Süleyman Demirel Üniversitesi
Fen Bilimleri Enstitüsü Dergisi

Suleyman Demirel University
Journal of Natural and Applied Science

18(SI: Biomechanics), 10-20, 2014

Indentation and Observation of Anisotropic Soft Tissues Using an Indenter Device

Parinaz ASHRAFI *1,2, **Ergin TÖNÜK** 1,2,3
[1] Department of Biomedical Engineering, Middle East Technical University, 06800 Ankara, Turkey
[2] BIOMATEN, CoE in Biomaterials and Tissue Engineering, METU, 06800 Ankara, Turkey
[3] Department of Mechanical Engineering, Middle East Technical University, 06800 Ankara, Turkey

(Received: 12 September 2014, Accepted: 27 November 2014)

Keywords
Indentation
Soft Tissue Modeling
Anisotropic Tissue

Abstract: Soft tissues of human body have complex structures and different mechanical behaviors than those of traditional engineering materials. There is a great urge to understand tissue behavior of human body. Experimental data is needed for improvement of soft tissue modeling and advancement in implants and prosthesis, as well as diagnosis of diseases. Mechanical behavior and responses change when tissue loses its liveliness and viability. One of the techniques for soft tissue testing is indentation, which is applied on live tissue in its physiological environment. Indentation affords several advantages over other types of tests such as uniaxial tension, biaxial tension, and simple shear and suction, thus it is of interest to develop new indentation techniques from which more valid data can be extracted. In this study a new indenter device was designed and constructed. Displacement and force rate cyclic loading, and relaxation experiments were conducted on human arm. The in-vivo force rate controlled cyclic loading test method which is novel is compared with the traditional displacement controlled cyclic loading tests. Anisotropic behavior of tissue cannot be determined by axi-symmetric tips, therefore ellipsoid tips were used for examining anisotropy and in-plane material direction of bulk soft tissues.

Eşyönsüz Yumuşak Dokuların İndentör Cihazı Kullanılarak İndentasyonu ve Gözlemi

Anahtar Kelimeler
İndentasyon
Yumuşak Doku Malzeme
Eşyönsüz Doku

Özet: İnsan bedeninde iskelet dışındaki neredeyse tüm dokular yumuşak dokulardır. Yumuşak dokuların mekanik davranışı çoğu mühendislik malzemesinden farklı ve daha karmaşıktır. Yumuşak doku mekanik özelliklerinin belirlenmesi ve malzeme modeli oluşturulması implantlar, protez ve ortezler ve hatta tanı koyma açısından önemlidir. Öte yandan yumuşak dokuların canlılığını kaybetmesi ile mekanik özelliklerinde farkedilir değişiklikler meydana gelir. Yumuşak doku mekanik özelliklerini belirlemek için kullanılan deneysel yöntemlerden birisi de indentasyondur. İndentasyonun tek veya iki eksenli çekme, kayma, emme gibi yöntemlere göre belirli avantajları olduğu bilindiğinden daha iyi veri almak üzere yeni indentasyon deneyleri geliştirlmesine gerek duyulmuştur. Bu çalışma kapsamında yeni bir indentör cihazı tasarlanıp üretilmiş, devirli yükleme, gevşeme ve sünme deneyleri yapılarak deneysel veriler incelenmiştir. İndentör cihazının göncellenen yapısı nedeniyle toplanan veri daha temizdir. Mullin (alışma) etkisi, viskoelastisite, eşyönsüzlük gibi özellikler gözlenebilmektedir. Sünme ve kuvvet denetimli yükleme deneyleri bu sistem aracılığıyla yapılabilmektedir. Dokuların eşyönsüz özelikleri olduğu bilindiğinden eksenel simetrik olmayan uçlarla düzlemsel eşyönsüzlük hakkında bilgi edinilmektedir. Ayrıca kuvvet denetimli deneyler ile yer değiştirme denetimli deney sonuçları incelenmiştir.

---

* Corresponding author: Parinaz.Ashrafi@metu.edu.tr

1. Introduction

Soft biological tissues have complex structures with complicated physiology .They display very different mechanical behavior in comparison to the traditional engineering materials. For improvement of soft tissue constitutive modeling and improvement in implants and prosthesis designing, as well as diagnosis of diseases, it is needed to perceive the mechanical behavior of soft tissues. For this there is a need for reliable constitutive equations that formulate and model the material behavior. Mechanical modeling relies on parameters that must be determined from experiments with determined boundary conditions, so to allow the inverse problem to be solved. Due to this aim it is needed to carry out tests and collect experimental information about the mechanics of the material. Recorded time-force-displacement data and determined geometry and boundary conditions were the input data used to evaluate the mechanical properties and to determine the constitutive model.

Many models exist in literature but because of the peculiar behavior of the live soft biological tissues, a completely acceptable model has not been proposed yet. Most of the existing models hardly simulate all experimentally observed behavior and some models are deficient in modeling even basic features (Zheng et al., 1999), and that is due to lack of the reliable experimental results. It is possible to conduct mechanical experiments on soft biological tissues by different methods. Most of the experimental data reported in the literature so far have been obtained ex vivo (Ahn & Kim, 2010; Carson et al., 2011; Fu & Chui, 2014; Seifzadeh et al., 2012; Zhang et al., 2014). Ex vivo measurements are obviously easier to perform and conditions can be made more repetitive these data are less accurate for realistic mechanical modeling since the properties of a living organ can change after removal from its natural environment with e.g. an intact blood perfusion and adequate water content of the tissue (Nava et al., 2008). In this study, in-vivo tests were conducted. In the in-vivo tests organ is studied at its original place and while it is alive. These two basic factors make in-vivo method as an ideal approach because firstly mechanical behavior and responses change when tissue loses its liveliness and viability. Secondly surrounding of the tissue, has great influence on the mechanical behavior of the tissue, thus the response of tissue in its original place is different than of it in separate place. Fung(1984) explains this fact during tests on blood vessels. In the studies carried out on pig brain (Gefen & Margulies, 2004) and on pig liver (Ottensmeyer et al., 2004) different in-vivo and ex-vivo test methods were conducted and compared. In Geffen and Margulies the nearest result to in-vivo test obtained in the ex-vivo perfused test and for stable cases, it showed a deviation of 17%. This deviation was above 50% forunperfused ex-vivo test.For these reasons, research in this area has been recently focused on examination of mechanical behavior of soft tissues in a living state and within the body(in vivo)(Carter et al., 2001; Kauer 2001; Ottensmeyer, 2001; Samur et al., 2007).

