

Achilles and patellar tendinopathy display opposite changes in elastic properties: A shear wave elastography study

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B. Coombes, K. Tucker, B. Vicenzino, V. Vuvan, R. Mellor, et al.. Achilles and patellar tendinopathy display opposite changes in elastic properties: A shear wave elastography study. Scandinavian Journal of Medicine and Science in Sports, 2018, 28 (3), pp.1201-1208. 10.1111/sms.12986 . hal-03409609

HAL Id: hal-03409609 https://hal.science/hal-03409609v1

Submitted on 30 Jun2022

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1	Achilles and patellar tendinopathy display opposite changes in elasticity: An ultrasound
2	shear wave elastography study.
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22	Running Head: Tendinopathy: A shearwave elastography study
23	Acknowledgements: The authors thank Wolbert Van den Hoorn and Ilze Willis for assistance

with Matlab.

Funding source: Dr Coombes is in receipt of a University of Queensland Postdoctoral
Fellowship for Women and received a travel fellowship by the France-Australia Science
Innovation Collaboration. Support was received from The French Ministry of Sport (17-
R-04) for publication costs.
Conflict of Interest: No conflict of interest, financial or otherwise, are declared by the
authors.
Original research
Word count 2868

35 ABSTRACT

Purpose: To compare tendon mechanical properties (elastic modulus) and structural
properties (thickness) of healthy individuals with those with Achilles or patellar
tendinopathy.

39 Methods: Sixty-seven participants (22 Achilles tendinopathy, 17 patellar tendinopathy, 28 40 healthy controls) were recruited between March 2015-March 2016. Shear wave velocity 41 (SWV), an index of tissue elasticity, and tendon thickness were measured bilaterally at mid-42 tendon and insertional regions of Achilles and patellar tendons by an examiner blinded to 43 group. Analysis of covariance, adjusted for age, body mass index and sex was used to 44 compare differences in tendon thickness and SWV between the two tendinopathy groups 45 (relative to controls) and regions. Tendon thickness was included as a covariate for analysis 46 of SWV.

47 Results: Compared to controls, participants with Achilles tendinopathy had lower SWV at the

48 distal insertion (Mean difference MD; 95% CI: -1.56; -2.49 to -0.62 m/s; P<0.001), and

49 greater thickness at the mid-tendon (MD 0.19; 0.05 to 0.33 cm; *P*=0.007). Compared to

50 controls, participants with patellar tendinopathy had higher SWV at both regions (MD 1.25;

51 0.40 to 2.10 m/s; *P*=0.005), and greater thickness proximally (MD 0.17; 0.06 to 0.29 cm;

52 *P*=0.003).

Conclusion: Compared to controls, participants with Achilles and patellar tendinopathy
displayed lower Achilles tendon elasticity and higher patellar tendon elasticity respectively.
More research is needed to explore whether maturation, aging or chronic load underlie these
findings and whether current management programs for Achilles and patellar tendinopathy
need to be tailored to the tendon.

58

59 Key words: jumper's knee; Aixplorer; ultrasound, elasticity, stiffness, musculoskeletal,

60 rehabilitation, pain

62 INTRODUCTION

Painful disorders of the Achilles and patellar tendons are a major problem in competitive and
recreational sports as well as the sedentary population. More than half (52%) of elite runners
develop Achilles tendinopathy during their lifetime,¹ while the prevalence of current or
previous patellar tendinopathy in volleyball or basketball athletes is similar (50-55%).²
Ultrasonography is widely used for diagnosis of tendinopathy, however classical ultrasound
findings show limited correlation with symptoms^{3, 4} and lack fundamental information on
tissue mechanical properties.

70

Shear wave elastography is a relatively new ultrasound imaging technique that allows noninvasive estimation of soft-tissue viscoelastic properties in vivo by measurement of Shear Wave Velocity (SWV) (in meters per second) generated by the ultrasound pulse.⁵
Importantly, as the SWV may be determined from a relatively small region of tissue (as opposed to the whole structure) it can provide direct measurement of specific regions of interest within tendon,^{6, 7} which is important because discrete areas of pathology are reported in people with tendinopathy.⁸

