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Fascia Research IV

Basic Science and Implications
for Conventional and
Complementary Health Care

KIENER

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Foreword

Welcome to the Fourth International Fascia Research Congress. This year we have invited presentations from scientists investigating various aspects of soft connective tissues using the broadest interpretation of the term “fascia.” This year’s book contains 35 research articles, published since the Congress in Vancouver (2012), which cover the most recent findings from 13 established and emerging research areas related to fascial tissue. These areas span a diverse range of topics from cellular and sub-cellular aspects of fascia through to the assessment and exploration of clinical aspects and therapeutic approaches to fascia. This year these topic areas have been expanded to include new research into the role of fascia in cancer, novel assessment methods, veterinary aspects, fascial perspectives in sports and movement, along with special considerations emerging in fascia-related research. These topics are complemented by abstracts from the Fourth International Research Congress, held near Washington, DC, September 18–20, 2015. The Fourth International Fascia Research Congress was created by a multidisciplinary committee of basic science researchers and practicing health care professionals whose respective fields share a common focus and interest in the human body’s soft connective tissue matrix. These abstracts were peer reviewed by the scientific committee of the International Fascia Research Congress and those accepted are presented as submitted without editorial input from the reviewers. The abstracts have been broadly organised into 13 chapters covering: *Anatomy; Biomechanics; Cytology and Histology; Pathology; Fluid Dynamics; Cancer; Veterinary and Animal Models; Assessment Modalities; Manual Therapy; Surgery and Scars; Low Back Pain and*

Innervation; Special Considerations; Fascia in Sport and Movement, Research Methods and New Hypotheses. While fundamental and basic science is highlighted, the Fourth International Fascia Research Congress is focussed on therapy, whether manual, tool-assisted or movement oriented.

This book is intended as a companion to the Fourth International Fascia Research Congress and to provide the latest and most up-to-date information, complementing the proceedings book from the First, Second and Third International Fascia Research Congresses. This book is written for the medical scientists interested in fascia as well as for clinicians who work with this tissue, including: acupuncturists; chiropractors; manual therapists; osteopaths; physiotherapists; podiatrists; practitioners of structural integration; as well as medical and orthopaedic clinicians; yoga instructors; sports coaches and other movement therapists. The aim of the Congress is to foster understanding and collaboration among scientists working in fascia research and the various clinical professionals who address fasciae in their work with clients and patients.

We trust you will find it a useful addition to your reference library and an aid to guide your participation at the Congress. For those of you not attending this congress in person, this book by itself, or in combination with the video replay, will give you the latest and most up-to-date perspective on the interactions between quite diverse pathways of scientific inquiry and the multidisciplinary nature of research in the emerging field of fascia.

This Congress is a joint effort of the Fascia Research Society and the Ida P. Rolf Research Foundation. We want to express our appreciation to the many people who so generously donated time, expertise, and money to the Fourth International Fascia Research Congress. In particular, we

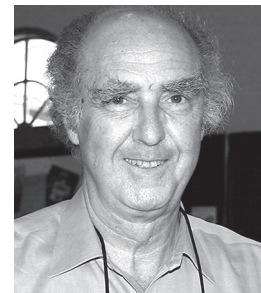
are indebted for the peer review of the abstracts to the scientific committee of the fascia congress and its chairs, Dr Serge Gracovetsky and Dr Antonio Stecco, and for the editorial assistance of Dr James Smeathers and Melina Simjanovic.



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Table of Contents

Index of Authors	VIII
Fascia Research 2015 – State of the Art	1
1 Fascia and Anatomy	15
2 Biomechanics of Fascia	35
3 Cytology and Histology of Fascia	57
4 Fascia Pathology	65
5 Fluid Dynamics in Fascia	75
6 Fascia and Cancer	95
7 Veterinary and Animal Models of Fascia	103
8 Assessment Modalities in Fascia	125
9 Muscle, Fascia and Manual Therapy	143
10 Fascia in Surgery and Scars	207
11 Fascia in Low Back Pain and Innervation	221
12 Fascia in Sports and Movement	259
13 Special Considerations in Fascia	293
14 Research Methods and New Hypotheses in Fascia	303

Fascia Research 2015 – State of the Art

In addition to accepted conference abstracts, this conference proceedings book, Fascia Research IV, also includes a number of key full-text articles that form an important basis for the scientific study of fascia. Since the first International Fascia Research Congress in Boston (2007), fascia has aroused increasing interest from scientists, clinicians and manual body therapists. The number of research papers on fascia in peer-reviewed journals has rapidly increased, particularly since the late 1980's and mid 2000 (see figure 1). Since the publication of the proceedings of the first Fascia Research Congress in 2007, there have been more than 10.5 thousand fascia-related papers published in peer-reviewed journals in more than 19 languages. This increase in fascia research has been, at least in part, a result of the relatively recent work that re-evaluated the anatomical and histological structure of fascia, coupled

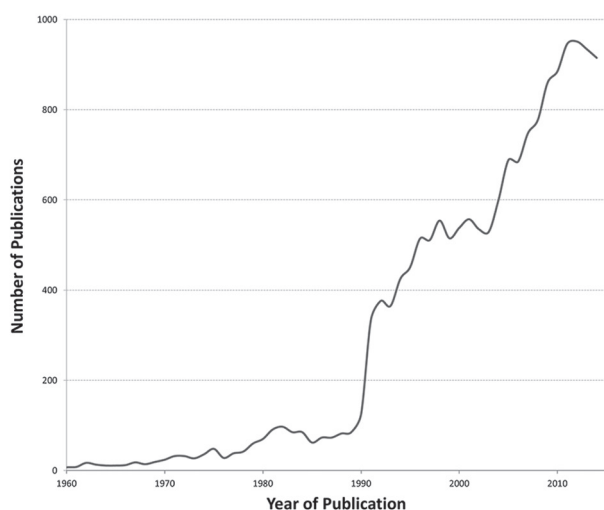


Fig. 1: Number of 'Web of Science' publications with the terms 'fascia*' or 'fasciitis' in their title or abstract. Note the rapid increase in publications since 1990, with almost 1000 fascia-related articles currently published per year.

with developments in assessment technologies, such as high resolution ultrasound and bioelectrical impedance, which have recently allowed *in vivo* measurement of fascial behavior and can be used to assess the effects of manual therapy. The purpose of the program book for the Fourth International Fascia Research Congress is to provide you with background material and the most up-to-date developments in fascia research.

At the first International Fascia Research Congress in Boston (2007), fascia was broadly defined as:

"... the soft tissue component of the connective tissue system that permeates the human body, forming a continuous, whole-body, three-dimensional matrix of structural support. It interpenetrates and surrounds all organs, muscles, bones, and nerve fibres, creating a unique environment for body systems functioning. The scope of our definition of and interest in fascia extends to all fibrous connective tissues, including aponeuroses, ligaments, tendons, retinaculae, joint capsules, organ and vessel tunics, the epineurium, the meninges, the periosteal, and all the endomysial and intermuscular fibres of the myofasciae." (Findley and Schleip, 2007).