Nevertheless there are some identified disadvantages of in-vivo indentation that should also be considered; For avoidingany detriment and harm, tests are carried out only on external organs of subjects, such as skin, though studies on the internal organs by employing non-invasive methods are alsopossible, yet the nonlinear properties of tissue would not be properly characterized and only a linear stress-strain relation would be observed. (Ottensmeyer 2002). Another difficulty is that due to not having a regular geometry of cross-section of tissue sample, boundary conditions, and loading direction, instead of simple calculation oneneeds advanced techniques like inverse finite element method for obtaining stress-strain relations (Hu et al., 2011; M Kauer, 2002; Kim, 2004; Samani & Plewes, 2004; Tönük & Silver-Thorn, 2004)

It is possible to carry out experimentsonsoft biological tissues by using different devices. Nava et al. (2008) used an aspiration device to conduct in-vivo suction tests on human liverduring open surgery. Compressive force exerted by the surgeon during the measurements in order to ensure a good initial contact between aspiration device and liver surface caused uncertainties.Indentation tests are frequently used in the investigation of the mechanical properties of soft biological tissues (Choi & Zheng, 2005; Korhonen, 2003; Yin et al., 2004). Pailler-Mattei et al. (2008) used an original light load indentation device to study in vivo the mechanical properties of human skin. Cox et al. (2008) used indentation tests with varying indenter sizes on linear elastic rubbers and compared to tensile tests on the same specimen for modeling of synthetic heart valve. Eight carotid atherothrombotic plaque samples harvested from patients were studied by indentation tests by Barrett et al. (2009). In Ahn & Kim, (2010), soft tissue indentation loading experiments on porcine livers were performed to measure the surface deformation and force response of tissue with various indentation depths and two different tip shapes. Fath El Bab et al. (2010) proposed a sensor with two probes configuration to address dependency on the pushing distance. Carson et al. (2011) used spherical indentation tests for ex vivo material characterization of prostate tissue. In Chao et al. (2010) a tomography-based air-jet indentation system was used for examination of forefoot plantar soft tissue and compared with resulting obtained from tissue ultrasound palpation system. W.-M. Chen et al (2011) developed an instrument-driven tissue tester that includes a portable motorized indenter within a special foot positioning apparatus for in vivo tests. Van Dommelen et al. (2010) conducted indentation experiments for comparing white matter and grey matter brain tissue.Iivarinen et al. (2011) compared the indentation stiffness ofin relaxed, physically stressed and oedemic human forearm by using a hand held stiffness meter. An optoelectromechanical tissue indenter was used by Luo et al. (2011) during experiments on human heel. Prevost et al. (2011) compared the results of in-vitro, in-vivo and in in-situ indenter tests on porcine brain tissue. Fu & Chui, (2014) combined compression and elongation data obtained from in vitro tests on porcine liver tissue for indentation simulations.

Indentation can be used in all test methods such as, in-vivo, ex-vivo, thus comparative studies are feasible. Zhang et al. (2014) conducted in vitro swine brain indentation tests. Yao et al. (2014) developed a spherical indentation technique to measure the time-dependent material properties of human cervical tissue taken from patients undergoing hysterectomy.

Indentation is the most suitable technique for in-vivo test method. During indentation tests viscoelasticity, relaxation, creep and in-plane anisotropy can be observed therefore important mechanical properties of tissue can be examined. Indentation affords several advantages over other types of in vivo tests such as uniaxial tension, biaxial tension, simple shear and suction, thus it is of interest to develop new indentation techniques from which more valid data can be extracted (Bischoff, 2004). During these tests the tip of indenter device moves forward toward the tissue and simultaneously records time, tissue reaction force and tip displacement.

In this study an indenter device was designed and constructed. Common soft tissue behaviors such as preconditioning effect and anisotropy were observed. The in-vivo force rate controlled cyclic loading test method which is novel is compared with the traditional displacement controlled cyclic loading tests.

Most biological tissues are characterized by anisotropy (Kroon & Holzapfel, 2008; Pandolfi & Vasta, 2012; Peña et al. 2008). Since soft tissues are composed of different materials, like elastin and collagen, in different combinations, soft tissue properties are direction dependent (Samur et al, 2007). The anisotropic characteristics of soft tissues arise due to the preferred orientation and distribution of the collagen fibers (Lokshin & Lanir, 2009). For example, transverse anisotropy is observed in nanofibrillar collagen scaffold that mimic the structure of collagen organization in blood vessels (Huang et al., 2013; Argatov et al., 2015). This important characteristic cannot be observed by using circular indenter tips, the use of axially symmetric tips for estimating material properties ignores pronounced anisotropy. Feng et al. (2013) proposed combination of dynamic shear tests with subsequent asymmetric indentation tests on the same sample, to measure the anisotropy of brain tissue. Bischoff (2004) in a computational study used ellipsoidal tips, and displayed anisotropy in his results. Petekkaya (2008) used these ellipsoidal tips in his experimental study.

2. Materials and Methods

2.1. Subjects and Equipment

A group of eight young subjects all having a normal healthy condition (age 25-29) voluntarily contributed to the study. The experiments were performed under the approval of the Ethics Committee of Middle East Technical University (Ankara- Turkey).

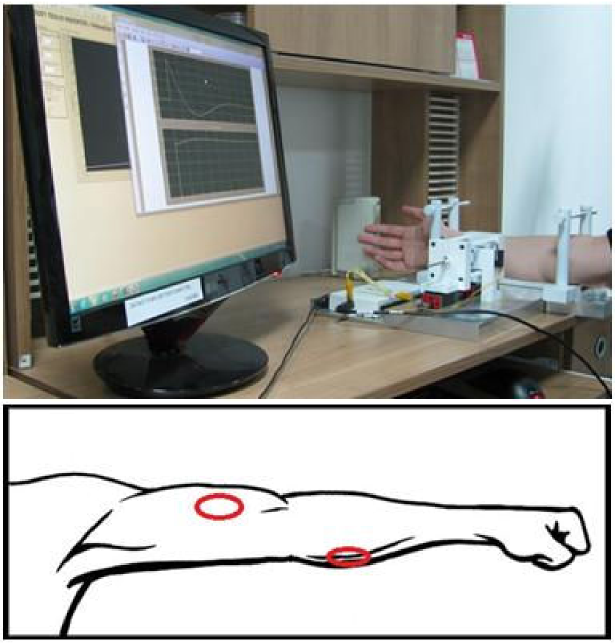


Figure 1. Indenter device set up and indentation regions on arm.

