NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of autologous blood injection for tendinopathy

Treating tendinopathy by injecting a patient's own blood around the painful tendon

Tendons are bands of fibrous connective tissue that connect muscle to bone. 'Tendinopathy' describes a range of conditions that affect tendons, usually caused by overuse. The most common tendons affected are in the elbow, the heel and the knee. Symptoms include pain, weakness and stiffness. In autologous blood injection, blood is taken from the patient and re-injected around the affected tendon. Sometimes the blood is separated into red blood cells and platelets (cell fragments that produce substances called growth factors) before injecting the sample containing mostly platelets. The aim is to supply the tendon with growth factors that start the healing process.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in April 2012 and updated in September 2012.

Procedure name

- Autologous blood injection for tendinopathy

Specialty societies

- British Elbow and Shoulder Society
- British Orthopaedic Association
- British Orthopaedic Foot and Ankle Society
- British Society for Rheumatology

- The Pain Society

Description

Indications and current treatment

‘Tendinopathy’ describes a range of conditions that affect tendons, causing pain, weakness and stiffness. The symptoms are usually associated with overuse. Sites commonly involved are the extensor (elbow), Achilles (heel) and patellar (knee) tendons. Tendinopathy also has other names – for example, tendonosis and tendonitis – and it encapsulates a range of pathologies, including inflammatory, non-inflammatory and degenerative changes.

Tendinopathy usually resolves over a period of several months. Conservative treatments include rest, analgesics, anti-inflammatory medication, use of orthotic devices, eccentric exercise and physiotherapy. Local injection of steroids, extracorporeal shockwave therapy, or sometimes surgery to release the tendon from the underlying bone or constricting surrounding tissues, can also be used. A period of rehabilitation is usually needed after any surgical intervention.

What the procedure involves

Autologous blood injection (using whole blood or platelet-rich plasma) is claimed to promote healing through the action of growth factors on the affected tendon.

A variable amount of blood is withdrawn from the patient by standard venesection. Sometimes the blood is centrifuged to produce a platelet-rich sample. About 2–3 ml of whole blood or platelet-rich plasma is injected into the area around the damaged tendon, sometimes with ultrasound guidance. Local anaesthetic is usually used. 'Dry needling' (repeatedly passing a needle through the tendon to disrupt the fibres and induce bleeding) may be performed before injection of the blood. A ‘peppering’ technique is sometimes used to inject the autologous blood; this involves inserting the needle into the tendon, injecting some of the blood, withdrawing without emerging from the skin, slightly redirecting and reinserting. After the procedure, patients are usually advised to avoid strenuous or excessive use of the tendon for a few weeks, after which physiotherapy is started. The procedure may be repeated if needed.

The mechanism of action is thought to be a healing response in the damaged tendons triggered by growth factors in the blood. These growth factors trigger stem-cell recruitment, increase local vascularity and directly stimulate the production of collagen by tendon sheath fibroblasts.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to autologous blood injection for tendinopathy. Searches were conducted of the following databases, covering the period from their commencement to 26 September 2012: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with tendinopathy.
Intervention/test	Autologous blood injection.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on approximately 460 patients from 5 randomised controlled trials[1–5] and 3 case series[6–8].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on autologous blood injection for tendinopathy

Abbreviations used: ABI, autologous blood injection; CI, confidence interval; CST, corticosteroid injection; DASH, 'Disabilities of the arm, shoulder and hand'; MRI, magnetic resonance imaging; NR, not reported; NS, not significant; NSAID, non-steroidal anti-inflammatory drug; PRP, platelet-rich plasma; PRTEE, 'Patient-related tennis elbow evaluation'; SD, standard deviation; US, ultrasound; UTC, ultrasonographic tissue characterisation; VAS, visual analogue scale; VISA-A, 'Victorian institute of sports assessment – Achilles'

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Creaney L (2011)[1]

Randomised controlled trial
UK
Recruitment period: not reported
Study population: patients with refractory elbow tendinopathy
n=150 (70 ABI vs 80 PRP) patients
Age: mean 51 years
Sex: 57% male

Patient selection criteria: Patients with symptoms for a minimum of 6 months and refractory to therapy using conservative measures including physical therapy exercises were included. Patients who had previously had a CST injection, dry needling or blood injection were excluded.

Technique: tendon's surface bathed with 2 ml bupivacaine. Under US guidance, blood collected from the antecubital fossa was injected into clefts of hypoechoicity within the tendon using minimal pressure. For plasma injection, blood was spun in a centrifuge (LC6; Sarstedt) and 1.5 ml siphoned from the buffy coat layer.</td>
<td>Number of patients analysed: 130 (60 ABI vs 70 PRP)
Success
(Defined as an improvement in the PRTEE score of 25 points at final analysis)
Success rate at 6 months (including all patients with complete datasets):
• ABI=72% (43/60) (95% CI, 61% to 83%)
• PRP=66% (46/70) (95% CI, 55% to 77%), p = 0.59

Composite failures
Failure was defined as an improvement of less than 25 points or progression to surgery
Failures
• ABI=8% (5/60)
• PRP=24% (17/70)
Progression to surgery
• ABI=20% (12/60)
• PRP=10% (7/70)

PRTEE score* (mean [95% CI])
<table>
<tr><th></th><th>ABI (n=48)</th><th>PRP (n=63)</th></tr>
<tr><td>Baseline (first injection)</td><td>52.5 (48.5, 56.5)</td><td>45.8 (41.9, 49.6)</td></tr>
<tr><td>1 month (second injection)</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>3 months</td><td>37.7 (32.2, 43.3)</td><td>33 (28.2, 37.8)</td></tr>
<tr><td>6 months +</td><td>46.8 (42.1, 51.5)</td><td>35.8 (30.3, 41.4)</td></tr>
</table>
*In addition to patients lost to follow-up, the analysis excludes patients who opted for surgery.
+The difference is significant, in favour of the PRP group.</td>
<td>The study did not report on safety.</td>
<td>Follow-up issues:
• 13% (20/150) loss to follow-up. 10 patients lost to follow-up in both the ABI and PRP groups.
Study design issues:
• Method of randomisation not described. Allocation concealment by sealed envelopes, patient and outcome assessors blinded to the treatment. Genuine intention-to-treat analysis was not possible because 20 patients were lost to follow-up. Instead, the paper reported a modified intention-to-treat analysis including all remaining patients with complete datasets.
• To detect a clinically significant difference of 10 points on mean improvement in the PRTEE scale, allowing for 20% loss to follow-up, at least 52 patients needed to be enrolled. (90% power and significance at p=0.05)
• PRTEE is a validated composite scale measuring pain and physical function on a scale of 0–100, with a higher score indicating more pain and functional disability.
Study population issues:
• Limited information reported on baseline comparability (age, sex, baseline PRTEE score).</td>
</tr>
</table>

Abbreviations used: ABI, autologous blood injection; CI, confidence interval; CST, corticosteroid injection; DASH, 'Disabilities of the arm, shoulder and hand'; MRI, magnetic resonance imaging; NR, not reported; NS, not significant; NSAID, non-steroidal anti-inflammatory drug; PRP, platelet-rich plasma; PRTEE, 'Patient-related tennis elbow evaluation'; SD, standard deviation; US, ultrasound; UTC, ultrasonographic tissue characterisation; VAS, visual analogue scale; VISA-A, 'Victorian institute of sports assessment – Achilles'			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Authors noted that a degree of 'dry needling' was unavoidable. Patients received 2 injections (1 at baseline and at 1 month). Patients were advised to continue normal activities but to avoid any physical activity for 48 hours and anti-inflammatory drugs. Follow-up: **6 months** Conflict of interest/source of funding: none			

Abbreviations used: ABI, autologous blood injection; CI, confidence interval; CST, corticosteroid injection; DASH, 'Disabilities of the arm, shoulder and hand'; MRI, magnetic resonance imaging; NR, not reported; NS, not significant; NSAID, non-steroidal anti-inflammatory drug; PRP, platelet-rich plasma; PRTEE, 'Patient-related tennis elbow evaluation'; SD, standard deviation; US, ultrasound; UTC, ultrasonographic tissue characterisation; VAS, visual analogue scale; VISA-A, 'Victorian institute of sports assessment – Achilles'

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Gosens (2011)[2]

Randomised controlled trial
The Netherlands
Recruitment period: 2006–8
Study population: patients with elbow tendinopathy
n=100 (51 PRP vs 49 CST) patients
Age: mean 47 years
Sex: 46% male

Patient selection criteria: patients with lateral epicondylitis for more than 6 months and pain of at least 50 on a VAS scale. Patients treated with surgical intervention or with CST injection in the previous 6 months, age less than 18 years, systemic disorders, history of carpal tunnel syndrome or cervical radiculopathy were excluded.

