



Draft manuscript for review

**Sclerosing polidocanol injections in mid-portion Achilles tendinosis:
remaining good clinical results and decreased tendon thickness at 2-year
follow-up**

Journal:	<i>Knee Surgery, Sports Traumatology, Arthroscopy</i>
Manuscript ID:	KSSTA-05-0315
Manuscript Type:	Original Article
Date Submitted by the Author:	28-Dec-2005
Complete List of Authors:	Lind, Bengt; Radiology, Radiology Öhberg, Lars; Radiology, Radiology Alfredson, Håkan; University of Umeå, Sports Medicine Unit, Dept of Surg and perioperative Science
Keywords:	Achilles tendinosis, treatment, sclerosing injections, ultrasound, Doppler

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3 **Sclectrosing Polidocanol injections in mid-portion Achilles tendinosis:**
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6 **remaining good clinical results and decreased tendon thickness at 2 year**
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8
9 **follow up.**

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11 Bengt Lind¹, Lars Öhberg¹, and Håkan Alfredson²
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18 Department of Radiology¹, Sports Medicine Unit, Department of Surgical and Perioperative
19 Science, Department of Musculoskeletal Research, National Institute for Working Life²,
20 University of Umeå, S-901 87 Umeå, Sweden
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31 Corresponding author: Håkan Alfredson, Professor,
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33 Sports Medicine Unit, Department of Surgical and Perioperative Science, Umeå University,
34 901 87 Umeå, Sweden
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38 Telephone 46-90-7853951
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40 Fax: 46-90-135692
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42 e-mail: hakan.alfredson@idrott.umu.se
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Abstract

The short-term results after treatment with sclerosing polidocanol injections have been shown to be good in patients with chronic painful mid-portion Achilles tendinosis. This study aimed to evaluate the longer term effects on tendon thickness, structure and vascularity, patient satisfaction with treatment, and pain during tendon loading activity. Ultrasonography (US)+Colour Doppler (CD) was used for evaluation of the tendon, and the patients graded the amount of pain during tendon loading activity on a VAS.

Forty-one patients-tendons (23 men and 18 women, mean age 53 years) with a long duration (mean 33 months) of pain symptoms from mid-portion Achilles tendinosis (US+CD showed a localised thickening, structural changes and neovascularisation), were at 3 (mean) occasions (6-8 weeks in between) treated with US and CD-guided injections of the sclerosing substance Polidocanol, targeting the area with neovessels ventral to the tendon. After treatment, 36 patients were satisfied with the results of the treatment and back to previous (before injury) activity level. At the 2-year follow up (mean 23 months), 37 patients were satisfied with the results of the treatment, and there was a significant reduction in VAS (from 75 to 7; $p<0.05$). US showed a significant reduction in the mean mid-portion tendon thickness (from 10 mm to 8 mm, $p<0.05$) and a "more normal" structure. CD showed no, or few, remaining neovessels in the majority of the successfully treated tendons.

In conclusion, treatment with sclerosing polidocanol injections in patients with chronic painful mid-portion tendinosis showed remaining good clinical results at 2-year follow-up. Decreased tendon thickness and improved structure after treatment might indicate a remodelling potential?

Introduction

Chronic painful Achilles tendinopathy was for many years considered to be a troublesome condition to treat [8,9,10]. However, new methods for treatment such as painful eccentric calf muscle training has been shown to give good clinical results, allowing for the patients to return to Achilles tendon loading physical activity [1]. Recently, a new type of injection therapy was introduced. In pilot studies, were the sclerosing agent Polidocanol under US and CD guidance was injected in the area with neovessels ventral to the tendon, promising short-term clinical results have been demonstrated [3,17]. Treatment with sclerosing injections is based on US and CD findings, together with immuno-histochemical studies of tendon biopsies, showing neovessels in painful but not pain-free tendons [16], and sensory nerves travelling together with the vessels [4,6]. Sclerosing therapy with polidocanol is widely used for treating varicose veins as well as teleangiectases, and very few side effects have been reported [5,7,14]. Polidocanol has a selective effect in the vascular intima causing thrombosis of the vessel. The agent also has an effect if the injection is performed outside the vessels, which is important when very small vessels are being targeted. It is plausible that the sclerosing effect of polidocanol on the vessels, might also affect nerves adjacent to the neovessels, either directly (by destruction) or indirectly (by ischaemia).

US is well known to be a reliable and cost effective method to study tendon structure [11,15], and simultaneous CD examination allows for studies of blood flow [12,13,16]. The normal tendon blood flow cannot be visualised due to the relatively low flow rate, but high flows, like in neovessels seen in the chronic stage of Achilles tendinosis, can often be detected.