Experimental data was acquired using a soft tissue indenter designed and manufactured in METU. It is designed to make in vivo (on live body) measurements on human arm. After fixing the arm device indents a predetermined point on it with forward and backward movements. The arm is at rest and lay on a mechanical support during each experiment. Indenter set up and indentation regions on arm are presented in Figure (1). The indentation force, displacement, and time are measured and controlled via a load cell, step motor and data acquisition system. For this Haydon switch hybrid stepper motor (28000 series size 11), Honeywell ELPF-T1-M-50N load-cell and AD620 amplifier was selected. For real time data collection a computer code with a graphical user interface was developed in LabVIEW programming software (version 11.0) and NI-6212 (16-bit resolution) data acquisition card with chosen input sampling rate between 50 to 100 samples per second (S/s) was used. Resolution requirements for force and displacement were 5mN and 2µm. Ellipsoidal tip made of a polymer (polyamide) wasused for indenting tissue during experiments. The top and front view of the contact surface of tip is illustrated in Figure (2). The dimensions are: Rx=6mm, Ry=1.5 mm, Rz=1.5 mm

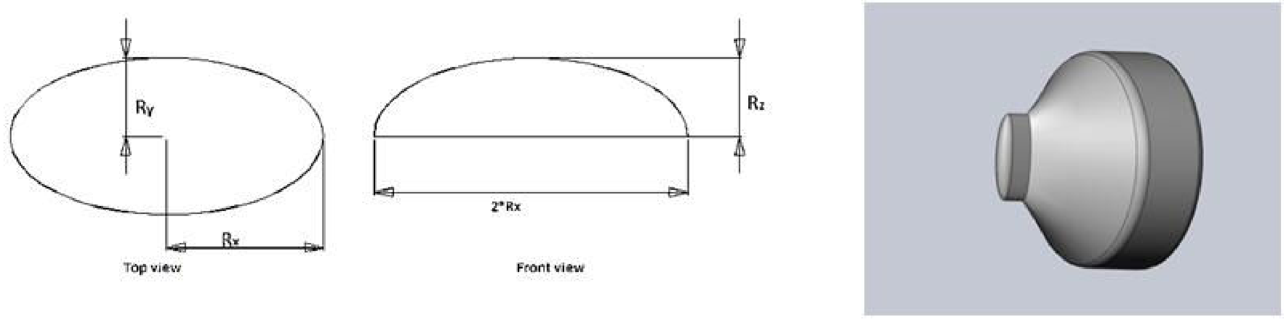


Figure 2. Indenter tip used in anisotropy tests; R_x=6mm, R_y=1.5 mm, R_z=1.5 mm

2.2. Experiment Procedure

2.2.1. Displacement rate controlled cyclic loading experiments

In this test, various scrutiny were made using two groups of data that are force-time and force-displacement. Soft biological tissues display preconditioning effect (Mullin's effect) under cyclic loading. During first load cycles tissue is more stiff and resistant to force, by repeating the cycles the reaction of tissue changes and shows repeatable and comparatively compliant response.

In “displacement rate controlled mode”, the amount of displacement is kept constant and force vs. time and force vs. displacement characteristics of the soft tissue are examined. Motor speed [mm/s], the displacement [mm] and number of cycles have to be taken as inputs by the help of the graphical user interface in LabVIEW. 5mm/s motor speed,15 mm displacement and 15 loops were chosen as inputs for the tests.

2.2.2. Force rate controlled cyclic loading experiments

In “force rate controlled mode”, the amount of force rate is kept constant [N/s], and displacement-time and force-displacement characteristics of the soft tissue areexamined. For example if input is 1 N/s and the cycle duration time is 10s, in 5s the indenting force linearly increases to 5N (the peak force of cycle) and then it linearly decreases back to zero force. The test is repeated until the desired number of cycles is reached. Therefore, in order to perform this test, parameters such as force rate [N/s], the time duration for every cycle, and number of cycles have to be taken as inputs by the help of the graphical user interface. In addition to these inputs the value of threshold to define tolerance domain of target force is also defined as user’s input parameter. The values used for the experiments were, force rate1.8N/s, duration was 6s for every cycle,15 loops, and a force tolerance of 0.01 N were chosen as inputs for the tests.

2.2.3. Relaxation experiments

In this test, after initial indentation the amount of displacement (penetration into tissue) was kept constant and the response of tissue was observed. After going forward and reaching the required input displacement into the soft tissue, the stepper motor and indenter tip was dwelled until input relaxation timeis reached and then at the end of this time indenter device is retracted. The input parameters to this test are the amount of displacement [mm], the speed of the motor [mm/s] and relaxation time [s]. Here the tests were conducted on forearm with 5 mm/s motor speed,6 mm displacement and 60 seconds relaxation duration. Due to sensitivity, relaxation experiments should be conducted in a noiseless environment. They are extremely influenced by muscle movements during relaxation time.

2.2.4. Determination of material directions and in-plane anisotropy

In literature, flat-ended cylindrical (Choi et al., 2008), spherical (Dimitriadis 2002), conical (Pelletier et al., 2006), pyramidal (Borodich et al., 2003) and cylindrical lateral (Argatov et al., 2015) that uses the lateral contact of a cylindrical indenter are widely used. The response of tissue to loads are different depend on the direction, this behavior cannot be determined by axi-symmetric tips, therefore ellipsoid tips which are theoretically examined by Bischoff (2004), and first experimentally used byPetekkaya et al. (2010) were used.

