, Khan KM, Kiss ZS, Purdam CR, Griffiths L. Reproducibility and clinical utility of tendon palpation to detect patellar tendinopathy in young basketball players. *Br J Sports Med* 2001;35:65–9.
- 23 Visentini PJ, Khan KM, Cook JL, Kiss ZS, Harcourt PR, Wark JD. The VISA score: an index of severity of symptoms in patients with jumper's knee (patellar tendinosis). *J Sci Med Sport* 1998;1:22–8.
- 24 Warden SJ, Kiss ZS, Malara FM, Ooi ABT, Cook JL, Crossley KM. Comparative accuracy of magnetic resonance imaging and ultrasonography in confirming clinically diagnosed patellar tendinopathy. *Am J Sports Med* 2007;35:427–36.
- 25 Purdam CR, Jonsson P, Alfredson H, Lorentzon R, Cook JL, Khan KM. A pilot study of the eccentric decline squat in the management of painful chronic patellar tendinopathy. *Br J Sports Med* 2004;38:395–7.
- 26 Crossley KM, Bennell KL, Cowan SM, Green S. Analysis of outcome measures for persons with patellofemoral pain: which are reliable and valid? *Arch Phys Med Rehabil* 2004;85:815–22.
- 27 Hoksrud A, Ohberg L, Alfredson H, Bahr R. Ultrasound-guided sclerosis of neovessels in painful chronic patellar tendinopathy: a randomized controlled trial. *Am J Sports Med* 2006;34:1738–46.
- 28 Jonsson P, Alfredson H. Superior results with eccentric compared to concentric quadriceps training in patients with jumper's knee: a prospective randomised study. *Br J Sports Med* 2005;39:847–50.
- 29 Wang CJ, Ko JY, Chan YS, Weng LH, Hsu SL. Extracorporeal shockwave for chronic patellar tendinopathy. *Am J Sports Med* 2007;35:972–8.
- 30 Coleman BD, Khan KM, Kiss ZS, Bartlett J, Young DA, Wark JD. Open and arthroscopic patellar tenotomy for chronic patellar tendinopathy. A retrospective outcome study. *Am J Sports Med* 2000;28:183–90.
- 31 Khan KM, Cook JL, Kiss ZS *et al*. Patellar tendon ultrasonography and jumper's knee in female basketball players: a longitudinal study. *Clin J Sport Med* 1997;7:199–206.
- 32 Lian Ø, Hølen KJ, Engebretsen L, Bahr R. Relationship between symptoms of jumper's knee and the ultrasound characteristics of the patellar tendon among high level male volleyball players. *Scand J Med Sci Sports* 1996;6:291–6.
- 33 Panni AS, Tartarone M, Maffulli N. Patellar tendinopathy in athletes. Outcome of nonoperative and operative management. *Am J Sports Med* 2000;28:392–7.
- 34 Khan KM, Visentini PJ, Kiss ZS *et al*. Correlation of ultrasound and magnetic resonance imaging with clinical outcome after patellar tenotomy: prospective and retrospective studies. *Victorian Institute of Sport Tendon Study Group. Clin J Sport Med* 1999;9:129–37.
- 35 Alfredson H, Ohberg L, Forsgren S. Is vasculo-neural ingrowth the cause of pain in chronic Achilles tendinosis? An investigation using ultrasonography and colour Doppler, immunohistochemistry, and diagnostic injections. *Knee Surg Sport Traumatol Arthrosc* 2003;11:334–8.
- 36 Barzelai S, Sharabani-Yosef O, Holbova R *et al*. Low-intensity ultrasound induces angiogenesis in rat hind-limb ischemia. *Ultrasound Med Biol* 2006;32:139–45.
- 37 Rawool NM, Goldberg BB, Forsberg F, Winder AA, Hume E. Power Doppler assessment of vascular changes during fracture treatment with low-intensity ultrasound. *J Ultrasound Med* 2003;22:145–53.
- 38 D'Vaz AP, Ostor AJ, Speed CA *et al*. Pulsed low-intensity ultrasound therapy for chronic lateral epicondylitis: a randomized controlled trial. *Rheumatology* 2006;45:566–70.