

1 **Fascial tissue Research in Sports Medicine: From Molecules to Tissue Adaptation,**
2 **Injury and Diagnostics**

3
4 *2018 consensus statement from the 2nd international CONNECT conference, Ulm,*
5 *Germany*

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37 **Abstract**

38

39 **Background:** The fascial system builds a three-dimensional continuum of soft, collagen-
40 containing, loose and dense fibrous connective tissue that permeates the body and enables all
41 body systems to operate in an integrated manner. Injuries to the fascial system cause a significant
42 loss of performance in recreational exercise as well as high performance sports and could have a
43 potential role in the development and perpetuation of musculoskeletal disorders, including lower
44 back pain.

45

46 Fascial tissues deserve more detailed attention in the field of sports medicine. A better
47 understanding of their adaptation dynamics to mechanical loading as well as to biochemical
48 conditions promises valuable improvements in terms of injury prevention, athletic performance
49 and sports-related rehabilitation.

50

51 This consensus statement reflects the state of knowledge regarding the role of fascial tissues in
52 the discipline of sports medicine. It aims to: (i) provide an overview of the contemporary state of
53 knowledge regarding the fascial system from the *micro level* (molecular and cellular responses)
54 to the *macro level* (mechanical properties), (ii) summarise responses of the fascial system to
55 altered loading (physical exercise), to injury and other physiological challenges including ageing,
56 (iii) outline methods available to study the fascial system, and (iv) highlight the contemporary
57 view of interventions that target fascial tissue in sport and exercise medicine.

58

59 Advancing this field will require a co-ordinated effort of researchers and clinicians combining
60 mechanobiology, exercise physiology and improved assessment technologies.

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62

63 Terminology and definitions

64
65 The term *fascia* was originally used to describe a sheet or band of soft connective tissue that
66 attaches, surrounds and separates internal organs and skeletal muscles. Advancing research on the
67 physiological and pathophysiological behaviour of a range of connective tissues has revealed that
68 this definition is too restrictive. Understanding of mechanical aspects of connective tissue
69 function depends on consideration of a host of interconnected and interwoven connective tissues
70 beyond these sheets or bands, and there is enormous potential gain from understanding the
71 convergence of biology underpinning adaptation, function and pathology.

72
73 The *fascial system* includes adipose tissue, adventitia, neurovascular sheaths, aponeuroses, deep
74 and superficial fasciae, dermis, epineurium, joint capsules, ligaments, membranes, meninges,
75 myofascial expansions, periosteum, retinacula, septa, tendons (including endo-/peri-/epi-
76 /paratendon), visceral fasciae and all the intra- and intermuscular connective tissues, including
77 endo-/peri-/epimysium.¹

78
79 With its diverse components, the fascial system builds a three-dimensional continuum of soft,
80 collagen-containing, loose and dense fibrous connective tissue that permeates the body and
81 enables all body systems to operate in an integrated manner (Fig. 1).¹ In contrast, the
82 morphological/histological definition describes *fascia* as ‘a sheet, or any other dissectible
83 aggregations of connective tissue that forms beneath the skin to attach, enclose, and separate
84 muscles and other internal organs’.¹ The proposed terminology distinguishing the terms ‘fascia’
85 and ‘fascial system’ allows for the precise identification of individual structures as well as
86 grouping them for functional purposes.

87 88 Consensus meeting

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90 The 2nd international CONNECT conference was held at the University of Ulm, Germany, during
91 16th–19th March 2017, as part of a conference series aimed at fostering scientific progress towards
92 a better understanding and treatment of fascial tissues in sports medicine. After the conference, a
93 meeting was held with conference speakers and other field-related experts to discuss and find
94 consensus regarding the role of fascial tissue in the field of sports medicine.

95
96 Injuries to a variety of fascial tissues cause a significant loss of performance in sports² and have a
97 potential role in the development and perpetuation of musculoskeletal disorders, including lower
98 back pain.³ A major goal of clinicians is to return athletes and patients to activity, training and
99 competition after injury.

