Curr Pain Headache Rep (2013) 17:352
DOI 10.1007/s11916-013-0352-9

MYOFASCIAL PAIN (R GERWIN, SECTION EDITOR)

Fascial Components of the Myofascial Pain Syndrome

Antonio Stecco · Marco Gesi · Carla Stecco · Robert Stern

Abstract Myofascial pain syndrome (MPS) is described as the muscle, sensory, motor, and autonomic nervous system symptoms caused by stimulation of myofascial trigger points (MTP). The participation of fascia in this syndrome has often been neglected. Several manual and physical approaches have been proposed to improve myofascial function after traumatic injuries, but the processes that induce pathological modifications of myofascial tissue after trauma remain unclear. Alterations in collagen fiber composition, in fibroblasts or in extracellular matrix composition have been postulated. We summarize here recent developments in the biology of fascia, and in particular, its associated hyaluronan (HA)-rich matrix that address the issue of MPS.

Keywords Fascia · Myofascial pain syndrome (MPS) · Hyaluronic acid · Densification · Myofascial trigger points (MTP)

This article is part of the Topical Collection on *Myofascial Pain*

A. Stecco
Department of Sport Medicine,
University of Padova, Padua, Italy

M. Gesi
Department of Human Anatomy,
University of Pisa, Pisa, Italy

C. Stecco (✉)
Department of Molecular Medicine,
University of Padova, Via Gabelli 65,
35127 Padova, Italy
e-mail: carla.stecco@unipd.it

R. Stern
Department of Basic Biomedical Sciences,
Touro/Harlem College of Osteopathic Medicine,
New York, NY 10027, USA

Published online: 26 June 2013

Introduction

MPS remains a medical mystery. The potential causes are unknown, except that myofascial trigger points (MTPs) appear to be involved. Knowing the potential causes of MPS is critical for developing effective treatment modalities. The muscle and nerve components of MPS are well-explored [1], involving motor, sensory, and autonomic components. However, the participation of fascia in MPS is less well described and far less understood. In the classic textbook "Myofascial Pain and Dysfunction" by Simons et al [1], the index does not contain a single entry for fascia. This reflects the extent to which fascia has been ignored by clinicians, and other members of the MPS community.

Only recently some authors [2–6] have suggested that connective tissue could become tighter in overuse syndromes or after traumatic injuries, but it is unclear if this is due to an alteration of collagen fiber composition, of fibroblasts, or of ground substance. The same authors suggest that the alteration of fascial pliability could be a source of body misalignment, potentially leading to poor muscular biomechanics, altered structural alignment, and decreased strength and motor coordination.

We now present an overview of fascia anatomy with an emphasis on new aspects of fascia biology and the various hypotheses to explain the role of fascia in MPS.

The Anatomy of Fascia

For the term deep fascia, we intend any dense fibrous sheath that interpenetrates and surrounds the muscles, bones, nerves, and blood vessels of the body, binding all these structures together into a firm compact mass. Over bones, it is called periosteum, around tendons, it forms the paratendon, around vessels and nerves, it forms the neurovascular sheath. Around joints, it strengthens the capsules and ligaments. So, we can

consider the paratendon, the neurovascular sheath, and the periosteum as specialization of the deep fascia, not only because they are in continuity with it, but also because they have the same histological features.

We can distinguish two main types of muscular fasciae however, according to their thickness and their relationships with the underlying muscles: the aponeurotic fasciae and the epimysial fasciae.

The Aponeurotic Fasciae

With the term aponeurotic fasciae we mean all the "well defined fibrous sheaths that cover and keep in place a group of muscles or serve for the insertion of a broad muscle" [7]. These fasciae are the better known; they correspond for example to the thoracolumbar fascia, the fascia lata, the crural fascia, etc. Inside the aponeurotic fasciae, many fibrous bundles running in different directions are macroscopically visible. For this reason, for a long time the aponeurotic fasciae were classified as irregular dense connective tissues. In reality, recent works [8–10] have demonstrated that the aponeurotic fasciae are formed of two or three layers of parallel collagen fiber bundles, each layer having a mean thickness of 277 μm (± SD 86.1 μm). These layers are composed of parallel collagen fiber bundles, presenting a woven arrangement. Moreover, the collagen fibers of adjacent layers are oriented in different directions, forming angles of 75°–80°. This pattern of deposition was confirmed by the 3D reconstruction of the crural and thoracolumbar fasciae. Each layer is separated from the adjacent one by a thin layer of loose connective tissue (mean thickness 43±12 μm) that permits the sliding of the layers over the adjacent ones, and so, from a mechanical point of view, each layer could be considered as independent, with a specific influence on the functionality of each tissue.

Several reports [11–17] suggest that the aponeurotic fascia is richly innervated, predominantly in the superficial sublayer [10]. Analyzing the relationship between these nerve terminations and the surrounding fibrous tissue, it becomes evident that the capsules of the corpuscles and the free nerve endings are closely connected to the surrounding collagen fibers. In this way, we can surmise that these nerve endings could be stretched, and become activated each time that the surrounding deep fascia is stretched. The mechanoreceptors, which are immersed in a fibrous stroma, are in this way sensitive to the traction of the underlying muscles, which the tendonous expansions transmit to the fascia. This hypothesis is also substantiated by embryogenetic studies that have established that the fibrous capsule of all mechanoreceptors is derived from the surrounding connective tissue; hence it is very likely that connections between these two elements persist into post-natal life.