The longer-term effects of treatment with sclerosing polidocanol injections are not known, and it is of interest to study the effects on tendon pain, structure and vascularity. The aims with this prospective study were to clinically and sonographically (US+CD) follow patients

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that have been treated with sclerosing Polidocanol injections for chronic painful mid-portion
Achilles tendinosis.

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Material and methods

Forty-one patients-tendons (23 men and 18 women, mean age 53 years, range 34-78) with the diagnose chronic painful mid-portion Achilles tendinosis, that had been treated with sclerosing polidocanol injections at the Sports Medicine Unit in Umeå, Sweden, were included.

Patients with mid-portion tendinosis, that previously (before sclerosing injection treatment) had been treated with intra- or peri-tendinous cortisone injections, were not included.

Gray-scale ultrasonography (US) and colour Doppler (CD) examination

All tendons were examined with high resolution grey scale-ultrasound and with colour doppler (CDV), Acuson Segovia (Siemens). A linear multifrequency (8 – 13 MHz) probe was used. Pathological changes (tendon thickness and structure) in the Achilles tendon were recorded. Colour Doppler was used to diagnose neovascularisation and to locate where the vessels entered the tendon. The same experienced radiologist performed all US and CD examinations.

Treatment with sclerosing polidocanol injections

Polidocanol (5 mg/ml) was used as sclerosing agent. Polidocanol has a sclerosing effect (primarily acting on the intima layer in the vascular wall), and a local anaesthetic effect. The active substance is an aliphatic non-ionised nitrogen-free surface anaesthetic. Participants lay in prone position. Before the treatment the skin was washed with a solution of chlorhexidine and alcohol. The skin was draped with a sterile paper-cover exposing only the middle part of the Achilles tendon. For injection, a 0.7 x 50 mm needle connected to a 2 ml syringe, was used. The injection was performed dynamically, with the aid of real-time grey-scale ultrasonography and colour doppler technique, to inject at the target vessels. The ultrasound

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3 probe was held on the dorsal side of the Achilles tendon, parallel with the fibres. The injection
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5 was always done from the medial side of the tendon to minimise the risk of contact with the
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7 sural nerve. When the tip of the needle was positioned correctly, a small amount of
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9 Polidocanol was injected in fractions until the vessels were no longer visible at all. Small
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11 volumes (1-2 ml) of polidocanol were injected into the area with local neovascularisation
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13 outside the ventral part of the Achilles tendon. All patients were pain-free immediately after
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15 the injection (local anaesthetic effect), but the symptoms returned after a few hours. The
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17 patients were allowed free activity such as; walking, bicycling, and light strength training the
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19 first 2 weeks after treatment. After 2 weeks, free tendon loading activity was allowed.
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21 The patients were followed up 6-8 weeks after treatment, and if there was remaining pain
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23 together with remaining neovessels in the area with structural changes, a second injection
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25 treatment was given. If there was no pain during tendon loading activity, no treatment was
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27 given.
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36 Outcome measures

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38 At baseline and at follow-ups, we assessed participants Achilles tendon pain during activity.
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40 Using a visual analogue scale (VAS) for pain, the patients recorded the amount of pain during
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42 their type of Achilles tendon loading activity on a 100 mm-long scale. Runners registered
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44 pain during or after running, walkers during walking etc. The amount of pain was recorded
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46 from 0-100 mm, where no pain is recorded as 0 and severe pain as 100. Patient satisfaction
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48 with treatment was also recorded, defined as satisfied or not satisfied with result of treatment.
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50 At baseline and at follow-ups, using US and CD, the same experienced radiologist (L.Ö)
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52 examined all tendons. Tendon thickness was measured at the thickest part of the mid-portion
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54 and tendon structure was observed. Unfortunately, there is no reliable method to quantify
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56 vascularity-flow in tendons. Therefore, the neovascularisation in the Achilles tendon was
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3 estimated as (0), (1+), (2++), (3+++), (4+++++) according to the appearance of vessels inside
4 the tendons. When there were no visible vessels the estimation was (0). When there were one
5 or two small vessels, mostly in the posterior part of the tendons, the estimation was (1+).
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10 When there were several irregular vessels throughout the tendon the estimation was (2+ to
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13 4+).

18 **Ethics**

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21 The study was approved by the ethical Committee of the Medical Faculty, University of
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23 Umeå, Sweden.
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28 **Statistics**

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30 Results are presented as mean and range.

