Content of the project

Diabetes mellitus, with a steadily increasing prevalence of 8.5%, is a multi-system disorder characterized by persistent hyperglycaemia that has both acute and chronic biochemical and morphological consequences. The neuro-musculo-fascial organ system is affected in more than 80% of diabetic patients leading to reduced quality of life, non-pharmacological treatment failure, increased treatment cost and work disability with consequent income loss. Unfortunately, the understanding of pathological changes and processes leading to neuro-musculo-fascial disability remains significantly limited.

The skeletal muscle accounts for 40-50% of the body weight and mediates 75% of insulin-stimulated glucose uptake, and is therefore one of the main potential targets for the treatment of diabetes. The reports of capillarization and muscle fibre type changes in diabetes are not consistent, especially when studied in humans. Since certain non-pharmacologic and pharmacologic measures can protect muscles from capillary regression and fibre type shifting and thus ameliorate insulin resistance, understanding the influence of diabetes on morphological characteristics of skeletal muscles with different functions is of great importance.

The fascial system consists of the three-dimensional continuum of connective tissues that interpenetrates and surrounds organs, muscles, bones and nerves, endowing the body with a functional structure, and providing an environment that enables all body systems to operate in an integrated manner. Disorders of the connective tissues are common in diabetic patients. Since fasciae transmit and detect force generated by muscles in different directions, it is important to understand how fascial tissue responses to various directional mechanical loadings and how diabetes influence the ability of such response in order to improve physical therapy procedures to more specifically target pathological and functional changes of fascial tissue imposed by diabetes.

Diabetic neuropathy and entrapment neuropathies are among the most common complications associated with diabetes. Fascicular involvement pattern can aid in diagnostic workup for peripheral neuropathies. Thus, non-invasive visualization of the intrinsic structure of the nerves has become important for understanding, diagnosis, treatment as well as follow-up of the peripheral nervous system disorders. Thus, studies with focus on transitional knowledge from histology to application in the clinical practice are needed. Detailed studies with histological verification are needed to explore capabilities and capacity of accurate fascicular differentiation of available radiologic modalities (high resolution ultrasound, conventional magnetic resonance imaging) to image nerve fascicular anatomy in order to provide reference values for morphologic and morphometric parameters of internal nerve structure.

The proposed project aims to accomplish three broad objectives. First, it will determine detailed changes of myosin heavy chain isoform expression and capillary network around individual muscle fibres of vastus lateralis muscle, splenius muscle, diaphragm and external intercostal muscle of diabetic patients compared to age-matched non-diabetic controls using 3D analytic approach with confocal microscopy and semiautomated analysis of myosin heavy chain expression. Second, it will attempt to identify changes of biomechanical properties of functionally diverse fascia lata, plantar fascia, masseteric fascia and thoracolumbar fascia of diabetic patients compared to age-matched non-diabetic controls using correlative microscopy with biaxial relaxation tests and atomic force microscopy, which will be correlated with histological changes on micro and meso-anatomic level in 3D. Third, it will investigate the feasibility of high-resolution ultrasound and conventional magnetic resonance imaging in visualizing 3D fascicular anatomy of ulnar, radial and median nerves with histological cross sections, magnetic resonance microscopy and optical projection tomography verification, and examine the influence of diabetes on internal nerve organization.