

1 **EPIMUSCULAR MYOFASCIAL FORCE TRANSMISSION BETWEEN NERVE**
2 **AND MYOTENDINOUS UNIT: A SHEAR-WAVE ELASTOGRAPHY STUDY**

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24

ABSTRACT

25

26

Introduction:

28 Epimuscular myofascial force transmission can occur bidirectionally between
29 muscles and nerves through a connecting neurovascular tract. The purpose of
30 this study was to determine whether a neurodynamic stress test produces
31 stiffness changes in the adjacent myotendinous complex. The authors also
32 assessed which anatomical variables had an impact on elasticity changes
33 provoked by the maneuver.

34

Methods:

36 A convenience sample of healthy adults (n=39) recruited from a university
37 population who met the inclusion criteria participated voluntarily in this study.
38 Using Shear-Wave elastography, stiffness data were obtained for the ulnar
39 nerve, flexor carpi ulnaris tendon and muscle before and after a neural
40 tensioning maneuver.

41

Results:

43 Following an ulnar nerve stretch, statistically significant differences were
44 obtained in neural stiffness increase in nerve ($p < 0.001$), tendon ($p < 0.001$) and
45 muscle ($p = 0.046$), with a moderate ($d = 0.538$), small ($d = 0.485$) and small
46 ($d = 0.224$) effect sizes, respectively. The changes obtained were greater in
47 those individuals with a smaller anatomical distance between nerve and tendon.

48

49 **Conclusions:**

50 Alterations in peripheral neural tissue tension involves elasticity changes in
51 adjacent musculoskeletal tissue mediated by the neurovascular tract. Collateral
52 force transmission was determined by the individual anatomical differences of
53 each subject.

54 Future research should assess whether the observed increase in myotendinous
55 stiffness due exclusively to the passive transmission of force through the
56 connective bridges between the two tissues studied or if there is a
57 “neuroprotective” muscle contraction following neural stress.

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59

60 **Keywords:**

61 Myofascial force transmission, Shear-Wave elastography, Neurovascular tract,
62 Neurodynamic, Connective tissue.

63

INTRODUCTION

64

65

66 Muscles are structurally and functionally related to connective tissue. The
67 epimysium surrounds each muscle, connecting with the tendons and
68 periosteum. Perimysium forms muscle fascicles, while endomysium covers
69 each muscle fibre. Functional demands and mechanical forces influence both
70 the quantity and composition of this connective tissue (Purslow, 2020, 2010)

71 In recent decades, interest in connective tissue has increased due to its
72 role in muscular force transmission (Huijing, 2009), proprioception, and pain
73 perception (Fede et al., 2020; Mense, 2019). The fascia's continuous structure
74 challenges the view of muscles as isolated functional units (Maas, 2019). The
75 neurovascular tract, in its role as a connective tissue, connects muscle to other
76 tissues mechanically (Huijing, 2009; Yucesoy et al., 2010)

77 The sliding filament theory, introduced over 60 years ago, posits that
78 muscle fibres shorten from end to end as "A" bands come together (Huxley and
79 Niedergerke, 1954). This model suggests longitudinal force transfer via
80 sarcomere shortening. However, a secondary matrix of proteins also transmits
81 force across the muscle fibre to the tendons, protecting fibres from damage.
82 The costamere, part of this matrix, connects the sarcolemma to the contractile
83 apparatus, playing a crucial role in muscle function and injury prevention
84 (Hughes et al., 2015).

85 Street et al. highlighted in 1983 that skeletal muscle force is transmitted
86 both longitudinally and transversely (Street, 1983).). Longitudinal transmission
87 occurs along the muscle fibre, while collateral pathways transmit force from

88 each sarcomere to the connective tissue and extracellular matrix, then to the
89 tendon (Gao et al., 2014). This collateral force transmission, known as
90 "epimuscular myofascial force transmission (EMFT)" (Huijing, 1999; Yucesoy,
91 2010), involves transmission from the entire myofibril surface without the direct
92 involvement of the myotendinous/myoaponeurotic unit (Pamuk et al., 2020).

93 Up to 80% of force transmission is suggested to occur through EMFT
94 (Hughes et al., 2015), underscored by muscular dystrophies like Duchenne
95 muscular dystrophy where protein complexes are altered.

