DEVELOPMENT OF A FOOT MULTISCALE MODEL FOR DIABETIC FOOT PREVENTION

Zimi Sawacha, PhD[(1)], Annamaria Guiotto, MsEng[(1)], Daniela Boso, PhD[(2)], Giuseppe Sciumè, MSEng[(2)], Gabriella Guarneri, MD[(3)], Alessandra Scarton, MsEng[(1)], Angelo Avogaro, MD, PhD[(3)], Bernard Schrefler, PhD[(2)], Claudio Cobelli, PhD[(1)]

[(1)] *Department of Information Engineering, University of Padova, Padova, Italy. email: zimi.sawacha@dei.unipd.it*
[(2)] *Department of Civil, Environmental and Architectural Engineering, University of Padova, Italy*
[(3)] *Department of Clinical Medicine and Metabolic Disease, University Polyclinic, Padova, Italy*

SUMMARY
Diabetic foot is an invalidating complication of diabetes mellitus, a chronic disease widely diffused in the aging population. Diabetic neuropathy and vasculopathy alter foot biomechanics resulting in callosity and ulcerations. The social and economic weight of the diabetic foot can be reduced through a prompt diagnosis and treatment [1].
In order to understand the aetiology of diabetic foot and allow a prompt diagnosis several finite element (FE) models of the foot have been developed in the last decades, see e.g. [2-4]. The aim of this work is to create a patient specific multiscale 3-dimensional (3D) FE model of a diabetic neuropathic subject (NS) foot. This multiscale model includes a biomechanical foot model (BFM) together with a biological-tissue model (BTM). The BFM integrates in-vivo kinematic, kinetic, magnetic resonance (MRI) data as input variables. The BTM considers the ulcerated region (if present) and the surrounding healthy tissue and integrates the plantar pressure output of the BFM as input together with a proper constitutive law to account for vasculopathy. The multiscale, patient-specific model allows to study the phenomenon at two levels: macro and micro. The BTM is the micro scale and uses BFM outcomes (i.e. foot contact pressure, both normal and tangential components) together with a proper vasculopathy law as input, to predict ulcer initiation risk. The model validity is assessed by means of comparison between experimental and simulated peak pressure values.

INTRODUCTION
The diabetic foot is one of the major complication of diabetes mellitus. It is determined by the simultaneous presence of both peripheral neuropathy and vasculopathy that, by altering the biomechanics of the foot, lead to callosity and ulcers formation. The social and economic burden of the diabetic foot can be reduced through a prompt diagnosis and treatment [1]. FE analysis allows to characterise and quantify the loads developed in the different anatomical structures and to understand how these affect foot tissue in dynamic conditions [3]. In this study an experimentally kinematics-kinetics based FE subject-specific multiscale model of the foot of a diabetic neuropathic subject is developed. This multiscale model accounts for two different levels, one micro and one macro, namely: BFM and BTM. The patient-specific, multiscale computational model can help in predicting ulcer formation and evolution on the foot of diabetic subjects.

METHODS
Experimental procedure
The biomechanical analysis of the foot was carried out as in [5] on one diabetic neuropathic subject (NS) ((age, 72 years, BMI, 25.1 kg/m^2). The experimental setup included a 6 cameras stereophotogrammetric system (60-120 Hz BTS S.r.l, Padova), 2 force plates (FP4060-10, Bertec Corporation, USA), 2 plantar pressure systems (Imagortesi, Piacenza). The signals coming from all systems were synchronized in post processing as in [5]. The patient's hindfoot, midfoot, forefoot and tibia subsegments 3-dimensional (3D) kinematic was calculated together with each subsegment 3D ground reaction forces and plantar pressure. The neurological evaluation included the assessment of symptoms, and signs compatible with peripheral nerve dysfunction. The Michigan Neuropathy Screening Instrument questionnaire was used [6]. Electroneurophysiological study, ankle-to-brachial systolic pressure ratio (Index of Winsor), cardiovascular autonomic tests, ophthalmologic examination, a urinary albumin-to-creatinine ratio measured (0–30 mg/g normal, 30–300 mg/g microalbuminuria, >300 mg/g macroalbuminuria), a carotid artery Doppler ultrasound examination, and a 12-leads electrocardiogram were also performed. HbA1c values from the preceding 10 years were collected. The protocol was approved by the local ethic committee.

Finite element models and BTM definition
The MRI of the foot of a diabetic neuropathic subject was acquired with 1.5T devices (Philips Achieva and Siemens Avanto, Spacing between slides: 0.6-0.7mm, Slice thickness: 1.2-1.5mm). MRI images were then segmented with Simpleware ScanIP-ScanFE (v.5.0) ABAQUS (Simulia, v.6.12) was used either to generate the mesh and/or to run FE simulation. BFM was meshed with quadrilateral elements according to the literature [3].