Although the renewed interest in fascia brought together clinicians and scientists from a variety of fields, it also highlighted new difficulties, which continue to hinder our understanding of the complexities of fascia. Chief amongst these is the various fascia-related definitions and terminologies that are adopted by the different clinical and scientific disciplines. There has been considerable recent debate, regarding the most appropriate definition of fascia (see for example volume 18, issue 3 of the Journal of Bodywork and Movement Therapies). Clearly there is a need for standardized definitions and nomenclature. Currently, there are three commonly used nomenclatures. The most restrictive but precise terminology is that offered

by the Federative Committee on Anatomical Terminology, which exclude membranous connective tissue layers within the anterior abdominal wall and peritoneum (commonly known as Scarpa's and Colle's fascia) and all subcutaneous connective tissue from descriptions of 'fascia' (FCAT, 1998). In contrast, the terminology put forward by the British edition of Gray's anatomy (Standring, 2008), specifically recognizes the entire range of loose subcutaneous connective tissues as 'superficial fascia' but excludes aponeuroses and intramuscular layers (perimysium and endomysium) from the definition of fascia. In Fascia Research IV, we have adopted the third common nomenclature, and the same broad definition used at the first International Fascia Research Congress, in which fascial tissues are seen as one interconnected tensional network that adapts its fibre arrangement and density according to local tensional demands. While each nomenclature has its strengths and weaknesses, we adopted the more inclusive terminology as it reflects the Latin root of the term 'fascia' (bundle, bandage, strap, unification, binding together) and is also synonymous with the non-professional's understanding of the term "connective tissue." We hope that the fourth International Fascia Research Congress will provide a vehicle to aid in the definition of a common nomenclature, which ultimately will help to focus and coordinate fascia-related research and practice into the future.

Given the resurgence of interest in fascia, the editors have reviewed the content of thousands of published research papers from a variety of scientific fields, including biology, engineering and medicine. As our understanding of the role of fascia in the maintenance of health and disease expands, we have also found an increasing number of fascia-related topic areas. For instance, in Fascia I (2007) and II (2009), eight fascia-related topic areas were covered including areas such as *Anatomy*, *Cellular Dynamics* and *Pain*. In Fascia III (2012), the number of fascia-related topics increased to ten, to include additional topics such as *Fluid Dynamics*, *Therapy*, and *Surgery & Scars*. In Fascia IV, we have identified fourteen fascia-related topics and have selected almost twice as many papers as in the first two fascia congress program books. These are organized by topic area to parallel the scientific abstracts submitted to the Congress. In the interest of green publication, the full text is included only for those papers, which are not freely available at www.pubmed.gov. We give you the DOI and encourage you to read the others online, and think you will find, as we do, that in the process of locating and downloading articles you will find another article you were not looking for but which turns out to be very interesting as well.

First, we will share key findings from anatomy regarding

connective tissue architecture in specific parts of the body, its relation to neurovascular structures and the potential importance of these tissues in common injuries. In the second area, the directional properties and biomechanics of these connections are shown to provide multi-directional bracing forces to form a functional myofascial force transmission system, which may accommodate varying degrees of injury. The spotlight then moves to the cellular and histologic levels, looking in detail at how individual cells respond to mechanical forces and how their response and physical properties change with disease and pathology. We then go on to discuss the role of interstitial fluid flow and its potential to accelerate cellular migration, healing and tissue repair but also highlight the role of remodelling of the extracellular matrix in cancer and related disorders. In the following sections, we then discuss the role of animal models in helping advance our understanding of the function and pathophysiology of fascial tissue and how new innovative and sophisticated measurement techniques provide exciting new avenues to further our understanding and to help assess the effect of clinical intervention. We next discuss models of clinical and surgical intervention affecting fascia, from the cellular, neuro-physiological, and mechanical standpoints. We then discuss new findings on fascial innervation and lumbar fascia in low back pain. This is followed by a chapter examining the role of fascia in sports and movement. Finally, we discuss emerging research exploring fascial involvement in a number of relatively uncharted populations and exciting new hypothesis regarding its role in musculoskeletal and systemic ailments, including cancer and arthritis. In doing so, we believe that Fascia Research IV provides the most recent findings from the broadest and most coherent perspective of fascia-related research to date.

1 Fascia and Anatomy

▶ **1.1.1** In this richly illustrated report, the authors dissected 48 unembalmed cadavers, to investigate the anatomical continuity between the proximal attachment of the hamstring muscles, the gluteal muscles and the associated fascia. The study describes the presence of an annular, retinacular-like structure with widespread myofascial expansions, which were continuous with the epimysium of the gluteal muscles and extend to envelope and compartmentalize the sciatic and posterior femoral cutaneous nerves. In contrast to a typical retinaculum, which provides a smooth surface for tendons to slide when their associated muscle contracts, fibrocartilage was not present in this dense fibrous tissue. The authors hypothesize that the "structure probably has a direct role in

force transmission during muscle contraction, establishing a synergy between the gluteus maximus muscle and the long head of the biceps femoris.” They further hypothesize that this structure is likely involved in injury of the proximal attachment of long head of biceps femoris and highlight the importance of mobilization of this fascial tissue especially in sciatic nerve involvement.

► **1.1.2** This paper comprehensively reviews the organization and composition of the thoracolumbar fascia (TLF), a girdling structure consisting of several aponeurotic and fascial layers which separate the paraspinal muscles from the muscles of the posterior abdominal wall. The superficial lamina of the posterior layer of the TLF (PLF) is dominated by the aponeuroses of the latissimus dorsi and the serratus posterior inferior. The deeper lamina of the PLF forms a retinacular sheath encapsulating the paraspinal muscles. The middle layer of the TLF (MLF) is derived from an intermuscular septum, which separates muscles that develop anterior (hypaxial) and posterior (epaxial) to the transverse processes of the vertebrae. The paraspinal retinacular sheath (PRS) forms a lumbar interfascial triangle (LIFT) with the MLF and PLF, which is in a key position to act as a ‘hydraulic amplifier,’ assisting the paraspinal muscles to support the lumbosacral spine. Along the lateral border of the PRS, a thickened complex of dense connective tissue, the lateral raphe, arises from the junction of the hypaxial myofascial compartment (the abdominal muscles) with the paraspinal sheath of the epaxial muscles and is well positioned to distribute tension from the surrounding hypaxial and extremity muscles into the layers of the TLF. At the base of the lumbar spine all of the layers of the TLF fuse together to attach firmly to the posterior superior iliac spine and the sacrotuberous ligament. This thoracolumbar composite (TLC) is suggested to assist in maintaining the integrity of the lower lumbar spine and the sacroiliac joint. This is an important concept for clinicians involved in the management of back pain and its biomechanical role is further investigated and explained in section ■2.1.3.

► **1.1.3** This study evaluated the gross and histological anatomy of the bicipital aponeurosis (BA), a fascial expansion which arises from the tendon of biceps brachii. In the 30 cadaveric upper limbs examined, fibres from the short head of the biceps brachii contributed to the formation of proximal part of aponeurosis, while its distal part was continuous with the fascial sheath overlying the tendon of long head of biceps brachii. The BA was angled at about 22° to the tendon and both blood vessels and adipose tissue were found between the tendon and the fascial sheath. The authors suggest the BA plays an important role in dissipating force away from the attachment site

of the biceps tendon and may assist in dual action of the biceps brachii as a supinator and flexor of the forearm.