100
101 This consensus statement reflects the current state of knowledge regarding the role of fascial
102 tissues in the discipline of Sports Medicine and will be updated as part of a consensus meeting
103 during the CONNECT conference. This paper aims to summarize the contemporary state of

104 knowledge regarding the fascial system from the *micro level* (molecular and cellular responses)
105 to the *macro level* (mechanical properties) and responses of the fascial system to altered loading
106 (physical exercise), to injury and other physiological challenges including ageing, methods
107 available to study the fascial system, and the contemporary view of interventions that target
108 fascial tissue in sports medicine. This document was developed for scientists and clinicians to
109 highlight common traps and truths of fascial tissue screening and imaging techniques and
110 intervention methods and to present a multidisciplinary perspective of future research in the field.

111 112 **Molecular adaptation of fascial tissues: effects of physical exercise, ageing, sex hormones** 113 **and inflammation**

114
115 Molecular crosstalk between extracellular matrix (ECM) molecules and cellular components is an
116 important determinant of fascial tissue physiology and pathophysiology. A molecular chain,
117 characterised by high functional and structural plasticity and bidirectional molecular interactions,
118 connects the cellular cytoskeleton to the ECM (Fig. 2). Small functional and structural alterations
119 in the ECM result in complex cellular adaptation processes and, vice versa, changes in cell
120 function and structure leading to ECM adaptation.⁴ Therefore, fascial tissue homeostasis is the
121 result of a complex interplay and dynamic crosstalk between cellular components and the ECM.
122 Especially under dynamic conditions such as growth and regeneration, strong alterations of local
123 ECM microenvironments are necessary to allow cellular adaptation and rebuilding of fascial
124 tissues. All factors influencing cell or ECM behaviour can result in changes in the structure and
125 homeostasis of tissues and organs.

126
127 The ECM also works as a molecular store, catching and releasing biologically active molecules to
128 regulate tissue and organ function, growth and regeneration. Molecules stored in the ECM
129 network can be cleaved to release biologically active cleavage products.⁵ Mechanical stress can
130 induce the release and activation of ECM-stored molecules, inducing the cleavage products of
131 collagen XVIII and other basement membrane components. It has been shown that endostatin
132 (the 20 kDa C-terminal fragment of collagen XVIII) can modulate vascular growth and
133 function.⁶⁻⁸ In addition, changes of the ECM by ageing or physical exercise may be involved in
134 triggering systemic effects via excreted circulatory molecules, such as the exercise-responsive
135 myokine irisin,⁹ which has been proposed to increase energy expenditure in mice and humans.

136
137 In fascial tissues such as tendons, acute and chronic loading stimulates collagen remodelling.¹⁰ As
138 the exercise-induced increase in collagen synthesis is lower in women than in men, and as injury
139 frequency and the expression of estrogen receptors in human fascial tissue are sex-dependent,
140 estrogens may play an important regulatory role in ECM remodeling.¹¹⁻¹³ The effects of estrogens
141 on collagen synthesis appear to differ between rest and response to exercise. While estrogen
142 replacement in elderly, post-menopausal women impairs collagen synthesis in response to
143 exercise, estrogen has a stimulating effect on collagen synthesis at rest.¹⁴ Oral contraceptives, on
144 the other hand, have an overall depressing effect on collagen synthesis.¹⁵

145

146 Physiological ageing is a highly individual process characterised by a progressive degeneration of
147 tissues and organ systems. Age-related alterations in fascial tissues include densification
148 (alterations of loose connective tissue) and fibrosis (alterations of collagen fibrous bundles).¹⁶
149 Functionally, these pathological changes can modify the mechanical properties of fascial tissues
150 and skeletal muscle, thereby contributing to pain- and age-related reductions in muscle force or
151 range of motion, which cannot be solely explained by the loss of muscle mass.¹⁷ ECM structural,
152 biochemical, cellular and functional changes occur during ageing.¹⁸ Interestingly, ageing is
153 characterised by chronic, low-grade inflammation—so-called *inflammaging*.¹⁹ As the ECM is the
154 main site of inflammatory responses taking place in tissues, it is not surprising that the ECM can
155 interact with immune cells to change their function, which is important for growth and
156 regeneration of tissues. Leukocyte extravasation depends on cleavage of the basal membrane by
157 locally released proteases. Tenascin and osteopontin are examples of ECM molecules important
158 for regulation of the local immune response.^{20 21} In addition, the ECM plays an important role as a
159 barrier for transmigration of immune cells in and out of the tissue. Although early inflammation
160 after tissue damage due to physical exercise or injury is crucial for tissue remodelling and
161 adaptation,^{22 23} stem-cell activity and collagen synthesis may be inhibited by the chronic intake
162 of non-steroidal anti-inflammatory drugs (NSAIDs) prior to exercise.^{24 25} However, limiting the
163 magnitude of inflammation might be beneficial for tissue regeneration and gains in muscle mass
164 and strength, depending on the nature of the injury,²⁶ and in elderly people.²⁷

