E D I T O R I A L

Fascia Research II: Second International Fascia Research Congress

KEYWORDS: Fascia, musculoskeletal manipulation, research, congresses

It is with pleasure that I introduce background materials to the Second International Fascia Research Congress, to be held October 26 – 30, 2009, at Vrije Universiteit (VU), Amsterdam, Netherlands. This conference is sponsored by the faculty of Movement Sciences of VU, a leading research university. The submitted abstracts are posted at the congress website, http://www.fasciacongress.org/2009. The key speakers are all new for 2009, although almost half the key presenters from 2007 will be returning with shorter presentations (Langevin, Solomonow, Mense, Standley, Bove, Huijing), and Guimberteau will have a new video presentation of fascia images obtained during human surgery. The conference proceedings book *Fascia Research II* includes full-text articles that form an important basis for the scientific study of fascia. Huijing is a muscle physiologist who has for many years been studying the connections between muscles and fascia. He has recently developed an interest in the clinical practice relating to fascia and has guided the selection of these papers; some of this information has not been widely published. Van der Wal presents his new findings on connective tissue architecture from his doctoral dissertation of 20 years ago (to appear in the next issue of *International Journal of Therapeutic Massage and Bodywork*). Other papers come from widely disparate scientific disciplines. Purslow, one of the key speakers and an author of one of the papers in the congress proceedings book, is a food scientist whose connective tissue studies are sometimes seen by other disciplines.

The organizers of the first Fascia Research Congress (Boston 2007) based their invitation for this next congress on a broad interpretation of the term "fascia": "Fascia is the soft tissue component of the connective tissue system that permeates the human body.... 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 periostea, and all the endomysial and intermuscular fibers of the myofasciae." This broad definition offers several important advantages. Rather than having to draw most often arbitrary demarcation lines between joint capsules and their intimately involved ligaments and tendons (as well as interconnected aponeuroses, retinacula, and intramuscular fasciae), fascial tissues are seen as one interconnected tensional network that adapts its fiber arrangement, length, and density according to local tensional demands. This terminology fits to 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."

The purpose of this editorial is to share with you information that I have learned from the papers to appear in *Fascia Research II,* from my perspective as both a clinician and a researcher.

First, I will share key findings from anatomy regarding connective tissue architecture and how joint motion mechanically affects nerves.[1,2] The biomechanics of these connections and the potential applications for human surgery is the second area in which papers are presented.[3–6] The spotlight then moves to the cellular and histologic levels,[7–10] looking in detail at how individual cells respond to mechanical forces.[11,12]

FASCIA ANATOMY

Based on his studies of the anatomic structures involved in myotendinous force transmission at the rat elbow joint, van der Wal[1] takes a new approach to muscle and connective tissue architecture.

Anatomical thinking has been limited by the traditional dissection process, in which connective tissue is removed to display underlying tissues. Connective tissue is usually named based on the nearby structures, suggesting little role for this tissue. From the structural viewpoint, connective tissue can be seen to have two distinct functions: to separate or allow gliding, or to connect and transfer forces. The same principles can be seen in the connective tissue of the abdomen as in the tissue of the extremities.

Van der Wal makes the argument that muscles and ligaments cannot be viewed as separate structures next to each other, each acting independently to handle mechanical stresses across a joint. He realized that because ligaments can bear stress only when they are stretched fairly tight, ligaments can serve to stabilize

joints only if the distance between the bones on each side of the joint remains fairly constant throughout the joint range of motion; however, only two joints in the body meet this criterion, and other joints are forced to use a different mechanism. Using a three-dimensional computer reconstruction program and a novel dissection approach that maintains the connections between muscles and connective tissues, he was able to show that there are specialized connective tissue structures running between the muscles and the bone of origin or insertion. This dynamic connection between connective tissue and muscle he terms the "dynament"—a structural support that can adapt to changing distances between bones throughout the joint range of motion. Some muscles have these specialized connective tissue structures at the proximal end only, some at the distal end only, some at both ends—and some at neither end. Furthermore, analysis of mechanical force transfer through such structures shows that nerve endings are concentrated where the stresses are the highest, especially in the proximal or distal end of the "dynament." This contrasts with the more traditional approach that describes the density of innervation by the named muscle, rather than by the type of load that that portion of the muscle or connective tissue is designed to bear.