Technique: 27 ml of blood was collected from uninvolved arm and 3 ml of platelet collected (Recover System, Biomet). Approximately 1 ml of platelet or CST (kenacort 40 mg/ml triamcinolone acetonide) was injected directly with bupivacaine hydrochloride 0.5% with epinephrine into the area of maximum tenderness. Using a peppering technique the remaining PRP or CST was injected into the</td>
<td>Number of patients analysed: 100 (51 PRP vs 49 CST)
Successful treatment
Defined as a reduction of 25% on the VAS pain score without a reintervention after 2 years.
• PRP=76% (39/51)
• CST=43% (21/49) (p<0.0001).
Failures
11.8% (6/51) patients treated by PRP and 28.6% (14/49) treated by CST needed reoperation or reintervention (timing for reintervention or reoperation ranged from 2 to 14 months).
• 6% (3/51) of patients treated by PRP and 12% (6/49) of patients treated by CST needed reoperations (no further details reported).
• 6% (3/51) of patients treated by PRP needed a re-injection with CST (in 1 patient re-injection within 3 months after initial treatment and in 2 patients within the first year after the initial treatment) and 16.3% (8/49) of patients treated by CST needed reintervention with CST every 3 months (n=1) or with PRP injection (n=7).

Mean VAS scores (Intention to treat analyses)
<table>
<tr><td>Timepoint</td><td>PRP</td><td>CST</td><td>p value</td></tr>
<tr><td>Baseline</td><td>69.0 (15.9)</td><td>66.2 (14.0)</td><td>0.34 (NS)</td></tr>
<tr><td>2 years</td><td>21.3 (28.1)</td><td>42.4 (26.8)</td><td><0.0001</td></tr>
</table>
Data reported as mean (SD)

Mean DASH disability symptom scores (intention to treat analyses)
<table>
<tr><td>Timepoint</td><td>PRP</td><td>CST</td><td>P value</td></tr>
<tr><td>Baseline</td><td>54.3 (19.5)</td><td>43.3 (16.1)</td><td>0.002</td></tr>
<tr><td>2 years</td><td>17.6 (24.0)</td><td>36.5 (23.8)</td><td><0.0001</td></tr>
</table>
Data reported as mean (SD)</td>
<td>Initial worsening of pain was observed in the PRP group (no further details reported).

No other complications observed.</td>
<td>Follow-up issues:
• 6% (6/100) loss to follow-up 'temporarily' (no further details reported).
Study design issues:
• Method of randomisation not described. Allocation concealment by sealed envelopes. Double-blind trial. Intention-to-treat analysis carried out.
• As part of the double-blind procedure, blood was also collected from the patients in the CST group.
• Authors noted the study may be underpowered at 2-year follow-up.
• DASH is a 30-item questionnaire to assess physical function and symptoms in musculoskeletal disorders of the upper limbs. Score range from 0 to 100, with lower score indicating better ability. VAS for pain, scores range from 0 (no pain) to 100 (maximum pain possible).

Study population issues:
• Baseline comparability reported for age, sex, hand dominance, and VAS scores. Significant difference in baseline DASH scores, with a higher score in the PRP group.
Other issues:</td>
</tr>
</table>

Abbreviations used: ABI, autologous blood injection; CI, confidence interval; CST, corticosteroid injection; DASH, 'Disabilities of the arm, shoulder and hand'; MRI, magnetic resonance imaging; NR, not reported; NS, not significant; NSAID, non-steroidal anti-inflammatory drug; PRP, platelet-rich plasma; PRTEE, 'Patient-related tennis elbow evaluation'; SD, standard deviation; US, ultrasound; UTC, ultrasonographic tissue characterisation; VAS, visual analogue scale; VISA-A, 'Victorian institute of sports assessment – Achilles'

Study details	Key efficacy findings	Key safety findings	Comments
common extensor tendon. Injection administered once. This technique involved a single skin portal and 5 penetrations of the tendon. Patients were instructed to rest the arm for approximately 24 hours and use acetaminophen if necessary. After a standardised stretching protocol for 2 weeks under the care of a physiotherapist, a formal programme was initiated. At 4 weeks, patients were allowed to proceed with normal activities. Follow-up: **2 years** Conflict of interest/source of funding: one or more of the authors declared potential conflict of interest. Biomet supplied the Recover system used at discounted rate.			• Information on patient selection criteria and technique obtained from Peerbooms 2010 (in appendix A) which reported outcomes at 1-year follow-up period.

Abbreviations used: ABI, autologous blood injection; CI, confidence interval; CST, corticosteroid injection; DASH, 'Disabilities of the arm, shoulder and hand'; MRI, magnetic resonance imaging; NR, not reported; NS, not significant; NSAID, non-steroidal anti-inflammatory drug; PRP, platelet-rich plasma; PRTEE, 'Patient-related tennis elbow evaluation'; SD, standard deviation; US, ultrasound; UTC, ultrasonographic tissue characterisation; VAS, visual analogue scale; VISA-A, 'Victorian institute of sports assessment – Achilles'

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>De Jonge S (2011)[3]

Randomised controlled trial
The Netherlands
Recruitment period: 2008–9
Study population: patients with chronic Achilles tendinopathy
n=54 (27 PRP vs 27 saline injection [placebo])
Age: mean 50 years
Sex: not reported

Patient selection criteria: patients with a clinical diagnosis of Achilles tendinopathy with a minimal duration of symptoms of 2 months were included. Patients were excluded if they had received PRP injection in the Achilles tendon, performed a full eccentric exercise programme, presence of a systemic illness, other musculoskeletal injury, pregnancy or use of fluoroquinolones.

Technique: Skin and subcutaneous tissue was anaesthetised with 2 ml of 0.5% Marcaine and blood collected from the cubital vein was centrifuged (Gravitation Platelet Separation III). Under US guidance 5 aliquots of a total amount of 4 ml was injected at 3 different needle locations.</td>
<td>Number of patients analysed: 54 (27 PRP vs 27 saline)

VISA-A (primary outcome measure)
<table>
<tr><th></th><th>PRP</th><th>Saline</th></tr>
<tr><td>Baseline</td><td>46.7 (40.3, 53.1)</td><td>52.6 (54.1, 60.2)</td></tr>
<tr><td>1 year</td><td>78.2 (68.0, 88.5)</td><td>77.6 (70.8, 84.4)</td></tr>
</table>
Results reported as: points (95% CI)
The adjusted between-group difference at 1-year follow-up was not significant (5.5 points on VISA-A score; 95% CI, −4.9 to 15.8) (adjusted for baseline VISA-A score and duration of symptoms); p value not reported.

Patient satisfaction
59.3% (16/27) patients in each group were satisfied with their allocated treatment (further details not reported).
Adjusted between-group difference for subjective patient satisfaction after 1 year was −2.7% (95% CI, −23.4 to 18.1; p=0.81).

Return to sporting activity
56.5% of the patients in the PRP group and 41.7% in the placebo group returned to their previous sports levels in the desired sport (actual numbers not reported).
The adjusted between-group difference for return to sports was 1.8% (95% CI, −24.5 to 28.1; p=0.89).

Ultrasound assessment
Neovascularisation
(Scores reported are mean (95% CI))
<table>
<tr><th>Timepoint</th><th>PRP</th><th>Saline</th></tr>
<tr><td>Baseline</td><td>2.3 (1.8, 2.7)</td><td>2.2 (1.6, 2.7)</td></tr>
<tr><td>12 weeks</td><td>3.0 (2.6, 3.5)</td><td>2.5 (2.1, 2.9)</td></tr>
<tr><td>1 year*</td><td>1.4 (0.8, 2.0)</td><td>1.2 (0.7, 1.7)</td></tr>
</table>
*Between-group difference at 1-year follow-up: 0.1 point (−0.6, 0.9) was not significant, p=0.71</td>
<td>'No complications were reported between 24-week and 1-year follow-up'.</td>
<td>Follow-up issues:
• No patients lost to follow-up.
Study design issues:
• Sequence generation by block randomisation (block size of 12 participants). Allocation concealment by a blank sealed envelope. Procedure performed by physician blinded to the allocated treatment.
• Patients remained blinded until 1-year follow-up.
• To show a difference of 12 points on the VISA-A score, a sample size of 27 patients in each group was needed (power 80% p=0.05; assuming a 10% loss to follow-up).
• Four patients, of which 1 patient was from the PRP group (failed to attend the visit), excluded from the UTC analysis.
• One patient treated by PRP excluded from the neovascularisation analysis (failure to attend).
• VISA-A scale assesses severity of Achilles tendinopathy on a scale of 0–100, with lower score indicating higher severity.
• Neovascularisation scored using the modified Ohberg score system: 0=no vessels to 4+ =more than 3 vessels throughout the tendon. Unclear if this is a validated method of scoring.</td>
</tr>
</table>