165
166 *Outlook and perspectives for future research:*

167 Insights into the structure–function relationship of the ECM, especially in ageing and injured
168 fascial tissues and skeletal muscle, are highly relevant for maintaining musculoskeletal function
169 in the elderly during daily life and exercise and for prevention of exercise-related overuse injuries
170 in athletes. While a body of literature exists on metabolic activity and ECM remodelling in
171 human tendons in response to exercise, much less is known and more research is needed to
172 investigate the molecular response of other fascial tissues (such as intramuscular fascial tissue) to
173 altered loading and ageing.

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175
176 **Myofascial force transmission**

177
178 Conventionally, skeletal muscles have been considered as primarily transmitting force to their
179 osseous insertions through the myotendinous junction.²⁸ However, in situ experiments in animals
180 and imaging studies in humans have shown that inter- and extramuscular fascial tissues also
181 provide a pathway for force transmission.²⁹⁻³³ Although the magnitude of non-myotendinous
182 force transmission under in vivo conditions is disputed,^{34 35} the contribution of these pathways is
183 thought to be dependent, in part, on the mechanical properties of myofascial tissue linkages.³⁶
184 Myofascial tissue that is stiffer or more compliant than normal has been shown to influence the
185 magnitude of intermuscular force transmission and, arguably, may have a significant effect on
186 muscle mechanics.³⁷⁻³⁹ The mechanical properties of fascial tissues can be modified by several
187 factors, which, inter alia, include a change in fluid content, cross-links and molecular

188 organization and content of specific ECM molecules and contractile activity of myofibroblast
189 cells.^{40 41} Changes can also be a consequence of muscle injury,⁴² disease,⁴³ surgical treatment³⁷ or
190 ageing (Fig. 3).⁴⁴

191
192 As fascial tissues connect skeletal muscles, creating a multidirectional network of myofascial
193 continuity⁴⁵, altered local forces (e.g. by muscular contraction) might also affect the mechanics
194 of adjacent tissues. In fact, a plethora of cadaveric and animal studies have demonstrated
195 substantial mutual interactions between neighbouring muscles arranged serially in slings (e.g. M.
196 latissimus and M. gluteus maximus)⁴⁶ and parallel to each other (e.g. lower limb synergists).⁴⁷
197 For example, when seen from a fascial perspective, the knee-joint capsule is not only influenced
198 by directly inserting tendons but also by more distant structures such as the gluteus maximus or
199 the tensor fasciae latae and their connecting fasciae.⁴⁸ However, it remains to be further
200 elucidated how such findings translate into human in vivo conditions.

201 Although scarce, initial in vivo evidence points towards a significant role of myofascial force
202 transmission for the locomotor system. Available data point towards the existence of (a) remote
203 exercise effects and (b) non-local symptom manifestations in musculoskeletal disorders, both of
204 which might be of relevance in athletic and therapeutic settings. It has been shown that stretching
205 of the lower limb increases range of motion of the cervical spine, and patients with sacroiliac pain
206 display hyperactivity of the gluteus maximus and the contralateral latissimus muscle.⁴⁹⁻⁵¹
207 Because the involved body regions are connected via myofascial chains, myofascial force
208 transmission might be the cause of the observations. Besides interactions between muscles
209 arranged in series, significant amounts of force have been shown to be transmitted in vivo
210 between muscles located parallel to each other; electrical stimulation of the gastrocnemius
211 muscle leads to a simultaneous displacement of the soleus muscle.³⁰ This intralimb myofascial
212 force transmission may be of relevance in diseases such as cerebral palsy.³⁸

213
214 *Outlook and perspectives for future research:*
215 Although the basic mechanisms of myofascial force transmission have been studied, there is a
216 need to discern the influence of variables, such as age, sex, temperature and level of physical
217 activity within healthy physiological and pathological settings. Furthermore, despite convincing
218 *in-vitro* evidence for the existence of myofascial force transmission, its relative contribution to
219 the occurrence of remote exercise effects under in vivo conditions has to be further elucidated.
220 Besides mechanical interactions between adjacent tissues, non-local changes of stiffness or
221 flexibility may also (at least partly) stem from neural adaptations, e.g. a systemic reduction of
222 stretch tolerance.