The nerve receptors have traditionally been divided into muscle or joint receptors; however, a continuum of receptor types can be seen across both tissues, defined by the types of stresses borne by the specific tissue. Van der Wal suggests four classes of nerve receptors: muscle spindles; Golgi tendon organs and Ruffini corpuscles; lamellated or paciniform corpuscles; and free nerve endings. The first three classes are found in muscles, and the latter three, in the connective tissue surrounding joints.

Several points from this paper are important for the study of therapies dealing with fascial tissues: A consideration of the types of receptors that are sensitive to dynamic force changes in compression (the laminated corpuscles) and tension or torsion (the spray-type endings), and whether such endings adapt slowly or rapidly to loading or have low or high thresholds, can help in the development of hypotheses regarding the potential effects of therapy on inputs to the nervous system. The paper by Standley and Meltzer[13] shows effects at a molecular level of pressure and shear, the major forces they see as involved in manual therapies. Many therapies address the tissues at the junctions between muscle and bone; defining the architecture at this location may help in understanding how such therapies work and in developing testable hypotheses for treatment effects and ways to improve treatments for specific conditions. The full text of this important paper by van der Wal will appear in the next issue of IJTMB.

The paper by Coppetiers and colleagues[2] from the research group led by key 2009 speaker Hodges shows clearly that motion at either the hip or the ankle results in nerve motion not only at the joint moving, but also at more distant joints. Motion at the ankle increased strain in the tibial nerve only by about 3%, which is below the range demonstrating physiologic changes in normal animal studies. However, local neural inflammation results in nerves that are sensitive to this level of strain and that cannot tolerate motion in the full normal range. Furthermore, motion at the hip combined with motion at the ankle results in higher strains in the nerves at the ankle to levels that can impair blood flow even in normal nerves. Hip flexion can be used as a test to strengthen the diagnosis of tarsal tunnel. Bove[14] addresses proximal and distal nerve effects from a physiologic perspective.

FASCIA BIOMECHANICS

Mechanical connections between a muscle and synergistic muscles have been the subject of many years of investigation by Huijing, a key speaker from the 2007 Fascia Congress, and two of the four papers in this section (Kreulen et al.,[5] and Huijing[6]) come from his research group. Maas and Sandercock[3] suggest that the existence of these connections does not mean that, in normal physiologic conditions, they are active, because these authors find that the soleus muscle in the cat (a single-joint muscle) acts mechanically independently of the neighboring muscles that cross both the ankle and the knee. As expected, passive ankle moment is indeed dependent on knee position, reflecting the two joint muscles that are also involved in passive movement. When the distal tendon of the soleus was cut, the soleus continued to exert force across the ankle, demonstrating strong connective tissue linkages to the neighboring muscles. However, active stimulation of the intact soleus muscle showed effects at the ankle that were independent of the knee position. Thus, they conclude that the strong connections between the muscles were not active at the normal ranges of motion in the intact limb in the specific positions of this experiment. Other scientists, including Huijing, suggest that this finding reflects limits on, rather than the absence of, myofascial force transmission. In either case, extrapolation of these results to other muscle groups must take into account the specific connective tissue architecture that differs from muscle to muscle.