The Myofascial Insertion

Many researchers have found that many muscles have fascial insertions [18–24], but their role is unknown. The best known expansion is the lacertus fibrosus, an aponeurosis that originates in the biceps tendon and then merges with the antebrachial fascia. But, in reality, every muscle has its own specific connection with the fascia. Usually these expansions are considered anatomical variations, but they are actually present constantly and provide precise organization [25]. These expansions permit selective stretching of the fascia, creating different types of lines of force inside the deep fasciae. Stecco et al [26] suggest that all of these fascial insertions provide an excellent illustration of how the thickness and strength of fasciae are a precise mirror of the forces generated by muscular action. Indeed, when these muscles contract, not only do the bones move, but thanks to these fascial expansions, they stretch also the deep fascia. For example, the quadriceps muscle inserts into the tibia by way of the quadriceps tendon, but also projects a myofascial expansion that passes anterior to the patella to contribute to the anterior knee retinaculum [27]. In a similar manner, the Achilles tendon not only attaches to the posterior aspect of the calcaneus, but also has fascial continuity both with the plantar fascia over the back of the heel [28–30], and with the fibrous septa of the heel fat pad [31]. Also, the pes anserinus and iliotibial tract contain a component inside the fascia. Dissections in the shoulder region of unembalmed cadavers [24, 32] reveal the constant presence of specific myofascial expansions originating from the pectoralis major, latissimus dorsi, and deltoid muscles; all of which merge into the brachial fascia.

If we consider all the myotendineous expansions into fasciae, the results indicate that the aponeurotic fasciae could be considered the convergence of all of these expansions, like a large flat tendon that receives all the tractions from underlying muscles and transmits them at a distance. Thus, if we consider all these insertions and map them [33], it is evident that this illustrates perfectly the arrangement of collagen fibers bundles inside the fascia lata, and by extension, the fascia lata could be considered the sum of all of these myotendonous expansions.

These myofascial expansions have a precise orientation, apparently correlated with the spatial planes and with the different activities performed by various muscles. The specific distribution of the myofascial expansions could also indicate their specific functional role. Indeed, when muscles contract to actuate a movement, they simultaneously stretch the same fascia into which they extend expansions. So, according to the various motions, specific muscles are activated, but also select portions of the deep fascia to be stretched by the action of their specific myofascial expansions.

This organization suggests that the fasciae functions as a transmission belt between two adjacent joints, and also between

synergic muscle groups, creating an anatomical continuity between different muscles involved in the same directional movement. This guarantees perceptive and directional continuity and provides anatomical basis for their myokinetic chains, their sequence actions, to the myofascial trains. and also to the meridians.

These expansions also permit a reciprocal feedback between fascia and muscles: a dynamic reciprocity between the two different tissues. The fascia can perceive a stretch produced by a muscle due to its expansions, and transmit this tension at a distance, informing the distal muscle regarding the state of contraction of the proximal muscle, possibly via muscle spindle activation. So, the aponeurotic fasciae connect various segments and joints, coordinating the synergic activation of various muscles and the correct disposition of the different joints involved. Beninghoff [34] described that in the inferior limb during the crouching movement, the angles of the hip, knee, and ankle are the same, and above all, they vary in the same manner. We suggest that it is the aponeurotic fascia that coordinates this synchronicity. In reality, if we have, for example, a damaged ankle, it depends less upon the angles involved. So, the aponeurotic fascia stresses more the other two joints in order to modify their angles as a compensation for this limitation.

Only the presence of different and autonomous fibrous planes inside the aponeurotic planes are different muscles permitted to contract, without opposing the action of other muscles inserted into the same aponeurotic fascia. After a trauma, surgery, or overuse syndrome, the sliding system within the aponeurotic fasciae can change. We speculate that the contraction of a muscle also influences the insertions of other associated muscles. In addition, the creation of an adhesion point involves the formation of new lines of force within the fasciae. This strengthens the supposition that the connective tissue surrounding muscles are major contributors to the phenomenon of MPS.

The Epimysial Fasciae

With the term epimysial fascia, we indicate all the thin collagenous layers that are strictly connected with muscle. They present a concise fibrous structure and are able to transmit forces between adjacent synergistic muscular fiber bundles, belonging or not belonging to the same motor unit. The epimysium and perimysium correspond to this definition, as do the deep fasciae of the pectoralis major, latissimus dorsi, deltoid muscles, and the deep fasciae of the majority of the muscles of the trunk. All of these could be considered epimysial fasciae. In addition, the epimysial fasciae are formed by superimposed layers. For this reason, in the fusiform muscles, the collagen layers have an angle of incidence of 55° in respect to the path of muscular fibers at rest [35]. It is evident that the epimysial fasciae have the same organization as do the aponeurotic fasciae; a multilayered organization of collagen fibers. The direction of the collagen fibers changes according to the state of the muscle [36–38], confirming the degree to which the epimysial fasciae are related to the activity of the muscle itself. According to Purslow [38], they have a fundamental role in the transmission of the force generated in the muscle towards the bone levers. Indeed the epimysial fasciae give insertions to aponeurotic expansion that introflex inside the muscle and the muscular fibers. It should also be noted that the space between the collagen fibers of the epimysial fasciae is occupied by the matrix or ground substance, rich in proteoglycans, and in particularly HA [39]. The increased presence of such macromolecules in the ground substance allows the collagen fibers to slide with little friction when an elicitation occurs, providing relative independence of each muscle belly from surrounding elements.

Gao et al [40] demonstrated that the epimysium from old rats is much stiffer than that of young rats. The increased stiffness cannot be attributed to variations in the ultrastructure and thickness of the epimysium or the size of the collagen fibrils. Microscopic analysis do not demonstrate any changes in the arrangement and size of the collagen fibrils in the epimysium between old and young rats. The age-related increase in the stiffness of the epimysium could play an important role in the impaired lateral force transmission in the muscles of the aged rats and in the alteration of intramuscular motor coordination.

The epimysial fasciae have free nerve endings, but not Pacini and Ruffini corpuscles. The free nerve endings are particularly numerous around vessels, but also distributed homogeneously throughout their fibrous components. Thanks to the strong connections between epimysial fasciae and muscles, it is easy to understand that each time an underlying muscle contracts, it stretches a specific portion of the corresponding fascia. For example, different portion of muscular fibers of the pectoralis major are activated in relation to the degree of shoulder joint movements. Thus, different portions of the corresponding fascia are stretched accordingly. Consequently, specific patterns of intrafascial receptors could be activated corresponding to the range of motion, and also to the specific directions of movement. Therefore, it is easy to imagine a proprioceptive role for the epimysial fasciae.