78

79 Using this technique, lower elasticity was demonstrated in patients with Achilles tendinopathy,^{9,10} whereas both higher¹¹ and lower¹⁰ elasticity were reported in separate 80 81 studies of patients with patellar tendinopathy. By estimating patellar tendon stiffness from the 82 relationship between the force applied to the tendon and its associated proximal insertion displacement assessed through B-mode ultrasound, inconsistent findings are also reported (no 83 change¹² or decreased⁸ stiffness). However, this indirect method to assess tendon stiffness has 84 85 two major drawbacks: i) the tendon force is indirectly estimated (as the force is applied externally to a body segment, rather than directly on the tendon), and ii) only global 86

87 properties of the whole tendon can be estimated. This is surprising given the similar histological appearance in patellar and Achilles tendinopathy,¹³ but other factors, including 88 age, body composition and training might also modulate the mechanical properties of 89 tendon.¹⁴ For example, athletes with patellar tendinopathy are significantly younger (mean 90 91 age 23 \pm 3 years), taller (mean height 185 \pm 10 cm) and heavier (mean weight 77 \pm 11 kg), although of similar body mass index (BMI) (mean BMI 23 $\pm 2 \text{ kg/m}^2$) than those without 92 93 symptoms.¹⁵ In comparison, participants with Achilles tendinopathy are older (mean age $53 \pm$ 12 years) and have higher BMI (mean 35 $\pm 8 \text{ kg/m}^2$) than control participants.¹⁶ 94

95

96 Methodological differences surrounding measurement of tendon properties may also contribute to the variability between studies.¹⁷ Of relevance to the shear wave elastography 97 98 technique for tendons, shear wavelengths can be greater than tendon thickness, leading to guided wave propogation.¹⁸ Within this context, the relationship between group velocity of 99 100 the shear wave estimated by commercialized ultrasound shear wave elastography techniques 101 and tendon elasticity is affected by tendon thickness. Thus, information about both SWV and 102 thickness must be sought to interpret changes in SWV as changes in elasticity. In addition, some authors9 have reported measurement artefacts during shear wave elastography 103 104 acquisition, including signal void areas within an elastogram. While their presence has been suggested to be a potential marker of intratendinous damage,⁹ comprehensive evaluation of 105 106 its presence is lacking.

107

108 The purpose of our study was to determine whether tendon elasticity and thickness of healthy 109 individuals differ from those with Achilles or patellar tendinopathy using shear wave 110 elastography. We proposed that regional differences in SWV and thickness would be present 111 in those with tendinopathy compared to controls. As other factors may also modulate the elastic properties of connective tissues, we also investigated the relationship between SWV
and age, sex and BMI. Last, we aimed to quantify elastography signal void in tendinopathic
and healthy tendon.

115

116 MATERIALS AND METHODS

117 Participants with or without tendinopathy were consecutively recruited by social media and 118 local advertisement between March 2015 and March 2016. Inquiries were directed to an 119 online screening questionnaire and eligible participants were invited to attend physical 120 screening by a musculoskeletal physiotherapist not involved in testing. The inclusion criteria 121 for patients with tendinopathy were self-reported tendon pain over the Achilles or patellar 122 tendon of at least 20 on a 0-100 numerical rating scale (NRS), and of duration 12 weeks or 123 more. Physical examination confirmed tendon pain on palpation and loading (by calf raise or 124 decline squat). The number of single leg calf raises or decline squats performed before pain 125 onset was recorded. Exclusion criteria were corticosteroid injection (in previous 6 months), 126 local surgery or other specific pathology (e.g., fracture, diabetes, inflammatory, systemic or 127 neurological disease, malignancy, radiculopathy). All participants were excluded if they had 128 experienced back or other leg symptoms requiring treatment or limiting work/sport in the 129 previous six months. This study was approved by the University of Queensland Medical 130 Research Ethics Committee and all participants provided written informed consent.

131

Participants with tendinopathy completed either the Achilles¹⁹ or Patellar²⁰ versions of the
Victorian Institute of Sport Assessment (VISA), to provide validated information about pain
and disability for their (most) affected leg. Total scores range from 0 to 100, 100 representing
an asymptomatic, fully performing individual. In addition to basic demographic information
(age, sex, height and weight), all participants completed the Active Australia Questionnaire,

to measure physical activity during the preceding week.²¹ Total activity time (minutes) was
calculated by adding the time spent in walking and moderate activity and twice the time spent
in vigorous activity.