Yu and colleagues[4] demonstrate the first in vivo evidence of epimuscular myofascial force transmission. They found that activation of the flexor pollicis longus (FPL), a muscle unique to human primates that contributes to manual dexterity by independently flexing the thumb, resulted in a load on the index finger about 5% of the force level of the thumb. This loading occurred without any time delay, which would be expected if the force transfer was through a viscoelastic mechanical connection between the muscles. For loading on the other fingers, about 1/3 of the motor units in the FPL produced loading, 1/3 produced unloading, and 1/3 had no effect; however, these effects were not as

closely synchronized in time as with the index finger. The authors concluded that the loading on the index finger reflected a neural synchronization with co-contraction of the muscles rather than direct force transmission, and they had no explanation for the variability of the effects on other fingers. Their technique for detecting synchronization of muscle forces will be useful in human studies to detect differences between neural and connective tissue connections between muscle groups. Yucesoy and Yaman will present additional in vivo evidence at the Fascia Congress 2009

Myofascial connections between adjacent muscle groups has been studied in animals, in which it is possible to isolate both the proximal and the distal tendons to a particular muscle. In children with cerebral palsy, orthopedic surgeons perform a tendon transfer procedure in which it is necessary to cut the distal tendons of the flexor muscles of the wrist, which are then dissected from the neighboring muscles and transferred to the other side of the joint to become wrist extensors. Smeulders and Kreulen[5] were able to study the flexor carpi ulnaris (FCU) in these patients during surgery. They looked at tendon excursion with wrist flexion/extension in the intact muscle, after distal tenotomy of the FCU, and after dissection of the FCU from the neighboring muscles just before transplantation. The proximal end of the tendon continued to move with wrist motion, showing 90% of the original excursion despite a tenotomy disconnecting it from the insertion. After dissection of the muscle, there was little motion with wrist movement, supporting the notion that there are connective tissue connections between adjacent muscles that allow forces to be transferred between those muscles. The FCU was maximally electrically stimulated to contract, comparing before/after tenotomy and before/after tissue dissection. Tenotomy changed the maximally shortened length by only 1.5%, compared with a 4% decrease after muscle dissection, again supporting the concept that connective tissue connection between adjacent muscles limits muscle excursion. They reviewed the implications of myofascial force transmission for tendon transfer in humans with spastic paresis. Spastic muscles have altered properties that, by themselves, do not explain muscle stiffness and contractures. Not only the muscle fiber and inter- and extramuscular connective tissue, but also the adaptation of these to muscle use and disuse, will affect functional results from tendon transfers. Studies on similar tendon transfers in rats will be presented by Maas at the Fascia Congress 2009.

Huijing[6] reviewed the concepts of myofascial force transmission between and within muscles, showing connections between both synergistic and antagonist muscles. Within a muscle fiber, up to half of the total force generated by the muscle is transmitted to surrounding connective tissues rather than directly to the origin and insertion of the muscle fibers. Force can be transmitted to adjacent muscles that are synergistic, as well as to extramuscular tissues such as the neurovascular tract and various septa and membranes; by this extramuscular pathway, such forces can reach antagonistic muscles. And so the findings that synergistic muscles are not mechanically independent seem also to apply to antagonistic muscles. These findings have implications for the management of muscle conditions found in people with spastic paresis, who often find themselves with joints fixed in a particular position—for example, wrist flexion or ankle plantar flexion. Immobilization of a highly pennate muscle results in atrophy if the muscle is in the shortened position, but if the muscle is in a lengthened position at immobilization, hypertrophy may even result. In any particular joint position, some of the sarcomeres in a given muscle may be shortened, and others lengthened, because of the local connective tissue connections with other muscles. The analysis of the impact on a given muscle therefore becomes quite complex. Huijing suggests several quite novel perspectives based on his anatomic and physiologic investigations. If the joint is kept in one position, the muscles on the stretched side may hypertrophy. Forces causing movement limitations in people with spasticity may come from the antagonist muscles, transmitted to the distal tendons of the synergistic muscles. He suggests that clinical dissection of the affected spastic muscle, without tendon transfer, may be sufficient to disrupt these pathways and provide clinical improvement.