Additionally, the epimysial fasciae make a connection with another type of nervous receptor: the muscle spindles. Indeed, the capsule of the muscle spindles corresponds to the perimysium, or to epimysium, or to fascial septae [41, 42]. Strasmann et al [43], analyzing the septum of the supinator muscle, affirm that a great number of muscle spindles are inserted directly into the connective tissue of the septum. Also, examining the evolution of the locomotor system, it becomes evident that the muscle spindles are firmly connected with the fascia, as has been demonstrated in the lamprey [44]. Muscle spindles are sensory receptors within the belly of a

muscle that primarily detect changes in the length of this muscle. The sensitive fibers of the muscle spindle are stimulated by minimal stretching; this threshold corresponds to a tension of 3 grams. In actuality, the epimysial fascia plays a fundamental role. The spindles can be shortened, responding to the gamma stimulus only if the perimysium is elastic and adaptable. If the epimysial fascia is more dense, it can block the shortening of the muscle spindle, and the co-activation of the fibers associated to that muscle spindle are prevented.

From a clinical point of view, this means that some parts of a muscle are not involved in the movement, causing an alteration in the vectors of force acting on a joint. This causes an unbalanced movement of the joint, with resulting uncoordinated movement and pain. It is evident that the patient feels pain at the joint, but the origin of the problem is in the connective tissue of the muscle that moves that joint.

The muscles spindles could be activated also by a passive stretching (see patellar reflex), stimulating the contraction of the corresponding muscle fibers. In actuality, if an epimysial fascia is stretched too far by a myofascial expansion, it is possible that the muscle spindles connected with this portion of fascia could be chronically stretched, and so become activated. It implies that the correlated muscular fibers are constantly stimulated to contract. This may explain the increased acetylcholine that is found in myofascial pain, and in particular around the trigger points [45, 46]. In addition, this second situation causes an imbalanced use of muscles, and is therefore an incorrect and unbalanced movement of the joint.

Dysfunction in the neck flexor muscles is associated with the neck pain observed in whiplash injury [47]. Taking into account the important role of deep cervical flexors (longus colli and capitis) in support of the physiological cervical lordosis [48], Jull and colleagues described the presence of altered patterns of coordination between the deep and superficial cervical flexors (sternocleidomastoid). They report an increased electromyographic activity of the superficial neck flexor muscles as compensation for reduced deep neck flexor muscle activation in patients with whiplash associated disorders (WAD) [47–49]. Moreover, cervical flexor endurance has been described as an important index of neck function in whiplash. This is consistent with previous studies that demonstrate a reduction in the neck pain following cervical flexion endurance training [50, 51]. A recent paper by Elliott et al [52] further emphasizes the role of neck flexors in WAD, describing the presence of fatty infiltration into muscle and changes in the cross-sectional area in the cervical anterior muscles during the chronic phase of illness. These authors observe that the most substantial changes in muscular fatty infiltration are present in the deeper muscles (longus capitis and colli), compared with the more superficial sternocleidomastoid muscle [52]. These authors describe that the fatty infiltration varies by cervical level, with the longus capitis/colli having the largest amount at the C2-C3 level [52]. It is interesting to note this, although histological modifications have been observed in neck muscles during the chronic phase of WAD [52]. Alterations in connective tissue after traumatic injuries have also been suggested [3, 53, 54] as a source of potential motor dysfunctions. To date, no previous studies have investigated the role of muscular fascia and its treatment as a method for improving neck mobility in patients with WAD.

The Physiology of Fascia

The Innervations

It is possible that the viscoelasticity of fascia can modify activation of the nervous receptors within fascia. These mechanoreceptors respond to surrounding tissue viscoelasticity and participate in their responses [55–60]. Viscoelasticity of the fascial tissue and associated HA shapes the dynamic response of the mechanoreceptors. The normal sliding lubricating function of HA decreases with increased viscosity. There are also decreases in the amounts of or changes in the fragment size of the HA, as discussed below. The adaptation of fascia to such changes is possible, but only within certain limits. These mechanisms permit a kind of "gate control" in the activation of intrafascial receptors. Beyond these levels, free nerve endings become hyper-activated, and can send a message of "pain". Deising et al [61] injected NGF (nerve grow factor) into the fascia of the erector spinae muscles at the lumbar level. He observed a long-lasting sensitization to mechanical pressure and to chemical stimulation when used with an acidic solution. Sensitization is confined to the deeper tissues, but not to the skin, suggesting that the sensitization of fascia nociceptors to mechanical and chemical stimuli may contribute to the pathophysiology of chronic musculoskeletal pain. Interestingly, the same authors demonstrate that the sensitized free nerve fibers endings within muscle fascia are stimulated more effectively when the fascia is "pre-stretched" by muscle contraction. Changes in innervations can occur pathologically in fascia. Sanchis-Alfonso and Rosello-Sastre [15] report the ingrowth of nociceptive fibers, immunoreactive to substance P, into the lateral knee retinaculum of patients with patello-femoral malignment problems. Furthermore, Bednar et al [62] find an alteration in both the histological structure (inflammation and micro-calcifications) and the degree of innervation of the thoracolumbar fascia in patients with chronic lombalgia, indicating a possible role of fascia in lumbar pain.

The Role of Hyaluronic Acid

HA is a large, remarkably simple, straight chain carbohydrate polymer of the ECM consisting of alternating units of

glucuronic acid and N-acetylglucosamine connected by beta linkages, with the total absence of any secondary modifications. This is in marked contrast with all other GAGs that are attached to core proteins and undergo reactions such as sulfation and epimerization. High molecular size HA (10^6 to 10^7Da) occurs in the body as a hydrating, space filling polymer [63, 64]. Such HA reflects normal, intact, healthy tissue, and does so by supporting normal homeostasis, suppressing cell proliferation, migration, angiogenesis [65], inflammation, and immunogenicity [66–68].

HA is ubiquitous in the ECM, particularly in that of loose connective tissue surrounding muscle bundles [69, 70]. HA is also present in the endomysium surrounding individual muscle fibers, and in perivascular and perineural connective tissue [69, 70, 71]. We have confirmed that HA is located in considerable amounts at the interface between deep fascia and the surface of muscle [39]. This provides a lubricant, as fascia glides over muscle epimysium.

