FASCIA SCIENCE AND CLINICAL APPLICATIONS: EDITORIAL

Findings from the frontiers of fascia research: Insights into ‘inner space’ and implications for health

The fifth International Fascia Research Congress (FRC) was held in Berlin, Germany November 14th and 15th of 2018, with a sold-out audience of almost 1000 registrants. FRC5 (Figs 1-5) was preceded by a ‘Think Tank’ meeting of the distinguished keynote speakers who are preparing a paper to define future directions for fascia research. Excitement amongst the internationally diverse and multi-modal conference attendees was palpable, with many sessions filled to capacity. This editorial will focus on material presented by the eight keynotes, with reference to research of a few additional speakers. Insights from the many other brilliant FRC presenters and contributors have also informed this summary paper.

1. What is fascia

Fasciae touch every system in the body. Research pertaining to fascia, therefore, span a range of topics from biomechanics to neurology to immunology. Because fascia is ubiquitous, multifaceted, and multifunctional, it is also challenging to define. As referenced in a recent article in the British Journal of Sports Medicine: “the fascial system builds a three-dimensional continuum of soft, collagen-containing, loose and dense fibrous connective tissue that permeates the body and enables all body systems to operate in an integrated manner” (Zügel et al., 2018). Fascia is distinct from other connective tissue including cartilage and bone (which are hard) and blood (which does not contain collagen); and from the three other major tissue types, which typically contain more densely organized cells: muscle tissue, nervous tissue, and epithelial tissue.

In addition to connection, fascial connective tissue provides separation and containment. Examples of fascial tissue include ligaments (connecting bone to bone), tendons (connecting muscle to bone), as well as aponeuroses, epineurium, joint capsules, periossea, retinacula, septa, membranes, meninges, neurovascular sheaths, adipose tissue, visceral fasciae, and all the intramuscular and intermuscular connective tissues including endo-/peri-/epimysium of muscles (Adstrum et al., 2017). Fascia has two distinct morphologies: loose connective tissue (which consists of areolar tissue, reticular tissue, and adipose tissue) and dense connective tissue.
(which has fibers as its main matrix element). Note that ligaments, tendons, and other fascial tissue that may appear distinct in textbooks are in fact continuous with the fascial connective tissue web that extends throughout the body. For a visualization of fasciae, we recommend the exquisite videos created by Dr. Jean-Claude Guimberteau, MD and the illuminating anatomical dissection projects of Dr. Gil Hedley, Drs. Carla and Antonio Stecco, Tom Myers, and many others.

2. Fibroblasts, hyaluronan, & hormonal effects

According to Dr. Carla Stecco, Orthopedic Surgeon and Professor of Anatomy and Movement Sciences at the University of Padova, Italy, fascia is indeed a complex organ. As she describes it, fasciae are comprised of cells, extracellular matrix, and nerve elements, all playing equally important roles. Fasciae contain fibroblasts, which create collagen, essential in tissue repair and remodeling, and which form structural elements of the extracellular matrix, as well as myofibroblasts. As described by Dr. Robert Schleip and Dr. Boris Hintz in a session on matrix biology, myofibroblasts have a small degree of contractility and are essentially activated fibroblasts, secreting large amounts of collagen. In addition to fibroblasts, the extracellular matrix contains telocytes, which were identified in fascial tissue last year by Dr. Stecco’s lab. Telocytes are similar to fibroblasts but have long extensions connecting different parts of the fascia and may play a role in quick communication. Recently, Dr. Stecco and her team discovered a unique type of fibroblast that secretes hyaluronan, the gel-like substance which lubricates joints and facilitates gliding between tissue layers. These new cells have been anointed ‘fasciacytes’.

Another finding important to facial tissue composition is that fascial fibroblasts contain sex hormone receptors, which can affect collagen expression. Dr. Stecco’s team has focused so far on female hormones and found receptors for estrogen, relaxin, and estradiol. These sex hormones, in particular estradiol, stimulate secretion of collagen type 3, which is elastic and organized more like a web; they also seem to decrease secretion of collagen type 1, which produces large bundles of strong collagen fibers to create stiffer and stronger fascia. In addition, fibrillin (a glycoprotein secreted by fibroblasts) was found to increase expression during the peri-ovulatory phase and pregnancy, making fascia more elastic. Increased elasticity in response to sex hormones makes the fascia of the trunk more adaptable to change of volume during pregnancy, and it is valuable to understand the biochemical mechanisms by which these changes occur. Looking at postmenopausal women, Dr. Stecco’s lab found decreased expression of sex hormone receptors, making fasciae less receptive to hormonal input and more likely to develop and maintain stiffness.