FASCIA CYTOLOGY AND HISTOLOGY

Ingber, one of the key speakers from the 2007 Fascia Congress, introduces the concept that "cells act locally but think globally" in sensing tensional forces in the extracellular matrix (ECM).[7] Integrin receptors on the cell surface are mechanically coupled to the actin cytoskeleton of the cell, forming a pathway to sense external forces and allow the cell to respond with changes in cell shape. Cells can activate internal chemical signaling pathways, increase stress-fiber assembly and adhesive strength, and form focal adhesions in response to externally applied mechanical forces. Ordinarily this mechanism is damped to lower its sensitivity to normal physiologic fluctuations. However, once a large-scale change occurs in the ECM, altering the cell shape, that cell then becomes more responsive to its immediate mechanical domain.

Grinnell[8] summarized his key presentation at the 2007 Fascia Congress with a description of his use of three-dimensional collagen matrices to demonstrate that cells adhere to matrix fibrils specifically, rather than to nonspecific matrix proteins, and that cells can remodel these matrix fibrils or can penetrate into the matrix. These interactions are controlled by the tension between cell and matrix, which in turn depends on collagen density, growth factor, and matrix restraint. Grinnell finds that cells under high tension show stress fibers, focal adhesions, and enzymatic activation related

to the adhesions. At low tension, cells lack these features and assume a different morphology, resembling dendritic cells. These cells resemble the mechanoreceptor osteocytes in bone, and the formation by soft-tissue fibroblasts of a mechanosensing network can be hypothesized. That hypothesis provides a cellular basis for the mechanoreceptors noted in the architectural scheme described by van der Wal.[1]

The paper by Engler and colleagues[9] describes specific effects of the ECM on the cells it surrounds. Differentiated cells contact and move within matrices whose stiffness ranges from as soft as the brain to as firm as collagen-coated glass. Among already differentiated cells, fibroblasts are the most responsive to the stiffness of the matrix, but undifferentiated stem cells are even more influenced. Mesenchymal stem cells (MSCs) are bone marrow–derived adult stem cells that can differentiate into neurons, myoblasts, and osteoblasts. These cells exert force against the ECM though a non-muscle myosin II mechanism that tensions actin structures linked to focal surface adhesions, which in turn are connected to the ECM. Depending on the force required to deform the matrix, neurogenic, myogenic, or osteogenic RNA transcriptional markers are produced if, respectively, the matrix is soft (brain-like, 1 kPa elasticity), more rigid (muscle-like, 10 kPa), or stiff (bone-like, 100 kPa). The myosin genes appear sensitive to matrix stiffness, so that as the matrix becomes stiffer, more myosin is produced, allowing the cell to generate sufficient force to accommodate an up-to-100-times difference in stiffness. Cells can also remodel their micro-environment, with effects going the other direction, from the cell to the matrix.

Physiologists have known for a long time that blood flow to tissues rapidly increases when muscles contract through local mechanisms. This change supports the increased metabolic demands of the tissues. Hocking et al.[10] were able to demonstrate mechanical coupling of skeletal muscle contraction with local arterioles through the ECM fibronectin, which uses a nitric oxide mechanism to stimulate an increase in arteriolar diameter. They found that actively contracting skeletal muscle generates tensile forces that change the conformation of fibronectin fibers surrounding the arteriolar wall. This change briefly exposes a heparin binding area of the fiber, which they hypothesize interacts with heparin sulfate proteoglycans on the smooth muscle of the vessel or on the skeletal muscle itself, releasing nitric oxide that initiates smooth muscle relaxation and hence vasodilation. This process demonstrates a novel method of mechanotransduction, which may serve in other capacities as well. While not mentioned by the authors, a testable mechanism is also suggested, whereby chronic low-level muscle contraction may cause a blunting or downregulation of this pathway, so that when the muscle contraction is stronger, the blood flow response is inadequate and tissue metabolites collect, causing pain and muscle dysfunction.