A layer of HA-secreting cells have been identified on the inner layer of deep fascia, apparently the source of the lubricant HA [72–74]. 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. We have termed these fascia-associated HA-secreting cells "fasciacytes". Whether or not these cells are of monocyte/macrophage origin is yet to be determined [75•].

The HA appears to provide a lubricating surface as fascia glides smoothly over muscles and tendons. Because of its considerable charge at neutral pH, HA is surrounded by an enormous volume of solvent water that can exert pressures on various adjacent structures.

Pathology of the Fascia

Alteration of HA

The biological properties of HA in physiological aqueous solutions are controlled by reversible tertiary structures, as documented by NMR (nuclear magnetic resonance) spectroscopy [76, 77].

Short HA chains have the ability to self-associate, particularly under the conditions provided by physiological solutions. This self-association generates a variety of intermolecular aggregated structures. This process is facilitated on the spread surfaces provided by the fascial sheath and muscle bundles [77]. By increasing their concentration and/or size, HA chains begin to entangle into complex arrays, conferring distinctive hydrodynamic properties, altering visco-elastic properties that are predicted to contribute to the etiology of MP and the MPS.

When the HA becomes adhesive rather than lubricating, the distribution of lines of force within the fascia become altered. By changes in viscosity, the receptors within the fascia can send a pain message from a degree of stretching that is even within the physiological range. An important component of pain therapy is to reverse these changes in HA. This includes a reversal of the aggregation of the HA fragments, using increased temperature, and local alkanization. This is accomplished with massage, manipulation, or physical therapies causing disaggregation of the pathologic chain-chain interactions through increase of the subcutis temperature. A physiological and biochemical validity is thus provided for the massage and other forms of body work that often provide relief for MPS.

Chemical Alterations (Acidification)

The loose connective tissue inside and around the fasciae is an important reservoir of water and salts for surrounding tissue. This provides a reservoir for the accumulation of different degradation products. The eventual variations in the contents of water, ions or other substances could alter the biomechanical proprieties of the loose connective tissue. This facilitates variations in the sliding motion of different fascial layers, and thus provides another potential cause of myofascial pathologies.

Particular attention should be placed in the interaction between HA, lactic acid and alterations of pH in fascial tissues. Different authors [78–80] document that the pH inside muscle can decrease until pH 6.6 is reached, representing the point of exhaustion. This value is even lower than the mean pH value found in the blood stream, which is 7.4 to 7.2.

At pH 6.6, the viscosity of HA present in the endomysium and perimysium of muscle can increase considerably. This is demonstrated by the experiment of Gatej et al [81]. He documents that at pH 6.6, the complex viscosity of the HA approaches 5 Pa s. (this is the measure of the dynamic fluid viscosity: N s m^{-2}) instead of the typical 3.8 (the normal value at pH 7.4). This increase in viscosity can explain the typical stiffness experienced by athletes after prolonged intense activity (marathons, endurance games, etc). We postulate that the lactic acid is not the only component that creates such stiffness, but is also the substance that catalyzes the reaction. The fascia assumes a fundamental role with its two components: dense connective tissue (collagen fibers type I and III) and loose connective tissue (adipose cells, GAGs (glycosaminoglycans), and HA). The alteration of pH stimulates the reaction that increases HA viscosity. The dense connective tissue spreads the stiffness throughout the surrounding areas, driving even further the sensation of muscle stiffness. The stiffness can be reversed soon thereafter, thanks to the degradation of the lactic acid in muscle. For this reason,

stiffness disappears quite soon with rest in athletes, with a full restoration of range of motion and cessation of symptoms. We postulate that this same mechanism can underlie alterations that do not permit full restoration nor relief of symptoms. We speculate that specific areas may not be restored to entirely normal viscosity; thus, the high viscosity profile is maintained. From the clinical point of view, such areas can be defined as undergoing densification and constitute potential MPS Trigger Points.

Treatment

Local Increase in Temperature

Manipulation and massage of muscles and their associated fascia increases local temperatures. The 3-dimensional superstructure of HA chains by inter- and intra-molecular water bridges (Van der Waals and hydrophobic forces) break down progressively when the temperature is increased to over 40 °C. There is a change in viscosity of HA solutions at precisely that temperature [78]. This decrease of the viscosity is able to restore normal gliding and normalizes the activation of the mechano-receptors in that area. It is reasonable to assume that the quantity of HA in that area will not be altered by increases in temperature, but rather its associative behavior and its three dimensional structure. For this reason it is postulated that the aggregative properties of HA with rest can be regenerated soon thereafter. This hypothesis can explain the short lasting effects of various body work therapies that simply increase temperature.

Self-Resolving Inflammatory Reaction Cascades

Paul et al [82] has defined that, under conditions of stress, HA becomes depolymerized and lower molecular mass polymers are generated.

These HA fragmentation reactions result in smaller polymers that in a size-dependent manner are highly angiogenic, inflammatory, and immunogenic [83–88]. Hyaluronan fragments promote inflammation, angiogenesis, and immune reactions by driving endothelial cell proliferation and migration, stimulating production of inflammatory cytokines, and by promoting macrophage chemotaxis.

We hypothesize that manual manipulation of the subcutis, with deep compression and friction, is able to catalyze this reaction. Stern et al [89] has demonstrated that as soon as fragments of 1000 Da are generated, particular inflammatory reactions are catalyzed. However, the smallest HA fragments, 4 Da in size, have no inflammatory effect but rather, do the opposite. They decrease the effect of the other larger HA fragments. by stopping the full reaction. This provides a mollifying feed-back reaction. We hypothesize a correlation between this reaction and the soreness referred to by patients in the days following manipulation treatments. Every clinician has observed the improvement of quality of life following this short period of an inflammatory reaction. We consider this self-resolving inflammatory reaction the actual mechanism that restores the correct quantity and quality of substances in the critical areas (as Trigger Points, area of high viscosity etc.) where the clinician has worked. In other word, the real efficacy of the manipulation of deep tissue is as a catalyst for resolving the inflammatory reaction.

