The 2013 World Congress on
Advances in Nano, Biomechanics, Robotics, and Energy Research (ANBRE13)
Seoul, Korea, August 25-28, 2013

Keynote Paper

Engineering Approaches to Age-related Diseases

*Taeyong Lee[1)], D Anitha[2)], Jee Chin Teoh[3)]

[1), 2), 3)] Department of Bioengineering, National University of Singapore,
9 Engineering Drive 1, Singapore 117576
[1)] bielt@nus.edu.sg

ABSTRACT

Age-related bone remodeling cause fragility of the femoral neck, thereby increasing fracture risk in elderly populations. We observed that the femoral necks of simulated young subjects manifested a marked predisposition to undergo yielding, whereas the femoral neck models of elderly subjects were generally more prone to buckling prior to yielding. Another diseases, diabetes mellitus is a ‘21st century epidemic’ affecting 8.3% of the world’s adult population especially the elderly. The degenerative change of glycation occurs at cellular level due to DM is reported to have stiffened the plantar soft tissue and lead to higher ulceration risk. Assessment was performed to investigate the effect of DM on plantar tissue stiffness.

1. INTRODUCTION

Age-related bone remodeling cause fragility of the femoral neck, thereby increasing fracture risk in elderly populations. We investigated the effects of age-remodeling and stress-reduction on the femoral neck using the Finite Strip Method (FSM). We verified the possibility that the femoral neck is likely to undergo fracture through two mechanisms: yielding and local buckling. Also, diabetes mellitus (DM) are prone to develop ulcers and gangrene of the feet. There are several existing tools used by clinicians to assess plantar foot health. Most methods, including monofilament testing and vibration perception threshold measurements (using tuning forks, biothesiometers or neurothesiometers), test only evaluates mechano-sensitivity of tissue but does not objectively quantify the tissue behavior. There has been data from a large diabetic cohort suggesting glycated collagen measured via skin biopsies to be a highly consistent parameter associated with diabetes complications, even comparable to HbA1c levels (Monnier et al., 1999). Accumulation of glycation end products accelerates age-related changes in the skin and connective tissue decreasing elasticity (Sell et al., 2005) and in turn making the tissues stiffer. There is clinical data suggesting diabetic plantar tissues to be significantly stiffer than aged-matched controls (Sun et al., 2011; Zheng, Choi, Wong, Chan, & Mak, 2000).

[1)] Professor
[2)], [3)] Graduate Student

2. FINITE ELEMENT MODELS

We observed that the femoral necks of simulated young subjects manifested a marked predisposition to undergo yielding, whereas the femoral neck models of elderly subjects were generally more prone to buckling prior to yielding (Fig. 1). The simulations showed that expansion could counter cortical thinning to ensure that the yield strength remained constant throughout the adult life but at the expense of reducing the pure buckling load.

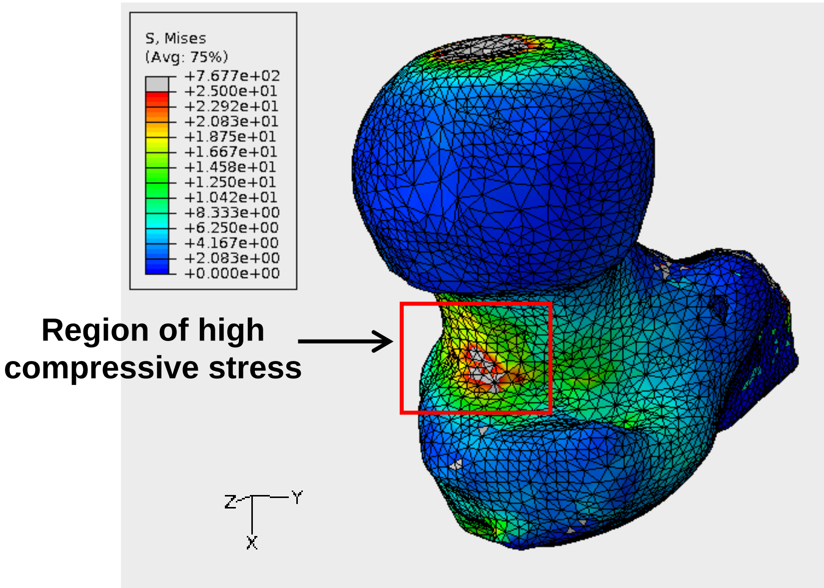

Figure 1. Local buckling of the elderly femoral neck by using Finite Element Method

Previous observational evidence from studies which relied on crude annulus model derived from DXA data showed that those with femur fractures have higher buckling ratios. Clearly the femoral neck cortex is not a smooth, uniform annulus. In the current study we evaluated realistic femoral models derived from CT scans of subjects. The instability of only the femoral neck was studied in this work as some earlier studies showed that it was the weakest region in an intact femur. Also, very little change in BMD over the follow-up study was observed, showing that BMD alone is not a good indicator of bone quality. This meant that both BMD and BR influenced bone strength significantly.

