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MYOFASCIAL PAIN (R GERWIN, SECTION EDITOR)

Painful Connections: Densification Versus Fibrosis of Fascia

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Abstract Deep fascia has long been considered a source of pain, secondary to nerve pain receptors becoming enmeshed within the pathological changes to which fascia are subject. Densification and fibrosis are among such changes. They can modify the mechanical properties of deep fasciae and damage the function of underlying muscles or organs. Distinguishing between these two different changes in fascia, and understanding the connective tissue matrix within fascia, together with the mechanical forces involved, will make it possible to assign more specific treatment modalities to relieve chronic pain syndromes. This review provides an overall description of deep fasciae and the mechanical properties in order to identify the various alterations that can lead to pain. Diet, exercise, and overuse syndromes are able to modify the viscosity of loose connective tissue within fascia, causing densification, an alteration that is easily reversible. Trauma, surgery, diabetes, and aging alter the fibrous layers of fasciae, leading to fascial fibrosis.

Keywords Fascia · Densification · Fibrosis · Connective tissue · Hyaluronan · Loose connective tissue · Aging · Overuse syndrome · Mechanics · Hysteresis · Stress–strain curves · Load · Lines of forces

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Introduction

Deep fascia has been considered one of the origins of pain [1•]. However, it has never been established what alterations in deep fascia must occur to account for pain. The terms "fibrosis" and "densification" are often used to indicate such fascial alterations [2, 3••]. However, the two terms are not interchangeable. On the one hand, fibrosis is similar to the process of scarring, with the deposition of excessive amounts of fibrous connective tissue, reflective of a reparative or reactive process. It can obliterate architecture and function of the involved tissue. On the other hand, densification indicates an increase in the density of fascia. This is able to modify the mechanical proprieties of fascia, without altering its general structure (Fig. 1).

Dupuytren's disease [4] and eosinophil fasciitis [5] could be considered typical examples of fascial fibrosis, while chronic, nonspecific neck pain seems to be associated with fascial densification [3••]. In reality, in the majority of cases, it is not clear whether it is fascial densification or fascial fibrosis that is involved. This lack of certainty not only causes confusion in terminology, but also implies that very different treatment modalities can be applied to fascia in an attempt to relieve pain.

Without a specific underlying mechanism being recognized, and no criteria or indicators commonly accepted, there is no basis for recommending a particular treatment. It is only with a clear understanding of fascial anatomy and structure that it will be possible to make accurate differential diagnoses, and to