The long axis of the ellipsoidal indenter tips was placed parallel to the longer axis of the biceps muscle and cyclic loading tests were conducted in every 30 degree up to 180 and a 210 degree for control. In these tests, for eliminating the preconditioning effect at first, 20 loops of cyclic loading were conducted at apre-determined point of muscle then the real tests were conducted consequently without waiting for the soft tissue to recover. Response of biceps muscle in different indenter tip alignments, to the same displacement controlled cyclic loading test were examined. The tests were carried out at same point with 5mm/s, 12 mm (test2) and 15mm (test1) tissue displacement with an ellipsoidal indenter tip. Displacement values of biceps muscle in every 30 degree indenter tip alignments, to the same force controlled cyclic loading test were examined. The tests were carried out at same point with 1N/s force rate,5 loops and 100s total experiment time.

3. Results

3.1. Displacement Rate Controlled Cyclic Loading Test Results

Mullin's effect in force-time graph shows up as a decrease in force; the force value drops progressively as time goes by and tends to an equilibrium value as time goes to infinity (Figure 3). Because of breathing and sensitivity of loadcell, in last cycles the exact equilibrium constant force was impossible to catch.

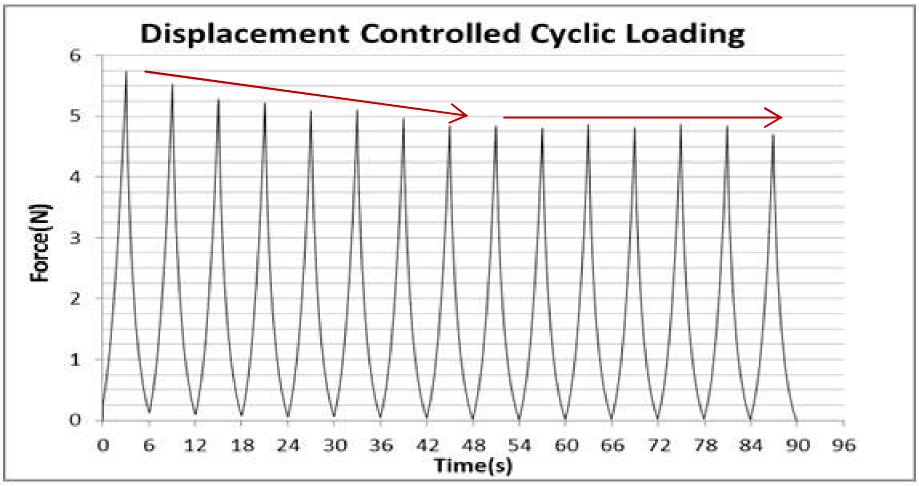


Figure 3. Displacement controlled cyclic loading test with 5 mm/s velocity,15 mm displacement and15 loops

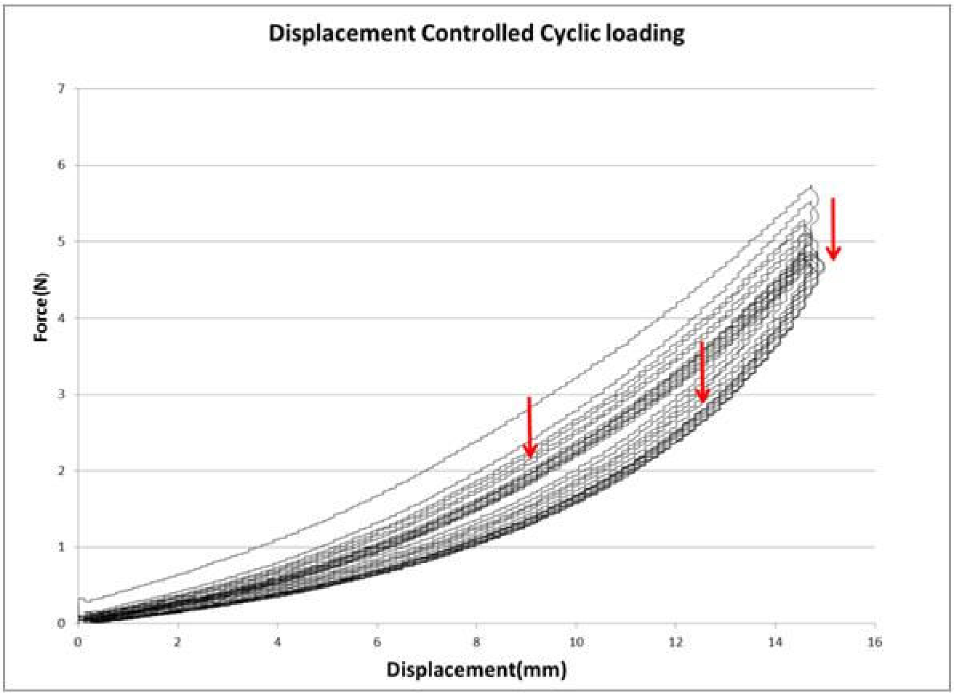


Figure 4. The observed downward shift in Hysteresis of cyclic loading test

3.2. Force Controlled Cyclic Loading Test Results

Mullin's effect on soft tissue during force controlled cyclic loading test was examined. The illustrated preconditioning effect observed in displacement-time and force-displacement graph is different than of it in displacement rate controlled cyclic loading tests. In displacement-time graph, as expected there was an increase in the displacement with progressing cycles that means a decrease in stiffness of tissue. Here we were trying to keep the force rate constant. In every cycle indenter sets out the movements in order to catch the target force pertinent to that current time, thus the peak forces were the same. Due to breathing, difficulties of in vivo tests, and good sensitivity of loadcell, we normally cannot see the exact equilibrium force (Figure 5).