223

224 **Injury of fascial tissues: cellular and mechanical responses to damage**

225

226 Excessive or prolonged loading or direct trauma to fascial tissues initiates micro and macro
227 changes necessary for tissue repair. These effects may also contribute to pathological changes
228 that modify tissue function and mechanics, leading to compromised function of healthy tissue.
229 Effects may become systemic, and thus not limited to the injured/loaded tissues.

230
231 Following an acute injury from overload or anoxia in fascial tissues, the immune response aims
232 to phagocytose injured cells. An acute inflammatory response is typically short-lived and
233 reversible and involves the release of a range of molecules, including pro-inflammatory cytokines
234 from injured cells and macrophages, along with other substances (e.g. bradykinin, substance P
235 and proteases) that sensitise nociceptive afferents⁵² and promote immune cell infiltration. If
236 loading is prolonged or repetitive, persistent inflammation may develop,^{53 54} leading to the
237 prolonged presence of macrophages and cytotoxic levels of cytokines in and around tissues
238 ultimately resulting in ongoing tissue damage. Some tissue cytokines (e.g. interleukin-1 β [IL-1 β ,
239 tumour necrosis factor [TNF] and transforming growth factor beta [TGF β -1]) are fibrogenic
240 cytokines that can promote fibrosis via excessive fibroblast proliferation and collagen matrix
241 deposition.⁵⁵

242
243 Overproduction of cytokines also maintains sensitisation of nociceptive afferents—a change that
244 would increase production and release of substance P (a known nociceptor neuropeptide). Recent
245 studies show that substance P can stimulate TGF β -1 production by tendon fibroblasts and that
246 both substance P and TGF β -1 can induce fibrogenic processes independently of each other.⁵⁶

247
248 Taken together, these findings suggest that both neurogenic processes (nerves are the primary
249 source of substance P) and loading/repair processes (TGF β -1 is produced by fibroblasts in
250 response to mechanical loading and during repair) can contribute to increased collagen in fascial
251 tissues. Fibrosis (e.g. collagen deposition) around tendon, nerve and myofascial tissues influences
252 dynamic biomechanical properties secondary to tissue adherence and can tether structures to each
253 other or induce chronic compression.⁵⁷ Increased collagenous tissues surrounding nerves can
254 tether nerves and also enhance pain behaviours.⁵⁸ Furthermore, inflammatory cytokines can ‘spill
255 over’ into the bloodstream, leading to widespread secondary tissue damage and central nociceptor
256 windup.^{53 59} Circulating TNF is elevated in chronic lower back pain,⁶⁰ and recent data highlight a
257 relationship between elevated TNF and greater risk for progression to chronic pain in some
258 individuals⁶¹ and in animal models of overuse.⁵⁹

259
260 Muscles also undergo changes in muscle fibre composition, adiposity and fibrosis in response to
261 injury to related structures (e.g. injury to an intervertebral disc) even in the absence of muscle
262 trauma (Fig. 4). These changes closely resemble those identified for direct muscle trauma, such
263 as supraspinatus tendon lesion,⁶² although with some differences (e.g. differences in the
264 distribution of infiltrating fat). After an injury to an intervertebral disc, deep back muscles
265 undergo rapid atrophy,^{63 64} most likely mediated by neural changes such as reflex inhibition.⁶⁵
266 This is followed by changes in muscle fibre composition (slow-to-fast muscle fibre transition),

267 fibrosis and fatty infiltration associated with increased production of pro-inflammatory cytokines
268 (e.g. TNF).⁶⁶ Increased cytokine expression was first identified from mRNA analysis of muscle,
269 but with an unclear origin. Recent work suggests this is mediated by an increased proportion of
270 pro-inflammatory macrophages,⁶⁷ hypothesised to result from altered metabolic profiles of
271 muscle as a consequence of transition to more fast (fatigable) muscle fibres.⁶⁸ Adipose tissue is a
272 potential source of pro-inflammatory cytokines and has been implicated in a range of
273 musculoskeletal conditions, including osteoarthritis.⁶⁹ Regardless of the underlying mechanism,
274 fibrotic changes in muscle have a substantial potential impact on tissue dynamics and force
275 generation capacity.