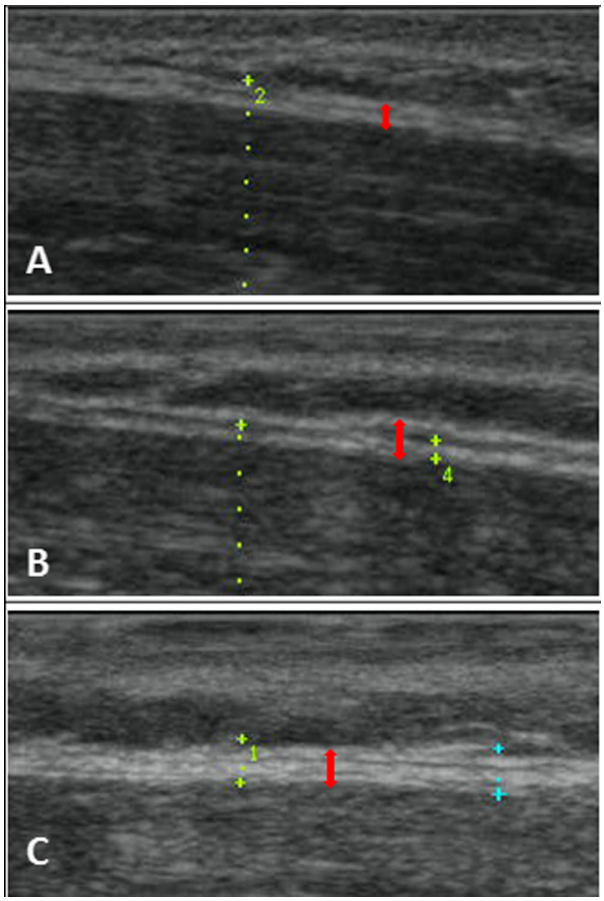

Fig. 1 Ultrasonography of the deep fascia of the neck over the sternocleidomastoid muscle. The deep fascia is highlighted with a red arrow. **a** Normal fascia, the two fibrous layers (white layers) and the loose connective tissue (in black) in the middle are visible. **b** Densification of the same fascia: the loose connective tissue is increased, the fibrous layers are normal. The total thickness of the deep fascia is increased. **c** Fibrosis of the same fascia. The fibrous component is increased as is the total thickness of the fascia (in this patient it measures 1.8 mm)

understand what alterations in fascia could underlie pain. Only then will it be possible to prescribe correct treatments.

Here, we attempt to provide an overall description of fascia, and its organization, its connective tissue and neuronal structures, as well as their relationship to adjoining tissues. The mechanical properties of fascia are also discussed. Through such descriptions, a basis may emerge for identifying the various alterations in fascia that lead to pain, and to evolve appropriate strategies for pain management.

Micro- and Macroscopic Characteristics of the Deep Fascia

The deep fasciae are essentially formed by collagen type I organized into numerous fibrous bundles that run in different directions. It must also be recognized that type III collagen, except in the case of bone, always accompanies type I collagen, though the ratio of I:III can vary widely. It is recognized that during periods of rapid growth, wound healing, regeneration and repair, and in fetal development, tissues contain more abundant amounts of collagen type III. Levels of type III collagen can also vary in different kinds of fascia, but this has not been investigated thoroughly.

The deep fasciae were formerly classified as an irregular dense connective tissue. But recent investigations [6–8] demonstrate that deep fasciae consist of 2–3 layers of parallel collagen fiber bundles, with each layer having a mean thickness of 277 μm (±SD 86.1 μm). These layers are composed of parallel collagen fiber bundles that occur in a wave-like arrangement. Moreover, the collagen fibers of adjacent layers are oriented in different directions forming angles of 75–80°. Each layer is separated from the other by a thin layer of loose connective tissue (mean thickness 43 ± 12 μm) that permits the sliding of the several layers upon adjacent ones. The tacit assumption is made that the loose connective tissue contains more abundant levels of collagen type III. Owing to such layers of loose connective tissue, from a mechanical point of view, each fibrous layer can be considered to function independently. Moreover, such a structure is able to work properly only if all the component layers are able to glide smoothly over one another.

Additional structural components of fascia have been identified. Elastin fibers are present in loose connective tissue. There are also proteoglycans, as well as the glycosaminoglycan hyaluronic acid (hyaluronan; HA). The latter occur at higher levels in loose connective tissue, and may play essential roles in the etiology of pain [9].

Mechanical Properties of Deep Fascia

Recently, investigators have attempted to describe the mechanical proprieties of deep fasciae, focusing predominantly on their capacity to transmit muscular forces at a distance, attributing this to the collagen fibers [10–14]. Up until now, the tissue has been evaluated by testing it in its entirety, for example applying the same mechanical conditions to all the adjacent dense layers. The approach is certainly justified because of the intrinsic difficulty in planning alternative experimental procedures. But this represents a major obstacle in understanding deep fascia, as the effects of the loose connective layers are not considered properly in this model.

In actuality, the multilayered organization of the collagen fibers implies a more complex mechanical behavior in comparison to a tendon. The orientation of the fiber bundles ensures the ability of the fasciae to provide strength in the case of tensile forces applied in different directions (multiaxial loading) and the anisotropy of the tissue, as pointed out by

experiments carried out on human donors [14, 15••] or animal models [16]. Furthermore, as with other connective tissues, the deep fascia shows distinct viscoelastic properties, with important functional implications. One of these is the fact the deep fascia shows high or low stiffness, depending on the rate of loading [17].

