Mechanical Characterization of Soft Connective Tissues with Aging

Arturo N. Natali, Piero G. Pavan, Emanuele L. Carniel, Paolo Dario and Ivano Izzo

***Abstract*—The effects of muskoskeletal disorders or degradation can be particularly evident in elderly people. Since the limitation of the functionality often lies in a field of mechanical behavior, the capability of characterizing the mechanics of soft connective tissues is important. In this paper it is shown how constitutive models can correctly describe the mechanical response of soft connective tissues and how these models can be adopted to account the modification of the micro-structural conformation of such tissues with aging. Through the use of numerical formulations capable of accounting for non linear-elastic behavior, visco-elasticity and damage phenomena, the change of the mechanical properties of the tissues are described and interpreted.**

I. Introduction

THIS paper deals with the constitutive modeling of soft connective tissues, such ligaments and tendons. In particular, the constitutive models proposed are aimed to describe the mechanical behavior of these tissues in the case of degenerative phenomena related to aging.

It is known that the functionality of connective tissues is reduced with aging. This fact is essentially related to the mechanical degradation of the microstructure [1-3] of the tissue and can induce heavy effects on the life of elderly people.

Understating the mechanics of soft connective tissues and their change through life [4], also from a quantitative point of view, is extremely important and can have at least two main applications: to design biomedical devices for improving the functional capability of elderly people; to contribute for a definition of strategies aimed to prevent, as much as possible, the structural degradation of connective tissues.

The constitutive models proposed in this paper have different peculiarities. First of all, it is possible to correlate the values of the constitutive parameters to some characteristics of the structural conformation of the tissues, for example the 'wave length' of the typical crimp of the collagen fibers and its effect on the stiffening behavior, or the percentage of liquid content and its relationship with the volumetric compressibility. Therefore, it can be stated that the constitutive models have some sort of coherence with the micro-structural conformation of the tissues. In addition, a change in the values of the constitutive parameters is associated to evident variations of important mechanical characteristics of the tissue, and these variations have a strong correlation with its full or reduced functional capabilities: flexibility and toughness, maximum strain and energy at failure, shock adsorbing capacity. Finally, the constitutive models are built to be coherent with the requirements of thermodynamics. This is important to confirm the rigorous mechanical approach adopted.

Manuscript received May 7, 2008.

A. N. Natali is with the Centre of Mechanics of Biological Materials (CMBM), University of Padova, Padova, I-35131 ITALY (phone: +39 049 827 5598; fax: +39 049 827 5604; e-mail: arturo.natali@unipd.it).

E. L. Carniel is with the Centre of Mechanics of Biological Materials (CMBM), University of Padova, Padova, I-35131 ITALY (e-mail: emanuele.carniel@unipd.it).

P. G. Pavan is with the Centre of Mechanics of Biological Materials (CMBM), University of Padova, Padova, I-35131 ITALY (e-mail: piero.pavan@unipd.it).

P. Dario is with the Scuola Superiore Sant'Anna, Pisa, I-56127, ITALY (e-mail: dario@arts.sssup.it).

I. Izzo is with the Scuola Superiore Sant'Anna, Pisa, I-56127, ITALY (e-mail: dario@arts.sssup.it).

II. Structure of Soft Connective Tissues

Soft connective tissues are composed of cells and extra-cellular matrix (ECM) that has a composition variable with the type of tissue considered and its specific mechanical function. The cells can occupy about 20% of the total volume of the soft connective tissue, while the ECM accounts for the remaining 80%. Therefore, the main mechanical characteristic of the tissue depends on the structural conformation of ECM.

The ECM mainly consists of protein fibers, as elastic fibers and collagen fibers, and amorphous matrix, said also ground substance. Elastic fibers have mechanical similarity to rubber, while collagen fibers show higher stiffness and form the main tensile load bearing components in the tissue. The ground substance is a sort of viscous gel composed of water, proteoglycans and other glycoproteins. While ground substance and elastic fibers have a randomly disposed structure, the collagen fibers can have distinct spatial orientation. The disposition of the collagen fibers is the result of an optimization process of the tissue to bear tensile stress. Therefore, according to the specific loading conditions associated to the main functional state of the tissue, this can show low or high anisotropic mechanical behavior.

Because of the different components making up the ECM, a soft connective tissue must be considered as a composite material whose mechanical behavior depends on the mechanical characteristics of the single components and their interaction. For example, the collagen fibers affect the tensile behavior of the tissue and, usually, reinforcing the ground matrix along specific spatial orientation, are responsible for the anisotropic response of the tissue. On the contrary, the compression behavior of the tissue is governed by the ground matrix, in particular by the phenomena of interaction between the liquid phases and the fibrous skeleton of ECM.