Imaging of the Fascial Components

Diagnosis of Myofascial Pain Syndrome

Physical examination of the patient with MPS provides little insight and is often unreliable. Various imaging procedures also are not contributory, and usually do not correlate with location of the pain. Even though MPS is a frequent reason that patients seek medical advice, the clinician often has little to offer. It is abundantly clear that the pathophysiological mechanisms underlying MSP have to be understood so that rational treatments can be undertaken.

Investigators have tried a variety of instruments in an attempt to assess and measure myofascial pain in an objective manner. These include electrodermal instrumentation, thermography, sonography, echography, and magnetic resonance imaging (MRI) scans. However, these often give variable results. None of these have been entirely satisfactory. Examination of fascia, using some of these imaging techniques, as has been documented recently [90], can provide clues however, to the etiology of MPS.

Jensen and Harms-Ringdahl [91] have addressed the clinical reality that patients presenting with neck pain can have several concurrent sources of pain: from joints, muscles, and ligaments. Often a specific origin of the neck pain is not recognizable. For this reason the term non-specific neck pain and myofascial pain is often used. But these diagnoses are done by exclusion and are based only on clinical aspects of the problem. There are very few studies describing objective and clinically applicable methods for identifying and classifying myofascial pain. Shultz [92] has quantified the most painful regions using electrodermal instruments. Arokoski [93] has demonstrated increasing superficial soft tissue stiffness. Sonography is a readily available, portable, and inexpensive imaging modality, suitable for use in a physiatrist's office to complement physical examination and to evaluate treatment outcomes. Different investigators and clinicians have used sonography or MRI scans to compare the thickness of fascia in different area of the body between healthy and symptomatic subjects [94–97]. In vivo studies using diagnostic ultrasound (DUS) demonstrate that this type of

imaging is a valid tool for use in measuring longitudinal and transverse movement of nervous tissue [98–102]. It is becoming commonplace to use dynamic ultrasonography methods in order to appreciate the gliding between different structures. This modality of evaluation permits collection of data regarding the movement of one structure in comparison with another. Software (the speckle tracking) can be used to evaluate the gliding of nerves in comparison with muscle or epineurium. The possibility of the nerve gliding inside the epineurium is fundamental to impaired intrafascicular gliding. An alteration of the viscosity, fibrosis or adhesions can create internal stretch lesions [103–106]. All these authors are in agreement that the thickening of the fascia is a well-established criterion for the diagnosis of MPS.

The variation in thickness of the fascia correlates with the increase in quantity of loose connective tissue (black layers) and not with the dense connective tissue (white layers). For this reason we suggest not to use the term "fibrosis" that correlates most closely with production of DCT from fibroblasts.

Fibrosis vs Densification

The real pathology or dysfunction of the fascia continues to be difficult to discern from the anatomical point of view. On the other hand, imaging and dissections have helped to clarify the differences between a simple alteration of function and morphological alteration of tissues. The latter correlates with a macroscopic rearrangement of the composition and conformation of the entire fascia tissue. This also correlates with an alteration in dense connective tissue (collagen types I and III) that is quite easy to recognize using common imaging procedures such as MRI, CAT scans, and ultrasonography. We suggest that the definition of fibrosis be defined as fibrotic tissue whenever the dense connective tissue component is altered. This can be recognized with an increase in quantity, most of the time recognized by a hyper-intense signal.

At the opposite end of the spectrum, dysfunction of fascia correlates only in an alteration of the loose connective tissue (adipose cell, GAG, and HA). This alteration can involve one or all three components. As we have explained in the previous paragraph, an alteration of the quantity or quality of the component of the LCT may change the viscosity and therefore the function of the lubricant that the LCT facilitates. This clinical situation does not create a macroscopic alteration of the morphology of the fascia tissue that can be appreciated during dissection or biopsy. For this reason it was and is still difficult for the clinician to make the diagnosis of MPS. We suggest this syndrome be defined as “densification of fascia.” This is different from the functional alterations observed from morphological alterations such as frank fibrosis. This distinction also appears abundantly clear for clinicians. A greater and different number of treatment modalities are available for fibrosis in comparison to simple densification. This is due to the simple fact that it is difficult to modify dense connective tissue in comparison to loose connective tissue.

Compliance with Ethics Guidelines

Conflict of Interest Stecco Antonio declares that he has no conflict of interest.

Marco Gesi declares that he has no conflict of interest.

Carla Stecco declares that she has no conflict of interest.

Robert Stern declares that he has no conflict 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.

References

Papers of particular interest, published recently, have been highlighted as:

- Of importance

1. Simons DG, Travel JG, Simons LS. Myofascial pain and dysfunction: the trigger point manual. Philadelphia: Lippincott, Williams and Wilkins; 1999.
2. Mayers TW. Anatomy trains. 1st ed. Oxford, UK: Churchill Livingstone; 2001.
3. Stecco L. Fascial manipulation. 1st ed. Padua: Piccin; 2004.
4. Day JA, Stecco C, Stecco A. Application of fascial manipulation technique in chronic shoulder pain anatomical basis and clinical implications. J Bodyw Mov Ther. 2009;13:128–35.
5. Pedrelli A, Stecco C, Day JA. Treating patellar tendinopathy with fascial manipulation. J Bodyw Mov Ther. 2009;13:73–80.
6. Langevin HM, Fox JR, Koptiuch C, Badger GJ, Greenan-Naumann AC, Bouffard NA, et al. Reduced thoracolumbar fascia shear strain in human chronic low back pain. BMC Musculoskelet Disord. 2011;12:203.
7. Stedman’s medical dictionary. 26th ed. Baltimore: Williams & Wilkins; 1995.
8. Stecco C, Pavan PG, Porzionato A, Macchi V, Lancerotto L, Carniel EL, et al. Mechanics of crural fascia: from anatomy to constitutive modeling. Surg Radiol Anat. 2009;31:523–9.
9. Benetazzo L, Bizzego A, De Caro R, Frigo G, Guidolin D, Stecco C. 3D reconstruction of the crural and thoracolumbar fasciae. Surg Radiol Anat. 2011;33:855–62.
10. Tesarz J, Hoheisel U, Wiedenhöfer B, Mense S. Sensory innervation of the thoracolumbar fascia in rats and humans. Neuroscience. 2011;194:302–8.
11. Stilwell Jr DL. Regional variations in the innervation of deep fasciae and aponeuroses. Anat Rec. 1957;127:635–53.
12. Tanaka S, Ito T. Histochemical demonstration of adrenergic fibers in the fascia periosteum and retinaculum. Clin Orthop Relat Res. 1977;126:276–81.
13. Palmieri G, Panu R, Asole A. Macroscopic organization and sensitive innervation of the tendinous intersection and the Lacertus Fibrosus of the Biceps Brachii muscle in the ass end of a horse. Arch Anat Histol Embryol. 1986;69:73–82.