Strength Properties of the Deep Fascia

Experimental testing has shown that strips of deep fascia with 1 cm of width can have a tensile strength of more than 390 N [12]. Furthermore, the strength appears to be related to muscular mass and maximum contraction force. This fact makes it possible to assume that the deep fasciae work like a tendon, transmitting force from one segment to another. For example, contraction of the gluteus maximus will stretch the fascia lata all the way to the point into which it inserts. The fascia lata will then transmit this force in a longitudinal direction along the iliotibial band, extending the tension into the antero-lateral portion of the crural fascia and the anterior knee retinaculum. Trindade et al. [18] demonstrate that the human deep temporal fascia plays a fundamental role in transmission of the tensile and shear loads generated by the temporal muscle to the masticatory system.

Stiffness Properties of the Deep Fascia

The spatial disposition of the collagen fibers result in anisotropic characteristics in relation to tissue stiffness. Hurschler et al. [19], for example, report an average structural stiffness per unit width of the deep fascia of the leg to be 50.9±33 N/mm in the longitudinal direction and of 46.4±16 N/mm in the transverse direction. Our studies confirm that deep fascia of the leg is stiffer in longitudinal than in the transverse direction [15••]. The lower stiffness in the transverse direction may be associated with the capability of deep fascia to adapt to muscle fiber contraction. The higher stiffness in a longitudinal direction could permit the fascia to transmit part of the muscle contraction force in a way similar to that of tendons. It is likely that any alteration of stiffness in longitudinal or transverse direction could result in the capability of generating and transmitting muscle contraction forces.

Nonlinear Stress–strain Behavior

Analyses of the mechanical responses of the aponeurotic fasciae to uniaxial loading tests demonstrate typical nonlinear behavior, similar to that of other connective tissues [20, 21]. Three typical regions of the aponeurotic fasciae stress–strain curve can be distinguished: a "toe" region, a linear region, and a failure region. The "toe" region is near the undeformed state. In this region the tissue has low stiffness, a mechanical characteristic that is related to the crimping conformation of the collagen fibers and high compliance of the elastin fibers. In experimental tests carried out on samples of the deep fascia of the leg [14, 15••], the "toe" region is found to extend up to 4 % of strain. Above this value (linear region), the tissue shows greater stiffness and an almost linear response. In this region, the stress increment is proportional to strain increment. With an increase of strain, the deep fascia undergoes a "damage phenomenon" that consists of an incremental reduction of the stiffness up to complete failure of the tissue. In some samples of leg deep fascia, a progressive failure is found, starting at about 12 % of strain. This failure is recognized to be the result of damage to the collagen fibers. Owing to the anisotropic characteristics of deep fasciae, the stress–strain curves have been found to depend on the direction of loading [15••, 16]. Furthermore, the mechanical responses differ, depending on the compartment being considered. For example, our research demonstrates that samples taken from the anterior leg compartment are stiffer than samples removed from the posterior leg compartment [15••]. These data may be one of the components that explain why, in clinical practice, the anterior compartment syndrome occurs more frequently than in the posterior one [22, 23].

Stress Relaxation of Deep Fasciae

Stress relaxation is one of the typical phenomena related to the viscoelastic nature of deep fasciae. It consists of stress reduction within tissue when it is suddenly stretched and kept stretched over a period of time. This behavior is due to a rearrangement of the structural components, and to the migration of the liquid phases throughout the time period, leading to stress decay as a macroscopic effect. The trend of stress relaxation is characterized by a significant decrease of the stress values during the early phase of the process. Experimental tests on leg deep fascia demonstrate a stress relaxation of about 30 % within the first 120 s, a stress drop that represent 90 % of the relaxation process in an observation time of 240 s [15••].

In the evaluation of the short-term behavior of leg deep fascia, this means that 90 % of stress relaxation takes place in the first minute following application of the strain, reaching an almost steady state within the aforementioned time interval. Functional implications derive from this experimental observation. For example, this indicates that to relax the fasciae, during stretching, the position must be maintained for at least 1 min. The stress relaxation property of the deep fasciae is often important in rehabilitation. Wójcik et al. [24] evaluated the effectiveness of fascial relaxation for tense muscles in patients after hip arthroplasty. The results indicate that the techniques of fascial relaxation significantly reduces recovery time and eliminates muscle tensing in the operated hip joint, thus also contributing to improvement in the range of motion.