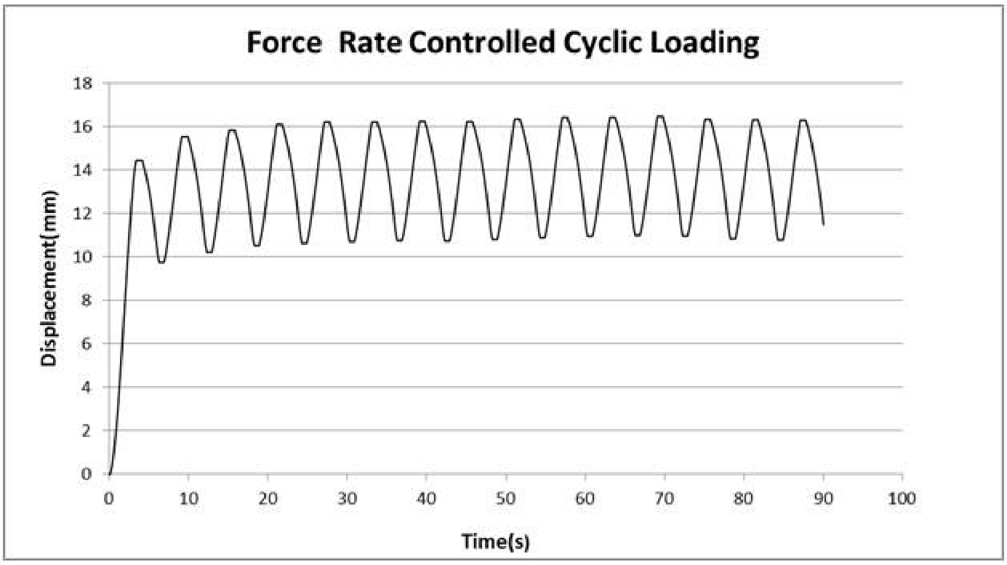


Figure 5. Force rate controlled cyclic loading test with 1.8N/s, 6s for every cycle and15 loop

In force-displacement graph of this experiment preconditioning was illustrated distinctly. There was a shift to right in curves by repeating cycles and during the last cycles almost repeating curves occurred. In addition to increase in the maximum displacements of the tissue (stretch), a decrease was observed in magnitude of hysteresis by increasing number of cycles and an approach to a repeatable pattern (Figure 6).

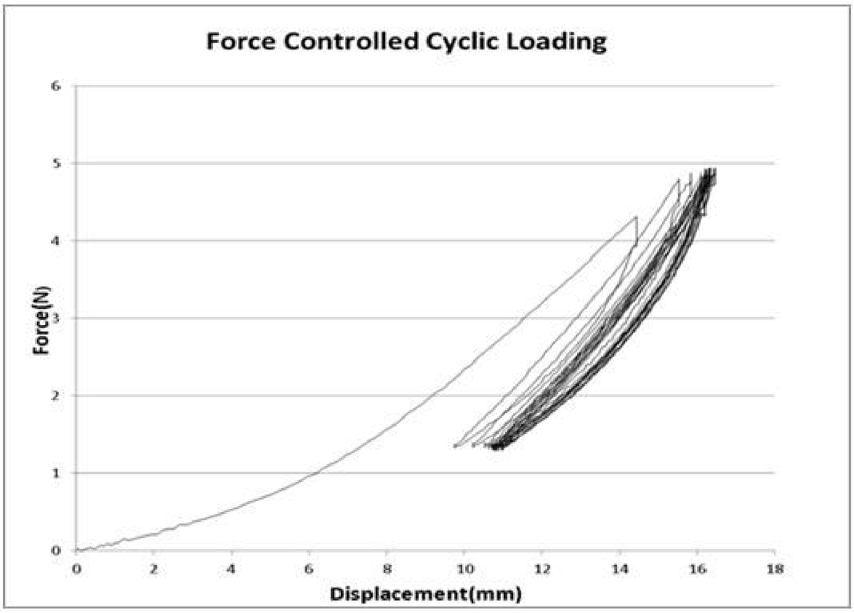
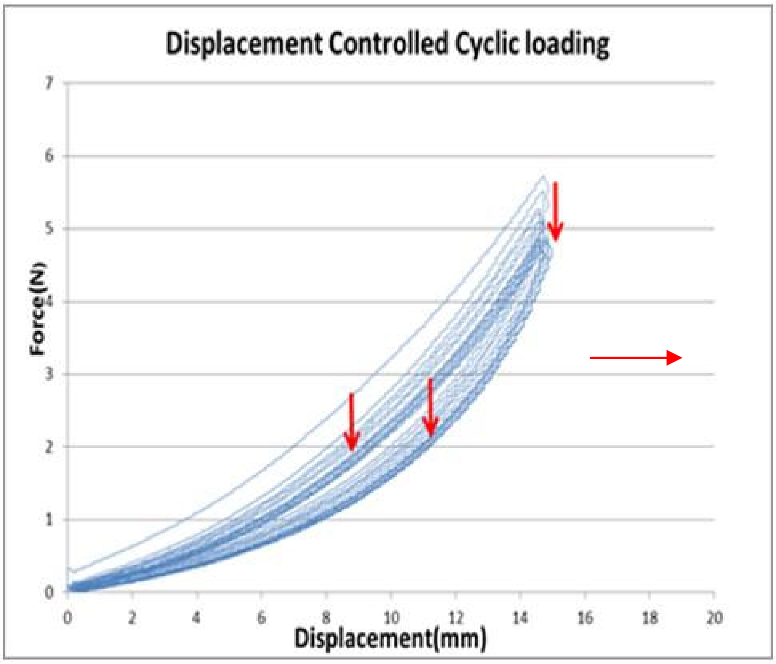


Figure 6. Obvious shift to right in maximum displacements by repeating cycles

In Figure (7), force-displacement relation under displacement rate control and load rate control for fifteen cycles is illustrated. The period of both experiment was 90 s but in different subjects. Mullin's effect shows up as a downward shift (i.e. decrease in force) in displacement rate controlled experiments whereas it shows up as a right shift (i.e. decrease in stiffness) in force rate controlled.