A. *Structural conformation and mechanical behavior*

In order to formulate a constitutive model capable of describing the effective behavior of a soft connective tissue, it is necessary to take into account the specific conformation of each component and to identify the relationship existing between the hierarchical structural organization and the corresponding mechanical behavior at the macroscopic level, i.e. at the level of the tissue.

The collagen fibers are structures with high hierarchical arrangement. The main substructure is the collagen fibril which is formed by tropocollagen molecules linked together. Adjacent collagen fibrils are linked together to form collagen fibers. The bonds between fibrils are given by the FACIT filaments, as well as by proteoglycans. A soft connective tissue not subjected to loading shows a wavy conformation of the collagen fibrils, known also as ‘crimping’. The crimp of the collagen fibers is the reason of the typical behavior shown by a fibrous-reinforced tissue under tensile loading.

The mechanical behavior of the collagen fibers [5,6] under elongation is characterized by an overall non-linear response with three main distinct regions shown in Figure 1 in terms of stress-versus-strain curve, up to failure. An initial toe-region, where the tissue has low stiffness, is followed by a region characterized by a quasi-linear stress-strain behavior. While the first is associated to the initial crimp conformation of the collagen fibers, which is typical of the tissue when unloaded, and the progressive un-crimping phenomena, the second is found in a strain range in which the collagen fibers must be considered as un-crimped and predominantly aligned along the loading direction. The third region is found for more large strains, when the elongation causes the progressive rupture of the fibers, with regard to inter-fibrillar and intra-fibrillar bonds. This third region is characterized by a progressive decreasing of the tangential stiffness. With the increase of strain the tissue goes towards the total failure.

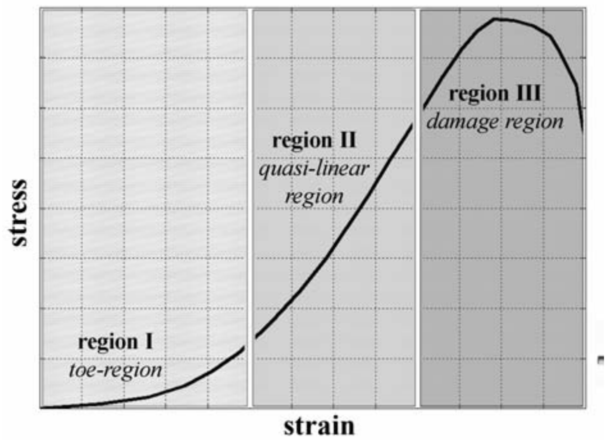

Fig. 1. Typical stress-strain behavior of a connective tissue rich in collagen fibers, up to failure.

With aging [7] the change in the collagen fibers can be a variation in the diameter of the fibrils, their number in unit of volume, their mutual bonding, as well as the level of crimp in the unloaded configuration. All these changes can be reflected in several aspects of the mechanical behavior.

The composition of the ground matrix is essentially an electrolytic water solution, in which the main components are positive sodium ions and proteoglycans. The latter are negative charged and this fact has influence when the tissue is compressed since the electrostatic interactions can increase the bulk modulus of the tissue. The viscous gel is non-Newtonian, thus with strain-rate dependent viscosity, and is partially free to move within the solid skeleton of the tissue. The movement of the viscous gel is a dissipative process that needs time to develop, influencing the macroscopic mechanical behavior of the tissue and determining a visco-elastic response. A tissue subjected to a high loading-rate shows a high bulk modulus because the water solution is more bounded and can contribute with its high volumetric stiffness to increase the bulk modulus of the tissue. On the contrary, if loaded with low loading-rate, the tissue shows, in general, higher compressibility. Even if the behavior of the ground matrix is more related to the compressive behavior of a tissue, the presence of the water solution is considered to have also lubrication effects in the phenomena related to the re-arrangement of the fibrous structures, thus affecting also the visco-elastic behavior of the tissue in tension.

Also in the case of the ground matrix [8,9] the aging causes a deep change in the macroscopic mechanical behavior, since a change of the water content or of the permeability of the connective tissue has direct effects on the volumetric compressibility of the tissue as well as on its viscoelastic properties.

III. Constitutive Formulation

The constitutive models proposed in this paper to describe the mechanics of soft connective tissues, include well known mechanical characteristics, such as anisotropy, non-linear elasticity, visco-elasticity [10] and damage [11].