140

Elastography acquisition Upon arrival participants rested in lying for five minutes prior to
examination using the supersonic shear imaging technique (Aixplorer version 8.2, Supersonic
Imagine, Aix-en-Provence, France) with 50 mm linear transducer (15-4MHz). A single
operator (BKC) performed all scans to eliminate inter-observer variability.²² Interday
reliability was examined by testing both legs in six healthy participants on two occasions
separated by 48 hours. Intraclass correlation coefficients (ICC) ranged from 0.71 to 0.80 for

147 measurement of SWV and 0.78 to 0.97 for thickness measurements (Table 1).

148

149 Examination was performed blind to the physical examination and group by scanning 150 bilateral patellar and Achilles tendons in a randomised order for all participants. For Achilles 151 measurements, participants lay in prone with their leg extended and ankle resting over the 152 edge of the plinth. The participant's resting ankle angle was measured using a hand-held 153 goniometer. For patellar tendon measurement, participants lay in supine, supported in 30° 154 knee flexion and neutral hip rotation. Based on previous report of the slack angle of the Achilles tendon $(43.7\pm3.2^{\circ} \text{ plantarflexion})^{23}$ and unpublished observations of the patellar 155 156 tendon, both positions were assumed to have some passive tension on the respective tendons. 157 The amount of signal void within each ROI, defined as the percentage of all pixels without 158 elastography colour was also calculated. For SWV measurement, we made sure that regions 159 with signal void were not confused with a low value. Participants were told to remain 160 completely relaxed during testing.

162 The ultrasound transducer head was aligned in the longitudinal plane with collagen fibres, applying minimal pressure.²⁴ Tendon thickness was measured from longitudinal B-mode 163 images using the inbuilt Aixplorer distance function. For the Achilles tendon, the maximum 164 165 perpendicular distance between anterior and posterior tendon boundaries was measured over 166 the free tendon (2-4 cm proximal to the Achilles insertion) and immediately proximal to the 167 calcaneal attachment. For the patellar tendon, the maximum perpendicular distance 168 immediately distal to the apex of the patellar and at the midpoint between patellar and tibial 169 attachments was measured. Using the shear wave elastography mode (penetration; 170 persistence low; smoothing 5), the transducer was held for ~ 10 s duration, and two or three 171 measurements were repeated in each location. For the Achilles tendon, separate images were 172 collected for measurement of mid-tendon and insertional regions, while both patellar regions 173 could be visualised without moving the transducer.

174

175 Data extraction Elastography clips (10 s duration, sampling rate of 1.5-1.8 Hz) were 176 converted into PNG images (~20-26 images), then processed offline using customised Matlab 177 scripts (R2016a, The Mathworks, Natick, MA, USA) by a research assistant who was blinded to group. The following regions of interest (ROI) were manually traced on the adjacent B-178 179 mode image keeping within the peritendinous boundary: For the Achilles tendon, ROI were 180 measured at the free tendon (ROI length \sim 3 cm) and immediately proximal to the calcaneal 181 attachment (ROI length ~1 cm). For the patellar tendon, ROI were measured mid-way 182 between proximal and distal attachments (ROI length ~ 2 cm) and 0.5 cm from the apex of the 183 patella (ROI length ~0.5 cm). The mean SWV (m/s) was averaged over the ROIs of 184 consecutive images. The amount of signal void within each ROI, defined as the percentage of 185 all pixels without elastography colour, was also calculated. For SWV measurement, the 186 Matlab script ensured that regions with signal void were not confused with a low value.

187 Examples of Achilles and patellar elastograms (highlighting signal void) are provided in188 Figure 1 and Figure 2, respectively.

189

190 Statistical analysis For Achilles tendinopathy (AT) and patellar tendinopathy (PT) groups, 191 only the affected leg or self-reported worst leg (in bilateral cases) was included in analysis. 192 For healthy control (HC) participants, we randomly matched Achilles and patellar tendons to 193 ensure an equivalent proportion of left/right legs in the analysed sample, as recommended by previous studies.²⁵ Repeated measures ANCOVAs were used to compare tendon SWV and 194 195 thickness between groups (AT vs HC or PT vs HC) and regions (mid-tendon vs insertion). 196 Where significant group-by-region interaction was observed, generalised linear models 197 (GLM) were used to estimate mean differences (MD) and 95% confidence intervals (CI) 198 between groups for each tendon region. Age, BMI and sex were included as covariates in all 199 models. In addition, we included tendon thickness as a covariate in analyses of SWV, based on evidence that tendon thickness may affect SWV.^{18, 26} We dichotomised signal void as 200 201 present if it affected more than 5% of pixels within the ROI and differences between groups 202 were compared using Pearson Chi-square statistic.