96 Due to the close morphological relationship between muscles and
97 connective tissue, changes in local stiffness can affect surrounding areas (Wilke
98 et al., 2018). Changing the length of a muscle alters the forces on adjacent
99 muscle tendons that remain unchanged in length. Stretching a muscle affects
100 its tension and that of neighbouring muscles (Yoshitake et al., 2018a).

101 Intermuscular force transmission also occurs between muscle and other
102 tissues. The neuromuscular tract links the intramuscular connective tissue
103 network with the neurovascular complex support matrix (Maas and Sandercock,
104 2010).

105 On another note, peripheral nerves must adapt their length to the
106 stretching and flexing movements of the extremities. They have a complex
107 structure of neuron bundles packed into fascicles, surrounded by connective
108 tissue layers, the perineurium and epineurium (Phillips et al., 2004). Due to
109 these characteristics, they can be subjected to mechanical stress through
110 tension. These manoeuvres, known as "neurodynamic", are used by

111 physiotherapists to evaluate and treat painful musculoskeletal disorders (Boyd
112 et al., 2009).

113 Neurodynamic assessment has become popular in evaluating and
114 treating neural and musculoskeletal disorders (Shacklock, 2005). Through
115 polyarticular movement, mobilizing the peripheral nervous system applies a
116 mechanical load on neural tissue, altering the length and dimensions of the bed
117 supporting these neurovascular structures, thus improving pain tolerance (Nee
118 and Butler, 2006; Zamorano-Zárate, 2013).

119 Besides mobilizing neural tissue, peripheral nerves can be "stretched"
120 through precise positioning of the joints that the selected nerve crosses
121 (Martínez et al., 2014). Cadaver studies confirm that neural stretching
122 techniques can increase nerve length (Byl et al., 2002). Likewise, a 65%
123 increase in ulnar nerve strain at the wrist level has been found when performing
124 this maneuver (Wright et al., 2001).

125 The development of Shear-Wave Elastography (SWE) enables the
126 evaluation of changes in the elastic properties of living tissues. SWE works by
127 analysing the speed at which perpendicular waves are formed as the main
128 ultrasound beam travels through tissue (Brandenburg et al., 2014; Franchi-
129 Abella et al., 2013). The relationship between the mechanical properties of
130 these shear-waves and tissues began being studied in 1960 (Drakonaki et al.,
131 2012; Taljanovic et al., 2017). Since then, studies have shown the relationship
132 between shear-wave speed and tissue stiffness (Guzmán Aroca et al., 2014;
133 Hug et al., 2015).

158 right-handed, without any episodes of neck pain the previous year or
159 neuropathies in the upper limb, without trauma or surgery in the neck or upper
160 limb) participated voluntarily in this study, which was approved by the Ethics
161 Committee of the Francisco de Vitoria University (Madrid, Spain) with n°
162 15/2017 and enrolled in *Clinical Trial* with ID n° NCT03509337. All individuals
163 signed an informed consent prior to their participation.

164

165 **Procedure**

166 The participants maintained a relaxed position, with minimal tension on
167 the peripheral neural system: supine, head and neck in a neutral position, left
168 hand on the abdomen with legs flexed and supported on a wedge (Zamorano-
169 Zárate, 2013). The right arm was held passively at 30° abduction, elbow in 10°
170 flexion and forearm in 30° supination. Wrist and distal joints held in a relaxed
171 position. This initial position guarantees a relaxed state of the flexor carpi
172 ulnaris muscle (FCUM) and its tendon (FCUT) as well as the ulnar nerve (UN),
173 which was confirmed by asking the patient for their perception. The lack of
174 sensation of tension in the upper limb confirmed the correct initial position. To
175 put tension on the UN without affecting the length of the FCUM (insertion in
176 pisiform, hamate and base of the 5th metacarpal) or its tendon, an expert
177 researcher in neural tissue mobilization with over 10 years of experience
178 performed extension of the 4th and 5th metacarpophalangeal joints and
179 corresponding distal joints. The other joints were maintained without changes
180 until an exponential increase in resistance of the tissues placed under tension
181 was perceived (Kwan et al., 1992). The participants also verbalized the moment

182 which they felt the increase in tension. Both the start and end positions are
183 shown in figure 1.