Of note, Dr. Antonio Stecco, who shared research in a concurrent FRC session, is currently evaluating new treatment options for muscle and fascial stiffness involving the enzyme hyaluronidase, which catalyzes the degradation of hyaluronic acid. High concentration of...
hyaluronic acid and glycosaminoglycans (which create turgor) have been shown inside fascia and muscle and correlated with tissue stiffness. He is currently evaluating injection of hyaluronidase and its effects on tissue stiffness and range of motion at his lab at New York University.

And in promising new research of Dr. Carla Stecco, CB1 and CB2 endocannabinoid receptors have been recently identified in fascial fibroblasts, which could contribute to modulation of fascial fibrosis. Prior research cited has shown that CB2 stimulation can reduce scarring and inflammation, although this has not yet been shown in fascial connective tissue.

3. Interstitial fluid, lymphatics, & cancer cell migration

Although fascia research has tended to focus more on fiber and cell components, well-deserved attention was recently brought to the fluid within the layers by Dr. Neil Theise, a Professor of Pathology, liver specialist, and stem cell researcher at the NYU School of Medicine in New York. Dr. Theise’s appreciation of the fluid-filled submucosal layer has played an important role in updating conventional medical perspectives on the significance of liquid content in interstitial space, which is elusive ex-vivo and commonly considered artifact in tissue samples. Dr. Theise and his team identified the more viscous gel-like fluid as well as faster-moving water-like fluid in the interstitial space, highlighting the potential for cancer cell migration through these channels. Although not technically new, the apt and intuitive term ‘interstitium’ has now been popularized as a name for this fluid-filled space within fascial connective tissue, enhancing our common language. Dr. Theise and his team have also identified an electrostatic current running through the interstitial space.

The relationship of interstitial fluid with lymphatics and cancer cell migration was discussed by Dr. Melody Swartz, who is a Professor of Molecular Engineering at the University of Chicago. Her research focuses on the lymphatic system, pathophysiology, and immunity. Interstitial fluid, which surrounds and suspends cells within the extracellular matrix, provides nutrients to the cells and removes waste. Small amounts of blood plasma leak out of the capillaries, which gets picked up by the lymphatic vessels, most of which is eventually returned to the blood. Lymphatics can actively pull in water when needed, but this can only happen if there is fluid flow. The more dense the interstitial space, the higher the resistance to flow. Hydrostatic pressure opens up channels to balance and diffuse pressure and allow flow through the matrix, sized and distributed according to need. The flow of liquid through the porous medium of the matrix is described by Darcy’s Law. As Dr. Swartz explained, the interstitial balance of water is essential for us to maintain our micro-environments and for proper function of the immune system.

Under normal conditions, proteoglycans, which form the ground substance of connective tissue matrix, help contain fluid within our tissues, due to electrostatic repulsion. The matrix provides adhesion sites, integrated with the cells, for secreted proteins including growth factor and immune cell secreted cytokines. As described by Dr. Swartz, cells are constantly sensing their environment and responding to pressure and chemical changes by remodeling the matrix to optimize local conditions, which can change dramatically in disease states. With inflammation, fluid is flushed to the lymph nodes where adaptive changes take place to remove pathogens, promote wound healing, and restore homeostasis. With loss of interstitial fluid flow in excessive untreated edema, communication with lymph nodes is lost, which can lead to fibrosis and susceptibility to infections and potentially lead to more serious issues.

Interstitial fluid flow is essential for a properly functioning immune system, however, it can also be exploited, as discussed by...
Dr. Swartz and elaborated on by Dr. Peter Friedl in another session. When cancer cells migrate, they can do so rapidly along fluid channels. So while manual therapy has been shown to significantly improve immune system function, caution should be exercised on and near cancer sites and if there is risk of metastasis. Gentle movement of fluid to reduce edema can be beneficial, however, once doctor-approved.