Abbreviations used: ABI, autologous blood injection; CI, confidence interval; CST, corticosteroid injection; DASH, 'Disabilities of the arm, shoulder and hand'; MRI, magnetic resonance imaging; NR, not reported; NS, not significant; NSAID, non-steroidal anti-inflammatory drug; PRP, platelet-rich plasma; PRTEE, 'Patient-related tennis elbow evaluation'; SD, standard deviation; US, ultrasound; UTC, ultrasonographic tissue characterisation; VAS, visual analogue scale; VISA-A, 'Victorian institute of sports assessment – Achilles'

Study details	Key efficacy findings	Key safety findings	Comments
4 ml of saline injection was prepared for the placebo group. Patients were advised to perform a stretching programme in the second week and to avoid sport activities for 4 weeks. All patients started an eccentric exercise programme for 12 weeks. Follow-up: **1 year** Conflict of interest/source of funding: One or more authors declared conflict of interest. Biomet provided financial support and donated the platelet-separation kits.	**Evaluation of tendon structure** Tendon structure evaluated quantitatively by UTC. Scores reported are percentage of echo types I and II (95% CI) **Timepoint** / **PRP** / **saline** Baseline / 76.9 (72.6, 81.1) / 72.1 (67.7, 76.5) 1 year* / 83.7 (79.6, 87.9) / 81.3 (77.3, 85.3) *Between-group difference at 1-year follow-up 1.2% (−4.1, 6.6) was not significant, p=0.65 **Reinterventions** Four patients treated by PRP and 1 patient treated by placebo underwent another treatment because of failure to improve after 24 weeks.		• Echo types I and II represent more or less organised (secondary tendon bundles); echo types III and IV represent smaller, disorganised and more amorphous or fibrillar structures. **Other issues:** • This study is a follow-up of De Vos (2010) which reported on outcomes at 24-week follow-up. No adverse events were reported. This study is included in appendix A. De Vos (2010) noted that there is uncertainty about the role of neovascularisation and suggested there may be a beneficial effect of increased neovascularisation in the first period of treatment and an opposing effect when neovascularisation is still present in the longer term.

Abbreviations used: ABI, autologous blood injection; CI, confidence interval; CST, corticosteroid injection; DASH, 'Disabilities of the arm, shoulder and hand'; MRI, magnetic resonance imaging; NR, not reported; NS, not significant; NSAID, non-steroidal anti-inflammatory drug; PRP, platelet-rich plasma; PRTEE, 'Patient-related tennis elbow evaluation'; SD, standard deviation; US, ultrasound; UTC, ultrasonographic tissue characterisation; VAS, visual analogue scale; VISA-A, 'Victorian institute of sports assessment – Achilles'

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Kazemi M (2010)[4]

Randomised controlled trial
(as described in the paper)
Iran
Recruitment period: 2007–8
Study population: patients with lateral elbow tendinopathy
n=60 (30 ABI vs 30 CST)
Age: mean 47 years
Sex: 18% male

Patient selection criteria: inclusion criteria included patients with new episode of lateral elbow tendinopathy within a year before recruitment, lack of upper limb function in activities of daily living. Exclusion criteria included active or history of arthritis or related disease, previous operation or any CST injection during the 3 months.

Technique: 2 ml of blood collected from distal region of the ipsilateral upper limb and mixed with 1 ml of 2% lidocaine and a single dose of the mixture was injected.
Patients in CST group were given a single dose of local CST (methylprednisolone 20 mg mixed with 1 ml of 2% lidocaine).
All patients advised to avoid pain-provoking activity for 48 hours and</td>
<td>Number of patients analysed: 60 (30 ABI vs 30 CST)

Severity of symptoms assessed using DASH, reported as mean score (SD)
<table>
<tr><td>Outcome</td><td>ABI</td><td>CST</td><td>p value</td></tr>
<tr><td>Baseline</td><td>51.6 (15.1)</td><td>52.3 (19.3)</td><td>0.88</td></tr>
<tr><td>4 weeks</td><td>21 (10.6)</td><td>32.3 (17.2)</td><td>0.004*</td></tr>
<tr><td>8 weeks</td><td>6.9 (12.6)</td><td>32.4 (19.4)</td><td><0.001+</td></tr>
</table>
*The mean difference 11.2 (SE 2.7) was statistically significant.
+The mean difference 25.5 (SE 4.2) was statistically significant.

Severity of symptoms (at 8-week follow-up)
<table>
<tr><td>Outcome</td><td>ABI</td><td>CST</td><td>p value</td></tr>
<tr><td>Modified Nirschl score</td><td>0.7 (0.7)</td><td>1.8 (1.1)</td><td><0.001</td></tr>
<tr><td>Limb pain at rest within last 24 hours</td><td>1.5 (1.2)</td><td>4 (2.6)</td><td><0.001</td></tr>
<tr><td>Limb function within the last 24 hours</td><td>1.5 (1.3)</td><td>3.4 (2.2)</td><td><0.001</td></tr>
<tr><td>Pain in maximum grip</td><td>1.4 (1.4)</td><td>4.2 (2.5)</td><td><0.001</td></tr>
<tr><td>Maximum grip strength</td><td>47.8 (15)</td><td>31.1 (15.7)</td><td><0.001</td></tr>
<tr><td>Pressure pain threshold (Newton/cm^2)</td><td>20.7 (10.6)</td><td>10.8 (5.7)</td><td><0.001</td></tr>
</table>
Scores reported as mean (SD)</td>
<td>There were 'no noticeable or reported side-effects' of the treatment in either group.</td>
<td>Follow-up:
• No loss to follow-up.

Study design issues:
• Method of randomisation: first patient randomly assigned with coin toss; remaining patients allocated sequentially. Single-blind trial.
• Sample size calculation: to detect a difference of 30% on VAS at 80% power, p=0.05, it was estimated 30 patients were needed in each group.
• Severity of symptoms assessed using: the Quick DASH scale, an 11-item questionnaire with score ranging from 0 to 100, with a lower score indicating lower difficulty; the modified Nirschl scale, with score ranging from 0 (no pain with exercise) to 5 (severe pain with normal activities of daily living). Pain intensity assessed using VAS, with scores ranging from 0 (no pain) to 9 (worst pain).
• No significant differences in baseline characteristics.</td>
</tr>
</table>

Abbreviations used: ABI, autologous blood injection; CI, confidence interval; CST, corticosteroid injection; DASH, 'Disabilities of the arm, shoulder and hand'; MRI, magnetic resonance imaging; NR, not reported; NS, not significant; NSAID, non-steroidal anti-inflammatory drug; PRP, platelet-rich plasma; PRTEE, 'Patient-related tennis elbow evaluation'; SD, standard deviation; US, ultrasound; UTC, ultrasonographic tissue characterisation; VAS, visual analogue scale; VISA-A, 'Victorian institute of sports assessment – Achilles'			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
a gradual return to normal activities. Patients were instructed not to use brace, NSAIDs or steroidal anti-inflammatory drugs throughout the duration of the study. Follow-up: **8 weeks** Conflict of interest/source of funding: none			

Abbreviations used: ABI, autologous blood injection; CI, confidence interval; CST, corticosteroid injection; DASH, 'Disabilities of the arm, shoulder and hand'; MRI, magnetic resonance imaging; NR, not reported; NS, not significant; NSAID, non-steroidal anti-inflammatory drug; PRP, platelet-rich plasma; PRTEE, 'Patient-related tennis elbow evaluation'; SD, standard deviation; US, ultrasound; UTC, ultrasonographic tissue characterisation; VAS, visual analogue scale; VISA-A, 'Victorian institute of sports assessment – Achilles'

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Thanasas C (2011)[5]

Randomised controlled trial
Greece
Recruitment period: not reported
Study population: patients with chronic lateral elbow epicondylitis
n=28 (14 ABI vs 14 PRP)
Age: mean 36 years
Sex: 25% male

Patient selection criteria: inclusion criteria included patients with a clinical diagnosis of lateral epicondylitis, no history of trauma, no previous local injection treatment and no history of rheumatic disorder. Exclusion criteria included recent onset of symptoms (<3 months), medical comorbidities and previous local injections.