In brief: what is known and what is new ...

In contrast to its depiction in many textbooks, fascia forms a complex network of sheets, bags, and strings that act to divert and transmit forces to assist in body movement. It was previously suggested in Fascia III, that muscles may not transmit their full force directly to the skeleton via tendons, but rather distribute a portion of their contractile or tensile force to other structures via fascial sheets. Fascial sheets transmit these forces to synergistic as well as antagonistic muscles to stiffen the respective joint, but also exert these effects on other regions, several joints further away, by forming a complex network of fascial sheets, bags, and strings. The relative importance of myofascial versus myotendinous force pathways in many common movements are currently being investigated (see section ■2). The papers in this section begin to map out the details of this network in specific parts of the body, highlighting their potential neuromechanical role and raising new questions about the importance of these tissues in common injuries, such as muscle strains and chronic low back pain.

2 Biomechanics of Fascia

► **2.1.1** The structural organization of fascia into sheet-like layers with multiple orientations, attachments and its intimacy with muscle groups provides fascia with a distinctly functional anisotropy. This has been investigated in fascia lata, using a biaxial mechanical test to determine the effect of interactions between lateral and longitudinal loading on overall material properties such as stiffness and strain energy storage. Histological sectioning and scanning electron micrographs provide anatomical evidence that correlates with the observed mechanical properties. The greater stiffness observed in the longitudinal direction corresponds with a thicker layer of longitudinally oriented collagen fibres and of large diameter. The thinner layer containing small diameter collagen fibres provides a lower transverse stiffness thereby permitting muscle expansion with minimal influence on the mechanical properties in the longitudinal direction.

► **2.1.2** A cadaveric investigation into the complex interactions between myofascial structures and functional movement attempts to answer questions about the relative functional importance of myofascial versus myotendinous force pathways. The relative contributions made by these pathways have been estimated by tracking the kinematics of cadaveric limbs following sequential tenotomies

in procedures that mimic surgical harvesting of the semitendinosus and gracilis tendons widely used in knee reconstructions. It was shown that the forces generated around the joint, are mostly dependent on the myofascial pathway and less reliant on the myotendinous connection. Supporting the notion that tendons are no longer the unique structures that transmit motive force to the skeleton.

▶ **2.1.3** Stability of the thoraco-lumbar spine is dependent on the highly complex arrangement of aponeurotic and fascial layers that surround the paraspinal and abdominal muscle groups. A recent cadaveric study used an ingenious arrangement of inflation devices to mimic muscle expansion and load cells to monitor tension generated within fascial layers in a series of transverse segments through the mid-lumbar region while under fluoroscopic visualization to explore load-sharing pathways. This study was able to simulate and manipulate the effects of paraspinal and abdominal muscle contractions on the throacolumbar fascia (TLF). Noticeable increases in the moment arms about the spinal axis were observed as posterior and lateral displacements in the TLF highlighting the importance of this mechanism in spinal stability. In addition, this study demonstrated the essential interplay between paraspinal and abdominal muscle contractions that are necessary for optimizing musculoskeletal bracing mechanisms in the spine.

In brief: what is known and what is new ...

These three papers highlight the complexity and functionality of major fascial groups throughout the body. The directional variability (anisotropy) and multiple interactions between neighbouring myofascial systems combine to enhance the overall efficiency and stability of functional movement patterns. Fascia has highly directional properties that correspond with the transfer and redirection of forces while simultaneously permitting length and shape changes in muscle groups. There also appears to be some advantageous interplay between the myotendionus and myofascial force transmission pathways that provides sufficient redundancy between these systems to accommodate varying degrees of injury or surgical insults while still remaining a functional force transmission system. The most complex myofascial arrangements are seen in the back where they help to enhance spinal stability during complex movement patterns. Stability is achieved by the multi-directional bracing forces generated during muscle contraction and further assisted by fascial realignment resulting from changes of shape and pressure within the muscle groups.

3 Cytology and Histology of Fascia

▶ **3.1.1** Fibroblasts are responsible for the production of collagen and elastin within the extracellular matrix (ECM). However, the discovery of separate lineages of fibroblasts helps to explain why scar formation in the skin fails to replicate true epidermal tissue. There are two lines of fibroblasts, arising separately from the upper dermal and lower dermal layers. Differences in the way cells respond to external protein triggers, via Wnt signalling (a pathway that regulates crucial aspects of cell fate determination, cell migration, cell polarity, neural patterning and organ development during embryonic development) and the interplay with T cell immune responses, are deemed responsible for the mechanism that influences dermal cell proliferation and hair follicle formation. Since it is the lower dermal lineage that dominates during the healing process, scar tissue is devoid of hair follicles that typify normal skin architecture. This linkage between tissue of origin for fibroblasts and variations in their functional response to Wnt activation provides new avenues for exploring mechanisms that underpin age related and pathological changes in the ECM.

▶ **3.1.2** The influence of mechanical therapies on chronic tendinopathies at the tissue level are explored by a murine model where tendinopathy is induced by injection of a transforming growth factor, TGF- β 1. This reduces tendon strength and induces cellular changes that closely typify the chondroid populations with raised levels of glycosaminoglycans seen in injured tendon. Presence of tendinopathy was validated by histological, gene expression and mechanical testing techniques. Following exposure to a controlled exercise regime, treadmill exercise was able to elicit in pathological tendon, a return to near normal strength, cellular make up and gene expression within four weeks. These results provide direct evidence for the role and efficacy of mechanical stimulation in the tendon healing process, albeit in the acute phase. It is anticipated that this murine model of induced tendinopathy will facilitate more detailed quantitative assessment of tissue repair processes induced by physical therapies and exercise-based rehabilitation modalities.

In brief: what is known and what is new ...

Previously in Fascia III, the question was asked whether manual treatments might have beneficial effects during early development of fibrotic processes. A useful model for addressing this issue has since been demonstrated and provides some necessary supporting evidence (see paper ■ 3.1.2). Cells within the ECM are demonstrably influenced by external mechanical factors resulting in an ECM protein

milieu that is modulated by exercise, inflammation and disease processes. A regular exercise protocol that is shown to be sufficient in countering some early degenerative changes within tendon permits more detailed mechanistic evaluations. For example, the relative contribution and explanatory mechanisms behind the different responses seen in concentric as opposed to eccentric exercise need further clarification. And can this difference be explained by the variations in load distribution and shear between muscle fascicles during contraction? (see papers ■2.1.2 and ■7.1.2)

4 Fascia Pathology

► **4.1.1** The complexity of the fascial structure and its intricate connectivity throughout the body make it vulnerable to strain and overuse injuries resulting in a number of chronic musculoskeletal pathologies and pain syndromes. The pathomechanics of painful musculoskeletal conditions is further complicated by the sensory and reactive capability of the myofascia to mechanical stimuli. Fascia is no longer considered to be a passive supporting structure within the body due to the presence and motility of contractile elements of actin containing myofibroblasts. The mechanosensory capacity of myofascial tissue is increasingly implicated in many painful conditions and diseases such as chronic neck and back pain, frozen shoulder and nerve entrapment syndromes. Extremes in movement, from hyperlaxity to increased stiffness and restricted shear in the fascial tissues are often found in painful conditions. Hence, more detailed investigations into the causal mechanisms of myofascial pain are required if we are to properly understand the rationale behind various massage and manipulative therapies. For example, how does reduction of compartmental pressure or mobilization of fibrous adhesions within the tissues help to resolve pain? Further information and some explanations are proposed in paper 12.1.4.