203

Receiver operating characteristic (ROC) analysis was performed to determine the threshold,
specificity and sensitivity to differentiate HC from AT or PT, using the Youden's index to
identify the cut-point.²⁷ Finally, Pearson correlations were computed to identify relationships
between SWV and demographic or injury factors (the latter for tendinopathy groups only).
Statistical analysis was performed using SPSS (22.0 IBM Corp). Significance was set at
P<0.05.

210

211 RESULTS

212 Participants Sixty-seven adults (22 with AT, 17 with PT and 28 HC who were free of tendon 213 pain) were recruited. Demographic and injury information is summarised in Table 2 and 214 reasons for participant exclusion are listed in Supplemental Figure 1. Participants with AT 215 were significantly older than those with PT (P < 0.001) and had higher BMI than HC 216 (P < 0.001). Total activity time was not statistically different between the three groups 217 (P=0.343). Similar symptom duration (P=0.943) and pain/disability levels (P=0.781) were 218 found for AT and PT groups. The resting ankle angle adopted during Achilles tendon testing 219 was not different between groups (mean plantarflexion angle $24.3\pm5.0^{\circ}$). 220 221 Achilles tendinopathy Compared to HC, participants with AT had greater thickness at the

mid-Achilles (MD 95% CI: 0.19; 0.05 to 0.33 cm; P=0.007), but not at the Achilles insertion

223 (*P*=0.80) (group-by-region interaction, *P*=0.035, Figure 3a). Compared to HC, participants

with AT had lower SWV at the Achilles insertion (MD -1.56; -2.49 to -0.62 m/s; P<0.001),

but not mid-tendon region (*P*=0.456) (group-by-region interaction, *P*<0.001, Figure 3c).

Signal void of more than 5% of the ROI was present in four HC (8.9%) and 10 AT (45.5%)
cases (Pearson Chi-square *P*=0.001).

228

Using ROC analysis, mid-Achilles thickness above 0.64 cm, SWV below 9.7 m/s and signal

void above 1.5% of the ROI were identified as cut-points to differentiate HC and AT (Table

3). Lower Achilles SWV was associated with higher age (r=-0.49, P<0.001), greater BMI

232 (r=-0.53, p<0.001), greater pain and disability as measured by VISA-A (r=0.49, P=0.046) and

fewer single leg calf raises before pain onset (r=0.646, P=0.001).

234

235 *Patellar tendinopathy* Compared to HC, participants with PT had greater thickness at the

236 proximal patellar (MD 0.17; 0.06 to 0.29 cm; *P*=0.003), but not mid-patellar (*P*=0.31) region

237	(group-by-region interaction, P=0.01, Figure 3b). Compared to HC, participants with PT had
238	higher SWV of the patellar tendon at both regions (MD 1.25; 0.40 to 2.10 m/s; $P=0.005$,
239	Figure 3d). Signal void of more than 5% of the ROI was present in 0 HC and 3 PT (17%)
240	cases (Pearson Chi-square P=0.021).
241	

Using ROC analysis, proximal patellar thickness above 0.62 cm, SWV above 6.9 m/s and signal void above 0.7% of the ROI were identified cut-points to differentiate HC and PT (Table 3). Lower proximal patellar SWV was correlated with age (r=-0.368, P=0.013) only.

246 DISCUSSION

247 Using the non-invasive ultrasound-based technique of shear wave elastography, we observed 248 lower insertional Achilles tendon elasticity and higher patellar tendon elasticity in 249 participants with tendinopathy relative to healthy controls. Lower elasticity in Achilles tendinopathy is consistent with two recent studies using shear wave elastography,^{9, 10} and 250 251 other force-deformation methods.²⁸ However, evidence for changes in patellar tendon mechanical properties in tendinopathy varies between methods^{8, 29} and studies.^{10, 11} Using 252 253 shear wave elastography, Zhang (2014) found significantly greater elasticity and thickness for 254 the proximal patellar tendon in 13 athletes with unilateral PT, compared to both the unaffected tendon and healthy control participants.¹¹ In contrast, Dirrichs et al (2016) 255 256 reported lower elasticity in symptomatic compared to asymptomatic tendons in 38 participants with patellar tendinopathy.¹⁰ However, Dirrichs et al (2016) reported using a 257 much smaller ROI (standardised size of 1 mm) placed in the stiffest area of tendon.¹⁰ 258 259 260 Although causal relationships cannot be inferred from this cross-sectional study, it is possible

that different pathobiological processes associated with maturation and aging may be at play