184

185 **Ultrasound and Shear-Wave Elastography**

186 A Canon TUS Ai800 (Aplio i800) ultrasound machine fitted with a PLT-
187 1005BT 14L5 multi-frequency linear probe (5-14 MHz) and Shear-Wave
188 elastography software (Canon Medical Systems, Japan) was used. The
189 researcher in charge of the ultrasound has over 10 years of experience in
190 musculoskeletal studies.

191 With the participant in the initial resting position, an image was obtained
192 in a transverse plane 5 cm proximal to the pisiform bone in which the structures
193 of interest for this study were identified (ulnar nerve, flexor carpi ulnaris muscle
194 and tendon) using 2D ultrasound mode and color Doppler (figure 2A). The
195 ultrasound parameters (depth, focal position, gain, and dynamic range) were
196 adjusted to obtain a high-quality image that allows for the unequivocal
197 identification of the structures of interest for this study. The images were stored
198 for later analysis. Images of the same structures were then obtained in the
199 longitudinal plane (figure 2B), on which the SWE study was then performed.
200 These measurements are performed in the longitudinal plane because of the
201 anisotropic properties of the neurovascular and musculoskeletal tissues (Dubois
202 et al., 2015; Lee et al., 2016; Miyamoto et al., 2015).

203 The colour scale extremes were adjusted for each tissue and each
204 participant to obtain a high-quality elastogram that allowed for the proper
205 positioning of the ROIs in the selected locations. As long as the area to be

206 quantified (the location of the ROIs) is covered by colour, modifying the colour
207 scale does not alter the shear wave velocity values and, therefore, the stiffness
208 measured in kilopascals. Colour void areas, whether due to excess or
209 deficiency, are beyond the software's reading capacity.

210 Three Regions of Interest (ROI) adjacent to each other were established
211 on the obtained elastogram, each one covering the total diameter of the ulnar
212 nerve. The stiffness measurements obtained were recorded in Kilopascals
213 (KPa) (figure 3). FCUM and FCUT tension measurements were also obtained
214 using a ROI size determined by the diameter of the nerve that was first
215 explored.

216 The same procedure for obtaining elastography data was repeated in the
217 final position with neural tension in order to compare the pre / post tension data.

218

219 **Anatomical relation of adjacent structures**

220 The anatomical location of the neurovascular bundle and its relationship
221 with the flexor carpi ulnaris tendon was visually analyzed. Those individuals in
222 whom both adjacent elements were identified and only separated by a
223 connective tissue interface were grouped under the term "wall-to-wall".
224 Meanwhile, those in which a connecting neurovascular tract of more than 4mm
225 was identified were termed "distant neighbors." Figure 4 illustrates this
226 classification, which is due to the individuality of each patient and their
227 anatomical variations (Kachare et al., 2020; Lung y Siwiec, 2020).

228

229 **Data and statistical analysis**

230 The R Ver. 3.3.3. was used for the statistical analysis (R Foundation for
231 Statistical Computing, Institute for Statistics and Mathematics, Welthandelsplatz
232 1, 1020 Vienna, Austria). The level of significance was established at $p < 0.05$.
233 The distribution of quantitative variables was tested with the Shapiro-Wilk,
234 which showed how the majority had a non-normal distribution. Quantitative
235 variables were described with median [interquartile range] or mean \pm standard
236 deviation depending on its distribution. Qualitative variables were expressed
237 with absolute and relative frequencies. The Wilcoxon Signed-Rank test was
238 applied between pre-test/post-test outcome variables and the U Mann-Whitney
239 test between outcome and baseline variables. The effect size (Cohen's d) was
240 defined as not relevant (< 0.20), small (between 0.20 and 0.50), moderate
241 (between 0.50 and 0.80), or large (≥ 0.80). Minimal Detectable Change (MDC)
242 was also calculated for pre-posttest outcome variables.

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244

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RESULTS

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247 39 healthy subjects were recruited, 17 men and 22 women of 20.69 ± 2.20
248 years with a BMI of 21.56 ± 2.90 considered as healthy status (Table 1).

249 The stiffness of the tissues was compared at rest versus the moment
250 when the participants reported a sensation of tension. Pre-test/post-test
251 outcome variables showed significant differences in the ulnar nerve ($Z = 4.7589$,
252 $p < 0.001$) with an increase of 39 KPa and a moderate effect size. In the ulnar
253 tendon ($Z = 4.2918$, $p < 0.001$) the stiffness values increased by 27 KPa with a

254 small effect size and, in the case of the flexor carpi ulnaris muscle, there was a
255 significant ($Z=1.9828$, $p=0.046$) increase of 3 KPa with a small effect size (Table
256 2).