14. Yahia L, Rhalmi S, Newman N, Isler M. Sensory innervation of human thoracolumbar fascia. An immunohistochemical study. Acta Orthop Scand. 1992;63:195–7.
15. Sanchis-Alfonso V, Roselló-Sastre E. Immunohistochemical analysis for neural markers of the lateral retinaculum in patients with isolated symptomatic patellofemoral malalignment. A neuroanatomic basis for anterior knee pain in the active young patient. Am J Sports Med. 2000;28:725–31.
16. Stecco C, Gagey O, Belloni A, Pozzuoli A, Porzionato A, Macchi V, et al. Anatomy of the deep fascia of the upper limb. Second part: study of innervation. Morphologie. 2007;91:38–43.
17. Corey SM, Vizzard MA, Badger GJ, Langevin HM. Sensory innervation of the nonspecialized connective tissues in the low back of the rat. Cells Tissues Organs. 2011;194:521–30.
18. Testut L, Jacob O. Trattato di anatomia topografica. Firenze: UTE. 1987.
19. Chiarugi G, Bucciante L. Istituzioni di Anatomia dell'uomo. Padova: Vallardi-Piccin; 1975.
20. Platzer W. Apparato locomotore. Milano: Ambrosiana; 1979.
21. Huijing PA, Baan GC. Myofascial force transmission causes interaction between adjacent muscles and connective tissue: effects of blunt dissection and compartmental fasciotomy on length force characteristics of rat extensor digitorum longus muscle. Arch Physiol Biochem. 2001;109:97–109.
22. Standring L. Single referrals for inpatient and community rehabilitation. Nurs Times. 2005;101:34–6.
23. Moore KL, Dalley AF, Agur AMR. Clinically oriented anatomy. 5th ed. Lippincott, Williams & Wilkins; 2006.
24. Stecco A, Masiero S, Macchi V, Stecco C, Porzionato A, De Caro R. The pectoral fascia: anatomical and histological study. J Bodyw Mov Ther. 2009;13:255–61.
25. Stecco C, Macchi V, Porzionato A, Morra A, Parenti A, Stecco A, et al. The ankle retinacula: morphological evidence of the proprioceptive role of the fascial system. Cells Tissues Organs. 2010;192:200–10.
26. Stecco A, Gilliar W, Hill R, Fullerton B, Stecco C. The anatomical and functional relation between gluteus maximus and fascia lata. J Bodyw Mov Ther. 2013 (in press).
27. Toumi H, Higashiyama I, Suzuki D, Kumai T, Bydder G, McGonagle D, et al. Regional variations in human patellar trabecular architecture and the structure of the proximal patellar tendon enthesis. J Anat. 2006;208:47–57.
28. Wood JF. Structure and function as seen in the foot. London: Baillière, Tindall and Cox; 1944.
29. Snow SW, Bohne WH, DiCarlo E, Chang VK. Anatomy of the Achilles tendon and plantar fascia in relation to the calcaneus in various age groups. Foot Ankle Int. 1995;16:418–21.
30. Milz S, Rufai A, Buettner A, Putz R, Ralphs JR, Benjamin M. Three-dimensional reconstructions of the Achilles tendon insertion in man. J Anat. 2002;200:145–52.
31. Benjamin M. The fascia of the limbs and back–a review. J Anat. 2009;214: 1–18. Review.
32. Stecco C, Gagey O, Macchi V, Porzionato A, De Caro R, Aldegheri R, et al. Tendinous muscular insertions onto the deep fascia of the upper limb. First part: anatomical study. Morphologie. 2007;91:29–37.
33. Gerlach UJ, Lierse W. Functional construction of the superficial and deep fascia system of the lower limb in man. Acta Anat. 1990;139:11–25.
34. Beninghoff G. Trattato di anatomia umana. Padova: Piccin; 1972.
35. Purslow PP. Muscle fascia and force transmission. J Bodyw Mov Ther. 2010;14: 411–7. Review.
36. Trotter JA, Purslow PP. Functional morphology of the endomysium in series fibered muscles. J Morphol. 1992;212:109–22.
37. Passerieux E, Rossignol R, Chopard A, Carnino A, Marini JF, Letellier T, et al. Structural organization of the perimysium in bovine skeletal muscle: junctional plates and associated intracellular subdomains. J Struct Biol. 2006;154:206–16.
38. Purslow PP. Strain-induced reorientation of an intramuscular connective tissue network: implications for passive muscle elasticity. J Biomech. 1989;22:21–31.
39. McCombe D, Brown T, Slavin J, Morrison WA. The histochemical structure of the deep fascia and its structural response to surgery. J Hand Surg Br. 2001;26:89–97.
40. Gao Y, Kostrominova TY, Faulkner JA, Wineman AS. Age-related changes in the mechanical properties of the epimysium in skeletal muscles of rats. J Biomech. 2008;41:465–9.
41. Boyd-Clark LC, Briggs CA, Galea MP. Muscle spindle distribution, morphology, and density in longus colli and multifidus muscles of the cervical spine. Spine. 2002;27:694–701.
42. Maier A. Proportions of slow myosin heavy chain-positive fibers in muscle spindles and adjoining extrafusal fascicles, and the positioning of spindles relative to these fascicles. J Morphol. 1999;242:157–65.
43. Strasmann T, van der Wal JC, Halata Z, Drukker J. Functional topography and ultrastructure of periarticular mechanoreceptors in the lateral elbow region of the rat. Acta Anat. 1990;138:1–14.
44. Von During M, Andres KH. Topography and fine structure of proprioceptors in the hagfish. Myxine glutinosa. Eur J Morphol. 1994;32:248–56.
45. Hubbard DR, Berkoff GM. Myofascial trigger points show spontaneous needle EMG activity. Spine. 1993;18:1803–7.
46. Mense S. [Pathophysiology of low back pain and the transition to the chronic state - experimental data and new concepts]. Schmerz. 2001;15:413–7.
47. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J R Stat Soc Ser B Stat Methodol. 1995;57:289–300.
48. Panjabi MM, Cholewicki J, Nibu K, Grauer JN, Babat LB, Dvorakd J. Mechanism of whiplash injury. Clin Biomech. 1998;13:239–49.
49. Jull GA, Kristjansson E, Dall'Alba P. Impairment in the cervical flexors: a comparison of whiplash and insidious onset neck pain patients. Man Ther. 2004;9:89–94.
50. Jull GA, O'Leary SP, Falla DL. Clinical assessment of the deep cervical flexor muscle: the creaniocervical flexion test. J Manipulative Physiol Ther. 2008;31:525–33.
51. Jull GA. Deep cervical neck flexor dysfunction in whiplash. J Muscoloskel Pain. 2000;8:143–54.
52. Elliott M, O'Leary S, Sterling M, Hendrikz J, Pedler A, Jull G. Magnetic resonance imaging findings of fatty infiltrate in the cervical flexors in chronic whiplash. Spine. 2010;35:948–54.
53. Schleip R, Vleeming A, Lehmann-Horn F, Klingler W. Letter to the editor concerning "A hypothesis of chronic back pain: ligament subfailure injuries lead to muscle control dysfunction" (M Panjabi). Eur Spine. 2007;16:1733–5.
54. Hammer WI. Functional soft-tissue examination and treatment by manual methods. 3° ed. Sudbury, ON: Jones & Barlett Pub; 2007.
55. Bell J, Holmes M. Model of the dynamics of receptor potential in a mechanoreceptor. Math Biosci. 1992;110:139–74.
56. Damiano RE. Late onset regression after myopic keratomileusis. J Refract Surg. 1999;15:160.
57. Loewenstein WR, Skalak R. Mechanical transmission in a Pacinian corpuscle. An analysis and a theory. J Physiol. 1966;182:346–78.
58. Swerup C, Rydqvist B. A mathematical model of the crustacean stretch receptor neuron. Biomechanics of the receptor muscle, mechanosensitive ion channels, and macrotransducer properties. J Neurophysiol. 1996;76:2211–20.
59. Husmark I, Ottoson D. The contribution of mechanical factors to the early adaptation of the spindle response. Physiol. 1971;212:577–92.