► **4.1.2** High levels of myofibroblast proliferation with uneven distribution are seen in the fascia of certain diseases such as Dupuytren's. Detailed analysis of the histology, immunohistochemistry and genetic factors within the ECM of tissues from symptomatic, asymptomatic and healthy tissue has helped to shed light on regional differences in disease development. This particular disease presents as a progressive flexion contracture of the fingers leading to disabling deformities. The main treatment for severe cases of Dupuytren's disease is fasciotomy, or failing that fasciectomy, of the affected tissue only. However, this paper cautions against considering asymptomatic tissue

as "normal" due to certain similarities in cellular make up and activity to the clinically affected tissue. This finding has implications for potential improvements to treatment and investigating the bilateral nature of some disease symptoms and processes.

In brief: what is known and what is new ...

Previously in Fascia III, proprioception in ligaments was discussed as a trigger for reflex muscle activity that helps protect the joint. In this issue a similar mechanism is also described in relation to the functional response of the fascia via mechanosensory pathways. Anomalies or resultant imbalances in this response found in a number of movement disorders such as hyperlaxity of joints or hypermobility syndrome; increased stiffness e.g. Dupuytren's contractures or restricted tissue shear, as in Duchenne dystrophy all of which, lead to painful musculoskeletal conditions. Since current treatments are often based on reversing the triggering conditions of either excessive laxity or stiffness, detailed investigations into the cellular responses to mechanical stimuli are becoming increasingly relevant. Understanding how the cellular make up and physical properties of tissue change with disease is proving increasingly beneficial to the advancement of surgical and manipulative therapies, as discussed in ■9 and ■10.

5 Fluid Dynamics in Fascia

► **5.1.1** The ability of myofibroblasts to directly exert tension on the ECM through integrin-mediated contraction is now well established. Less, however, is known about the contractile nature of fibroblasts. This paper suggests that healthy fibroblasts embedded within fascia may also dynamically influence the tension of connective tissue by rapidly remodelling their cytoskeleton but without transforming into myofibroblasts. Tension modulation by fibroblasts is suggested to regulate interstitial fluid pressure and flow by altering the permeability (pore size) of the ECM, and thus the movement of water toward the normally under-hydrated glycosaminoglycans. Movement of water in or out of the tissue also serves as the mechanism by which fibroblasts sense a change in osmotic pressure and accordingly adjust their size, to control fluid movement. These cytoskeletal responses appear to be unique to loose connective tissues, such as those forming interfaces between subcutaneous and perimuscular layers, and does not occur in other more densely packed connective tissues.

► **5.1.2** Nearly every cell in the human body has a primary cilium, a solitary, non-motile, microtubule-based

antenna that extends from the cell surface. The primary cilium controls the balance between the canonical and non-canonical Wnt pathways (see ■ 3.1.1 for example), which regulate gene transcription, intra-cellular calcium levels and components of the cytoskeleton responsible for cell shape. Recently, the primary cilium has also been shown to play an important mechanosensory role, and in particular, in sensing fluid flow. Application of oscillating fluid flow to cultured cells that have an intact primary cilium was shown to alter the microtubule network within the cell; increasing the number and density of microtubules in a magnitude- and time-dependent manner. Cytoskeletal microtubules are thought to work together with integrins in extracellular matrix adhesions and cadherins in cell-cell junctions to resist tensile forces generated within the actin component of the cytoskeleton and thereby establish a mechanical force balance that stabilizes the shape of the entire cell. This reinforcement mechanism did not occur after primary cilia removal from the cell. It is possible therefore that, following fluid shear across a cell, microtubule networks are developed to stabilize the cell in response to the mechanical stimulus.

▶ **5.1.3** Numerous *in vitro* studies have shown that fibroblasts regulate their cellular functions in response to fluid flow over a range of shear stress (0.005 to 2.5 Pa). During inflammation and in certain cancers, interstitial fluid flow can increase 10-fold ($>10 \mu\text{m/s}$) and can influence cell migration. This *in vitro* study used a novel culture chamber to investigate the migration behaviour of human breast cancer cells to physiologically relevant fluid shear flows. Interstitial flow increased the percentage of migratory cells, and also increased migration speed in about 20% of cancer cells. The migratory behavior of cancer cells, however, was heterogeneous, with some cells migrating towards flow and others migrating against flow. Flow-directed invasion occurred in roughly 10% of cells, suggesting that fluid flow can enhance tumor cell invasion by directing a subpopulation towards the draining lymphatic vessels, a major route of metastasis.

In brief: what is known and what is new ...

In Fascia II and III it was shown that in scar, chronically inflamed tissue and cancer-associated tissues, fibroblasts have the ability to transform into contractile cells, or myofibroblasts, which can increase ECM stiffness by generating sustained and continued tension on the ECM. This increase in ECM stiffness is accompanied by greater interstitial pressure and lymphatic flow, which may predispose an individual to fibrosis, cancer invasion and metastasis. Healthy fibroblasts embedded within loose fascia, however, would also appear to dynamically

influence the tension of adjacent tissues by remodelling their cytoskeleton but without stress fibre formation and transforming into myofibroblasts. This restrains the fluid-retaining capacity of the adjacent proteoglycans, which are normally underhydrated. Stretching of the matrix or partial detachment of the cell, likely increases the permeability of the tissue allowing flux of fluid into the peri-cellular ground substance. Local changes in osmolarity or fluid shear stress are sensed by cell structures, such as the primary cilia, which influence gene transcription, intra-cellular calcium levels and provide a direct connection to the cytoskeletal machinery, which governs cell shape and motility. Such changes in cell shape may oppose further fluid movement and stabilize the cell but may also direct the migration of fibroblasts toward the flow of fluid in a dose-dependent manner. Thus therapies that promote interstitial fluid flow could have the potential to accelerate cellular migration, healing and tissue repair. However, care is needed when manipulating these tissues to avoid the formation of myofibroblasts and caution is also required in cancer-associated tissues.

6 Fascia and Cancer

▶ **6.1.1** Tumor associated Collagen Signature (TACS) outside the immediate tumor in surgical samples of breast surgery for cancer, independent of the cancer lesion itself, is correlated with patient outcome. 10-year survival rates are 46% for those with increased collagen deposition near the tumor, compared to 78% without. This paper explores potential mechanisms. The adult mammary gland responds to biochemical and mechanical signaling from the extracellular matrix. The stroma outside the tumor affects survival in several ways: 1) Reorganization of the extracellular matrix to promote tumor invasion – increased breast density, increased collagen alignment, increased expression of syndecan-1 (which promotes alignment), and higher expression of COX-2 and the gene for type I collagen, COL1A1; 2) changes in expression of stromal cell types – beta lymphocytes, macrophages (which stimulate collagen fibrillogenesis and remodel and align collagen), and carcinoma associated fibroblasts (CAF); 3) changes in stromal gene expression, including changes associated with the wound healing response of fibroblasts and 4) stromal and mechanical signaling pathways – increased caveolin-1, matrix metalloproteinase (MMP) and chemokines.