FASCIA CYTOLOGY AND MECHANICS

The first section of the paper by van der Wal[1] notes that connective tissue comes as either dense or loose tissue. Iatridis et al.[11] focus on the lesser-studied loose tissue. Many therapeutic techniques are based on the stretching of connective tissues, but whether that stretching is greater than the stretching applied in daily life, or whether it is of a normal range applied to tissues that have themselves been subjected to less-than-normal stresses is not known. Iatridis and colleagues found a very low, but linear, viscoelastic biomechanical response to applied stress in subcutaneous tissues. The tensile modulus is similar to levels reported by others for the pericellular matrix of the cell, articular chondrocytes, skin, and the nucleus pulposus, and about 2.5×10^{-6} that of the medial collateral ligament. This tissue has a much lower tensile elastic modulus and relaxes faster than do most other tissues, suggesting that it is already bearing load even at the lowest strain levels. Iatridis interprets this finding as indicating that, rather than having a load-bearing function, it serves to transmit mechanical signals.

The "separating" function of connective tissue described by van der Wal[1] is most evident in the connections between a tendon and the tendon sheath, which allows for a great deal of excursion. Readers interested in pictures at surgery of this loose connective tissue and in a theoretical framework for a structure that remains under relatively constant load throughout a wide range of displacement are directed to the work by hand surgeon Guimberteau (speaker at Fascia 2007), both in video[15] and in papers.[16,17]

Key 2009 speaker Purslow[12] addresses the three distinct layers of intramuscular connective tissue (IMCT): epimysium surrounding whole muscles, perimysium separating fascicles or bundles of muscle fibers within the muscle, and endomysium covering the individual muscle fibers. These structures provide intramuscular pathways and reinforcement for nerves, blood vessels, and lymphatics. Although types I and III collagen are the major components of these tissues, with type IV predominating at the basement membrane immediately next to the sarcolemma, small amounts of types V, VI, XII, and XIV are present as well. The interaction between the myoblast and the ECM is critical to muscle growth and development (see also the paper by Engler et al.[9]), and the number of muscle fibers within the muscle does not change after birth. In performing the ultimate connective tissue–sparing dissection proposed by van der Wal[1] (digesting the muscle tissue and leaving only the network of collagen fibers), the IMCT can be seen as an extensive matrix of connected tunnels. Continued interaction between the muscle cells and the ECM governs muscle turnover, hypertrophy, and injury repair throughout growth and adult life, affecting the size of each of these connective tissue compartments. Several functions are found for these layers. Mechanical support for large

and small nerves and blood vessels parallels the connections between tendon and tendon sheath observed by Guimberteau.[16]

Purslow hypothesizes that, as muscles change shape during contraction, the connective tissue layers allow these tissues to slide past each other with a controlled amount of resistance. He also notes that the very thick outer layer of fascia that divides muscles into various compartments (for example, the anterior compartment of the lower leg) is usually seen by physicians only as a source of trouble when the pressure rises too high, creating a "compartment syndrome" that becomes a surgical emergency. However, in normal activity, contraction of one muscle within the compartment results in a small elevation of pressure, which increases the contractile efficiency of other muscles within that compartment. Not noted by Purslow is another function of this layer: these normal pressure changes result in cyclical changes throughout the gait cycle, which assists in venous return of blood to the heart, with the calf muscles serving as a "second heart pump"[18,19] and assisting with perfusion to the muscle itself.[20] Furthermore, the arteriolar dilation previously noted by Hocking[10] may further contribute to this muscle pumping mechanism.

Whereas the academic field of "connective tissue research" has shifted its main focus mostly to molecular dynamics (with particular attention to bone dynamics, cartilage, and genetic analysis), the newly emerging field of fascia research pays particular attention to aspects in which the body's collagenous soft connective tissues work together as a body-wide three-dimensional fibrous network for support. Huijing and Langevin[21] propose a further recommendation for describing fascial tissues with more specification. Depending on morphology and arrangement, they suggest criteria by which a local tissue can be correctly described as "superficial fascia," "deep fascia," "epimysium," and so on. The inclusion of specified descriptions such as these can be extremely helpful in understanding the differences in the structural function of the tissue.

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CONFLICT OF INTEREST NOTIFICATION

Dr. Findley receives limited travel reimbursement and no salary support from the Fascia Research Congress. The author declares that there are no conflicts of interest.

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