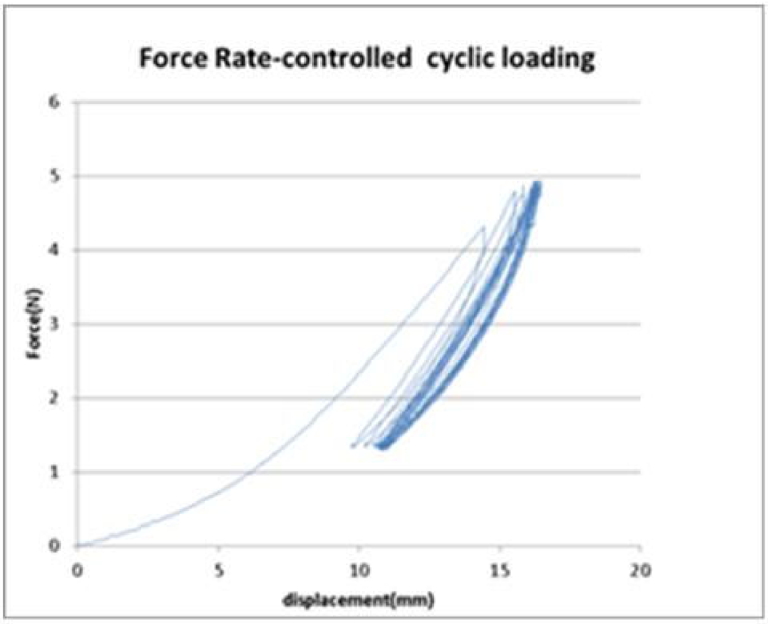


Figure 7. Force versus Displacement curves for indentation tests under displacement and load control for fifteen cycles. The period of both experiment was 90 s but in different subjects. Note the obvious shift to the right of the curves in the load controlled test.

3.3. Relaxation Experiment Results

In relaxation tests some periodic fluctuations were observed despite to the very small pulses related to heartbeats. After examinations and some experiments on dummy objects instead of individuals, as it was anticipated from previous studies (Tonuk.2004 and Petekkaya.2008) the source of these fluctuation was because of breathing. The number of periodic fluctuations and breathing times were in harmony. In relaxation tests, during constant imposed deformation, the resulting force drops progressively as time goes by and tends to an equilibrium value as time goes to infinity (Figure 8).

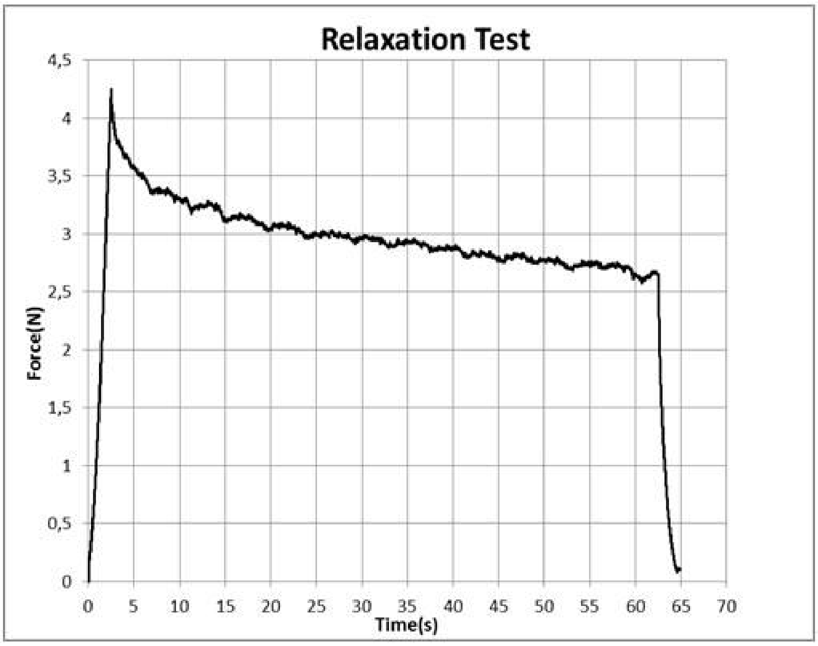


Figure 8. Relaxation test conducted on forearm with 5 mm/s motor speed, 6 mm displacement and 60 seconds relaxation duration

3.4. Determination of Material Directions and In-Plane Anisotropy

In results obtained from displacement controlled cyclic loading tests, by changing the alignment of indenter tip, the mean maximum force of the tissue was increased from 0° to 90°. This means that the stiff direction of the muscle is at 90 degree and perpendicular to the contraction direction of muscle fibers and the compliant direction is in 0° (Figure 9). In 0° the long axis of elliptic tip was positioned parallel to the long axis of biceps muscle therefore parallel to the alignment direction of muscle fibers. In 90° the long axis of elliptic tip is perpendicular to long axis of the biceps muscle. As a result the alignment direction of the muscle fibers and sarcomeres is a factor that determines the stiff and compliant direction of muscle; the direction parallel to fibers is most compliant direction, and the direction perpendicular to fibers is the stiffest.

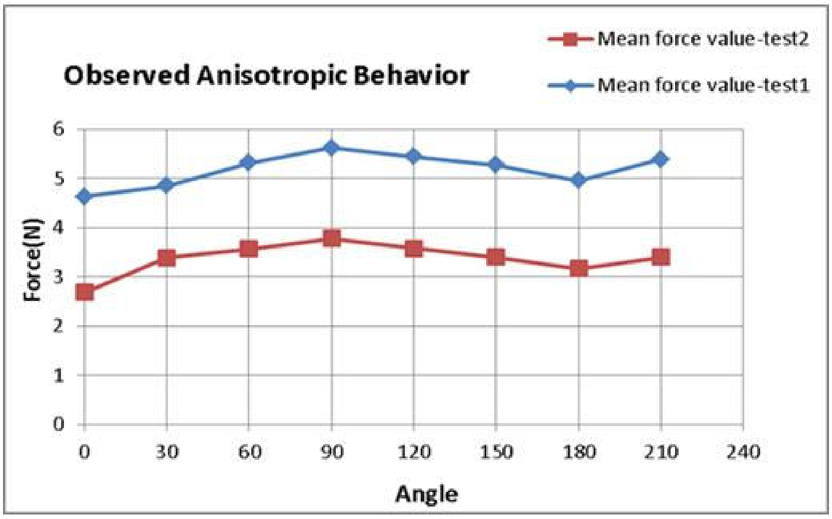


Figure 9. Response of biceps muscle in different indenter tip alignments, to the same displacement controlled cyclic loading test. The experiments were carried out at same point with 5mm/s, 12mm (test2) and 15mm (test1) tissue displacement.

In force rate controlled tests the displacement of indenter into the tissue was decreased from 0°to 90° and then increased from 90° to 180°. This means that in 90 degree, the muscle is stiffer, therefore the indenter travels less to catch the target force(Figure 10).