▶ **6.1.2** There is recent interest in structural components of the extracellular matrix (ECM) and how they play an active and not just a passive role in adult tissue changes. This paper reviews the collagens and proteoglycans in the

ECM and highlights recent research of individual components and their effects on cells through specific receptors. Both cancer and fibrosis in liver, lung and other tissues share a number of common changes in the ECM structure and function; formation and degradation both increase, resulting in greater tissue turnover. There are now clinical tests of biomarkers in serum to measure the degree of liver fibrosis, which in Europe are often used instead of liver biopsy. Genetic modifications lead to different expression of ECM collagen and proteins. There are also post-transcriptional modifications (PTM) which affect how a single gene can produce as many as 1,000 protein subtypes. Changes in cross-linking and matrix remodeling can now be followed with markers in the serum. Examples are given for bone metastasis in breast and prostate cancer, and liver fibrosis. It is not yet known whether such changes are merely a result of another underlying disease process, or if they actually are involved in causation of the observed pathology.

► **6.1.3** There is normally a dynamic but stable interaction between cells and their surrounding extracellular matrix (ECM). Changes in either the cells or the ECM result in a reorganization of this interaction to restore the previous equilibrium as much as possible. Wound healing provides a good example of this, and the activated myofibroblasts die when the wound is closed. Loss of this normal homeostasis occurs during cancer development and results in alteration of the ECM to facilitate cell invasion. Biochemical factors in this process can be produced by Cancer Associated Fibroblasts (CAF), particularly the family of enzymes known as matrix metalloproteinases (MMP), lysyl oxidase (LOX) and fibroblast activation protein (FAP). Rho-ROCK is another signaling pathway which regulates a number of cell functions including the internal cytoskeleton and gene expression. Rho-ROCK stands for Rho(Ras homology small GTPase) and ROCK (Rho-associated coiled-coil containing protein kinase). Mechanical factors can directly align the ECM by physical force, or indirectly by aligning the cells, which then deposit the ECM. Fluid flow through the ECM affects alignment of both collagen fibrils and the ECM fibroblasts. The interaction between biochemical and mechanical factors is a potential target for therapeutic intervention.

► **6.1.4** Stiffening of the extracellular matrix is a hallmark of cancer. The tumor associated ECM shows increased collagen deposition, particularly type I, increased lysyl oxidase and crosslinking which stiffens the tissue, and increased tumor cell and fibroblast contractility which in turn increases the tension in the tissue, leading to further remodeling and stiffening. Mechanosignaling and

cellular tension foster increased tumor aggressiveness. In response to mechanical cues from the ECM, cells modulate their shape and nuclear architecture which then remodels the ECM. ECM stiffness and tissue mechanics can be measured experimentally at a high resolution with atomic force microscopy, and at lower resolution with ultrasound and MRI elastography and tissue compression and shear rheology testing. Tumor cells show increased anaerobic glycolytic metabolism. There is emerging evidence of a connection between the altered ECM stiffness and these metabolic changes.

In brief: what is known and what is new ...

AT Still, MD posited a connection between cancer and fascia more than 100 years ago. Epidemiological studies show that persons with diseases of increased systemic fibrosis such as scleroderma have a much higher rate of cancer. People, who exercise, particularly resistance or weight training, are less likely to die of their cancer (and other diseases). Muscle is the largest organ in the body, but rarely is the site for metastatic cancer, and then it is often at a site of earlier trauma to the muscle. Cancer has been likened to a wound healing process that never stops. It has been noted that both cancer and the surrounding tissues become stiffer, and the pathophysiology underlying this observation are only now being described in detail. These four papers provide a starting point for the serious student, covering both biomechanical and biochemical processes and genetic and post genetic transcription influences. From the clinical side, the effect of resistance training suggest several paths for research: Muscles and their tendons secrete cytokines (which get renamed myokines since they come from muscle), some of which are mentioned in these papers. These circulate throughout the body, to both tumor sites and potential metastatic locations. Muscles also exert forces laterally through myofascial force transmission. This travels at least as far as measurements in the antagonist muscles on the other side of the limb. Muscle contraction increases circulation, and the concomitant fluid flow through the extracellular matrix and lymphatic system. Muscles affect overall metabolism of glucose, which is the preferred substrate for tumor cells. So the mechanical and biochemical factors in the ECM may well be found at a larger scale in fascial tissues throughout the body. Finally, nutrition plays a role in reducing inflammation. The anti-inflammatory diet is presented in abstract 6.2.1 by Cotter and Hankinson with application to musculoskeletal disorders. The same diet is also useful for cardiac conditions, and for cancer.

As Dr Peter Purslow showed in detail at FASCIA II in Amsterdam, the fascial fibres surrounding muscle can be

seen at higher and higher magnification connecting to the muscle cells themselves. Dr Guimberteau demonstrated the unique connections between the tendon and the tendon sheath and carried those observations starting with the skin and going deeper into the body. The complex connections between the extracellular matrix and cancer are the subject of numerous investigations, but there is much less work connecting the ECM to the larger framework of the body. The Web of Science analysis of publications in the year 2014 shows 1346 papers on both the topic of the ECM and cancer, but a much smaller number, 93, for fascia and cancer. The field is in its infancy, and will have an inaugural conference on Acupuncture, Fascia and Oncology at Harvard Medical School in November 2015, just as the initial Fascia Research Congress was launched there in 2007.

7 Veterinary and Animal Models of Fascia

▶ **7.1.1** Equine tendon provides a useful model for studying tendinopathies due to the comparable size and mechanical properties with human Achilles tendon. The frequency and intensity of loads encountered during equine racing and training also allow tendon overuse injuries to be investigated. Recent advances in the use of ultrasound transmission velocities to measure mechanical properties of tissue have enabled the non-invasive tracking of elastic modulus in tendon. The axial speed of sound through tendon is related to the elastic modulus which is known to decrease during injury and repair. Thus axial speed of sound currently used as an indicator of tendon function, health in equine tendon might soon become available for routine studies on human tendon.

▶ **7.1.2** Tendon injuries are widely attributed to the gradual accumulation of micro-damage caused by exposure to repetitive loading over time. How this relates to tendinopathy is still uncertain but in vitro studies of fascicle sliding in response to prolonged cyclic loading highlight some intriguing anomalies. Fatigue tests on bovine tendon have shown there is greater displacement of collagen fibres than found between neighboring cells indicating a degree of independence between the load bearing fibres and constituent fibrocyte networks within the tendon. Importantly, this may indicate a delayed awareness of fatigue failure by the cell-strain sensing mechanisms.