Hysteresis

The hysteresis is another typical phenomenon related to the viscoelastic nature of deep fascial tissue. In general, hysteresis can be defined by the amount of energy lost during a loading–unloading cycle in a tissue. Several experimental tests on different connective tissues show that the hysteresis decreases with the increment of the loading rate characteristic of the loading–unloading cycle [25]. For the deep fascia, this has important consequences from a functional point of view in cases in which mechanical efficiency, namely low energy loss, becomes important, such as in rapid movements. In fact, in relation to tendon structure, the reduction of the hysteresis of deep fascia with the increase of loading rate improves the capacity of elastic energy storing and recoiling.

Mechanical Properties of the Loose Connective Tissue

From a mechanical point of view, the loose connective tissue has the fundamental role of assuring the autonomy of the two dense fibrous layers. Only if the loose connective tissue has low viscosity can the adjacent dense fibrous layers be stretched and transmit forces along different directions without interfering with each other. In addition, the loose connective tissue plays a fundamental role in the ability of the deep fascia to adapt to volume variations of the underlying muscles during contraction.

Despite the ubiquitous presence throughout the body of loose connective tissue, and its potential importance in a variety of therapies that utilize mechanical stretch, as well as in normal movement and exercise, very little is known about the biomechanical behavior of loose connective tissues. To better understand this, it is necessary to investigate its composition. The main components of the loose connective tissue are water, ions, and glycosaminoglycans, with a prevalence of HA. HA is present both between the dense layers of deep fascia and between the deep fascia and the underlying muscle. In skeletal muscle, HA is present in the epimysium, perimysium, and endomysium [26, 27], which are extensions of the fascia.

Perivascular and perineural fascia also contain high levels of HA. HA is secreted by specific cells inside the fascia called fasciacytes [9]. These fibroblast-like cells may be of monocyte/macrophage origin, similar to the HA-secreting cells of joints and the eye. In joints, these are termed synoviocytes, secreting the HA of the synovial fluid. In the eye, they are called hyalocytes, responsible for the HA of the vitreous fluid. Hyaluronan occurs both as individual molecules, and as macromolecular complexes that contribute to the structural and mechanical properties of fascia. Hyaluronan is a lubricant that allows normal gliding of joint and connective tissue. It is likely that these gliding interactions are influenced by the composition and efficacy of the HA-rich matrix.

Goetz and Baer [28] analyzed the subsynovial connective tissue of the carpal tunnel, which could be considered comparable to the loose connective tissue associated with fasciae. It is arranged in layers around the digital flexor tendons and the median nerve. Its thickness is about 0.22 mm, similar to that of fascial loose connective tissue. Its main role is to assist in the gliding of tendons. The aim of that study was to characterize the permeability of the tissue and its time-dependent response to compressive loads, in relation to the capability of having free flow of the permeating fluid. The average tissue permeability is 8.78×10^{-15} m^4/Ns, a value slightly greater than that of articular cartilage. Behavior under a constant compressive load demonstrated time-dependency, with an average initial modulus of 395 kPa, gradually decreasing to a value of 285 kPa in the steady-state phase (about 25 mins from the initial application of the load). The authors found a wide range of mechanical responses under constant load. This does not correlate with age, sex, or harvest location.

In the future, similar experimental tests could be performed on the deep fascia to clarify the role of the loose tissues in ensuring sliding capability of the dense connective layers. At present, similar tests are not available. Because of the paucity of data in the literature, we can only postulate what the necessary conditions are to keep fasciae functional, and the reasons for the possible alteration in their physiological behavior.