276
277 Exercise, physical modalities and pharmacological interventions have all been shown to reduce
278 the inflammatory processes associated with fascial tissue injury and fibrosis. For example, early
279 treatment with anti-inflammatory drugs can prevent/reverse pain behaviours induced by TNF
280 signalling and reduce downstream collagen production in animal models.⁷⁰ Stretching of fascial
281 tissues can promote resolution of inflammation both in vivo and in vitro,⁷¹ and manual therapy
282 can prevent overuse-induced fibrosis in several fascial tissues.⁷² In terms of muscle changes,
283 resistance exercise is necessary to reverse fatty changes (and perhaps fibrosis) in chronic
284 conditions,⁷³ whereas gentle muscle activation is sufficient to reverse early muscle atrophy⁷⁴ and
285 whole body exercise can prevent inflammatory changes in back muscles that follow intervertebral
286 disc injuries.⁷⁵

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289 *Outlook and perspectives for future research:*

290 Future research is needed to gain a deeper understanding of the mechanisms underlying the
291 impact of treatments on fibrosis and fatty changes in fascial tissues. Although there is evidence
292 that exercise, physical therapies or pharmacological approaches can impact inflammatory
293 processes, and reduce consequences, further work is required to understand how best to tailor
294 interventions based on the time-course of pathology and type of exercise, or whether there is
295 additional benefit from combined treatments.

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297

298 **Imaging and non-imaging tools for diagnosis and assessment**

299

300 Pathological changes in the mechanical properties of fascial tissues have been hypothesised to
301 play an essential role in musculoskeletal disorders such as chronic pain conditions and overuse
302 injuries.⁷⁶ As a result, considerable demand for diagnostic methods examining fascial tissue
303 function has arisen. In basic research, an oft-used approach is to study molecular and mechanical
304 changes in myofibroblasts and other biomarkers via needle biopsy and subsequent
305 immunohistochemistry.⁷⁷

306

307 To evaluate the effects of treatment and exercise in clinical settings, a series of methods are
308 available (Table 1). Changes in water content can be analysed via bio-impedance assessment,⁷⁸

309 but there is no data on reliability and validity of measurements in smaller body regions. Manual
310 palpation represents a cost-neutral and widely used screening method aimed at assessing
311 viscoelastic properties (e.g. stiffness); however, similarly, its reliability is limited.^{48 79-81}
312 However, the approach is based on a number of assumptions, and available devices often lack a
313 thorough proof of validity.^{77 82} Moreover, no tissue-specific conclusions can be drawn due to the
314 black-box character of the measurements.⁸³ Imaging methods such as ultrasound or elastography,
315 in contrast, are promising tools for explicitly quantifying the mechanical properties of fascial
316 tissues under in vivo conditions.⁸⁴

317
318 Producing a distortion of the measured tissue (e.g. through compression or shear waves),
319 elastography provides ultrasound images reflecting the relative hardness of the targeted area.
320 Recently, the technique has been increasingly applied in musculoskeletal research. However, the
321 existence of several different methods, lack of standardisation and frequent appearance of
322 artefacts during measurements threaten the validity of achieved results.⁸⁵ Without the use of
323 elastography, the conventional ultrasound image can be reliably used to display and measure the
324 morphology of fascial tissues, such as myofascial tissues, ligaments and tendons.⁸⁶ Some initial
325 studies have, moreover, attempted to quantify relative movement (e.g. sliding of fascial layers
326 and shear strain) using cross-correlation calculations.⁸⁷

327
328 Despite some initial applications to myofascial tissues, most data on ultrasound imaging are
329 available for tendon measurements (Fig. 5). In the late 1990s, advancements made in the
330 application of B-mode ultrasonography allowed quantification of the tensile deformation of
331 human tendons, in vivo, based on tracking of anatomical features in the tendon when pulled on
332 by the force exerted in the in-series muscle during static contraction.⁸⁸ Unfortunately, the in vivo
333 stiffness and Young's modulus results often disagree with findings from in vitro material tests,
334 when forces and elongations are precisely controlled and measured. Errors are likely being
335 caused by in vivo measurement simplifications in the quantification of both tendon deformation
336 and the loading applied during the static muscle contraction. The former includes simplifications
337 regarding the tendon's resting length, line of pull and uniformity in material properties. The latter
338 includes simplifications regarding the effect of loading on tendon moment arm length, the effect
339 of antagonist muscle co-activation and the uniformity in tendon cross-sectional area. Most of
340 these simplifications can be avoided by appropriate measurements to quantify the neglected
341 effects. In addition, recent developments in ultrasound shear-wave propagation⁸⁹ and speckle
342 tracking⁹⁰ have the potential to substantially improve experimental accuracy and physiological
343 relevance of in vivo findings.