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33 Wilcoxon Signed Ranks Test was used to study the differences in VAS, and tendon
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35 thickness, before and after treatment.
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38 A p-value < 0.05 was considered significant.
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42 **Results**

43 *Before treatment*

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46 Basic characteristics and activities are shown in Table 1.

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49 Before treatment with sclerosing polidocanol injections, all patients had a painful thickening
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51 in the Achilles tendon mid-portion. US showed a thickening (mean 10 mm), including
52
53 irregular tendon structure and hypo-echoic areas, corresponding to the painful area. CD
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55 showed a neovascularisation inside and outside the area with structural changes.
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59 Forty-one tendons in 41 patients (23 men and 18 women) were treated with a mean of 3
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Polidocanol injection treatments, with 6-8 weeks in between.

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3 The mean VAS before treatment was 75 (range 27-99)
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8 *After treatment*
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10 After treatment, 36/41 patients (tendons) were satisfied with the results of the treatment and
11 back to previous (before injury) activity level. The mean VAS was significantly ($p < 0.05$)
12 reduced to 10 (range 0-43).
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17 Five patients were not satisfied with the result of the treatment (2 patients were later
18 surgically treated).
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22 Four of these patients had remaining vascularity in the structurally abnormal and thick tendon.
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24 In one patient, there were no remaining neovessels, but remaining structural changes.
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27 *2-year follow-up*
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29 At the 2-year follow-up (mean 23 months), 37 patients (tendons) were satisfied with the
30 results of treatment and active at desired level of Achilles tendon loading activity.
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34 One patient that initially was not satisfied with the result after the treatment and then had no
35 remaining neovessels, was now satisfied and had no remaining neovessels.
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38 The mean VAS was 7 (range 0-45). From baseline there was a significant reduction in VAS
39 (from 75 to 7; $p < 0.05$). The mean tendon thickness was significantly reduced compared to
40 baseline (from 10 to 8mm, $p < 0.05$). In the successfully treated tendons, the tendon structure
41 had an ultrasonographically “more normal” appearance in 30 tendons, but in 7 tendons minor
42 structural abnormalities remained. There were no remaining neovessels in 29 tendons, but a
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few (1+ and 2+) remaining neovessels in 8 tendons.

Discussion

This study shows remaining good clinical results, decreased tendon thickness, and “ultrasonographically improved” tendon structure, at the 2-year follow-up after treatment with sclerosing polidocanol injections for chronic painful mid-portion Achilles tendinosis.

US is a reliable method to measure tendon thickness and study structure [11,15,16]. However, it is important to add that considering tendon structure, an ultrasonographically normal looking structure does not exclude the possibility of tendinotic changes. For the purpose to properly evaluate tendon structure, US needs to be combined with biopsies [10].

The findings of a decreased tendon thickness and a “more normal” structure are similar to what our group previously have been reported in a US follow-up of patients who were treated with painful eccentric calf muscle training [18]. Interestingly, chronic painful tendinosis tendons has for many years been considered to be degenerated and weak [8], indicating a poor state with no remodelling capacity. However, the results of these follow-up studies together, clearly demonstrates findings resembling a remodelling of the tendon. It should also be kept in mind that the patients involved in these studies have a mean age that is relatively high (>50 years), but despite that it seems that after successful treatment there is potential for the tendon to regain a more normal thickness and structure. Also, there were no partial or total ruptures among the tendons in the current study, and in the previous study on eccentric training [18], indicating that these tendons are most likely not weak. Studies focusing on evaluation of tensile strength in normal and tendinosis tendons are consequently of high interest.

In the current study, at follow-up there was no remaining vascularity in 29/37 of the tendons.

However, because there was no reliable method to quantify vascularity, we couldn't involve vascularity in the statistical evaluation. Evaluation of vascularity is very much operator dependant, and factors like angulation and pressure on the probe markedly affect the results.

Standardisation of the procedure is a major problem, and to try to limit the risk for errors, the