Technique: under US guidance, a single injection of 3 ml autologous peripheral whole blood was injected at the origin of wrist extensors with a peppering technique (single skin insertion, deep peripheral multiple sites of injection).
For the PRP, 27 to 55 ml of autologous peripheral blood was collected and prepared (Biomet GPS III) and a single injection of</td>
<td>Number of patients analysed: 28 (14 ABI vs 14 PRP)

Mean improvement in VAS scores
<table>
<tr><th>Timepoint</th><th>ABI</th><th>PRP</th><th>p value</th></tr>
<tr><td>Baseline</td><td>6.0 (5.3, 6.7)</td><td>6.1 (5.4, 6.8)</td><td>NR</td></tr>
<tr><td>6 weeks</td><td>2.5 (1.9, 3.1)</td><td>3.8 (3.1, 4.5)</td><td><0.05</td></tr>
<tr><td>3 months</td><td>3.2 (2.3, 4.1)</td><td>4.2 (3.5, 4.9)</td><td>0.11</td></tr>
<tr><td>6 months</td><td>3.4 (2.4, 4.4)</td><td>4.4 (3.4, 5.4)</td><td>0.32</td></tr>
</table>
Scores reported as mean (95% CI)

Improvement in Liverpool elbow score
<table>
<tr><th>Timepoint</th><th>ABI</th><th>PRP</th><th>p value</th></tr>
<tr><td>Baseline</td><td>6.9 (6.7, 7.2)</td><td>6.9 (6.9, 7.3)</td><td>NR</td></tr>
<tr><td>6 weeks</td><td>1.9 (1.4, 2.3)</td><td>2.0 (1.6, 2.4)</td><td>0.45</td></tr>
<tr><td>3 months</td><td>1.9 (1.4, 2.3)</td><td>2.2 (1.7, 2.6)</td><td>0.45</td></tr>
<tr><td>6 months</td><td>2.0 (1.4, 2.5)</td><td>2.3 (1.9, 2.7)</td><td>0.53</td></tr>
</table>
Scores reported at follow-up are change scores (95% CI)</td>
<td>Local pain and discomfort:
• ABI=29% (4/14)
• PRP=64% (9/14)

Pain and discomfort started from the day of injection and gradually subsided (assessed at end of the first week).

No other complications were noted.</td>
<td>Follow-up:
• One patient from the ABI group was lost to follow-up. Reasons not reported.

Study design issues:
• Computer-generated blocked randomisation with an odd sequence number randomly allocated to one group. Single-blind study. Outcome assessors blinded to treatment patient received.
• Pain intensity assessed using VAS, with scores ranging from 0 (no pain) to 9 (agonising pain). The Liverpool Elbow score evaluates range of motion, daily activities, and ulnar nerve function with scores ranging from 0 to 10, with higher scores indicating better function.

Study population issues:
• Study reported baseline characteristics (age, sex, duration of symptoms, dominancy of hand and occupation) 'did not differ substantially between the 2 groups'.</td>
</tr>
</table>

Abbreviations used: ABI, autologous blood injection; CI, confidence interval; CST, corticosteroid injection; DASH, 'Disabilities of the arm, shoulder and hand'; MRI, magnetic resonance imaging; NR, not reported; NS, not significant; NSAID, non-steroidal anti-inflammatory drug; PRP, platelet-rich plasma; PRTEE, 'Patient-related tennis elbow evaluation'; SD, standard deviation; US, ultrasound; UTC, ultrasonographic tissue characterisation; VAS, visual analogue scale; VISA-A, 'Victorian institute of sports assessment – Achilles'			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
3 ml of PRP was injected using a peppering technique. All patients were advised to refrain from heavy activities for 1 week, and provided with a stretching and eccentric loading exercise to be performed for 5 weeks. No cortisone or NSAIDs were prescribed during follow-up. Follow-up: **6 months** Conflict of interest/source of funding: none			

Abbreviations used: ABI, autologous blood injection; CI, confidence interval; CST, corticosteroid injection; DASH, 'Disabilities of the arm, shoulder and hand'; MRI, magnetic resonance imaging; NR, not reported; NS, not significant; NSAID, non-steroidal anti-inflammatory drug; PRP, platelet-rich plasma; PRTEE, 'Patient-related tennis elbow evaluation'; SD, standard deviation; US, ultrasound; UTC, ultrasonographic tissue characterisation; VAS, visual analogue scale; VISA-A, 'Victorian institute of sports assessment – Achilles'

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Kon E (2009)[6]

Case series
Italy
Recruitment period: 2007–8
Study population: patients with chronic patellar tendinosis
n=20
Age: mean 26 years
Sex: 100% male

Patient selection criteria: Patients with a chronic patellar tendinosis, history of pain and failed treatment.

Technique: 150 ml blood was withdrawn for every lesion treated, centrifuged and 5 ml of platelet-rich plasma was injected followed by penetrations of the tendon using a needle. Injections were performed without ultrasound guidance.
After injection participants were advised to limit the use of leg for at least 24 hours, use cold therapy/ice on the affected area and non-steroidal medication was allowed.
Rest was indicated between the first and second injection, stretching exercises and mild activities after the second injection</td>
<td>Number of patients analysed: 20

Functional recovery
Six patients showed 'complete recovery', 8 'marked improvement', 2 'mild improvement' and in 4 cases 'no improvement' (definition and timing of assessment not reported).

Patient satisfaction
80% (16/20) reported satisfaction with the results of treatment.

Quality of life
A statistically significant improvement in all domains of the SF-36 questionnaire at end of therapy and at 6-month follow-up (p value not reported).
<table>
<tr><th>Domain</th><th>Before therapy</th><th>6-month follow-up</th></tr>
<tr><td>Physical function</td><td>56.7</td><td>86.7</td></tr>
<tr><td>Pain</td><td>35.7</td><td>71.6</td></tr>
<tr><td>General mental health</td><td>64.9</td><td>78.5</td></tr>
<tr><td>Vitality</td><td>59.1</td><td>68.7</td></tr>
<tr><td>Social functioning</td><td>49.1</td><td>84.3</td></tr>
<tr><td>General health perceptions</td><td>69.1</td><td>85.9</td></tr>
<tr><td>Role limitation (physical factors)</td><td>13.9</td><td>87.0</td></tr>
<tr><td>Role limitation (emotional factors)</td><td>40.7</td><td>91.4</td></tr>
</table>
Activity level
Sport activity level, assessed on Tegner activity score, showed a statistically significant improvement from pretreatment level to 6-month follow-up (p<0.0005) but no statistically significant difference compared with pre-injury activity level (p value not reported).
Pre-injury: mean score 7.5; pretreatment: mean score 4.
Follow-up: mean score 7.</td>
<td>In all cases, moderate pain and stiffness after the injections, which persisted for a few days. In 1 patient, marked pain response occurred after the injection (3 weeks to resolve).

No severe adverse events observed.</td>
<td>Study design issues:
• Prospective study with consecutive patient recruitment.
• Quality of life assessed with SF-36, score on a scale of 0–100, with higher score indicating better outcome.
• Tegner activity level score, range from 0 to 10, with 0 indicating disability and 10 indicating playing sports at competitive level.

Other issues:
• Data on Tegner activity score extracted from graph.
• Study reported that 'all results are presented as number of tendons treated (not number of individuals)'.</td>
</tr>
</table>

Abbreviations used: ABI, autologous blood injection; CI, confidence interval; CST, corticosteroid injection; DASH, 'Disabilities of the arm, shoulder and hand'; MRI, magnetic resonance imaging; NR, not reported; NS, not significant; NSAID, non-steroidal anti-inflammatory drug; PRP, platelet-rich plasma; PRTEE, 'Patient-related tennis elbow evaluation'; SD, standard deviation; US, ultrasound; UTC, ultrasonographic tissue characterisation; VAS, visual analogue scale; VISA-A, 'Victorian institute of sports assessment – Achilles'			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
and after the third injection, patients were advised to begin a strengthening programme. Patients were advised to proceed to normal sport or recreational activities as tolerated after 1 month. Three injections administered in total. Injections administered every 15 days. Follow-up: **6 months** Conflict of interest/source of funding: not reported			

Abbreviations used: ABI, autologous blood injection; CI, confidence interval; CST, corticosteroid injection; DASH, 'Disabilities of the arm, shoulder and hand'; MRI, magnetic resonance imaging; NR, not reported; NS, not significant; NSAID, non-steroidal anti-inflammatory drug; PRP, platelet-rich plasma; PRTEE, 'Patient-related tennis elbow evaluation'; SD, standard deviation; US, ultrasound; UTC, ultrasonographic tissue characterisation; VAS, visual analogue scale; VISA-A, 'Victorian institute of sports assessment – Achilles'

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Edwards SG (2003)[7]

Case series
USA
Recruitment period: not stated
Study population: patients with lateral epicondylitis
n=28
Age: mean 46 years
Sex: 50% male

Patient selection criteria: inclusion criteria: lateral epicondylitis, without prior surgery or steroid injections within past 3 months. Refractory to any combination of physiotherapy, splinting, NSAIDs or steroids.

Technique: 2 ml blood mixed with 1 ml 0.5% bupivacaine, or 1 ml 2% lidocaine injected. The needle was positioned into the undersurface of the extensor carpi radialis brevis. Patients were placed in splints, and a physiotherapy programme initiated at 3-week follow-up. If pain did not resolve fully the procedure was repeated at 6 weeks

Follow-up: mean 10 months</td>
<td>Pain
Whole group
<table>
<tr><th>Mean (range)</th><th>Baseline(n=28)</th><th>9.5 months (n=28)</th><th>p value</th></tr>
<tr><td>VAS</td><td>7.8 (4–10)</td><td>2.3 (range not reported)</td><td>NR</td></tr>
<tr><td>Nirschl</td><td>6.5 (5–7)</td><td>2.0 (range not reported)</td><td>NR</td></tr>
</table>
Maximal benefit was reached at an average of 3 weeks.