344
345 In contrast to static muscle contraction tests aimed at assessing human tendon stiffness and
346 Young's modulus, scanning during dynamic activities has typically been applied to document
347 tendon deformations directly, through morphometric analysis on scans,^{91 92} or indirectly, through
348 ultrasound propagation speed analysis,^{93 94} to investigate the interaction between tendon and
349 muscle in the studied task. These experimental approaches are relatively immune to problems
350 caused by erroneous quantification of tendon forces; however, appropriate measurements need to

351 be taken to validate the assumption that the usual practice of tracking a single tendon anatomical
 352 point, or a tendon region limited by the size of the scanning probe, can give a representative
 353 picture for the entire tendon.

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356 *Outlook and perspectives for future research:*

357 In view of the current diagnostic methods' limitations, further research investigating the
 358 measurement properties (e.g. validity) is warranted to provide evidence-based recommendations.
 359 Hence, within the clinical assessment of mechanical soft-tissue properties, collected data should
 360 be interpreted with caution, and, as long as no clear gold standards exist, a combination of
 361 methods seems advisable instead of focusing exclusively on one technique. Ultrasound-based
 362 assessments of tendon deformability on loading have grown in popularity but can provide
 363 erroneous conclusions due to several invalid assumptions and approximations typically made to
 364 simplify the experimental protocol. Most of these errors can be eliminated by appropriate
 365 measurements.

366

367 **Mechanobiology of fascial tissues: effects of exercise and disuse**

368

369 The main principles of the above ultrasound-based methodology have been implemented in
 370 numerous studies over the last 20 years to study the adaptability of human tendons to exercise
 371 and disuse.^{95 96} The findings convincingly show that human tendons respond to the application of
 372 chronic overloading by increasing their stiffness and to chronic unloading by decreasing their
 373 stiffness. The mechanisms underpinning these adaptations include changes in tendon size and
 374 changes in Young's modulus. One common finding among studies is that tendon adaptations
 375 occur quickly, within weeks of mechanical loading/unloading application.^{97 98} Importantly,
 376 however, some studies report adaptations in tendon size but not tendon material,⁹⁹ and others in
 377 tendon material but not size,⁹⁷ while some report adaptations in both tendon size and material.¹⁰⁰

378

379 To study human tendon mechanobiology and explore the basis of the above distinct adaptability
 380 features, both cross-sectional and longitudinal experimental designs have often been adopted.
 381 Cross-sectional designs have been used for the following purposes: (a) to compare tendons
 382 subjected to different habitual loads due to their specific anatomical location,¹⁰¹ (b) to compare
 383 tendons between limbs with muscle strength asymmetry,⁹⁹ (c) to compare tendons in humans
 384 with different body mass but similar habitual activities⁹⁶ and (d) to compare tendons in athletes
 385 with those in sedentary individuals.¹⁰⁰ Study designs (a), (b) and (c) support the notion that
 386 adjustments in tendon stiffness to accommodate changes in physiological loading are
 387 accomplished by adding or removing tendon material rather than altering Young's modulus of the
 388 tendon. Importantly, the addition or removal of tendon material does not seem to always occur
 389 uniformly along the tendon, but in some regions only, which can go undetected unless the whole
 390 tendon is examined.¹⁰² In contrast to study designs (a), (b) and (c), findings from study design (d)
 391 show that improvements in Young's modulus of the tendon may occur and account fully for, or

392 contribute to, the increased tendon stiffness in response to loading. Interestingly, exercise-
 393 training intervention studies also report improvements in Young's modulus of the tendon.⁹⁵⁻⁹⁷ In
 394 combination, these findings indicate that stiffening of the tendon through alteration of its material
 395 requires 'supra-physiological' loading features (e.g. in terms of loading magnitude, frequency
 396 and/or duration). Once this rapid adaptation occurs and the exercise becomes a habitual daily
 397 activity, alterations in tendon size might mediate any further changes in tendon stiffness.