257 The Mann-Whitney U test showed that neural tensioning caused a
258 greater increase in tendon stiffness in the “wall-to-wall” group than in the
259 “distant neighbors” group (53.5 KPa and 12 KPa respectively. $P < 0.05$). Tension
260 changes in nerve or muscle were not statistically significant. There were no
261 significant differences in the other variables analyzed. MDCs are very high
262 indicating a low sensitivity to change.

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DISCUSSION

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267 The results of our study confirm that there is evidence of a
268 transmission of forces between different tissues. Specifically, an increase in
269 stiffness within the myotendinous unit is evidenced following an increase in
270 tension of the adjacent neural tissue. In accordance with other authors, the
271 neurovascular tract seems to be the route of lateral force transmission (Huijing,
272 2009).

273 Previous studies in animal models have been able to successfully
274 predict the amount of EMFT under different experimental conditions (Bernabei
275 et al., 2016). Other researchers (Freitas et al., 2019; Yoshitake et al., 2018b)
276 showed the existence of EMFT mediated by collagen bonds between the
277 epimysium of adjacent muscles, as well as by the presence of the

278 neurovascular tract. The authors demonstrated tension changes induced within
279 a muscle during the relative stretching of an adjacent muscle. Similarly, there is
280 evidence of EMFT in synergistic and antagonist muscles in patients with
281 cerebral palsy (Kaya et al., 2020).

282 However, our study has confirmed that this transmission of forces also
283 occurs between different tissues. More specifically, force transmission is seen
284 between muscles, tendons and neural tissue. This transmission is mediated by
285 the presence of the neurovascular tract (Huijing, 2009), which serves as a link
286 between the different tissues, as can be seen in ultrasound images obtained.

287 The muscle offers less resistance to elongation than nerves and
288 tendons, so generating neural elongation increases the stiffness of both this
289 tissue and the tendon, as we have shown in the study; however, the muscle
290 modifies its stiffness to a lesser extent, relative to its intrinsic mechanical
291 properties, which are very different from those of the other two tissues studied
292 (Feng et al., 2018). On the other hand, the slight increase observed could be
293 due to a "neuroprotective" contraction. The reason for this slight increase in
294 stiffness should be addressed by future studies specifically designed to answer
295 this question.

296 The morpho-functional union described supports observations made in
297 spastic patients in whom tenotomy was performed in order to return the wrist
298 and hand to a functional position. This procedure failed to reverse the flexion
299 seen in spastic ulnar deviation (Smeulders y Kreulen, 2007). The authors of this
300 study observed "*in vivo*" that the neurovascular tissue of the ulnar nerve was
301 connecting and, therefore, possibly triggering the displacement of the proximal

302 end of the severed tendon during passive wrist flexion and extension
303 movements performed "*in situ*".

304 In addition, increase in myotendinous stiffness in the flexor carpi ulnaris
305 is observed when applying physical stress (stretching) to the ulnar nerve. This
306 may be due to either simultaneous stretching or to a neuroprotective contraction
307 of the muscle.

308 From a clinical point of view, further research is needed to reveal if the
309 presence of the neurovascular tract serves exclusively as a passive route of
310 transmission of forces or plays a more active role. Studies looking at
311 electromyographic recordings of median nerve tension tests reveal the activity
312 of the arm muscles, which show the appropriate biomechanical conditions to
313 resist stretching of the median nerve (Jaberzadeh et al., 2005). It is important to
314 point out that the activity of these muscles precedes the moment in which the
315 examined individuals report painful sensations. This means that there is muscle
316 activity caused by neural stretching outside of the pain range. It seems that the
317 presence of mechanoreceptors in the connective structures of the nerves would
318 justify the fact that the stretching of the nerve triggers a reflex muscle
319 contraction of certain muscle groups, in a sequenced way and in relation to
320 different ranges of motion.