262 in patellar and Achilles tendinopathy, respectively. Animal work demonstrates that 263 maturation and aging have different influences on the physical, chemical and mechanical properties of tendon.³⁰ In their experimental study in rats, Vogel et al (1980) observed a sharp 264 rise in elasticity during maturation and a smaller but significant decrease during aging.³⁰ 265 266 These changes in mechanical parameters were closely related to cross-linking of collagen. Significant increases in tendon elasticity with maturation³¹ may explain why adolescent 267 athletes have three times greater odds of patellar than Achilles tendinopathy.³² In our study, 268 269 older age was associated with lower Achilles tendon elasticity, which is in agreement with previous investigations using shear wave elastography,^{7, 24} and other methods.³³ Differences 270 271 in chronic load may alternatively contribute to our findings. Cassel et al (2015) reported that 272 athletes with patellar tendinopathy were taller and heavier and performed higher training volumes than athletes without patellar tendinopathy,³² attributes which may induce adaptation 273 274 by increased tendon elasticity. Conversely, sedentary lifestyles adopted by some people with 275 Achilles tendinopathy may contribute to lower elasticity. Interestingly, biomechanical studies 276 demonstrate that the effects of stress deprivation on connective tissue are more prolonged at 277 the insertion than mid-tissue region,³⁴ potentially explaining the significant reduction of 278 mechanical properties at the Achilles insertion. Of clinical importance, Achilles tendon 279 elasticity was significantly correlated with self-reported pain and disability over the 280 preceding week and with a rudimentary measure of the loading capacity of the Achilles 281 tendon.

282

The strengths of this study include the blinded design and concurrent investigation of two different lower limb tendinopathies. We acknowledge that interpretation of differences in SWV as differences in elasticity is not straightforward, as larger tendon thickness can lead to a higher SWV due to the effects of guided wave propagation, independent of any change in

actual tissue elasticity.^{18, 35} In the present study, no between-group difference in thickness 287 288 was observed for the mid-patellar tendon and the Achilles tendon insertion, increasing our 289 confidence in our interpretations that mechanical properties were altered. However, it is 290 possible the technique failed to detect a less stiff (but thicker) mid-Achilles tendon. This 291 study extends upon previous ones by quantifying signal void within the measured ROI. 292 Signal void was highly specific (82-96%) to cases with tendinopathy. Although currently speculative, its presence may be due to intra-tendinous swelling or tears,⁹ greater attenuation 293 of shear waves as a result of altered viscosity,²⁶ or severe matrix disruption and increased 294 anisotropy.³⁶ Further studies are needed to determine the impact of attenuation on SWV in 295 296 the considered region, and relate signal void to changes in matrix proteoglycan concentration 297 due to tendinopathy.

298

299 Limitations of the current study include the moderate reliability estimates, small sample size 300 and heterogenous tendinopathy population, which included participants with symptoms at 301 either mid-tendon or insertional regions. We chose to recruit both male and female control 302 participants with a range of ages, rather than individually match participants on the basis of 303 age or sex. Although not without limitation, statistical adjustment by including age, sex and 304 BMI as covariates in all models, was performed in an attempt to explore which factors 305 modulate changes in tendon properties. Other potential confounding factors such as sporting 306 history and muscle strength were not measured.

307

In summary, in the positions tested here, Achilles tendon SWV less than 9.7 m/s and patellar
tendon SWV more than 6.9 m/s showed high specificity (81% and 82% respectively) and
sensitivity (79% and 77%) for detecting Achilles and patellar tendinopathy respectively,

suggesting this method may have important clinical utility for early detection of patients atrisk of tendon pathology.

313

314 PERSPECTIVE

315 Achilles and patellar tendinopathy share similar histopathology, but affect different age

316 groups. The present study suggests that the two lower limb tendinopathies display different

317 mechanical properties when compared to tendons from healthy individuals. More research is

318 needed to explore whether maturation, aging or chronic load underlie these findings and

319 whether current management programs for Achilles and patellar tendinopathy need to be

tailored to the tendon.