Possible Alterations of the Deep Fasciae

Considering our understanding of the complex structure of deep fasciae, we postulated that they could be subjected to at least two different kinds of alterations: (1) damage of the loose component that affects the sliding system between different layers, and (2) damage of the fibrous component that affects the capacity of loading transmission. Recent work by Langevin et al. [29•] focuses attention on the sliding capability of dense layers, which is a direct effect of the shear strain occurring in the interposed loose connective tissue layer. They find significant correlations in men with chronic low back pain between shear strain capability of the loose connective layer and the following variables: perimuscular connective tissue thickness; echogenicity; trunk flexion range of motion; and trunk extension. This demonstrates the importance of altered sliding of the thoracolumbar fascial layers in low back pain. More recently, Stecco et al. [3••] have documented that a correlation exists between a decrease in the range of motion and increases in the thickness of neck deep fasciae. These authors analyzed, using ultrasonography, the fascia of the stenocleidomastoid (SCM) muscle in healthy participants and in patients with chronic, nonspecific neck pain. They found a mean thickness of fascia of 1.1 mm in the first group,

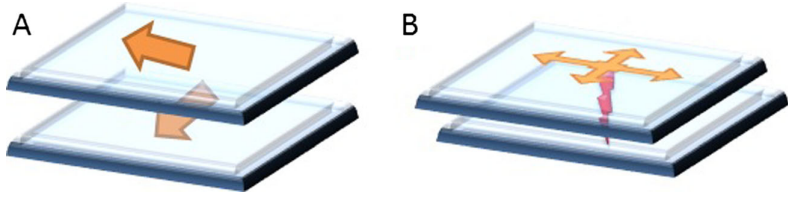

Fig. 2 **a** The two fibrous layers are free to glide thanks to the presence of low viscous loose connective tissue. This permits these layers to transmit the forces (represented by the orange arrows) independently and in different directions. **b** The densification of the loose connective tissue, represented with a red flash, alters the gliding between the two fibrous layers. The transmission of the forces can be altered in a way that is not easily defined. The tissue around the densification point can be subjected to intense mechanical stress

and 1.8 mm in the second group. For the Pearson correlation rank test between the range of motion and the fascia thickness in case and control groups, a value of r=0.915 was obtained. Consequently, these authors suggest the use of ultrasonography for the evaluation of deep fasciae in clinical practice. A thickness of >1.5 mm for the SCM fascia could be considered a cut-off value for the diagnosis of myofascial disease in subjects with chronic neck pain. In addition, this study suggests that variations in thickness of fascia correlate with increases in quantity of loose connective tissue, but not with dense connective tissue. Indeed, in the healthy participants, the deep fascia of SCM appears as a white, fibrous layer, while in all patients, the sublayers forming the deep fascia are recognized by the increased thickness of the loose connective tissue. A black layer appears (with a mean thickness of 0.36 mm) between the two fibrous sublayers (mean thickness 0.53 mm).

In the following sections, possible causes of alterations of these two components and the consequences for fascial functions will be examined.

Causes of Alterations of Loose Connective Tissue

Piehl-Aulin et al. [26] demonstrate accumulation of HA following exercise. We can postulate an increase in the quantity of HA in and on the surface of fascia occurring in all overuse syndromes. Similarly to a synovial joint, increased production of HA is the initial attempt to increase the gliding efficiency between two surfaces Increased HA correlates not only with improved lubricating function, but also with increasing viscosity, particularly if it is structured within thin layers. Indeed, at high concentrations, HA behaves like a non-Newtonian fluid and becomes more viscous [30, 31] because the HA chains entangle, contributing to the hydrodynamic properties of the solution. In addition, Tadmor et al. [32] show that when HA is organized into layers, viscosity increases considerably with increasing distance between the two surfaces. The increased viscosity of the loose connective tissue inside the fascia may cause decreased gliding between the layers of collagen fibers of the deep fasciae. This may be perceived by patients as an increase in fascial stiffness.

Some authors are attempting to modify the molecular structure of exogenously added HA with the aim of altering the mechanical proprieties of the extracellular matrix (ECM). For example, Chin et al. [33] demonstrate that the fascial ECM treated with high molecular weight tyramine-substituted HA exhibits low-load elastic mechanical properties, in particular a lower toe modulus, a trend toward lower toe stiffness, and a higher transition strain compared with water-treated controls.