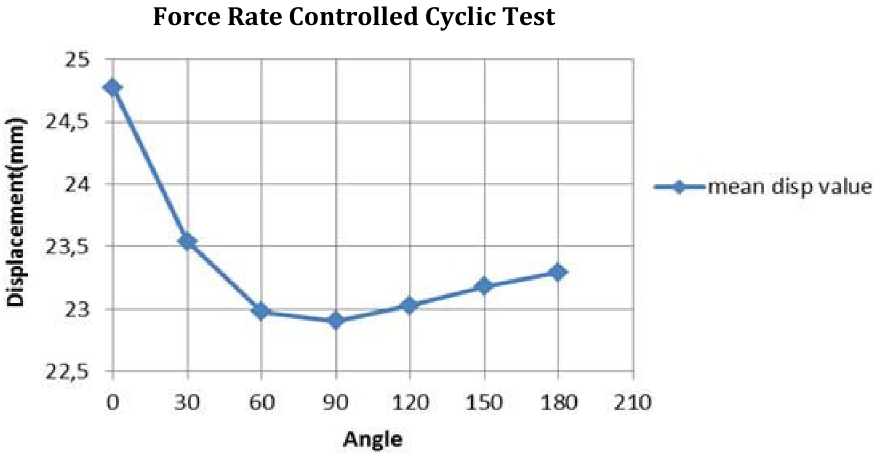


Figure 10. Displacement values of biceps muscle in different indenter tip alignments, to the same force controlled cyclic loading test. The tests were carried out at same point with 1N/s force rate, 5 loops and 100s total experiment time

4. Conclusion

This investigation is an experimental study to examine mechanical behavior of human soft tissues. One of the main reasons of doing material tests on soft biological tissues is to obtain a precise constitutive equation which can be used in finite element simulations of mechanical interaction of human body with surrounding. Better design of prosthesis, orthoses, identification of diseases, accident protection of passengers etc. are all based on accurate simulations where the bottle neck is material model. In this study in-vivo indentation experiments by an in-house indenter device were conducted on human arm muscles. Displacement rate and force rate cyclic loading, and relaxation experiment protocols were used. This study demonstrates the difference between Mullin’s effect during in-vivo force rate controlled cyclic loading and the traditional displacement controlled test method. Ellipsoidal tip was used to examine in-plane anisotropy and material direction of bulk soft tissues. It was observed that the stiffer material direction is perpendicular to contraction direction of muscle in both displacement rate and force rate cyclic loading protocols. In addition it was observed that in relaxation tests, during constant imposed deformation, the resulting force drops slowly as time progresses and tends to an equilibrium value as time goes to infinity.

References

Ahn, B., & Kim, J., 2010. Measurement and characterization of soft tissue behavior with surface deformation and force response under large deformations. Medical Image Analysis, 14(2), 138–148.

Argatov, I. I., Mishuris, G. S., & Paukshto, M. V., 2015. Cylindrical lateral depth-sensing indentation testing of thin anisotropic elastic films. European Journal of Mechanics - A/Solids, 49, 299–307.

Barrett, S. R. H., Sutcliffe, M. P. F., Howarth, S., Li, Z.-Y., Gillard, J. H., 2009. Experimental measurement of the mechanical properties of carotid atherothrombotic plaque fibrous cap. Journal of Biomechanics, 42(11), 1650–1655.

Bischoff, J. E., 2004. Static Indentation of Anisotropic Biomaterials Using Axially Asymmetric Indenters—a Computational Study. Journal of Biomechanical Engineering, 126(4), 498.

Borodich, F. M., Keer, L. M., Korach, C. S., 2003. Analytical study of fundamental nanoindentation test relations for indenters of non-ideal shapes. Nanotechnology, 14(7), 803–808.

Carson, W. C., Gerling, G. J., Krupski, T. L., Kowalik, C. G., Harper, J. C., Moskaluk, C. A., 2011. Material characterization of ex vivo prostate tissue via spherical indentation in the clinic. Medical Engineering & Physics, 33(3), 302–309.

Carter, F. ., Frank, T. ., Davies, P. ., McLean, D., Cuschieri, A., 2001. Measurements and modelling of the compliance of human and porcine organs. Medical Image Analysis, 5(4), 231–236.

Chao, C. Y. L., Zheng, Y.-P., Huang, Y.-P., Cheing, G. L. Y., 2010. Biomechanical properties of the forefoot plantar soft tissue as measured by an optical coherence tomography-based air-jet indentation system and tissue ultrasound palpation system. Clinical Biomechanics (Bristol, Avon), 25(6), 594–600.

Chen, W.-M., Phyau-Wui Shim, V., Park, S.-B., Lee, T., 2011. An instrumented tissue tester for measuring soft tissue property under the metatarsal heads in relation to metatarsophalangeal joint angle. Journal of Biomechanics, 44(9), 1801–1804.

Choi, A. P. C., Zheng, Y. P., 2005. Estimation of Young's modulus and Poisson's ratio of soft tissue from indentation using two different-sized indentors: Finite element analysis of the finite deformation effect. Medical & Biological Engineering & Computing, 43(2), 258–264.

Cox, M. A. J., Driessen, N. J. B., Boerboom, R. A, Bouten, C. V. C., Baaijens, F. P. T., 2008. Mechanical characterization of anisotropic planar biological soft tissues using finite indentation: experimental feasibility. Journal of Biomechanics, 41(2), 422–429.

Dimitriadis, E. K., Horkay, F., Maresca, J., Kachar, B., Chadwick, R. S., 2002. Determination of elastic moduli of thin layers of soft material using the atomic force microscope. Biophysical Journal, 82(5), 2798–2810.

Fath El Bab, A. M. R., Sugano, K., Tsuchiya, T., Tabata, O., Eltaib, M. E. H., Sallam, M. M., 2010. New compensation technique for the soft tissue stiffness measurements using two sensor probes configuration. Procedia Engineering, 5, 1304–1307.

Feng, Y., Okamoto, R. J., Namani, R., Genin, G. M., Bayly, P. V., 2013. Measurements of mechanical anisotropy in brain tissue and implications for transversely isotropic material models of white matter. Journal of the Mechanical Behavior of Biomedical Materials, 23, 117–132.