321 A greater transmission of forces was observed in the participants with
322 the "wall-to-wall" morphology in contrast to the reduction in force transmission
323 seen in those with the "distant neighbors" type morphology. This may be
324 explained by the inverse square law formulated by Sir Isaac Newton. This law
325 states that an object (in our study a tendon) distant to the origin of a mechanical

326 stimulus (for example the stretching of the ulnar nerve) will perceive said
327 stimulus four times less if the distance from that mechanical stimulus is
328 doubled. In living tissues such as those discussed here, however, biophysical
329 aspects inherent to each participant should be considered, such as
330 viscoelasticity or hydration, which could also affect the muscular response
331 obtained (Denslow, 2000). Studying these factors are beyond the objectives
332 initially set for this study but could be considered as possible limitations. Deeper
333 anatomical studies could provide further information related to the EMFT and
334 intersubject variability.

335 However, this anatomical configuration and the tension changes
336 obtained in our study could partly explain the different clinical behavior and
337 therapeutic response to the same mobilization or neural stretching maneuver
338 performed in patients with different clinical conditions, who show different
339 degrees of mechanosensitive (Denslow, 2000; Schmid et al., 2009; Szikszay
340 et al., 2018).

341 Finally, our study has some limitations, as detailed below: Sample size
342 was determined for convenience. Electromyography was not used to ensure
343 muscle silence in the resting position. Having only one investigation group does
344 not allow for understanding individual or natural stiffness variations or
345 measurement errors.

346 Subsequent studies with a larger sample could be useful to advance
347 the degree of understanding of the functional aspects of fascial tissue and,
348 specifically, of the neurovascular tract.

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350

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CONCLUSIONS

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353 The modification of stiffness in peripheral neural tissue also involves
354 tension changes in adjacent musculoskeletal tissue mediated by the
355 neurovascular tract. The amount of lateral force transmission is related to the
356 anatomical characteristics of the individual.

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358

359

CLINICAL RELEVANCE

360

- 361 1. Neuromuscular tract plays an important role in the transmission of forces
362 between different tissues.
- 363 2. Anatomical particularities of each subject confer different degrees of
364 force transmission between different tissues.
- 365 3. Shear-Wave Elastography is an effective tool for demonstrating changes
366 in tissue stiffness under stress by therapists.

367

368 **Clinical Trial Registration number**

369 NCT03509337

370

371 **Ethical Approval:**

372 This study was approved by the Ethics Committee of the Francisco de
373 Vitoria University (Madrid, Spain) with nº 15/2017.

374

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377

378 **Declaration of competing interest:**

379 Authors declare no conflict of interest.

380

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TABLES AND ILUSTRATIONS

570

571 **Table 1**

TABLE 1: Clinical and demographic baseline characteristics.

n		39
Age		21 [19, 22]
Gender, n(%)	Female	22 (56.4)
	Male	17 (43.6)
Weight		63.72±12.42
Height		170.90±9.94
BMI		20.83 [19.76, 22.69]
Physical Activity, n(%)	Active	26 (66.7)
	Sedentary	13 (33.3)
Schedule, n(%)	Afternoon	18 (46.2)
	Morning	21 (53.8)
Regional morphology	Wall-to-wall	18 (46.2%)
	Distant neighbors	21 (53.8%)

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573

574 **Table 2**

Table 2: Pre-test / post-test outcome variables

	Pretest (KPa)	Posttest (KPa)	Difference (95%CI)	^ap value	Cohen's d	MD C
nerv e	62 [45.5, 74]	101 [80, 126]	39 (29.999- 52.5)	<0.00 1	0,538	65,8 21
tend on	107 [91, 129]	134 [109.5, 175]	27 (15.999- 39)	<0.00 1	0,485	98,9 06
mus cle	16 [14.5, 19.5]	19 [13, 27.5]	3 (0.0008- 5.499)	0,046	0,224	37,8 48