Of the risedronate-treated subjects (n=10), all finite element models showed a region of high compressive stress at the superior cortex and a region of high tension at the inferior cortex. This is evident onto how useful these models could be in the clinical scenario. Also, buckling ratio was computed from the CT-scans to complement the finite element models and high buckling ratios (greater instability) were found at regions coinciding with high compression and tension, as mentioned above.

3. PLANTAR TISSUE ASSESSMENT

Identification of the localized mechanical response of the plantar soft tissue to external loading is the key to understanding diabetic foot abnormality and predicting whether ulceration will take place. The tissue mechanical response depends on various parameters, such as the external load (direction and rate), the tissue properties (anisotropy and viscoelasticity), and the configuration of the metatarsophalangeal (MTP) joint overlying the tissue.

In this study, an instrument-driven tissue tester, which incorporates a portable motorized indenter within a special foot positioning apparatus, was developed for realistic in vivo mechanical characterization (i.e. tissue stiffness and force relaxation behaviour) of the local plantar soft tissue pad with the MTP joint configured at various dorsiflexion angles associated with gait (Figure 2).

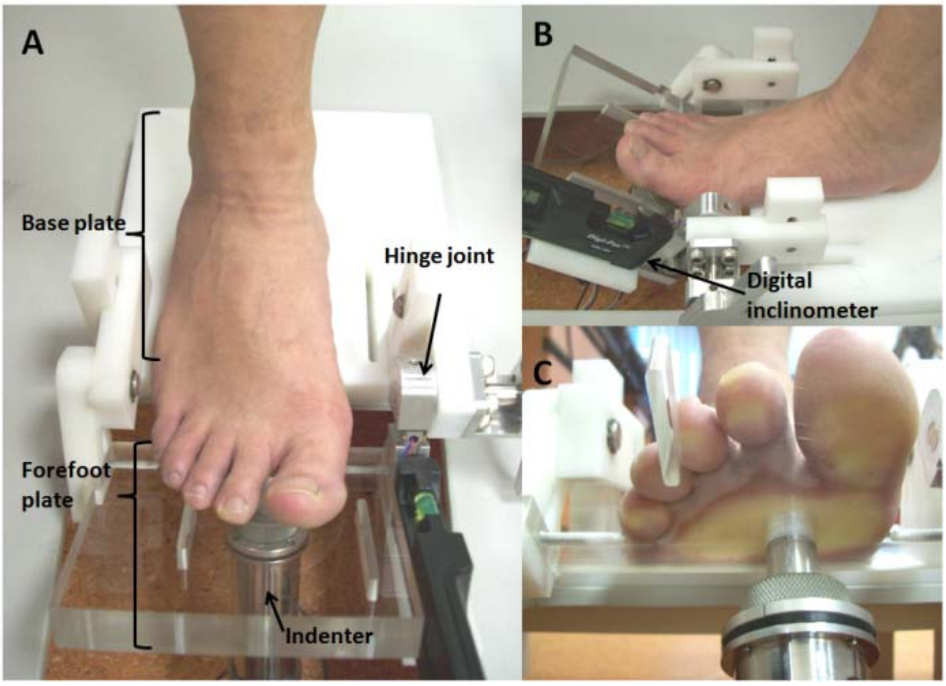

Figure 2. (A) Top view (B) side view (C) bottom view of experimental set up. The integrated indenter on the forefoot plate indents the plantar site and measures directly the force applied to the deformed tissue via a load cell mounted at the other end of the probe tip.

Pilot study has been conducted to compare the plantar soft tissue stiffness of diabetes patients (n=5) and age matched healthy participants (n=35). The tissue stiffness of diabetic subject is found to be stiffer (Figure 3). Nonetheless, to make statistically significant remark, more diabetes participants that fulfill the inclusion and exclusion criteria have to be recruited.