4. Inflammation, nociception, & pain

The relationship between inflammation, nociception, and pain was explored by Dr. Paul Hodges, Professor of Spinal Pain, Injury, and Health at the University of Queensland, Brisbane, Australia. Inflammation can be generated peripherally or centrally. When inflammation occurs, chemicals from white blood cells are released into the blood and in affected tissues to protect against foreign substances. Once secreted, these elements create a kind of inflammatory soup, as he describes it, which can excite and sensitize neurons, making them more responsive than they would normally be. Inflammation can therefore play an important role in generating and modifying pain response, and can lead to central sensitization, peripheral sensitization, tissue effects, and neuroimmune reactions, according to Hodges. And macrophages, which exist in every cell in the body, are key to inflammatory response including type M1 pro-inflammatory and type M2 anti-inflammatory. In injured muscle, accumulation of M1 macrophages has been observed. In recently submitted promising research, Dr. Hodges showed that in mice with spontaneous intervertebral disk lesions, inflammatory changes were observed in the nearby undamaged multifidus muscle, leading to atrophy, fatty infiltration, connective tissue accumulation, and muscle fiber changes; and that these changes were dramatically reduced by physical exercise.

Dr. Hodges highlighted the difference between nociception, which is information about a threat, and pain, which is the nervous system's response to perceived threat. He made the point that pain is non-linear, that input does not necessarily equal output, and that psychological and social factors can amplify or reduce pain experience. He emphasized a holistic bio-psycho-social approach for treating pain, including a focus on improving sleep, depression/stress, negative affect, as well as work and family support. He also highly recommended exercise to reduce muscle atrophy and tissue fibrosis that can result from disuse and altered movement patterns in response to pain stimuli. Gentle exercise can be initially used to turn muscles on, and more targeted and intensive exercise can be used at a later stage to stimulate muscle fibers and connective tissue. Exercise has a myriad of psychological benefits as well as benefits to immune response, which can further help to reduce pain and promote healing.

5. Back pain & the spine

Another strong proponent of exercise to improve health outcomes is Dr. Frank Willard, Professor of Anatomy and Neuroanatomy at the College of the Osteopathic Medicine of the University of New England. Dr. Willard's work focuses on spinal anatomy and neurology of spine pain. Low back pain can be debilitating and is a common and growing problem. Because fascial connective tissue is now known to be densely innervated and contain nociceptors, much research is being focused on the role of fascia in low back pain, particularly due to its important role in force transmission.

According to Dr. Willard, there are four types of back pain:
1. Axial - muscle tendon, ligament, bone, joint capsule, and associated fascia
2. Radicular - from compression of a nerve as it passes out of the lumbar spine
3. Myelopathy - coming from the spinal cord itself, when injured
4 Referred - referred to the back, rather than coming out of the back

Although herniated disks are a commonly discussed potential cause of low back pain, they seem to only contribute to approximately 4% of low back pain cases, possibly a little higher for men in their 30’s but no more than 6%. He found that osteoporosis also accounts for about 4% of low back pain cases based on available data, and osteoarthritis accounts for about 10% of cases. Recurrent referred visceral pain seems to contribute to another 2%, although this may be understated as this condition is often overlooked. By far the biggest source of low back pain from what Dr. Willard has found in the literature is myofascial-ligamentous pain, which seems to contribute to another 70%, although this may be understated as this condition is often overlooked. By far the biggest source of low back pain from what Dr. Willard has found is myofascial-ligamentous pain, which seems to contribute to another 70%. A common symptom with this type of injury according to Dr. Willard is a dull achy feeling in their shoulders, which is a common symptom with this type of injury according to Dr. Willard. As a side note - based on the sequential relationship between pain, compensatory movement patterns, and disuse with atrophy and fibrosis, it would follow that whiplash, in this example, could lead to frozen shoulder. No matter the origin, for back pain, neck pain, and many other conditions, exercise has been found time and again to be the best medicine (if you don’t use it, you lose it).

6. Biomechanics, biomaterials, & bioenergy optimization

Since 1990, several studies have described the presence of mechanoreceptors in spinal ligaments, suggesting an active role for fascial connective tissue beyond simple elastic stabilizers of the spinal column. Involved in this pioneering research was Dr. L’Hocine Yahia, professor of Biomaterials and Biomechanics at the Department of Surgery of Montreal University. He has also studied visco-elasticity properties and sensory innovation of the thoracolumbar fascia, which has been found to be integral in spinal movement. With regard to the neurology of biomechanics, we learn from Dr. Yahia that control of muscles is an emergent property of the neuron and that each movement (in human adults) is initiated by just one action of the nervous system.