398

399 *Outlook and perspectives for future research:*

400 Combining ultrasonography with dynamometry methods has now made it possible to assess in
 401 vivo human tendon plasticity under conditions of altered mechanical loading. Two important
 402 questions warrant further research. (1) What is the mechanism underpinning regional differences
 403 in tendon adaptability in terms of tendon size? Possibilities worth investigating include
 404 differences in local stress, local Young's modulus, local blood flow and mechanotransduction
 405 sensitivity. Finite element modelling of the tendon may be an appropriate avenue to examine the
 406 first two possibilities. (2) What is the limiting factor in tendon plasticity to exercise? An intuitive
 407 answer is that the magnitude and time-course of tendon plasticity are merely determined by how
 408 much and how fast the in-series muscle force increases as the muscle adapts to the chronically
 409 increased load, but confirming this requires systematic research.

410

411 **Interventions for fascial tissue pathologies in sports medicine**

412

413 Fascial tissue dysfunction in the field of sports medicine is rarely treated surgically. Anti-
 414 inflammatory drugs are used for sports-related overuse pathologies; however, they may impair
 415 regeneration and diminish tissue adaptation.^{24 25} Gyrase-inhibiting antibiotics often contribute to
 416 an increased likelihood of tendon injuries in sports.¹⁰³ In addition, injections of platelet-rich
 417 plasma seem to be successful in some cases of tendinopathy, although efficacy remains
 418 inconclusive.^{67 104} Moderate evidence exists for the value of shockwave therapy and eccentric
 419 loading in tendon healing.^{105 106} Similarly, foam rolling (tool-assisted massage of myofascial
 420 tissues) seems to improve short-term flexibility and recovery from muscle soreness^{75 107 108} and
 421 decrease latent trigger point sensitivity.¹⁰⁴ Nevertheless, the physiological mechanisms of these
 422 reported effects remain unclear although initial evidence suggests increases in arterial perfusion,
 423 enhanced fascial layer sliding and modified corticospinal excitability following treatment.¹⁰⁹⁻¹¹¹
 424 Finally, manual therapies, such as massage, osteopathy or Rolfing (a massage technique based on
 425 achieving symmetrical alignment of the body), are frequently used to improve fascial tissue
 426 regeneration or athletic performance, although their efficacy still remains to be validated.^{112 113}

427

428 *Outlook and perspectives for future research:*

429 Hopefully, current and future improvements in assessment methodologies will generate more
 430 conclusive research regarding which treatment modalities are most promising for specific
 431 conditions. While commercial and other interests often favour the promotion of premature
 432 positive conclusions about specific fascia-related treatments, strict application of scientific rigour
 433 is essential for the development of this promising field.

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Key messages

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- The *fascial system* is a three-dimensional continuum of soft, collagen-containing, loose and dense fibrous connective tissue that permeates the whole body
- Non-myotendinous (myofascial) force transmission via inter- and extramuscular fascial tissues provides a relevant pathway for force transmission. Its contribution to remote exercise effects and non-local symptom manifestations in musculoskeletal disorders remains to be elucidated
- Excessive or prolonged loading or direct trauma to fascial tissues initiate micro and macro changes (e.g. inflammation, fibrosis, fatty changes) resulting in ongoing tissue damage
- Diagnostic methods to examine fascial tissue function include bio-impedance assessments, manual palpation, indentometric measurements and imaging methods (ultrasound, elastography). As long as no clear gold standard exists, a combination of methods seems advisable instead of focusing exclusively on one technique
- Future improvements in assessment methodologies will generate more conclusive research regarding which treatment modalities are most promising for specific conditions. While commercial and other interests often favour the promotion of premature positive conclusions about specific fascia-related treatments, strict application of scientific rigour is essential for the development of this promising field

458 **Competing interests:** None declared
459 **Funding:** PH is supported by a research Fellowship from the National Health and Medical
460 Research Council of Australia (NHMRC; **APP1102905**)
461 **Partial Funding provided by the Ida P Rolf Research Foundation**
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735 **Table 1.** Currently used diagnostic methods to examine fascial tissue structure and function