Patients needing two or more treatments (n=9)
<table>
<tr><th>Mean</th><th>Baseline</th><th>After first injection</th><th>After second injection</th><th>p value</th></tr>
<tr><td>VAS</td><td>7.2</td><td>4.6</td><td>0.9</td><td>NR</td></tr>
<tr><td>Nirschl</td><td>6.6</td><td>4.1</td><td>0.9</td><td>NR</td></tr>
</table>
Two patients needed a third injection after which both VAS pain score and Nirschl score fell to 0 within 1 week.

50% (14/28) of patients were relieved of pain even after strenuous exercise after the first treatment, and 79% (22/28) were free of pain after the final treatment. No patient reported worsening or recurrence of pain.

Joint function
4% (1/28) of patients failed to respond satisfactorily and were treated surgically for lateral epicondylitis.</td>
<td>Complications
There were no occurrences of infection, reflex sympathetic dystrophy, elbow flexion contracture or other adverse events.

7% (2/28) of patients needed short-term narcotics after autologous blood injection, but most reported that their pain was similar to the pain they had experienced after previous steroid injections.</td>
<td>This study was included in the main extraction table in the original guidance.

Follow-up issues:
• Follow-up was curtailed when patients received a treatment outside the blood re-injection protocol.

Study design issues:
• Prospective study with consecutive patient recruitment. Patients were offered a range of surgical and non-surgical treatment options; this study population represents those who chose autologous blood injection.
• Full individual patient data also provided in study report.
• Pain was evaluated using VAS-score ranging from 0 to 10 (high score worse), and the Nirschl staging score, which has a scale of 1–7 points ranging from 'mild pain with exercise; resolves within 24 hours' to 'constant pain at rest; disrupts sleep' (high score worse).

Other issues:
• Time of 'post-procedure' follow-up for pain score not stated. If immediately after period of immobilisation, benefit related to lack of use of joint cannot be</td>
</tr>
</table>

Abbreviations used: ABI, autologous blood injection; CI, confidence interval; CST, corticosteroid injection; DASH, 'Disabilities of the arm, shoulder and hand'; MRI, magnetic resonance imaging; NR, not reported; NS, not significant; NSAID, non-steroidal anti-inflammatory drug; PRP, platelet-rich plasma; PRTEE, 'Patient-related tennis elbow evaluation'; SD, standard deviation; US, ultrasound; UTC, ultrasonographic tissue characterisation; VAS, visual analogue scale; VISA-A, 'Victorian institute of sports assessment – Achilles'			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Conflict of interest: none			distinguished from that related to blood injection. • Authors state that it was difficult to define the relative contribution to healing of the blood injection or the injury created by the injection itself. • Authors acknowledge the potential bias inherent in a non-blinded study design

Abbreviations used: ABI, autologous blood injection; CI, confidence interval; CST, corticosteroid injection; DASH, 'Disabilities of the arm, shoulder and hand'; MRI, magnetic resonance imaging; NR, not reported; NS, not significant; NSAID, non-steroidal anti-inflammatory drug; PRP, platelet-rich plasma; PRTEE, 'Patient-related tennis elbow evaluation'; SD, standard deviation; US, ultrasound; UTC, ultrasonographic tissue characterisation; VAS, visual analogue scale; VISA-A, 'Victorian institute of sports assessment – Achilles'

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Suresh SP (2006)[8]

Case series
UK
Recruitment period: 2004–5
Study population: patients with refractory medial epicondylitis; duration of symptoms 12 months
n=20
Age: mean 48 years
Sex: 65% male

Patient selection criteria: Patients with refractory medial epicondylitis confirmed by US and MRI, without steroid injections within 3 months. Refractory to physiotherapy, rest or steroids.

Technique: under US guidance 2 ml bupivacaine injected for local anaesthesia. The needle was positioned in the area of maximum tendon injury and dry needled. 2 ml autologous blood was slowly injected. Patients were told to avoid activities that aggravate symptoms. The procedure was repeated at 4 weeks

Follow-up: mean 10 months

Conflict of interest: none</td>
<td>Pain
Pain was evaluated using a visual analogue scale ranging from 0 to 10 (high score worse), and the Nirschl staging score, which has 1 to 7 points ranging from 'mild pain with exercise; resolves within 24 hours' to 'constant pain at rest; disrupts sleep' (high score worse).
Treatment was unsuccessful in 3 patients, who had (or were awaiting) surgical repair.

<table>
<tr><td>Mean (range)</td><td>Baseline (n=17)</td><td>4 weeks (n=17)</td><td>6 months (n=17)</td><td>p value</td></tr>
<tr><td>VAS</td><td>8 (5–10)</td><td>5.65 (2–9)</td><td>2.15 (0–9)</td><td><0.001</td></tr>
</table>
p = for both time points compared with baseline

<table>
<tr><td>Median (inter-quartile range)</td><td>Baseline (n=17)</td><td>4 weeks (n=17)</td><td>6 months (n=17)</td><td>p value</td></tr>
<tr><td>Nirschl</td><td>6 (5–7)</td><td>4 (2.25–5.0)</td><td>1 (1.0–1.75)</td><td><0.001</td></tr>
</table>
p = for both time points compared with baseline
Ultrasound assessment
Neovascularity (0–10) change score decreased from 6.10±1.62 points at baseline to 3.60±2.56 points at 10-month follow-up (p<0.001) (n= R).
Echo texture of the tendon was evaluated with a semi-quantitative score from 1 to 10, with 0 representing normal tendon and 10 representing diffuse hypo-echoic change seen throughout the entire tendon. Hypo-echoic change score decreased from 6.45±1.47 points at baseline to 3.85±2.37 points at 10-month follow-up (p<0.001).
There were significantly fewer interstitial tears noted at 10-month follow-up (mean 3; range 0–4) than at baseline (mean 6; range 5–8) in 11/20 patients evaluated (p=0.006).</td>
<td>Complications
There were no occurrences of infection, neurovascular damage or tendon rupture after the autologous blood injection procedure.</td>
<td>This study was included in the main extraction table in the original guidance.
Study design issue:
• 15% (3/20) of patients for whom treatment was unsuccessful were excluded from the efficacy outcome analysis.

Study population issue:
• 10% (2/20) of the patients underwent a third treatment course.

Other issues:
• All US assessments and injections were undertaken by one clinician with 10 years of experience.
• Authors state that there was no histopathological correlation between the procedure and improved tendon structure, and that the exact mechanism of action is not completely understood.</td>
</tr>
</table>

Efficacy

Procedural success

In a randomised controlled trial of 150 patients with tennis elbow, 70 were treated by autologous blood injection and 80 were treated by platelet-rich plasma injection. Technical success was defined as an improvement in patient-related tennis elbow evaluation (PRTEE) score (a composite scale measuring pain and physical function on a scale of 0–100, with a higher score indicating more pain and functional disability) of 25 points at final analysis. Of those patients followed up at 6 months, technical success was achieved in 72% (43/60) treated by autologous blood injection and 66% (46/70) of patients treated by platelet-rich plasma injection (p=0.59)[1].

In a randomised controlled trial of 100 patients with tennis elbow, 51 were treated by platelet-rich plasma injection and 49 were treated by corticosteroid injection. Successful treatment was defined as a reduction of 25% on the visual analogue scale (VAS) pain score (scores range from 0–100, with a higher score indicating more pain) and no reintervention after 2 years. At 2-year follow-up, successful treatment was achieved in 76% (39/51) of patients treated by platelet-rich plasma and 43% (21/49) of patients treated by corticosteroid injection (p<0.0001)[2].

Functional outcomes

In the randomised controlled trial of 150 patients mean improvement in PRTEE score was from 53 at baseline to 47 (95% confidence interval [CI], 42 to 52) in patients treated by autologous blood injection and from 46 at baseline to 36 (95% CI, 30 to 41) in patients treated by platelet-rich plasma injection at 6-month follow-up. This difference was significant (p value not reported)[1].

In a randomised controlled trial of 54 patients with Achilles tendinopathy, 27 were treated by platelet-rich plasma injection and 27 were treated by placebo injection. The mean difference on the ‘Victorian Institute of Sports assessment – Achilles’ (VISA-A) scale (assessing the severity of Achilles tendinopathy on a scale of 0-100, with a lower score indicating higher severity) was not significant (6 points [95% confidence interval [CI] −5 to 16]) at 1-year follow-up (p value not reported)[3].