MDC: Minimal Detectable Change

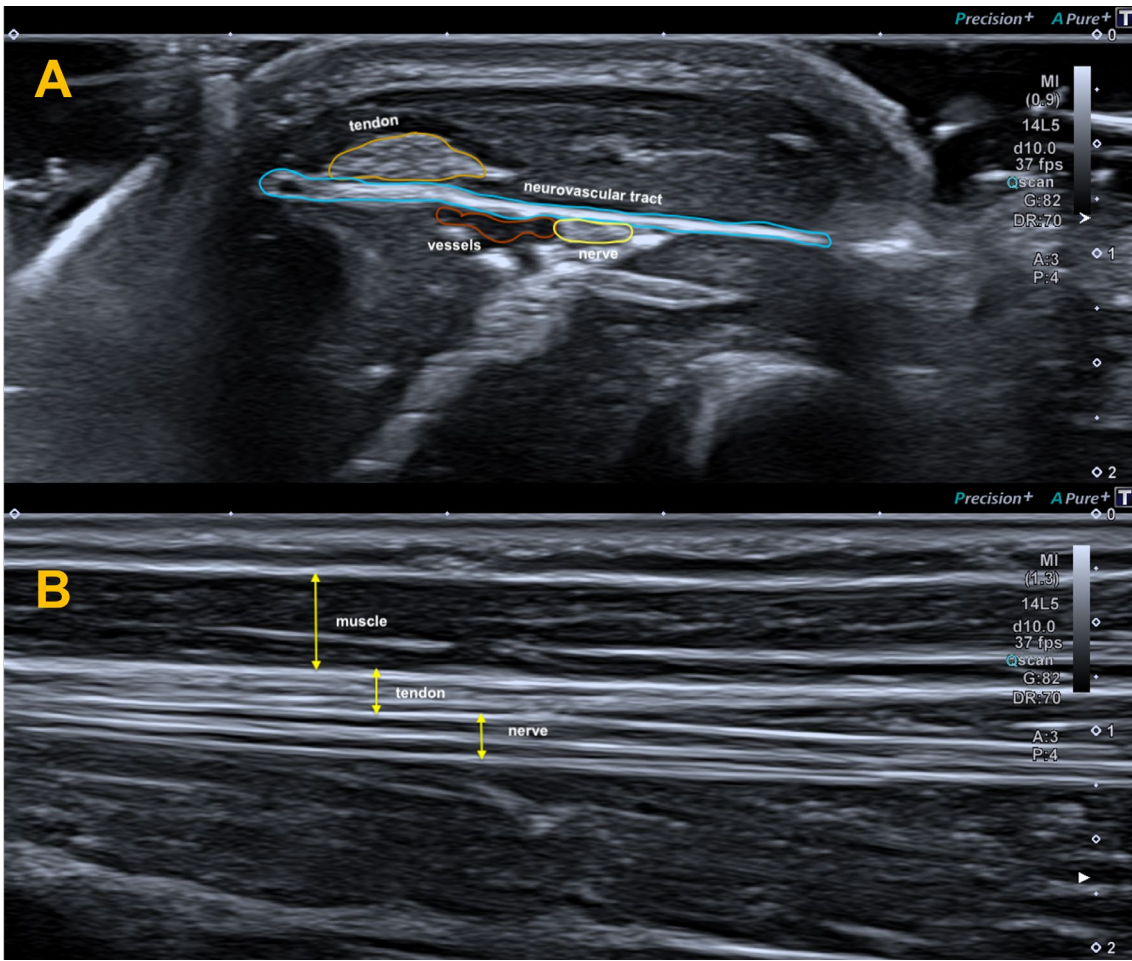
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576 **Fig. 1**



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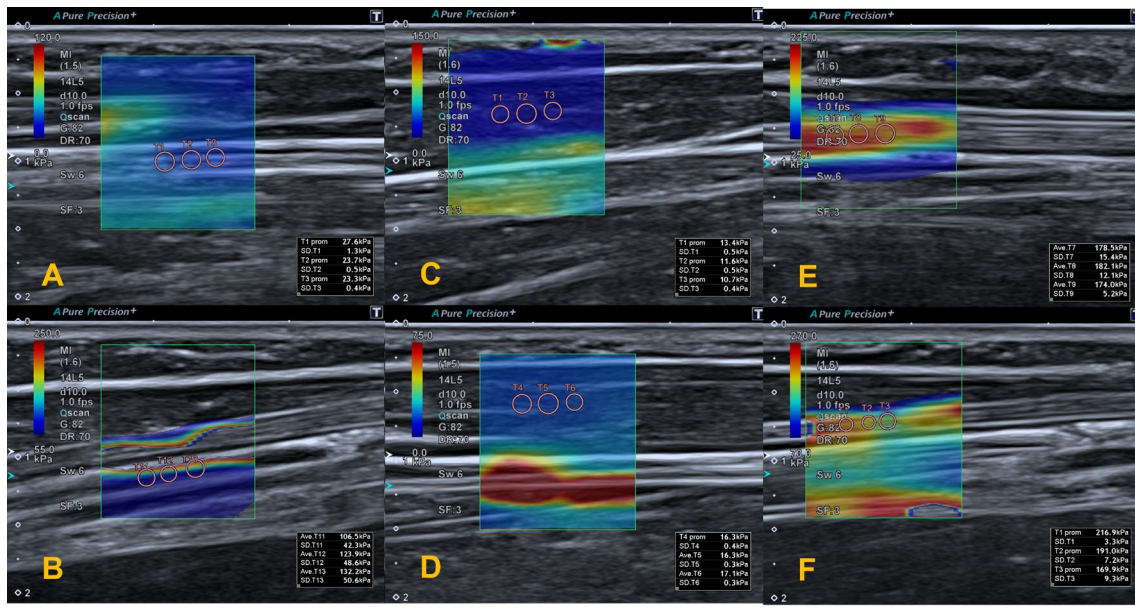
Fig. 2