Recently, Dr. Yahia has been involved in the development of a new predictive model for monitoring bone remodeling using a thermodynamic equation linking dynamic loading, metabolic biological, and chemical factors. This model can be used to predict long-term bone density distribution around implants, informing surgeons’ decision on if and when to proceed with hip replacement surgery. This biochemical modeling approach can also be used to analyze intervertebral disks. Related to tissue properties and biomechanics, we learned from Dr. Yahia that there is evidence that some fascia may have an ‘auxetic’ property, becoming thicker when stretched and typically having a honeycomb arrangement, although more research is needed. Some research has shown healthy tendons to exhibit a negative Poisson’s ratio (auxeticity) when stretched up to 2% along their length (within normal range), expanding radially when stretched axially. Negative Poisson’s ratio is also apparently observed in some materials near phase transitions. Synthetic auxetic material are also being used to support hip implants and as stents. Since the Poisson ratio is dependent on a material’s microstructure which may be lost if fascia is damaged or diseased, this property may provide a diagnostic tool to assess fascia health, according to Dr. Yahia.

The role of contractile elements of tendons in biomechanics was discussed by Dr. Adamantios Arampatzis, Professor of Movement Science at Humboldt-University in Berlin, Germany. We learned from Dr. Arampatzis that during state to state running, mechanical energy changes are low, minimizing metabolic cost
and saving mechanical energy; however, during jumping, muscles produce a huge amount of mechanical work at take-off to achieve the goal of maximum height. For the Achilles tendon, average elongation of 10–12mm was measured during running (4–6% strain). Active stretch-shortening cycle of vastus lateralis and vastus medialis muscles were assessed by Dr. Arampatzis and his team, with notable fascia length changes of up to 25% of optimal length during running and about 20% during walking. Focusing on the soleus and vastus lateralis, his research verified an important contribution of the series-elastic element of both muscles' fascicle dynamics, and found an average shortening of 27% of optimal length for soleus fascicles. Comparing biomechanics of a squat-jump (SJ) with counter-movement jump (CMJ) that includes a preparatory squat phase, CMJ was found to produce 5% greater height as compared to SJ and 56% greater power, due to greater force-length potential, greater power-velocity potential, and greater muscle activation. Clearly, by optimizing biomechanics, we can improve power and reduce strain, improving both performance and health.

7. Adaptive solutions for chronic strain

In order to prevent pathology instead of 'just' alleviating symptoms, we must identify cause, and for this an evolutionary perspective of anatomy and physiology is essential. To this end, Dr. Daniel Lieberman, a professor of human evolutionary biology at Harvard University, Cambridge, MA, shared an evolutionary perspective on human walking and running, shedding light on common strain patterns of the iliotibial band and plantar fascia.

Focusing first on iliotibial band (ITB) syndrome, Dr. Lieberman pointed out that the 'consensus' story on the ITB is that it is a thickening of the fascia lata, and that most people think of it as a lateral hip stabilizer. However, no one seems to have a clear idea about the cause. Potential causes for ITB syndrome include overuse, for example too much flexed posture or uphill running/hiking, as well as high arches or low arches, high Q angle, weak abductors, too much pronation, and too much supination. The ITB evolved independently in humans, but is not unique to humans. The ITB also exists in chimps, but plays a somewhat different role. In the frontal plane, ITB contribution to abductor force is no more than 5% in humans and 5% in chimps. In the sagittal plane, ITB acts as a spring during running, shedding light on common strain patterns of the iliotibial band and plantar fascia.

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8. In conclusion

Fascial connective tissue has clearly achieved a center stage of interest among a wide range of clinicians and researchers seeking to understand disease and optimize health. Once mechanisms for pathology and improved prognosis are identified, work can be done to leverage findings to improve health outcomes. Clearly, much progress has been made and is being made in this direction. In the meantime, there are many scientifically validated options immediately available to reduce pathology and pain and improve wellness, including manual therapy and exercise. In closing, an apt quote from Dr. Theise: “When any real progress is made, we unlearn and learn anew what we thought we knew before” – Henry David Thoreau.

9. Keeping connected

The Fascia Research Congress was founded in 2007 by Dr. Thomas Findley and Dr. Robert Schleip, with the goal of connecting clinicians and researchers to foster collaboration and knowledge sharing. Subsequently, the Fascia Research Society was launched in 2012 with help from both Tom Findley and Susan Shockett to facilitate ongoing collaboration. To learn more about fascia research and to stay connected, please consider joining the Fascia Research Society www.fasciaresearchsociety.org. Also, plan to join us for the next Fascia Research Congress in 2021 in Montreal, Canada. The presentations of the key speakers at FRC5 are available for purchase at http://fasciacongress.org/dvd-recordings-and-books/.

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References


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