A 3D horizontal plate was drawn in Abaqus to simulate the ground support and the foot-floor contact during stance. It was meshed with 8 mm side quadratic elements with the aim of obtaining contact pressures values comparable with the experimental ones (according to plantar pressure system sensors dimension). The plantar soft-tissue was represented as a continuum and its nonlinear material behaviour was modelled using an isotropic, incompressible, hyperelastic second-order polynomial formulation with parameters provided by [4]. Both the floor and the bones were modelled as homogeneous isotropic linear elastic materials [3]. The foot-floor interface was modelled using contact surfaces with a coefficient of friction of 0.6 [3]. The bones were tied to the soft tissues. During the simulation, the superior surfaces of the bones and soft-tissues were fully fixed to simulate the effects of constraints from superior-lying tissues [3]. Also the position of the foot with respect to the floor was considered matching the FE model angle between the floor and the mediolateral axis of the ankle (the axis passing through the prominences of malleoli) to the experimental one obtained from the kinematic data in the corresponding instant of the stance phase of gait. The loading conditions were set according to the ground reaction force registered with the force plate during gait. In order to cover the range of foot contact over the ground, four instants of the stance phase of gait when critical loads occurred [7] were chosen for the BFM FE simulations (heel strike (HS), loading response (LR), midstance (MS), push-off (PO)). Simulations of the phases were run using the foot subsegments vertical force and the whole foot vertical force. Abaqus CAE/pre-processor was adapted by altering its loading characteristics and its geometric positioning [4] for each of the investigated gait sub-phases. In BTM, a novel mathematical approach based on the Thermodynamically Constrained Averaging Theory (TCAT) is applied to define diabetic ulcer initiation [8]. It provides a rigorous yet flexible method for developing multiphase, continuum models at any scale of interest. In detail, the BTM consists of two phases: one solid for the tissue cells and their extracellular matrix (ECM) (i.e. ECM components and the tissue cells are treated as a single solid phase), and one fluid (the interstitial fluid). Transport of nutrients and possible drugs delivery within the microvasculature is also considered by means of the introduction of an effective diffusion coefficient which is estimated from the real degree of vascularization of the zone of interest. The cells maintain tissue integrity by cell to cell contact and thanks to the extracellular matrix which acts as a scaffold to give the tissue more structure and rigidity. The solid phase may become necrotic depending on the stress level (stresses from the BFM, see Figure 1) and on the nutrients availability.
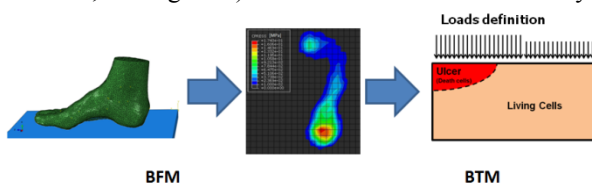

Figure 1: BFM to BTM workflows.

The solid and the liquid phases are closely connected in space and time, over multiple scales, thanks to the mentioned rigorous mathematical framework of the TCAT.

The validity of the model is assessed by comparing the experimental and the simulated peak plantar pressures data and by evaluating the Root Mean Square Error in percentage of the experimental peak value (RMSE%), in order to consider the spatial information.

RESULTS AND DISCUSSION

Results showed that when applying the foot subsegments ground reaction vertical component as input together with the subject specific kinematics there was a better agreement between the experimental and the simulated data than when applying the whole foot ground reaction vector (see Figure 2). The BFM predicted contact areas were 15.4 cm^2, 71.7 cm^2, 69.1
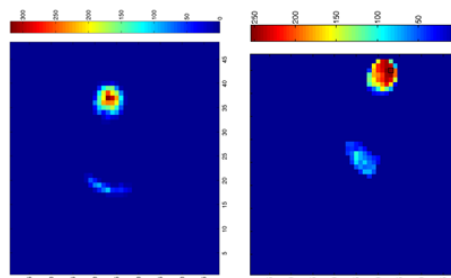

Figure 2. From left to right: simulated and experimental pressure distribution during the midstance phase of gait.

cm^2 and 51.8 cm^2 for the heel strike, loading response, midstance and push-off respectively, compared to 19.2 cm^2, 62.1 cm^2, 69.1 cm^2 and 49.3 cm^2 obtained from the experimental measurements. With the exception of the midstance, for the BFM the error in the contact surface prediction was below the 20% of the experimental value. Peak stress level were also calculated from the internal plantar soft-tissues and from the bones and expressed in terms of von Mises stress. In correspondence of the bone structure, peak of stress were present at the metatarsal and talus bones. The insertion points of the fascia (the 5 connector elements) at the phalanges connection region and plantar aspect of the calcaneus, experienced large stress due to the generated plantar fascia tension. The peak von Mises stresses occurring in the four instants of simulation of the BFM were respectively: 46KPa (heel), 326 KPa (heel), 150 KPa (heel), 447 KPa (the connection between the metatarsal heads and the phalanx).

CONCLUSIONS

In general, model predicted plantar pressures were in good agreement with those measured during the considered sub-phases of the stance phase of gait. The in-vivo gait analysis-based patient specific multi-scale model of the foot developed herein allows to characterise and quantify the loads developed in the different foot anatomical structures.

REFERENCES
1. Boulton AJM, et al. *Lancet* 366:1719–**24**, 2005.
2. Cavanagh et al, *J Foot Ankle Res.* **(Suppl 1)**: K4, 2008.
3. Chen WM et al., *Med Eng Phys*, **32(4):**324-31, 2010.
4. Cheung JT et al., *J Biomech*, **38(5)**: 1045-1054, 2005.
5. Sawacha Z, et al. *Gait & Posture.* **6(1)**:20-6. 2012.
6. Feldman EL, et al. *Diabetes Care.***17 (11)**, 1281–9.1994
7. Gefen A, et al. *J Biomech Eng.* **122(6)**:630-9, 2000.
8. Sciumè G, et al. *Cellular and Molecular Biomechanics.* **9(3)** 193-212. 2012.