▶ **7.1.3** The ECM within muscle appears to play a significant role in the transfer of tensile load during muscle contraction. This load transfer mechanism redistributes the tensile forces of muscle contraction in a lateral direction via shear forces in the endomysium. The thickness of ECM and

perimysium in particular, increases with age and is shown to interfere with the lateral transmission of force. Notably, the increased thickness of the ECM is also implicated in age related reduction in muscle strength.

In brief: what is known and what is new ...

Tendon injury can be readily observed and described at the macro-level but increasingly our understanding of injury mechanisms are becoming focused on the micro and cellular levels. These three papers provide examples of animal models that monitor changes in macro-injuries through the generic mechanical properties of tendon to subtle differences in fascicle sliding, cellular movement and force transfer mechanisms within the ECM in response to micro-injury. Such models are likely to be crucial in improving our understanding of the hierarchical function of fascial tissue in humans.

8 Assessment Modalities in Fascia

▶ **8.1.1** Disease processes that influence the functional properties of tissues and in particular those of the ECM can benefit from techniques that determine mechanical properties at the microscopic scale. One such measurement technique is based on the concept of Brillouin light, which uses the shift in frequency between incident and scattered light that is proportional to the mechanical strain within the medium under investigation. This feature can be used to determine a range of elastic, shear and bulk moduli in translucent materials and tissues. When applied to collagen and elastin within the ECM, this technique demonstrated that it is possible to determine the viscoelastic properties at very short nanosecond timeframes. Such short timeframes are most relevant to molecular scale events, well above the glass transition temperature, where the two materials appear to have very similar properties as opposed to the marked differences in moduli observed when measured macroscopically over longer physiologically relevant timeframes and where viscoelasticity dominates. However, the use of Brillouin light scattering as a non-invasive technique for assessing elastic properties of connective tissues in health and disease may well become a useful supportive diagnostic tool in future.

▶ **8.1.2** Quantitative assessment methods such as electrical impedance myography (EIM) and quantitative ultrasound (QUS) can provide useful diagnostic and prognostic indicators for certain diseases that affect muscle structure. In the case of EIM, localized anomalies in muscle structure, reduced fibre size, and changes in composition with increased fat alter the electrical resistance and

capacitance of the tissue to levels that are distinguishable between healthy and diseased states. QUS detects alterations in tissue structure and composition based on the number and reflectivity of interfaces indicated by the greyscale intensity. These changes are indicative of muscle health and so by combining the results from these two techniques a new and non-invasive, impartial indicator of muscle health becomes available.

In brief: what is known and what is new ...

Observations and measurement in biological systems primarily require good precision followed by the best available accuracy. Ideas derived from the underlying physical principles of non-destructive and non-contact methods of measurement are particularly desirable when testing human tissue for diagnostic purposes. Three such methods, some novel, some tried and tested, are provided as examples that may assist in the study and early diagnosis of certain connective tissue diseases and chronic injury (see paper ■7.1.1). These papers demonstrate how the innovation and sophistication of measurement and imaging techniques leads to many new avenues for research, which are only achievable through the availability of increasingly finer resolution and detail.

9 Muscle, Fascia and Manual Therapy

► **9.1.1** Satellite cells, which are adult skeletal muscle stem cells, are important for muscle regeneration. After injury, quiescent satellite cells, which reside beneath the basal lamina of each muscle cell, are activated to form myoblasts that differentiate to repair or replace of damaged muscle cells. This in vitro study used a novel approach to demonstrate that fibroblasts, which are located within the adjacent interstitial fascia of muscle, significantly promote myoblast migration in a simulated muscle injury.

► **9.1.2** Fat accumulation in skeletal muscle is thought to impair the regeneration, metabolism and contractile function of muscle cells and is a feature of obesity, type-2 diabetes, sarcopenia and muscular dystrophies. This in vitro study tested the potential of myoblasts and fibroblasts found in human muscle to differentiate into adipocytes in the presence of adipocyte-inducing media. Although some fibroblast populations reportedly exhibit little to no adipogenic capacity, the findings of this study highlight that fibroblasts located within the muscle fascia, are the main source of adipocytes in human-muscle-derived cultures.

► **9.1.3** This in vitro contraction study investigated the effect of cyclic short-duration stretch and acyclic

long-duration stretch of fibroblasts on nearby muscle cell contractility. This in vitro model highlights that stretch-activated fibroblasts promote the differentiation of highly contractile myotubes. Fibroblasts exposed to a long duration stretch, as used in myofascial release, increased the number and size of nicotinic acetylcholine receptors (nAChR) on myotubes, which is important for muscle contraction and for muscle homeostasis. In contrast, fibroblasts exposed to cyclic short duration stretch, which simulated repetitive stress injury, disrupted nAChR clusters on muscle cells. Long-duration stretch, therefore, would appear to activate extramuscular fibroblasts to stabilize nAChR on nearby skeletal muscle and may be beneficial to muscle cell function.

In brief: what is known and what is new ...

To date, research investigating the adaptation of the muscle-tendon unit has largely focused on contractile skeletal muscle proteins and collagen, with relatively little research directed toward interstitial muscle fascia. Fibroblasts, which are embedded within this interstitial fascia, however, comprise more than 50% of the extra-muscular cell population of skeletal muscle. Since the publication of Fascia III, there is exciting new evidence that these fascia-embedded cells respond to mechanical strain by secreting cytokines that direct myoblast differentiation, promote myoblast migration, influence myotube contractility and stabilize post-synaptic muscle receptors which are important for muscle contraction, homeostasis and muscle regeneration. Conversely, these fibroblasts can also synthesize fibrotic and inflammatory molecules, and may promote fatty infiltration, which is pathogenic to nearby skeletal muscle cells. Clinically relevant biomechanical strain serves as one stimulus regulating the phenotypic shift in fibroblasts leading to either pathogenesis or regenerative effects in nearby muscle cells. We believe this is an exciting new area of research that could lead to novel manual therapy approaches for improved skeletal muscle regeneration.

10 Fascia in Surgery and Scars

► **10.1.1** It is well known that the mechanical and physiological conditions of injured skin greatly influence the degree of scar formation, scar contracture, and generation and progression abnormal hypertrophic and keloid scar. This study used a rodent model to investigate the role of Focal Adhesion Kinase (FAK), a gap junction protein that regulates cell-matrix interactions and is activated by both inflammatory and physical signals, on the formation of pathological fibroproliferative scars. FAK was found to act through extracellular-related kinase (ERK) to mechanically

trigger the secretion of monocyte chemoattractant protein-1 (MCP-1) a potent chemokine that is linked to inflammatory cell recruitment, myofibroblast formation and human fibrotic disorders. Both mechanical and inflammatory stimuli induced robust MCP-1 secretion, and when the two were applied simultaneously, MCP-1 secretion was potentiated. Molecular strategies targeting FAK may also prove effective in uncoupling mechanical force from pathologic scar formation.