The loose connective tissue mechanical proprieties also change with temperature. In particular, the three-dimensional superstructure of HA chains progressively breaks down when the temperature is increased to >40 °C [34]. This may explain the effects of many physical therapies that increase temperature (laser, etc.) and with warming up in general. The increased temperature breaks down superstructures, with a consequent decrease in viscosity.

Also, alterations of pH can change the viscosity of loose connective tissue. It is known that loose connective tissue is an important reservoir of water and salts for surrounding tissues. But it also has the capacity to accumulate varieties of waste products. The biomechanical properties of loose connective tissue may be altered depending upon accumulated lactic acid content after intense exercise, with its attendant acidity. Indeed, pH has a direct relationship to HA viscosity [35]. It has been demonstrated that in the muscle compartment, pH can reach a value of 6.60 [36–38] with an increase of approximately 20 % in HA viscosity, with a consequent sensation of momentary stiffness.

Finally, HA is also thixotropic. This means that its viscosity is reduced under any loading condition. This determines strain states, and that the rest condition allows HA to return to a more viscous state. Dintenfass [39] demonstrates that synovial fluid has thixotropic and elastic (instantaneous dilating) properties. He finds that its viscosity decreases with an increase in shear rate, but it is pressure-resistant under sudden impacts. Owing to its viscoelastic properties and to its affinity to cartilage surfaces, it cannot be squeezed out from between opposing surfaces. This property can also be assumed for the key element of the fascial loose connective tissue and explains why immobility reduces fascial gliding and, consequently, range of motion.

Causes of Alterations in the Fibrous Component

Trauma or Surgery

Damage to fasciae always causes an inflammatory reaction that promotes the healing process. The fibrous layers of the fascia can be perfectly restored; indeed, they are formed by collagen type I, the key molecule involved in the process of scar formation. When deep fascia is disrupted, three sequential, yet overlapping, phases of the reparative wound healing process occur: inflammation, proliferation, and remodeling. During the inflammation phase, cell debris is phagocytosed and removed from the wound by white blood cells. Blood factors are released into the wound that cause the migration and division of cells during the proliferative phase. The proliferation phase is characterized by angiogenesis, collagen deposition, and wound contraction [40]. Fibroblasts grow and form a new, provisional ECM by excreting collagen type III, and then type I collagen and fibronectin. In this phase, the collagen forms an irregular connective tissue that has the main function of closing the wound gap.

However, for the correct healing of the deep fascia to occur, it is fundamental that collagen be remodeled and realigned along the correct lines representing components of local tensile stress Remodeling can last for years, depending on the size and nature of the wound [41, 42]. In actuality, this process is fragile and susceptible to interruption or failure. In particular, it seems that a fundamental role is played by the mechanical stress acting on the injury site, which guides the neuroinflammatory response. For example, in the leg, a horizontal scar causes a tensile state three times greater than a vertical scar [43, 44]. If the tissue in which tensile state can be observed was previously in an unbalanced condition or is immobilized, the remodeling process does not lead to physiological spatial reconstitution, but instead causes random deposition of collagen fibers.

Diabetes

Nonenzymatic glycation of proteins is one of several theories advanced in recent years to explain the pathogenesis of complications of diabetes. It is a condensation reaction between glucose and free amino groups of proteins. The extent of glycation is largely dependent on the glucose concentration to which the protein is exposed, and to the biologic half-life of the involved protein. Additionally, Cohen [45] indicates that glycated proteins, through a series of rearrangement reactions, give rise to abnormal cross-links and complexes that are believed to alter structure–function properties. The collagen nonenzymatic glycation reaction was thoroughly studied for its effect on the development of diabetic long-term complications in eyes, kidneys, and peripheral nerves and vessels. Arkkila et al. [46] demonstrate that in people with diabetes, there is increased synthesis of type III and type IV collagen, reflecting deposition of matrix and basement membrane connective tissue. There is a concomitant decreased synthesis of type I collagen, which can result in weakened vascular integrity, particularly in patients with retinopathy.