60. Wilkinson RS, Fukami Y. Responses of isolated Golgi tendon organs of cat to sinusoidal stretch. J Neurophysiol. 1983;49:976–88.
61. Deising S, Weinkauf B, Blunk J, Obreja O, Schmelz M, Rukwied R. NGF-evoked sensitization of muscle fascia nociceptors in humans. Pain. 2012;153:1673–9.
62. Bednar DA, Orr FW, Simon GT. Observations on the pathomorphology of the thoracolumbar fascia in chronic mechanical back pain. A microscopic study. Spine. 1995;20:1161–4.
63. Toole BP. Hyaluronan is not just a goo! J Clin Invest. 2000;106:335–6.
64. Lee JY, Spicer AP. Hyaluronan: a multifunctional, megaDalton, stealth molecule. Curr Opin Cell Biol. 2000;12:581–6.
65. Feinberg RN, Beebe DC. Hyaluronate in vasculogenesis. Science. 1983;220:1177–9.
66. Day AJ, Sheehan JK. Hyaluronan: polysaccharide chaos to protein organization. Curr Opin Struct Biol. 2002;11:617–22.
67. Delmage JM, Powars DR, Jaynes PK, Allerton SE. The selective suppression of immunogenicity by hyaluronic acid. Ann Clin Lab Sci. 1986;16:303–10.
68. McBride WH, Bard JB. Hyaluronidase-sensitive halos around adherent cells. Their role in blocking lymphocyte-mediated cytolysis. J Exp Med. 1979;149:507–15.
69. Laurent TC, Fraser JR. Hyaluronan. FASEB J. 1992;6:2397–404.
70. Fraser JRE, Laurent TC, Laurent UBG. Hyaluronan: its nature, distribution, functions and turnover. J Internal Med. 1997;242:27–33.
71. Piehl-Aulin K, Laurent C, Engström-Laurent A, Hellström S, Henriksson J. Hyaluronan in human skeletal muscle of lower extremity: concentration, distribution, and effect of exercise. J Appl Physiol. 1991;71:2493–8.
72. Klein DM, Katzman BM, Mesa JA, Lipton JF, Caligiuri DA. Histology of the extensor retinaculum of the wrist and the ankle. J Hand Surg Am. 1999;24:799–802.
73. Ellis FD, Seiler 3rd JG, Sewell CW. The second annular pulley: a histologic examination. J Hand Surg Am. 1995;20:632–5.
74. Katzman BM, Klein DM, Garven TC, Caligiuri DA, Kung J. Comparative histology of the annular and cruciform pulleys. J Hand Surg Br. 1999;24:272–4.
75. • Stecco C, Stern R, Porzionato A, Macchi V, Masiero S, Stecco A, et al. Hyaluronan within fascia in the etiology of myofascial pain. Surg Radiol Anat. 2011;33:891–6. *These authors were the first to correlate the alteration of the viscosity of the hyaluronic acid with the alteration of the deep fascia and the etiology of myofascial pain*.
76. Scott JE, Heatley F. Biological properties of hyaluronan in aqueous solution are controlled and sequestered by reversible tertiary structures, defined by NMR spectroscopy. Biomacromolecules. 2002;3:547–53.
77. Matteini P, Dei L, Carretti E, Volpi N, Goti A, Pini R. Structural behavior of highly concentrated hyaluronan. Biomacromolecules. 2009;10:1516–22.
78. Juel C, Bangsbo J, Graham T, Saltin B. Lactate and potassium fluxes from human skeletal muscle during and after intense, dynamic, knee extensor exercise. Acta Physiol Scand. 1990;140:147–59.
79. Nielsen JJ, Mohr M, Klarskov C, Kristensen M, Krustrup P, Juel C, et al. Effects of high-intensity intermittent training on potassium kinetics and performance in human skeletal muscle. J Physiol. 2004;554:857–70.
80. Juel C, Klarskov C, Nielsen JJ, Krustrup P, Mohr M, Bangsbo J. Effect of high-intensity intermittent training on lactate and H+ release from human skeletal muscle. Am J Physiol Endocrinol Metab. 2004;286:E245–51.
81. Gatej I, Popa M, Rinaudo M. Role of the pH on hyaluronan behavior in aqueous solution. Biomacromolecules. 2005;6:61–7.
82. Noble PW. Hyaluronan and its catabolic products in tissue injury and repair. Matrix Biol. 2002;21:2529.
83. Noble PW. Hyaluronan and its catabolic products in tissue injury and repair. Matrix Biol. 2002;21:25–9.
84. Noble PW, Lake FR, Henson PM, Riches DW. Hyaluronate activation of CD44 induces insulin-like growth factor-1 expression by a tumor necrosis factoralpha- dependent mechanism in murine macrophages. J Clin Invest. 1993;91:2368–77.