Method	Assessment target	Advantages	Disadvantages	References
<i>Biopsy</i>	Histological properties incl. molecular analysis	Permits analysis of tissue damage, infiltration of inflammatory cells, cytokines, etc.	Invasiveness	66, 75, 77
<i>Bioimpedance</i>	Hydration changes	High sensitivity	Lacking data on reliability and validity for smaller regions	78
<i>Manual palpation</i>	Stiffness, elasticity and shearing-mobility of tissue	Cost effectiveness Psychosocial factors	Limited reliability	79-82
<i>Indentometry</i>	Stiffness and elasticity	Established reproducibility	Limited depth	81, 83-85
<i>Ultrasound (US) imaging</i>	Thickness of layers, tendon elongation	Permits diagnosis of a fibrotic thickening (e.g. of a particular endomysium), or of tendon strain response during loading	Difficulty in standardizing the exact viewing angle	86, 88
<i>US with correlation software</i>	Relative shearing motion of adjacent layers	Permits diagnosis of adhesive tissue connections, such as in chronic low back pain	Lacking standards for selection of regions of interest	89
<i>Compression based US elastography</i>	Stiffness	Measurements possible at further depth than e.g. with indentometry	Lack of standardization Frequent appearance of artefacts	87
<i>Shear wave US elastography</i>	Stiffness	Enhancement by propagation analysis permits morphological analysis	Lack of standardization	91, 92
<i>B-mode ultrasonography</i>	Tendon structure and mechanical/material properties	1) In vivo methodology 2) application in perspective studies 3) relatively inexpensive	1) Accuracy is user-dependent 2) Applicability is limited to superficial tendons mainly 3) Limited control of any medio-lateral deviation of the tendon line of pull off the scanning plane 4) Tendon slack length (ie, at 0% strain) and tendon force cannot be directly measured and need to be estimated 5) Scanning frame rate is currently limited	90, 97,98,99,104

736 **Figure legends**

737
738 **Figure 1. Components of the fascial system.** The fascial system includes large aponeuroses like
739 the first layer of the thoracolumbar fascia (A), but also a myriad of enveloping containers around
740 and within skeletal muscles (B) and most other organs of the body. The internal structure of
741 fascial tissues is dominated by collagen fibers which are embedded in a semi-liquid ground
742 substance (C). Images with friendly permission of fascialnet.com (A) and thomas-
743 stephan.com (C).

744
745 **Figure 2. Transmission electron microscopy reveals the close cell-ECM interaction in human**
746 **skeletal muscle (*musculus vastus lateralis*, 25,000 x magnification) allowing a bidirectional cell-**
747 **ECM interaction.** Myofilaments (MF) are connected by Z-lines (Z) and costameres (C) to the
748 adjacent basal lamina (BL) and the surrounding reticular lamina (RL). Crossbridging structures
749 (arrows) connect the Z-lines and costameres to the dense part of the basal lamina. The reticular
750 lamina is structured by a network of collagen fibrils (CF) and additional ECM molecules, which
751 have a close connection to the basal lamina allowing bidirectional transmission of mechanical
752 forces.

753
754 **Figure 3. Factors influencing the mechanical stiffness of fascial tissues and their hypothesized**
755 **impact.** Up arrows symbolize a positive effect (e.g. increased cellular contractility increases
756 stiffness), down arrows symbolize a negative effect (e.g. increased use of corticosteroids
757 decreases stiffness) and double arrows symbolize an ambiguous association (e.g. hyaluronan
758 decreases stiffness if mobilized by mechanical stimuli, but leads to increased stiffness if no
759 stimuli are applied).

760
761 **Figure 4. Proposed timeline and mechanisms for fascial, adipose and muscle changes in the**
762 ***multifidus* muscle after intervertebral disc lesion.** Three phases, acute (top), subacute-early
763 chronic (middle) and chronic (bottom), are characterized by different structural and inflammatory
764 changes. TNF - Tumour Necrosis Factor; IL-1 β – Interleukin-1 β .

765
766 **Figure 5. Tendon displacement measured by B-mode ultrasound.** Sonographic images of the
767 human tibialis anterior (TA) muscle at rest (top) and in response to electrical stimulation at 75 V
768 (middle) and 150 V (bottom). The white arrow indicates the TA tendon origin. Notice the
769 proximal shift of the TA tendon origin upon electrical stimulation.⁸⁸

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