In a randomised controlled trial of 60 patients with tennis elbow, 30 were treated by autologous blood injection and 30 were treated by corticosteroid injection. Severity of symptoms was assessed with the quick ‘Disabilities of the arm, shoulder and hand’ (DASH) questionnaire (0–100, with lower score indicating less difficulty). Mean difference in score between the groups was 26 at 8-week follow-up (p<0.001)[4].

In the randomised controlled trial of 100 patients, mean pain score as assessed on a VAS scale improved from 69 at baseline to 21 for the platelet-rich plasma

group, and from 66 at baseline to 42 in the corticosteroid injection group at 2-year follow-up ($p<0.0001$)[2].

Two case series evaluated the outcome of autologous blood injection using the Nirschl staging score, which has a scale of 1–7 points ranging from 'mild pain with exercise; resolves within 24 hours' to 'constant pain at rest; disrupts sleep'. One case series of 28 patients with refractory lateral epicondylitis reported that the mean score improved from 6.5 points at baseline to 2.0 points at 9.5-month follow-up (measure of significance not stated)[7]. A second case series of 20 patients with refractory medial epicondylitis reported that median score improved from 6 points at baseline to 1 point in 17 patients at 6-month follow-up ($p<0.001$)[8].

Reinterventions

In the randomised controlled trial of 100 patients, 12% (6/51) of patients treated by platelet-rich plasma injection and 29% (14/49) of patients treated by corticosteroid injection needed reoperation or reintervention. In this trial, 6% (3/51) of patients treated by platelet-rich plasma and 12% (6/49) of patients treated by corticosteroid injection needed 'reoperation' (no further details reported). Of the patients initially treated by platelet-rich plasma, 6% (3/51) were retreated by corticosteroid injection, and 16% (8/49) of patients initially treated by corticosteroid injection were retreated by corticosteroid injection (n=1) or by platelet-rich plasma injection (n=7) (timing for reintervention or reoperation ranged from 2 to 14 months; p values not reported)[2].

In the randomised controlled trial of 150 patients, 20% (12/60) of patients treated by autologous blood injection elected to proceed to surgery compared with 10% (7/70) of patients treated by platelet-rich plasma (level of significance not reported)[1].

Return to sporting activity

In the randomised controlled trial of 54 patients, 57% of patients in the platelet-rich plasma group and 42% of patients in the placebo group returned to their previous level of sporting activity (absolute figures not reported). The adjusted between-group difference for return to sports was 2% (95% CI, −25 to 28; $p=0.89$) at 1 year follow-up[3].

Quality of life

In a case series of 20 patients, statistically significant improvement in all domains of the SF-36 questionnaire was reported at end of therapy and at 6-month follow-up (p value not reported)[6].

Safety

Pain

In the case series of 28 patients with tennis elbow, 7% (2/28) needed narcotic analgesia because of pain after autologous blood injection. Most patients in this series reported that the pain was similar to the pain they had experienced after previous steroid injections into the tendon[7].

Moderate pain and stiffness after the injections, which persisted for a few days, was reported in all patients in the case series of 20 patients with patellar tendinosis. One patient had more severe pain after the injection which took 3 weeks to resolve (no further information reported)[6].

Validity and generalisability of the studies

- There were differences in postoperative rehabilitation protocol and duration.
- The procedure used varied across the studies. Studies reported re-injection of whole blood and platelet-rich plasma re-injection.
- The majority of the studies reported on tendinopathy of the elbow.
- There is currently no study comparing blood re-injection with dry needling alone.
- The mode of action of blood re-injection is uncertain.
- There is some variation in injection technique. One study described a degree of dry needling of the tendon before blood re-injection, and ultrasound guidance was not used in all studies.
- The relative benefits of the blood re-injection and the follow-up physiotherapy regimen are difficult to determine.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed below.

Interventional procedures

- Extracorporeal shockwave therapy for refractory plantar fasciitis. NICE interventional procedures guidance 311 (2009). Available from www.nice.org.uk/IPG311
- Extracorporeal shockwave therapy for refractory Achilles tendinopathy. NICE interventional procedures guidance 312 (2009). Available from www.nice.org.uk/IPG312

- Extracorporeal shockwave therapy for refractory tennis elbow. NICE interventional procedures guidance 313 (2009). Available from www.nice.org.uk/IPG313
- Extracorporeal shockwave lithotripsy for calcific tendonitis (tendinopathy) of the shoulder. NICE interventional procedures guidance 21 (2003). Available from www.nice.org.uk/IPG021

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Dr Jonathan Rees and Dr Hasan Tahir (British Society for Rheumatology)

- One Specialist Adviser has performed this procedure and the other has not.
- One Specialist Adviser noted that this was a novel procedure with uncertain safety and efficacy. Another Specialist Adviser noted that this was an established practice.
- Comparators to the procedure are 'wait and see' approach, placebo, corticosteroid injection, dry needling or physiotherapy.
- One Specialist Adviser noted key efficacy outcomes to be pain relief and improved function.
- Anecdotal adverse events: increased level of pain, flare of pain, reduced functioning, and damage to surrounding tissues. Theoretical adverse events include tendon rupture, damage to the tendon and infection.
- In terms of numbers of patients eligible for treatment and use of resources, the potential impact of this procedure on the NHS was considered to be minor by 1 Specialist Adviser and moderate by another Specialist Adviser.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme was unable to gather patient commentary for this procedure.

Issues for consideration by IPAC

- Treatment may be offered by the private healthcare industry, particularly for professional athletes.
- Most of the studies included in the overview describe patients with long-term or refractory tendinopathy.
- It is not clear whether the procedure might complicate subsequent surgical repair.
- Two studies[7–8] that were included in the original guidance are included in the main extraction table (table 2).
- Ongoing trials:
  - NCT00947765; location: India; RCT [Autologous Blood Injection vs corticosteroid injection for treatment of lateral epicondylitis]; estimated enrolment: 60; estimated completion date: 2008.

References

1. Creaney L, Wallace A, Curtis M et al. (2011) Growth factor-based therapies provide additional benefit beyond physical therapy in resistant elbow tendinopathy: a prospective, double-blind, randomised trial of autologous blood injections versus platelet-rich plasma injections. British Journal of Sports Medicine 45 (12): 966–71

2. Gosens T, Peerbooms JC, van Laar W et al. (2011) Ongoing positive effect of platelet-rich plasma versus corticosteroid injection in lateral epicondylitis: a double-blind randomized controlled trial with 2-year follow-up. American Journal of Sports Medicine 39 (6): 1200–8

3. de Jonge S, de Vos RJ, Weir A et al. (2011) One-year follow-up of platelet-rich plasma treatment in chronic Achilles tendinopathy: a double-blind randomized placebo-controlled trial. American Journal of Sports Medicine 39 (8): 1623–9

4. Kazemi M, Azma K, Tavana B et al. (2010) Autologous blood versus corticosteroid local injection in the short-term treatment of lateral elbow tendinopathy: a randomized clinical trial of efficacy. American Journal of Physical Medicine & Rehabilitation/Association of Academic Physiatrists 89 (8): 660–7

5. Thanasas C, Papadimitriou G, Charalambidis C et al. (2011) Platelet-rich plasma versus autologous whole blood for the treatment of chronic lateral elbow epicondylitis: a randomized controlled clinical trial. American Journal of Sports Medicine 39 (10): 2130–4

6. Kon E, Filardo G, Delcogliano M (2009) Platelet-rich plasma: new clinical application a pilot study for treatment of jumper's knee. Injury: International Journal of the Care of the Injured 40: 598–603

7. Edwards SG, Calandruccio JH (2003) Autologous blood injections for refractory lateral epicondylitis. Journal of Hand Surgery (American Volume) 28: 272–8

8. Suresh SP, Ali KE, Jones H et al. (2006) Medial epicondylitis: is ultrasound guided autologous blood injection an effective treatment? British Journal of Sports Medicine 40: 935–9

Appendix A: Additional papers on autologous blood injection for tendinopathy

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Brown J, Sivan M (2010) Ultrasound-guided platelet-rich plasma injection for chronic patellar tendinopathy: a case report. Physical Medicine and Rehabilitation 2 (10): 969–72	N=1 Follow-up=6 weeks	A marked reduction of resting pain and pain that occurred during active knee range of motion was reported.	Larger studies included in table 2.
Connell DA, Ali KE, Ahmad M et al. (2006) Ultrasound-guided autologous blood injection for tennis elbow. Skeletal Radiology 35: 371–7	N=35 Follow-up=6 months	There was a significant improvement in VAS and Nirschl staging score from baseline ($p<0.001$) following autologous blood re-injection. There were no incidences of infection, neurovascular damage or tendon rupture following the procedure. 71% (25/35) of patients reported temporary pain (resolved within 2 days).	Larger studies included in table 2.