85. Hodge-Dufour J, Noble PW, Horton MR, Bao C, Wysoka M, Burdick MD, et al. Induction of IL-12 and chemokines by hyaluronan requires adhesion-dependent priming of resident but not elicited macrophages. J Immunol. 1997;159:2492–500.
86. Horton MR, Olman MA, Noble P. Hyaluronan fragments induce plasminogen activator inhibitor-1 and inhibit urokinase activity in mouse alveolar macrophages: a potential mechanism for impaired fibrinolytic activity in acute lung injury. Chest. 1999;116:17S.
87. McKee CM, Penno MB, Cowman M, Burdick MD, Strieter RM, Bao C, et al. Hyaluronan (HA) fragments induce chemokine gene expression in alveolar macrophages. The role of HA size and CD44. J Clin Invest. 1996;98:2403–13.
88. McKee CM, Lowenstein CJ, Horton MR, Wu J, Bao C, Chin BY, et al. Hyaluronan fragments induce nitric-oxide synthase in murine macrophages through a nuclear factor NF-kB-dependent mechanism. J Biol Chem. 1997;272:8013–8.
89. Stern R, Asari R, Sugahara KN. Size- specific fragments of hyaluronan: an information-rich system. Eur J Cell Biol. 2006;85:699–715.
90. Stecco A, Meneghini A, Stern R, Stecco C, Imamura M. Ultrasonography in the diagnosis of myofascial neck pain. J Rehabil Med. 2013. [In press].
91. Jensen I, Harms-Ringdahl K. Strategies for prevention and management of musculoskeletal conditions. Neck pain. Best Pract Res Clin Rheumatol. 2007;21:93–108. Review.
92. Shultz SP, Driban JB, Swanik CB. The evaluation of electrodermal properties in the identification of myofascial trigger points. Arch Phys Med Rehabil. 2007;88:780–4.
93. Arokoski JP, Surakka J, Ojala T, Kolari P, Jurvelin JS. Feasibility of the use of a novel soft tissue stiffness meter. Physiol Meas. 2005;26:215–28.
94. Ekman EF, Pope T, Martin DF, Curl WW. Magnetic resonance imaging of iliotibial band syndrome. Am J Sports Med. 1994;22:851–4.
95. Cardinal E, Chem RK, Beauregard CG, Aubin B, Pelletier M. Plantar fasciitis: sonographic evaluation. Radiology. 1996;201:257–9.
96. Wall JR, Harkness MA, Crawford A. Ultrasound diagnosis of plantar fasciitis. Foot Ankle. 1993;14:465–70.
97. Yu JS. Pathologic and post-operative conditions of the plantar fascia: review of MR imaging appearances. Skeletal Radiol. 2000;29:491–501. Review.
98. Greening J, Lynn B, Leary R, Warren L, O'Higgins P, Hall-Craggs M. The use of ultrasound imaging to demonstrate reduced movement of the median nerve during wrist flexion in patients with non-specific arm pain. J Hand Surg Br. 2001;26:401–6.
99. Hough AD, Moore AP, Jones MP. Reduced longitudinal excursion of the median nerve in carpal tunnel syndrome. Arch Phys Med Rehabil. 2007;88:569–76.
100. Dilley A, Lynn B, Greening J, DeLeon N. Quantitative in vivo studies of median nerve sliding in response to wrist, elbow, shoulder, and neck movements. Clin Biomech. 2003;18:899–907.
101. Ellis R, Hing W, Dilley A, McNair P. Reliability of measuring sciatic and tibial nerve movement with diagnostic ultrasound during a neural mobilization technique. Ultrasound Med Biol. 2008;34:1209–16.

102. Dilley A, Greening J, Lynn B, Leary R, Morris V. The use of cross-correlation analysis between high-frequency ultrasound images to measure longitudinal median nerve movement. Ultrasound Med Biol. 2001;27:1211–8.
103. Lundborg G, Rydevik B. Effects of stretching the tibial nerve of the rabbit. A preliminary study of the intraneural circulation and the barrier function of the perineurium. J Bone Joint Surg Br. 1973;55:390–401.
104. Abe Y, Doi K, Kawai S. An experimental model of peripheral nerve adhesion in rabbits. J Plastic Surg Br. 2005;58:533–40.
105. Lundborg G, Dahlin LB. Anatomy, function, and pathophysiology of peripheral nerves and nerve compression. Hand Clin. 1996;12:185–93.
106. Rydevik B, Lundborg G, Nordborg C. Intraneural tissue reactions induced by internal neurolysis. Scand J Plast Reconstru Surg. 1976;10:3–8.