▶ **10.1.2** Massage is often used in the management of hypertrophic scars and has been suggested to reduce the stiffness and shorten the time required for formation of a mature scar tissue. This study used a rodent model to evaluate the effect of massage (2 × 5 min per day) with and without topical agents on the thickness and histological appearance of burn-induced scars. In all groups, scar thickness decreased over the 17-week study period. Massage with a topical agent resulted in a significantly greater reduction in thickness (90 % reduction) compared to massage with a lubricant alone (72 % reduction) which in turn, produced a greater reduction in scar thickness than no treatment (53 % reduction). Thus, as little as 10 minutes of massage per day, with either a topical agent or lubricant, is an effective method for decreasing the thickness of post-burn scars.

In brief: what is known and what is new ...

Mechanical force or stress is an important factor that influences the extent and quality of scar tissue and in some instances may promote the growth hypertrophic and Keloid scars. It is important that scar mechanobiology be understood from the perspective of the extracellular matrix and extracellular fluid, in order to develop new strategies for scar prevention and treatment. Mechanical forces such as tension, shear, compression or hydrostatic stresses and osmotic pressure can be perceived by skin receptors including mechanoreceptors and sensory nerve fibres. As highlighted in Section ■11 (Low Back Pain and Innervation), mechanical stimuli received by mechanically sensitive nociceptors are transmitted to the dorsal root ganglia that contain neuronal cell bodies in the afferent spinal nerves. Neuropeptides are subsequently released by primary afferent sensory neurons in the skin, modulating scarring via skin and immune cell functions. While further research identifying factors that initiate pathological hypertrophic scar development are required, inhibition of mechanoreceptors, cell-adhering complexes and controlled force application provide additional openings for the development of novel methods for scar prevention and treatment.

11 Fascia in Low Back Pain and Innervation

▶ **11.1.1** Chronic musculoskeletal pain is often attributed to muscle. In order to function as a pain source, however, tissues have to be equipped with appropriate innervation, such as peptidergic nociceptors, which contribute to central transmission and modulation of pain by both peripheral and central actions. In Fascia III, Mense demonstrated that free nerve endings containing calcitonin gene-related peptide (CGRP) and substance P (SP) were common in thoracolumbar fascia of animals and humans. Both of these peptides contribute to sensitization of peripheral nerves by stimulating pro-inflammatory cytokines. When released centrally, these peptides also contribute to central sensitization of pain by actions in the dorsal horn of the spinal cord. Here, Barry et al. extend this work to identify cells in the dorsal root ganglion (central nervous system) that are associated with muscle and fascia. The density and distribution of nerve fibres in muscle and fascia were compared in a mouse model. The innervation density of these peptidergic neurons was found to be three times higher in fascia than in muscle. Although further research into the role of the two types of neurons is required, the greater number of peptidergic neurons in fascia than muscle suggests it may make a more important, though under recognized, contribution particularly in chronic musculoskeletal pain.

▶ **11.1.2** Free nerve endings in soft tissues can be activated by both mechanical and chemical stimuli. There is now compelling evidence that nerve growth factor (NGF) which is made in large quantities by inflamed tissues, increases sensitivity to pain (hyperalgesia) and acts as an important mediator in chronic pain conditions. Administration of NGF into skin or muscle is known to result in a profound hyperalgesia to mechanical stimuli, which in skin may last for weeks. This study, undertaken in humans, demonstrates that a single dose of NGF induced stronger mechanical hyperalgesia in fascia than muscle. Although the magnitude and duration of NGF-induced sensitization did not reach that previously reported for skin, thoracolumbar fascia was found to be even more sensitive to NGF-induced mechanical hyperalgesia than tibial fascia. These findings have important clinical implications and suggest that sensitization of fascia rather than muscle by NGF may be an important mechanism contributing to the pathophysiology of musculoskeletal pain, especially low back pain.

▶ **11.1.3** In Fascia III, it was shown that the thoracolumbar fascia (TLF) is equipped with nociceptors and, as such, may act as a source of pain. However,

the neuronal mechanism underlying pain arising from pathology of the fascia is not known. This paper builds upon this earlier research, to show how dorsal horn neurons of the spine, which govern the response to noxious mechanical and chemical stimulation, react to input from a chronically inflamed thoracolumbar fascia (TLF) in a rat model. Spinal processing of pain input from the TLF is not normally processed by neurons in the lumbar segments (L3–L6). In chemically induced inflammation of the fascia (injection of Freund's adjuvant), a proportion of L3 neurons ($\approx 11\%$) acquired new input from the fascia. This suggests that some neurons had silent synaptic connections with the TLF, which became active under the increased input from the inflamed fascia. Moreover, the proportion of neurons responding to stimulation from deep tissues rose from 11% to 33%. Surprisingly many neurons acquired new receptive fields most of which were located in deep somatic tissues (mainly muscles) of the hind limb. Thus, the increased input from the inflamed TLF had facilitated the transmission of spinal information from muscles and deep tissues outside the low back. Collectively, the expansion of the spinal target region of fascial afferents to L3 and the appearance of new receptive fields provide a potential explanation for the spread of pain in patients with non-specific fascia-related low back pain.

► **11.1.4** This article extends the anatomical and neurophysiological observations in the papers above to speculate that changes in the density of fascial tissue, as opposed to overt pathology within fascia, may be sufficient to entrap nociceptive nerve endings and cause pain. It is widely held that adhesions between the fascia and adjacent tissues may become painful, possibly because nociceptive nerve endings are trapped in the fibrotic adhesion and excited by shear forces between the tissues involved. In contrast to the fibrotic change that occurs with adhesions, so called 'densifications' are thought to reflect a change in the properties of the loose connective tissue component which allows sliding of adjacent overlaying fascial layers. These 'densifications' are proposed to alter the mechanical tension between adjacent fascial layers and subsequently in the entrapment or shear-induced excitation of nociceptive nerves leading to pain.

What causes 'densification' is unknown, however, the authors speculate that changes in tissue pH, temperature and the rate of tissue loading may influence the levels of water and proteoglycans in the loose connective tissue between the fascial layers. Proteoglycans, which are comparatively abundant in this tissue component, are thought to be critical in governing the sliding of adjacent fascial layers. Proteoglycans such as Hyaluronan are known to be hydrophilic and reversibly bind with water

to lubricate and permit relative sliding between adjacent layers of collagen-rich tissue. However, with reduced water content, Hyaluronan side chains become entangled resulting in greater viscosity, which is thought to decrease gliding between the fascial layers. Other factors such as tissue pH, temperature and loading rates in shear will also affect the viscosity of loose connective tissue components within the fascia. Thus sliding of adjacent tissue layers will be further enhanced with increased pH, elevated temperature and slow shear rates. Although the concept of a reversible 'densification' of fascial tissue supports many therapeutic interventions aimed at increasing temperature and/or shearing between fascial layers, clear quantifiable diagnostic criteria of the pathology and its connection to pain remains elusive and represents an important emerging area for future research.

In brief: what is known and what is new ...

Understanding pain perception is clinically important as it helps clinicians to initiate, guide and evaluate treatment. The clinician needs to recognize that fascia, rather than muscle, is an important source of pain and that pathological change within the fascia, such as inflammation, can stimulate additional nociceptive neurons and the spread of pain receptive fields. Moreover, recognizing that changes in fascia density and sliding, which do not have clear pathological changes, but may be sufficient to cause pain, highlights the potential of existing and new therapeutic approaches, such as those outlined in section 9.