Collagen glycation can also affect the deep fascia, causing thickening and fibrosis. Duffin et al. [47] demonstrate that patients with type I diabetes have a plantar fascia significantly thicker than that of normal controls. Also, Li et al. [48] demonstrate that collagen cross-linking by advanced glycation end-products alters the physical properties of collagen structures and tissue behavior, and reduces tissue stress relaxation ($p<0.01$), with a concomitant increase in tissue yield stress ($p<0.01$) and ultimate failure stress ($p=0.04$). Such collagens are also more susceptible to degradation by collagenases, and the panoply of matrix metalloproteinases.

All of these changes have been demonstrated for tendons, but it is probable that this also applies to fasciae, causing loss of fascial viscoelasticity driven by matrix-level loss of fiber–fiber sliding. Potentially, this has important implications for tissue damage accumulation, mechanically regulated cell signaling, and for matrix remodeling.

Hormones

Human connective tissue harbors receptors for various hormones, such as estrogen receptor β. Lee et al. [49] demonstrate that women that use oral contraceptives (OCPs) present with anterior cruciate ligament elasticity significantly lower than non-OCP users. In addition, knee flexion extension hysteresis is significantly higher in OCP users than in non-OCP users ($p<0.05$).

Aging

Wojtysiak [50] demonstrated, in pigs, numerous changes occurring during growth in the structure and properties of the intramuscular and perimuscular connective tissue of the longissimus lumborum muscle. More specifically, in newborns, the perimuscular collagen fibrils have a wavy disposition and form a loose network. Only with increasing age does the arrangement of collagen fibrils become denser and more regular. In contrast, the intramuscular collagen fibers decrease gradually with age of the pigs. These factors can influence the shear force value of connective tissue and the underlying muscles.

Trindade et al. [18] demonstrate that the human deep temporal fascia is stiffer in older people than in younger

people, and that a significantly higher *secant moduli* occurs with increasing age. Thus, increasing age creates stiffer, stronger, and more stable connective tissues, although they are much less flexible.

Conclusion

The complex structure of deep fasciae is associated with different kinds of pathological changes. If there is only an alteration of the loose connective tissue, the term fascial densification is probably preferred. If there is alteration of collagen fibrous bundles, the term fascial fibrosis is the term of choice. In reality, the two alterations are not incompatible. Indeed a chronic densification certainly affects the gliding between two adjacent fibrous layers. This can alter the distribution of the forces inside the fibrous layers, because they are unable to act independently. So, we have several possibilities:

1. Diet, exercises, and overuse syndromes that cause an alteration of the loose connective tissue inside the deep fascia, causing fascial densification. This alteration is easily reversible because we can modify the mechanical properties of the ECM by increasing the temperature, or increasing local strain with a (controlled) mechanical stimulus.
2. Trauma, surgery, and diabetes can alter the fibrous layers of the deep fasciae, causing a fascial fibrosis. This alteration is difficult to modify because only a local inflammatory process can destroy the pathological collagen fibers and permit deposition of new collagen fibers. Such deposition is based on optimized structural conformation with respect to the local mechanical state. Only early-guided mobilization permits correct healing of the deep fasciae in order to avoid the formation of fibrosis.

Chronic densification alters the gliding action between adjacent fibrous layers. This affects collagen fiber deposition, even at a site distant from the first site of densification. Indeed, the fascia is always subjected to remodeling pressures responding to the local mechanical state. If spatial deposition of fibers is altered with respect to physiological conditions, the rebuilding will be pathological. In rehabilitation during the densification phase, it is desirable to follow these principals, in order for effective treatment to take place to obtain a better result in a faster time and to avoid unwanted sequelae (Fig. 2).

In conclusion, deep fascia has been considered the source of pain, second to nerve pain receptors becoming enmeshed within the pathological changes to which fascia are subject. Densification and fibrosis are among such changes. By distinguishing between these two different changes in fascia, and understanding the connective tissue matrix within fascia, together with the mechanical forces involved, it will be possible to assign more specific treatment modalities to relieve chronic pain syndromes.

Compliance with Ethics Guidelines

Conflict of Interest Dr. Piero G. Pavan, Dr. Antonio Stecco, Dr. Robert Stern, and Dr. Carla Stecco each declare no potential conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- •• Of major importance

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