Fu, Y. B., Chui, C. K., 2014. Modelling and simulation of porcine liver tissue indentation using finite element method and uniaxial stress-strain data. Journal of Biomechanics, 47(10), 2430–5. doi: 10.1016/j.jbiomech.2014.04.009

Gefen, A., Margulies, S. S., 2004. Are in vivo and in situ brain tissues mechanically similar? Journal of Biomechanics, 37(9), 1339–1352.

Hu, J., Klinich, K. D., Miller, C. S., Rupp, J. D., Nazmi, G., Pearlman, M. D., Schneider, L. W., 2011. A stochastic visco-hyperelastic model of human placenta tissue for finite element crash simulations. Annals of Biomedical Engineering, 39(3), 1074–1083.

Iivarinen, J. T., Korhonen, R. K., Julkunen, P., Jurvelin, J. S., 2011. Experimental and computational analysis of soft tissue stiffness in forearm using a manual indentation device. Medical Engineering & Physics, 33(10), 1245–1253.

Kauer, M., No, D. E. T. H. (n.d.). Inverse Finite Element Characterization of Soft Tissues with Aspiration Experiments Inverse Finite Element Characteriza- tion of Soft Tissues with Aspiration, (14233).

Kauer, M., Vuskovic, V., Dual, J., Szekely, G., Bajka, M., 2002. I nverse finite element characterization of soft tissues, 6, 275–287.

Kim, J.,2004. Virtual Environments for Medical Training : Graphic and Haptic Simulation of Tool-Tissue Interactions By Virtual Environments for Medical Training :

Korhonen, R. K., Saarakkala, S., Juha, T. (n.d.). Experimental and numerical validation for the novel configuration of an arthroscopic, 1565.

Kroon, M., & Holzapfel, G. A., 2008. A new constitutive model for multi-layered collagenous tissues. Journal of Biomechanics, 41(12), 2766–71.

Lokshin, O., Lanir, Y., 2009. Viscoelasticity and preconditioning of rat skin under uniaxial stretch: microstructural constitutive characterization. Journal of Biomechanical Engineering, 131(3), 031009. doi:10.1115/1.3049479

Luo, G., Houston, V. L., Garbarini, M. A., Beattie, A. C., Thongpop, C., 2011. Finite element analysis of heel pad with insoles. Journal of Biomechanics, 44(8), 1559–1565.

Nava, A., Mazza, E., Furrer, M., Villiger, P., Reinhart, W. H., 2008. In vivo mechanical characterization of human liver. Medical Image Analysis, 12(2), 203–216.

Ottensmeyer, M. P., 2001. Minimally Invasive Instrument for In Vivo Measurement of Solid Organ Mechanical Impedance by.

Ottensmeyer, M. P., Kerdok, A. E., Howe, R. D., Dawson, S. L., 2004. The Effects of Testing Environment on the Viscoelastic Properties of Soft Tissues, 3078, 9–18.

Pailler-Mattei, C., Bec, S., Zahouani, H., 2008. In vivo measurements of the elastic mechanical properties of human skin by indentation tests. Medical Engineering & Physics, 30(5), 599–606.

Pandolfi, A., Vasta, M., 2012. Fiber distributed hyperelastic modeling of biological tissues. Mechanics of Materials, 44, 151–162.

Pelletier, H., Krier, J., Mille, P., 2006. Characterization of mechanical properties of thin films using nanoindentation test. Mechanics of Materials, 38(12), 1182–1198.

Peña, E., Peña, J. A., Doblaré, M., 2008. On modelling nonlinear viscoelastic effects in ligaments. Journal of Biomechanics, 41(12), 2659–2666.

Prevost, T. P., Jin, G., de Moya, M. A., Alam, H. B., Suresh, S., Socrate, S., 2011. Dynamic mechanical response of brain tissue in indentation in vivo, in situ and in vitro. Acta Biomaterialia, 7(12), 4090–4101.

Samani, A., Plewes, D., 2004. A method to measure the hyperelastic parameters of ex vivo breast tissue samples. Physics in Medicine and Biology, 49(18), 4395–4405.

Samur, E., Sedef, M., Basdogan, C., Avtan, L., Duzgun, O., 2007. A robotic indenter for minimally invasive measurement and characterization of soft tissue response. Medical Image Analysis, 11(4), 361–373.

Seifzadeh, A., Oguamanam, D. C. D., Trutiak, N., Hurtig, M., Papini, M., 2012. Determination of nonlinear fibre-reinforced biphasic poroviscoelastic constitutive parameters of articular cartilage using stress relaxation indentation testing and an optimizing finite element analysis. Computer Methods and Programs in Biomedicine, 107(2), 315–326.

Structure and Stress-Strain Relationship of Soft Tissues Author(s): Y. C. Fung Stable URL : http://www.jstor.org/stable/3882748 . Your use of the JSTOR archive indicates your acceptance of the Terms & Conditions of Use , available at . content in a t. (2014), 24(1), 13–22.

Tönük, E., Silver-Thorn, M. B., 2004. Nonlinear Viscoelastic Material Property Estimation of Lower Extremity Residual Limb Tissues. Journal of Biomechanical Engineering, 126(2), 289. doi:10.1115/1.1695575

Van Dommelen, J. A. W., van der Sande, T. P. J., Hrapko, M., Peters, G. W. M., 2010. Mechanical properties of brain tissue by indentation: interregional variation. Journal of the Mechanical Behavior of Biomedical Materials, 3(2), 158–166.

Yao, W., Yoshida, K., Fernandez, M., Vink, J., Wapner, R. J., Ananth, C. V, … Myers, K. M., 2014. Measuring the compressive viscoelastic mechanical properties of human cervical tissue using indentation. Journal of the Mechanical Behavior of Biomedical Materials, 34, 18–26.

Yin, Y., Ling, S.-F., Liu, Y., 2004. A dynamic indentation method for characterizing soft incompressible viscoelastic materials. Materials Science and Engineering: A, 379(1-2), 334–340.

Zhang, G. Y., Wittek, A., Joldes, G. R., Jin, X., Miller, K., 2014. A three-dimensional nonlinear meshfree algorithm for simulating mechanical responses of soft tissue. Engineering Analysis with Boundary Elements, 42, 60–66.

Zheng, Y., Mak, A. F. T., Lue, B., 1999. Objective assessment of limb tissue elasticity : Development of a manual indentation procedure, 36(2).