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Fig. 3



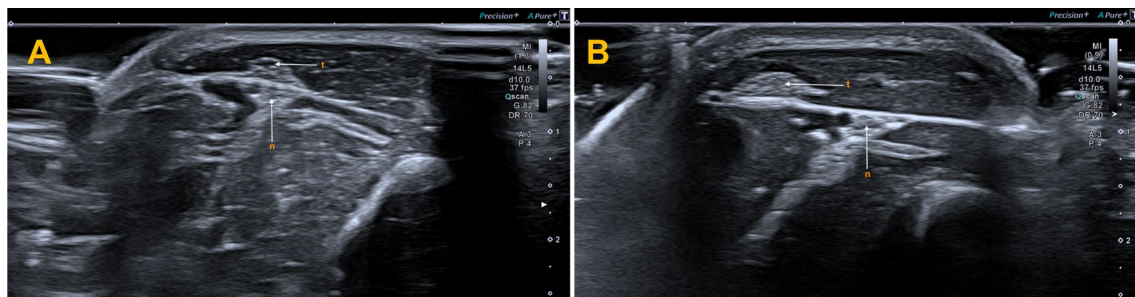
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Fig. 4



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CAPTIONS TO TABLES AND ILLUSTRATIONS

595

596

597 **Table 1: Clinical and demographic baseline characteristics.**

598 Data expressed with median [interquartile range] or mean±standard deviation
599 and with absolute and relative values (%).

600

601 **Table 2: Pre-test / post-test outcome variables.**

602 Data expressed as median [interquartile range]. 95%CI: 95% confidence
603 interval. ^asignificant if p<0.05.

604

605 **Fig. 1:** Ulnar nerve tension maneuver and positioning of the ultrasound probe
606 for the acquisition of elastographic images. **(A)** Overview of the patient's starting
607 position. **(B)** Initial position of the carpal and distal joints, with the relaxed
608 position of the 4th and 5th fingers. **(C)** Final position of the wrist and fingers
609 applying ulnar nerve tension without affecting the length of the flexor carpi
610 ulnaris muscle.

611

612 **Fig. 2: Initial ultrasound images.** **(A)** Cross-sectional image showing the
613 anatomical relationship between the vascular structures, ulnar nerve, flexor
614 carpi ulnaris muscle and tendon, and the neurovascular tract connecting them.
615 **(B)** Longitudinal plane of the ulnar nerve, flexor carpi ulnaris muscle and
616 tendon.

617

618 **Fig. 3: Shear-Wave Elastography** in the longitudinal plane and the average
619 data obtained in Kilopascals (KPa) of the different ROIs. **(A)** Ulnar nerve in the
620 initial resting position. **(B)** Ulnar nerve at the end of the tensioning manoeuvre.
621 **(C)** Flexor carpi ulnaris muscle at rest. **(D)** Flexor carpi ulnaris muscle at the
622 end of the neural tensioning manoeuvre. **(E)** Carpi ulnaris tendon in the initial
623 position. **(F)** Carpi ulnaris tendon in the nerve tensioning position.

624

625 **Fig. 4: Regional anatomy** seen in 2D ultrasound mode in a transverse plane 5
626 cm proximal to the pisiform bone. t = flexor carpi ulnaris tendon. n = ulnar nerve.
627 **(A)** Regional “wall-to-wall” anatomy; Note that the fascia that constitutes the
628 neurovascular tract is the only structure providing direct contact between the
629 tendon and nerve. **(B)** Regional anatomy of the “distant neighbors” type; both
630 structures are distant from each other and connected through the neurovascular
631 tract.