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3 same experienced radiologist did all examinations in our study. It is interesting to notice that
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5 in 8/37 pain-free tendons there were still some remaining neovessels. This could possibly
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7 indicate that the most important effects of polidocanol injection treatment are actions on
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9 nerves? However, only a few neovessels were seen in these tendons and compare to before
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11 treatment the amount of neovessels was decreased also in these tendons. We yet don't know
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13 whether the beneficial effects of polidocanol injections are due to effects on nerves, vessels,
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15 or a combination. Theoretically, there might be a critical point upon were the vascularity is
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17 symptomatic? Or, maybe the vessels mainly are guiding us to find the nerves, that have been
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19 shown to be localised in close relation to the vessels [4]. Also, the nerves are predominantly
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21 Substance-P (SP)- and Calcitonin Gene Regulated Peptide (CGRP) nerves [4,6], well known
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23 to be potent vasodilators, and interference with these nerves might potentially cause a
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25 secondary vasodilatation of importance for the effects of the treatment? US and CD follow-
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27 ups from day to day after treatment, could possibly add information about the tendon
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29 vascularity, helping to understand mechanisms of importance.
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36 Our technique for treatment with sclerosing polidocanol injections seems to be safe, because
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38 there were no complications in the current study material. There has been no local irritation in
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40 the skin, and no cases with subcutaneous fat atrophy, something that sometimes is seen after
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42 local cortisone injections. Despite that the patients were allowed to go back to full Achilles
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44 tendon loading activity already 2 weeks after treatment, there are no tendon ruptures in this
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46 follow-up material. However, one patient that was excluded from this follow-up material
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48 because he had been treated with multiple intra-tendinous cortisone injections before
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50 treatment with sclerosing polidocanol injections, sustained a total rupture after treatment.
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52 There is also one patient treated for insertional tendinosis (not in focus for this follow-up)
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54 who sustained a total rupture 8 weeks after treatment.
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3 In conclusion, in this 2-year follow-up, treatment with sclerosing polidocanol injections
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5 showed remaining good clinical results in patients with chronic painful mid-portion
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7 tendinosis. Decreased tendon thickness and improved structure after treatment might indicate
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9 a remodelling potential for the chronic painful Achilles tendinosis tendon?
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Acknowledgements

Financial support was obtained from the Swedish National Centre for Research in Sports.

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Table 1.

Basic data on the 37 patients with chronic painful mid-portion Achilles tendinosis that have been successfully treated with sclerosing polidocanol injections.

Variable	
Sport or recreational activity	
Walking	(n=16)
Jogging	(n=11)
Skiing*	(n=3)
Aerobics	(n=3)
Soccer	(n=1)
Floor-ball	(n=1)
Body-building	(n=1)
Golf	(n=1)
* Cross country skiing	
Duration of symptoms (months)	33 (mean) (range 5-240)
Body characteristics (mean+range)	
Age (years)	53 (34-78)
Height (cm)	170 (158-192)
Weight (kg)	81 (56-120)

Legends to the figures

Figure 1 A-C.

Ultrasound (US) and colour Doppler (CD) findings before and after treatment with sclerosing injections in a patient with chronic painful mid-portion Achilles tendinosis.

- A. Before treatment. There is a thickening in the mid-portion of the tendon, including an irregular structure with hypo-echoic areas. CD is showing neovessels (coloured structures) inside and ventral to the thickened tendon.
- B. After treatment with 3 polidocanol injections. There is a thickening in the mid-portion of the tendon, including minor irregularities in the structure. There are no neovessels (coloured structures) inside the thickened tendon.
- C. Follow-up after 2 years. The tendon thickness in the mid-portion of the tendon has decreased. There is a more normal tendon structure and no hypo-echoic areas. There are no neovessels.

Figures 1 A-C

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1B

1C

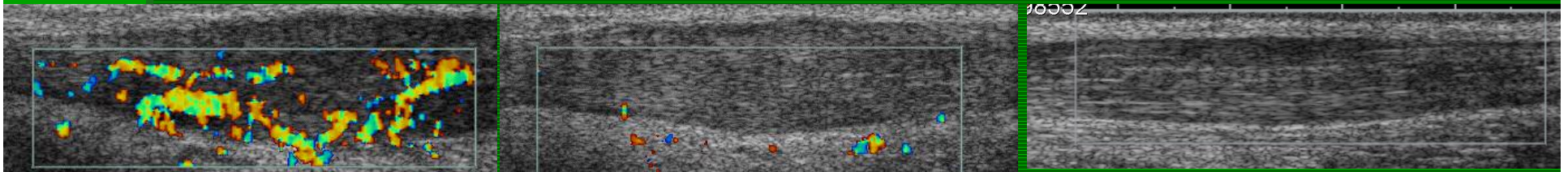


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Aerobics	(n=3)
Soccer	(n=1)
Floor-ball	(n=1)
Body-building	(n=1)
Golf	(n=1)
* Cross country skiing	
Duration of symptoms (months)	33 (mean) (range 5-240)
Body characteristics (mean+range)	
Age (years)	53 (34-78)
Height (cm)	170 (158-192)
Weight (kg)	81 (56-120)