12 Fascia in Sports and Movement

► **12.1.1** Vertebrate animals use elastic recoil of tendinous tissues for locomotion. This review examines the specific advantages of this phenomenon in kangaroos, antelopes, horses, birds, dogs, whales, dolphins, and – of course – also humans. It describes three different ways how the elasticity of tendons enables these vertebrates to improve their muscular function: Firstly, metabolic energy can be saved in locomotion if tendons stretch and then recoil, thereby storing and returning elastic strain energy. This happens in the leg tendons of running birds and mammals, in the aponeurosis of the back in galloping mammals, and may also happen in the tails of swimming whales and dolphins. Secondly, tendons can recoil much faster than muscles can possibly shorten, thereby enabling animals to jump further than they otherwise could. Thirdly, tendon elasticity affects the control of muscles, improving force control at the expense of position control. In short: elastic recoil provides many different improvements for rapid locomotion.

► **12.1.2** Three different training methods were compared in this study: strength training, recreational soccer and running. All were conducted by untrained adult persons for a period of 12 weeks, and their potential effects on jumping performance in a bilateral counter-movement jump were examined. Surprisingly neither running nor soccer had any effects on jumping performance, although soccer did induce increased muscle fiber cross-sectional area and quadriceps activity. However, strength training resulted in clear improvements in jumping performance. These effects of the strength training group were related to an enhanced neuromuscular activity in their hamstrings and plantar flexors, in addition to an increased myofiber fiber size.

► **12.1.3** This article introduces the theoretical foundations of a fascia oriented training approach. In addition, it also gives some practical examples of fascia oriented exercises. While conventional health-oriented sports focus primarily on an enhancement of muscular strength, cardiovascular conditioning, and/or sensomotor coordination, this approach tries to complement these training dimensions with a more specific stimulation of the fascial network of the human body, including tendons, aponeuroses, muscular envelopes, joint capsules, etc. Fibroblasts continually but slowly adapt the morphology of these tissues in response to repeatedly applied challenging loading stimulations. The exercises therefore attempt to orchestrate such mechanical challenges by different stretching methods, elastic recoil motions as well as rehydration practices. Given the slower adaptation times of fascial tissues – compared with myofibers – a more patience-oriented training mentality is advocated.

In brief: what is known and what is new ...

Elastic recoil capacities of fascial tissues are important features in locomotion. These elastic attributes depend on specific biomechanical properties of collagenous connective tissues, such as in tendons and aponeuroses. How these properties can be specifically fostered by different exercise methods is a new and promising field of scientific inquiry. Most likely this novel field in sports science will continue to offer inspiring surprises, which may not always confirm our traditional assumptions. Clearly, an augmentation of fascial elasticity needs to go hand-in-hand with muscular performance and appropriate sensory coordination. Whether such a training approach will lead towards an improved injury prevention in sports remains to be seen.

13 Special Considerations in Fascia

► **13.1.1** In this anatomical study, potential mechanisms underlying observed limitations in the range of passive joint motion in spastic cerebral palsy (CP) are explored. Although muscle adaptation is thought to be the primary cause of limited joint motion in CP, this histological study found no difference in length-tension properties of myofibre segments of flexor carpi ulnaris muscle biopsies (FCU) from CP patients (n=29) and healthy controls (n=10). Rather in the majority of CP patients (19/23) there was a three-fold increase in the thickness of tertiary perimysial fascia, which enters and crosses the muscle transversely to connect intra- and extra-muscular neurovascular structures. These authors hypothesize that heightened myofascial loads in spastic muscle is one among several factors contributing to the limitation of joint movement in CP.

In brief: what is known and what is new ...

As awareness of the role of fascia in myofascial force transmission, mechanotransduction and mechanosensation increases, there is emerging evidence that fascial tissue that surrounds muscle tissue may also be involved in conditions, such as spastic cerebral palsy, which was thought to mainly reflect dysfunction of the central nervous system. In section ■12, fascial involvement in a number of relatively uncharted populations will be explored.

14 Research Methods and New Hypotheses in Fascia

► **14.1.1** Similar to fibromyalgia, people with chronic fatigue syndrome (CFS) also have heightened sensitivity and symptoms following various physical and cognitive challenges. This clinical paper puts forward the hypothesis that restrictions in tissues adjacent to nerves, or adhesions of the nerve itself, increase mechanical tension within the nerve, resulting in mechanical sensitization, altered nociceptive signalling, altered proprioception, adverse patterns of muscle recruitment, reduced intra-neural blood flow, and release of inflammatory neuropeptides. The authors argue that neuromuscular restrictions are common in CFS, and that these restrictions contribute to the pathogenesis of CFS symptoms, including cognitive dysfunction. Although symptoms of fatigue not been fully explained by central sensitization, the role of peripheral contributors, such as fascial adhesions, presents an interesting and potentially testable hypothesis for future research.

► **14.1.2** This paper provides the first preclinical evidence for a new paradigm in which mechanical forces are hypothesized to be the underlying cause of enthesitis and new bone formation in spondyloarthritis (SpA); a group of chronic inflammatory disorders characterized by axial inflammation and asymmetrical peripheral arthritis. Inflammation of the attachment sites of ligaments and tendons to bones, or enthesitis, is a particular hallmark of SpA, which distinguishes it from other inflammatory rheumatic disorders. Using a mouse model of spondyloarthritis, limb unloading was shown to significantly suppress inflammation at the enthesis of the Achilles tendon compared with weight bearing controls, while new bone formation was strongly promoted at enthesal sites by biomechanical stress and also correlated with the degree of inflammation. The hypothesis that a mechanotransduction-associated inflammation is involved in chronic inflammatory arthropathies, such as SpA, opens new avenues for the therapeutic management of these conditions, particularly those that focus on modifying mechanotransduction pathways. The effectiveness of clinical applications of mechanotransduction, as with many physical therapeutic approaches, is still to be tested.

► **14.1.3** This study used ultrasonography to test the hypothesis that loose connective tissue inside the fascia plays a significant role in the pathogenesis of chronic neck pain. Morphometric and clinical data from 28 patients with chronic neck pain (CNP) and 25 healthy controls were compared. Significant differences were found in the thickness of the upper side of the sternocleidomastoid fascia and the lower and upper sides of the right scalene

fascia between healthy and CNP groups. The variation in thickness of the fascia correlated with the increase in quantity of the loose connective tissue but not with dense connective tissue. While the results suggest a clinical association between fascia and neck pain, whether the loose connective tissue is a cause or consequence of neck pain remains unknown.

In brief: what is known and what is new ...

As highlighted in section ■4.1.1, fascial involvement may be key in many musculoskeletal complaints, and even conditions previously considered unrelated or primarily systemic in nature. New hypotheses regarding the role of fascia in musculoskeletal force transmission, mechanoregulation, and neuromuscular control and its dysfunction in musculoskeletal and systemic ailments, including cancer and arthritis, are emerging. Carefully considered research designs and innovate measurement techniques are required, however, to adequately test many of these new hypotheses. There is a particular need for coordinated and well-controlled prospective studies to further advance our understanding of the function of fascia and to enrich the range of effective treatment options.

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