De Vos RJ, Weir A, van Schie HTM et al. (2010) Platelet-rich plasma injection for chronic Achilles tendinopathy. Journal of the American Medical Association 303 (2):144–9	N=54 Follow-up=24 weeks	The mean VISA-A score improved significantly after 24 weeks in the PRP group by 21.7 points (95% confidence interval [CI], 13.0–30.5) and in the placebo group by 20.5 points (95% CI, 11.6–29.4). The increase was not significantly different between both groups (adjusted between group difference from baseline to 24 weeks, −0.9; 95% CI, −12.4 to 10.6).	Larger studies included in table 2.
De Vos RJ, Weir A, Tol JL et al. (2011) No effects of PRP on ultrasonographic tendon structure and neovascularisation in chronic midportion Achilles tendinopathy. British Journal of Sports Medicine 45 (5): 387–92	N=54 Follow-up=24 weeks	A significant improvement in echo-types I+II was found after 24 weeks within both the PRP group (n=27) and the placebo group (n=27), but there was no significant between-group difference (95% CI, −1.6 to 7.8, p=0.169). After 6 weeks, the neovascularisation score increased within the PRP group (p=0.001) and the placebo group (p=0.002), but there was no significant between-group difference in change in neovascularisation score at any point in time.	Larger studies included in table 2.
De Vos RJ, van Veldhove PLJ, Moen MH (2010) Autologous growth factor injections in chronic tendinopathy: a systematic review. British Medical Bulletin 95: 63–77	N=13 studies	All studies showed that injections of autologous growth factors (whole blood and PRP) in patients with chronic tendinopathy had a significant impact on improving pain and/or function over time. However, only 3 studies using autologous whole blood had a high methodological quality assessment, and none of them showed any benefit of an autologous growth factor injection when compared with a control group. At present, there is strong evidence that the use of injections with autologous whole blood	Relevant studies included in table 2 or appendix A.

		should not be recommended. There were no high-quality studies found on PRP treatment. There is limited evidence to support the use of injections with PRP in the management of chronic tendinopathy.	
Filardo G, Kon E, Della villa S et al. (2010) Use of platelet-rich plasma for the treatment of refractory jumper's knee. International Orthopaedics 34: 909–15	N=30 Follow-up=6 months	A statistically significant improvement in all scores was observed at the end of the PRP injections in patients with chronic refractory patellar tendinopathy and a further improvement was noted at 6 months, after physiotherapy was added. Moreover, comparable results were obtained with respect to the less severe cases in the EQ-VAS score and pain-level evaluation, as in time to recover and patient satisfaction, with an even higher improvement in the sport activity-level achieved in the PRP group.	Larger studies included in table 2.
Gaweda K, Tarczynska M, Krzyzanowski W (2010) Treatment of Achilles tendinopathy with platelet-rich plasma. International Journal of Sports Medicine 31 (8): 577–83	N=14 Follow-up=18 months	The AOFAS scale improved from a baseline median of 55 points to 96 points at 18 months, while the VISA-A scale improved from a baseline of 24 to 96 in the final evaluations. During the final evaluation, 1 subject experienced minor pain following prolonged daily activity, while another subject complained of pain following overloading activity.	Larger studies included in table 2.
Gosens T, den Oudsten BL, Fievez E et al. (2012) Pain and activity levels before and after platelet-rich plasma injection treatment of patellar tendinopathy: a prospective cohort study and the influence of previous treatments. International Orthopaedics 36:1941–	N=36 Group1 (n=14): Patients treated before with cortisone and/or surgical treatment Group 2 (n=22): Patients who had not been treated before Follow up =unclear	Mean scores in VISA-patellar questionnaire significantly improved in group 2 from 39.1 to 58.6 at follow-up (p=0.003). The mean score in VISA-patellar questionnaire increased from 41.8 to 56.3 in group 1; this was not a significant change.	Larger studies included in table 2.

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Ibrahim M, Groah L, Libin A et al. (2012) Use of Platelet Rich Plasma for the Treatment of Bicipital Tendinopathy in Spinal Cord Injury: A Pilot Study. Topics in Spinal Cord Injury Rehabilitation 18(1):77–9.	N=8 Follow -up=8 weeks	No adverse events observed. Change in pain score measured using VAS (at baseline2,4,6 and 8 weeks) (p=0.061) in the treated arm but not for the untreated arm.	Larger studies with longer follow-up included in table 2.
James SL, Ali K, Pocock C et al. (2007) Ultrasound guided dry needling and autologous blood injection for patellar tendinosis. British Journal of Sports Medicine 41: 518–21	N=44 Follow-up=mean 15 months	Treatment failure occurred in 6% (3/47) of patients. A significant improvement in VISA score was reported (p<0.001) post-procedure.	Larger studies included in table 2.
Mishra A, Pavelko T (2006) Treatment of chronic elbow tendinosis with buffered platelet-rich plasma. American Journal of Sports Medicine 34: 1774–8	N=20 Follow-up=mean 26 months	At final 26-month follow-up, pain had decreased by 93% (p<0.001) in the group treated by autologous blood injection. No complications including infection, neurovascular changes, or worsening of epicondylar pain.	Larger studies included in table 2.
Monto RR. (2012) Platelet rich plasma treatment for chronic Achilles tendinosis. Foot and Ankle International 33:379–85.	N=30 Follow -up=24 months	Clinical success was achieved in 28 of 30 patients. The average AOFAS score increased from 34 to 88 at 24 months post-treatment. Pretreatment imaging abnormalities present in the Achilles tendon on MRI and ultrasound studies resolved in 27 of 29 patients at 6 months post-treatment.	Larger studies included in table 2.
Omar AS, Ibrahim M E, Ahmed AS et al. (2012) Local injection of autologous platelet rich plasma and corticosteroid in treatment of lateral epicondylitis and plantar fasciitis: Randomized clinical trial. The Egyptian Rheumatologist 34: 43–9	N=60 (30 patients with tennis elbow; [15 platelet rich plasma injection vs 15 steroid injection]; 30 with plantar fasciitis) Follow-up=6 weeks	The VAS score significantly reduced from 8.0 to 3.0 in the PRP group and from 8.6 to 4.3 in the control group (p<0.001). The DASH score significantly reduced from 58.9 to 19.9 in the PRP group and from 57.3 to 20.2 in the control group (p<0.001).	Larger studies with longer follow-up comparing platelet-rich plasma with steroid injections included in table 2.
Owens Jr RF, Ginnetti J, Conti SF et al. (2011) Clinical and magnetic resonance imaging outcomes following	N=14 Follow-up=2 years	The average SF-8 score improved from 24.9 to 30.0, the average FAAM score improved from 55.4 to 65.8, and the	Larger studies included in table 2.

platelet-rich plasma injection for chronic midsubstance Achilles tendinopathy. Foot and Ankle International 32 (11): 1032–9		average FAAMS score improved from 14.8 to 17.4. Complete MRI data were available for 6 patients. Only 1 in 6 Achilles tendons demonstrated qualitative MRI improvement post-injection. Conclusion: Patients who received PRP injection demonstrated modest improvement in functional outcome measures, however MRI appearance of diseased Achilles tendons remained largely unchanged following PRP injection.	
Ozturan KE, Yucel I, Cakici H et al. (2010) Autologous blood and corticosteroid injection and extracorporeal shock wave therapy in the treatment of lateral epicondylitis. Orthopedics 33 (2): 84–91	N=60 Follow-up=8 weeks	Autologous blood injection and extracorporeal shock wave therapy gave significantly better Thomsen provocative test results and upper extremity functional scores at 52 weeks; the success rate of corticosteroid injection was 50%, which was significantly lower than the success rates for autologous blood injection (83.3%) and extracorporeal shock wave therapy (89.9%). Corticosteroid injection provided a high success rate in the short term. However, autologous blood injection and extracorporeal shock wave therapy gave better long-term results, especially considering the high recurrence rate with corticosteroid injection.	Larger studies included in table 2.
Pearson J, Rowlands D, Highet R (2012) Autologous blood injection to treat achilles tendinopathy? A randomized controlled trial. Journal of Sport Rehabilitation 21 (3) 218–24.	N=33 patients (40 injured Achilles tendons: 20 autologous blood injection vs 20 control) Follow-up=12 weeks	At 12 weeks, VISA-A score improved to 18.9 units (SD 7.4) in the treatment group (n=12), revealing a blood-injection effect of 9.6 units (SD11.5), relative to a comparatively unchanged condition in the control group (9.4 units; SD9.0) (n=14). 21% rate of severe	Studies with longer follow-up included in table 2.