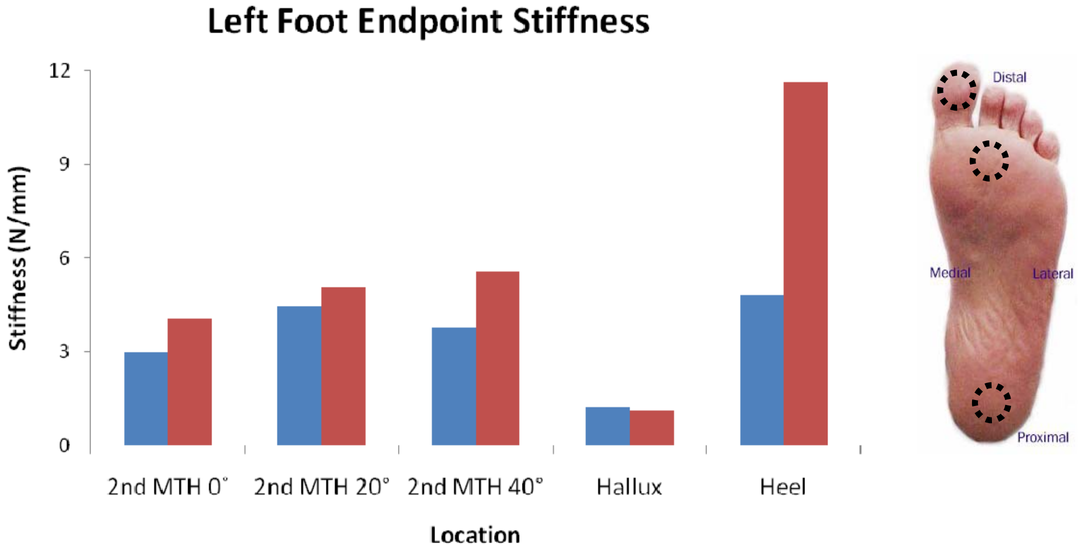

Figure 3. Computed effective Young's modulus (E) for plantar soft tissue of normal and DM subjects. MTH: metatarsal head

4. CONCLUSIONS

The trabecular degradation and cortical thinning involved in aging render the femoral neck more susceptible to failure by buckling. Knowledge gained from the foot model and plantar tissue assessment studies will eventually help to bridge the gap between increased risks of tissue damage and altered biomechanical properties in diabetic foot of DM population.

REFERENCES

Lee, T., Choi, J.B., Schafer, B.W., Loveridge, N., Reeve, J., and Beck, T.J. (2009), "Assessing the susceptibility to local buckling at the femoral neck cortex to age-related bone loss", *Ann. Biomed. Eng., ASCE,* **37**(9), 1910-1920.

Carpenter, R.D., Sigurdsson, S., Zhao, S., Lu, Y., Eiriksdottir, G., Sigurdsson, G., Jonsson, B.Y., Prevrhal, S., Harris, T.B., Siggeirsdottir, K., Guethnason, V. and Lang, T.F. (2011), "Effects of age and sex on the strength and cortical thickness of the femoral neck", *Bone*, **48**, 741-747.

Keyak, J.H. (2001), "Improved prediction of proximal femoral fracture load using nonlinear finite element models", *Med. Eng. Phys.,* **23**, 165-173.

Monnier, V. M., Bautista, O., Kenny, D., Sell, D.R., Fogarty, J., Dahms, W. and Genuth, S. (1999), "Skin collagen glycation, glycoxidation, and crosslinking are lower in subjects with long-term intensive versus conventional therapy of type 1 diabetes: Relevance of glycated collagen products versus HbA(1c) as markers of diabetic complications", *Diabetes, **48***(4), 870-880.

Sell, D. R., Biemel, K.M., Reihl, O., Lederer, M.O., Strauch, C.M., and Monnier, V.M. (2005), "Glucosepane is a major protein cross-link of the senescent human extracellular matrix: Relationship with diabetes", *J. Bio. Chem., **280***(13), 12310-12315.

Sun, J. H., Cheng, B. K., Zheng, Y. P., Huang, Y. P., Leung, J. Y., and Cheing, G. L. (2011), "Changes in the thickness and stiffness of plantar soft tissues in people with diabetic peripheral neuropathy", *Arch. Phys. Med. Rehab., **92***(9), 1484-1489.

Zheng, Y.P., Choi, Y.K.C., Wong, K., Chan, S. and Mak, A.F.T. (2000), "Biomechanical assessment of plantar foot tissue in diabetic patients using an ultrasound indentation system", *Ultrasound Med. Biol*., **26**(3), 451-456.