- Table 1: Inter-day reliability (48 hour interval) for measurement of tendon thickness and
- 322 shear wave velocity in six healthy individuals. ICC: Intraclass correlation coefficient.

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- 326 Table 2: Demographic and injury characteristics for Healthy Control, Patellar tendinopathy
- 327 and Achilles tendinopathy cohorts.

	Healthy Control	Patellar Tendinopathy	Achilles Tendinopathy
n	28	17	22
Demographic information			
Age (years)	38.3 (16.7)	29.4 (6.6)	47.5 (11.4)*
BMI (kg/m ²)	22.8 (2.7)	25.4 (3.3)	28.1 (5.3)*
Female sex n (%)	17 (61%)	4 (24%)*	9 (41%)
Total activity time (mins)	582.2 (451.9)	797.9 (481.3)	642.4 (491.3)
Injury information			
Injury duration (years)		3.8 (3.4)	3.7 (6.9)
VISA-A or VISA-P (0-100)		57.1 (14.4)	58.6 (16.5)
Worst pain (NRS, 0-10)		5.2 (2.3)	6.0 (2.1)
Average pain (NRS, 0-10)		3.4 (2.1)	4.2 (1.9)
Resting pain (NRS, 0-10)		1.2 (2.4)	1.4 (1.5)
Calf raises (repetitions to pain onset)		NA	9.7 (8.6)
Decline squats (repetitions to pain onset)		2.1 (1.7)	NA
Symptom distribution n (%)			
Bilateral tendinopathy		9 (53%)	14 (64%)
Proximal: distal symptoms		15 (88%): 2 (12%)	NA
Mid-tendon: insertional symptoms		NA	19 (87%): 9 (41%)

328 329 Data represents mean (SD) unless otherwise specified. * Significant (p<0.05) differences

330 compared to healthy controls.

	Mean	Specificit	Sensitivit
	Threshold	У	У
		Thickness	
Mid-Achilles	\geq 0.64 cm	89.3 %	72.7 %
Insertional Achilles	\geq 0.44 cm	67.9 %	59.1 %
Proximal patellar	\geq 0.62 cm	100.0 %	58.8 %
Mid-Patellar	\geq 0.33 cm	50.0 %	82.4 %
	Shea	r wave veloci	ity
Mid-Achilles	\leq 6.80 m/s	68.2 %	75.0 %
Insertional Achilles	\leq 9.68 m/s	81.0 %	78.6 %
Proximal patellar	\geq 6.90 m/s	82.1 %	76.5 %
Mid-Patellar	$\geq 7.03 \text{ m/s}$	92.9 %	35.3 %
		Signal void	
Mid-Achilles	\geq 1.5 %	82.1 %	59.1 %
Insertional Achilles	≥ 5.1 %	96.4 %	38.1 %
Proximal patellar	$\geq 0.7~\%$	96.4 %	41.2 %
Mid-Patellar	\geq 0.5 %	82.1 %	41.2 %

332 Table 3: Results of Receiver Operating Characteristic analysis.

Thresholds for tendon thickness (in cm), shear wave velocity (in m/s) and signal void (as a

percentage of total ROI) to differentiate healthy and tendinopathic tendon have been

336 calculated using the Youden's index. Specificity and sensitivity were generated at these cut-

337 points.

³³³

339	Figure 1: Example shear wave elastograms of the Achilles tendon from healthy control (1a)
340	and Achilles tendinopathy participants (1b and 1c). Signal void highlighted (asterisk) in 1c.
341	
342	Figure 2: Shear wave elastograms of the patellar tendon from healthy control (1a) and
343	Achilles tendinopathy participants (1b and 1c). Signal void highlighted (asterisk) in 2c.
344	
345	Figure 3: Thickness and Shear wave velocity (SWV) of the Achilles tendon (a and c) and
346	patellar tendons (b and d) for Healthy Control (Blue), Achilles tendinopathy (Red) and
347	patellar tendinopathy (orange). Values represent mean and SD. *Significant (P <0.05)
348	differences between tendinopathy and healthy control groups (determined by Generalised
349	linear model adjusted for age, body mass index, sex and thickness (for SWV measures).
350	

352 Supplemental Content Figure 1: Recruitment numbers and participant eligibility information

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