		worsening of pain (over 48 hours following injection) was reported.	
Peerbooms JC, Sluimer J, Bruijn DJ et al. (2010) Positive effect of an autologous platelet concentrate in lateral epicondylitis in a double-blind randomized controlled trial: platelet-rich plasma versus corticosteroid injection with a 1-year follow-up. American Journal of Sports Medicine 38 (2): 255–62	N=100 Follow-up=1 year	The results showed that, according to the visual analogue scores, treatment was successful in 24 of the 49 patients (49%) in the corticosteroid group and 37 of the 51 patients (73%) in the PRP group, which was significantly different (p<0.001). Furthermore, according to the DASH scores, treatment was successful in 25 of the 49 patients (51%) in the corticosteroid group and 37 of the 51 patients (73%) in the PRP group, which was also significantly different (p=0.005). The corticosteroid group initially had improvement and then declined, whereas the PRP group had progressive improvement.	This study is an interim report and study with longer follow-up (Gosens 2011) is included in table 2.
Randelli P, Arrigoni P, Ragone V et al. (2011) Platelet rich plasma in arthroscopic rotator cuff repair: a prospective RCT study, 2-year follow-up. Journal of Shoulder and Elbow Surgery 20 (4): 518–28	N=53 Follow-up=2 years	There were no significant differences in the healing between the PRP and control group after 6, 12, 24 months.	Larger studies included in table 2.
Sampson S, Aufiero D, Meng M et al. (2011) Platelet-rich plasma therapy as a first-line treatment for severe Achilles tendon tear: a case report. International Journal of Therapy and Rehabilitation 18 (2): 101–7	N=1 Follow-up=24 weeks	At 24 weeks post-injection, the tear was completely resolved on MRI and the patient returned to full functional activity. Conclusions: Currently there are limited data, with mixed results, regarding PRP treatment for Achilles tendinopathy, and limited reports of using PRP in humans within the first few weeks of injury.	Larger studies included in table 2.
Schepull T, Kvist J, Norrman H et al. (2011) Autologous platelets have no effect on the healing of human Achilles tendon ruptures: a randomized single-	N=30 Follow-up=1 year	In patients with acute Achilles tendon tear, complications reported included tendon re-rupture and infection.	Larger studies included in table 2.

blind study. The American Journal of Sports Medicine 39 (1): 38–47			
Sheth U, Simunovic N, Klein, G et al. (2012) Efficacy of autologous platelet-rich plasma use for orthopaedic indications: a meta-analysis. Journal of Bone and Joint Surgery, American Volume 94 (4) 298–308	N=446 Follow-up=24 months	The use of platelet-rich plasma (PRP) provided no significant benefit up to (and including) 24 months across the randomised trials (standardised mean difference, −0.34; 95% confidence interval [CI], −0.75 to 0.06) or the prospective cohort studies (standardised mean difference, −0.20; 95% CI, −0.64 to 0.23).	The meta-analysis pooled results for patients treated by PRP for a variety of orthopaedic indications.
Volpi P, Quaglia A, Schoenhuber H et al. (2010) Growth factors in the management of sport-induced tendinopathies: results after 24 months from treatment. A pilot study. Journal of Sports Medicine and Physical Fitness 50 (4): 494–500	N=15 Follow-up=24 months	After 90 days the VISA score significantly improved from 36±12 (range 21–64) to 74±17 (range 40–92). Reduction of irregularities was found in 80% of the tendons. After 24 months patients reported an average VISA score of 73±16 (range 42–100). No changes in IL, TNF-alpha and interferon gamma were observed. VEGF, EGF and CCL2 decreased progressively from 30 minutes to 3 hours after the treatment and returned to near the baselines after 24 hours.	Larger studies included in table 2.
Wolf JM, Ozer K, Scott F et al. (2011) Comparison of autologous blood, corticosteroid, and saline injection in the treatment of lateral epicondylitis: a prospective, randomized, controlled multicenter study. Journal of Hand Surgery - American Volume 36:1269–72.	N=34 (9 autologous blood injection vs 9 steroid injection vs 10 saline) Follow-up =6 months	There were no significant differences in DASH scores among the 3 groups; mean score of 20 for autologous blood compared with 13 for steroid injections and 10 for saline at 6-month follow-up.	Larger studies with longer follow-up included in table 2.

Appendix B: Related NICE guidance for autologous blood injection for tendinopathy

Guidance	Recommendations
Interventional procedures	**Extracorporeal shockwave therapy for refractory Achilles tendinopathy. NICE interventional procedure guidance 312 (2009)** 1.1 The evidence on extracorporeal shockwave therapy (ESWT) for refractory Achilles tendinopathy raises no major safety concerns: there have been reports of occasional tendon rupture in treated patients, but this may also occur when the procedure has not been used. However, current evidence on efficacy of the procedure is inconsistent. Therefore, ESWT for refractory Achilles tendinopathy should only be used with special arrangements for clinical governance, consent and audit or research. 1.2 Clinicians wishing to undertake ESWT for refractory Achilles tendinopathy should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients understand the uncertainty about the procedure's efficacy, and about its safety in relation to a possible risk of tendon rupture, and provide them with clear written information. In addition, the use of NICE's information for patients ('Understanding NICE guidance') is recommended. • Audit and review clinical outcomes of all patients having ESWT for refractory Achilles tendinopathy (see section 3.1). 1.3 NICE encourages further research into ESWT for refractory Achilles tendinopathy. Future research should take the form of clinical studies with clearly described patient selection and treatment protocols, including a description of local anaesthesia use and the type of energy applied (see section 2.5). The studies should include validated outcome measures and be based on a minimum of 1-year follow-up. NICE may review the procedure on publication of further evidence. **Extracorporeal shockwave therapy for refractory plantar fasciitis. NICE interventional procedure guidance 311 (2009)** 1.1 The evidence on extracorporeal shockwave therapy (ESWT) for refractory plantar fasciitis raises no major safety concerns; however, current evidence on its efficacy is inconsistent. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research. 1.2 Clinicians wishing to undertake ESWT for refractory plantar fasciitis should take the following actions.

	• Inform the clinical governance leads in their Trusts. • Ensure that patients understand the uncertainty about the procedure's efficacy and provide them with clear written information. In addition, the use of NICE's information for patients ('Understanding NICE guidance') is recommended. • Audit and review clinical outcomes of all patients having ESWT for refractory plantar fasciitis (see section 3.1). 1.3 NICE encourages further research into ESWT for refractory plantar fasciitis. Future research should take the form of clinical studies with clearly described patient selection and treatment protocols, including a description of local anaesthesia use and the type of energy applied (see section 2.5). The studies should include validated outcome measures and be based on a minimum of 1-year follow-up. NICE may review the procedure on publication of further evidence. **Extracorporeal shockwave lithotripsy for calcific tendonitis (tendinopathy) of the shoulder. NICE interventional procedure guidance 21 (2003)** 1.1 Current evidence on the safety and efficacy of extracorporeal shockwave lithotripsy for calcific tendinopathy of the shoulder appears adequate to support the use of the procedure, provided that normal arrangements are in place for consent, audit and clinical governance.

Appendix C: Literature search for autologous blood injection for tendinopathy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	26/09/2012	September 2012
Database of Abstracts of Reviews of Effects – DARE (CRD website)	26/09/2012	September 2012
HTA database (CRD website)	26/09/2012	September 2012
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	26/09/2012	September 2012
MEDLINE (Ovid)	26/09/2012	1946 to September Week 2 2012
MEDLINE In-Process (Ovid)	26/09/2012	September 25, 2012
EMBASE (Ovid)	26/09/2012	1974 to 2012 Week 38
CINAHL (NLH Search 2.0 or EBSCOhost)	26/09/2012	N/A
JournalTOCS	26/09/2012	N/A

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1 Tendinopathy/
2 Tendonit$.tw.
3 tendinit$.tw.
4 Tendinop$.tw.
5 Tendon Injuries/
6 (tendon$ adj3 injury$).tw.

7 Tenosynovitis/
8 Tenosynov$.tw.
9 exp Bursitis/
10 ((Inflammat$ or irritat$ or Pain$) adj5 (elbow$ or ankle$ or hip$ or wrist$ or knee$ or patella$ or shoulder$ or tendon$ or bursa$)).tw.
11 ((peri-achill$ or peri achill$ or periachill$) adj5 tendonit$).tw.
12 Bursit$.tw.
13 ((Tennis$ or golfer$) adj5 elbow$).tw.
14 Tennis Elbow/
15 (Housemaid$ adj5 knee$).tw.
16 (prepatell$ adj5 bursit$).tw.
17 Cumulative Trauma Disorders/
18 (Repetit$ adj5 strain$ inju$).tw.
19 RSI.tw.
20 (Cumulat$ adj5 trauma$ disord$).tw.
21 or/1-20
22 exp Blood Transfusion, Autologous/
23 (blood adj5 (inject$ or autolog$ or transfus$)).tw.
24 or/22-23
25 21 and 24
26 Animals/
27 Humans/
28 26 not (26 and 27)
29 25 not 28
30 from 29 keep 1-40