The starting basis is a hyperelastic fiber-reinforced constitutive model, which is here specified for the case of a soft tissue locally reinforced by one only family of collagen fibers. Adopting a decoupling of the strain energy function W in volumetric and iso-volumetric terms, it is written:

$$W = U_m(I_3) + \tilde{W}_m(\tilde{I}_1, \tilde{I}_2) + W_f(I_4), \tag{1}$$

being U_m and $\tilde{W}_m$ the terms related to the ground matrix depending on the volumetric and iso-volumetric parts of strain, while W_f is the term related the collagen fibers. Because of the isotropic characteristics assumed for the ground matrix, the associated terms of the strain energy depend on the right Cauchy-Green tensor through its principal invariants:

$$I_3 = \det \mathbf{C},$$
$$\tilde{I}_1 = \mathrm{tr}\left(I_3^{-1/3}\mathbf{C}\right), \quad \tilde{I}_2 = \frac{1}{2}\left[\tilde{I}_1^{\,2} - \mathrm{tr}\left(I_3^{-1/3}\mathbf{C}\right)^2\right], \tag{2}$$
$$I_4 = \mathbf{A}\cdot\mathbf{C}\mathbf{A}\,.$$

where the modified first and second invariants are adopted according to the split of the strain in volumetric and iso-volumetric components. The fourth invariant affecting the value of the strain energy of the collagen fibers in equation (1) depend both on strain and the spatial disposition of the fibers, which is locally given by a unit tensor **A** in the undeformed configuration.

The typical strong non-linear stress-strain behaviors of a soft connective tissue need to choose specific formulations of the strain energy terms. For the volumetric part of strain energy of the ground matrix it is assumed:

$$U_m^\infty(I_3) = \frac{K_v^\infty}{2 + r^\infty(r^\infty + 1)}[(I_3^{1/2} - 1)^2 + I_3^{-r^\infty/2} + r^\infty I_3^{1/2} - (r^\infty + 1)], \tag{3}$$

where K_v^∞ is an elastic parameter corresponding to the tangential bulk modulus of the material in the undeformed configuration, while r^∞ is a parameter that is set to fit the behavior of equation (3) to the experimental data. The iso-volumetric term of the ground matrix in equation (1) is assumed as:

$$\tilde{W}_m^\infty(\tilde{I}_1, \tilde{I}_2) = \frac{C_1^\infty}{\alpha_1^\infty}\left\{\exp\left[\alpha_1^\infty(\tilde{I}_1 - 3)\right] - 1\right\} + \frac{C_2^\infty}{\alpha_2^\infty}\left\{\exp\left[\alpha_2^\infty(\tilde{I}_2 - 3)\right] - 1\right\}. \tag{4}$$

The elastic constants C_1^∞, C_2^∞ are related to the shear modulus in the undeformed configuration and $\alpha_1^\infty, \alpha_2^\infty$ are constitutive parameters obtained through a fitting to the experimental data.

Finally, the strain energy term related to the collagen fibers is written in the following form:

$$\tilde{W}_m^\infty(\tilde{I}_1, \tilde{I}_2) = \frac{C_4^\infty}{(\alpha_4^\infty)^2}\left\{\exp\left[\alpha_4^\infty(I_4 - 1)\right] - \alpha_4^\infty(I_4 - 1) - 1\right\}, \tag{5}$$

where constitutive parameter C_4^∞ is related to collagen fibers initial stiffness, while α_4^∞ can be associated to the crimped conformation.

The mechanical response described by the strain energy function (1) corresponds to a condition in which very low strain-rate is applied to the tissue. In such a case, if the strain is limited in a range not inducing damage phenomena, the tissue behaves elastically in a regime of thermodynamic equilibrium.

In the case of generic strain rate, the tissue behaves visco-elastically and its constitutive model is defined by assuming a Helmoltz free-energy function of the type:

$$\psi(\tilde{I}_1, \tilde{I}_2, I_3, I_4, \mathbf{q}_\alpha^i) = \psi_{mv}(I_3, \mathbf{q}_{mv}^i) + \psi_{mi}(\tilde{I}_1, \tilde{I}_2, \mathbf{q}_{mv}^i) + \psi_f(I_4, \mathbf{q}_f^i) \tag{6}$$

that, similarly to what done in equation (1), is split in the terms related to the volumetric behavior of the ground matrix ψ_{mv}, iso-volumetric behavior of the ground matrix ψ_{mi} and mechanical response of the collagen fibers ψ_f. The internal variables $\mathbf{q}_{mv}^i$, $\mathbf{q}_{mi}^i$ and $\mathbf{q}_f^i$ can be interpreted as the change in stress due to the viscous phenomena. To define a thermodynamic consistent visco-elastic model, the three terms of the Helmoltz free-energy function are written as:

$$\psi_{mv}(I_3, \mathbf{q}_{mv}^i) = U_m^\infty(I_3) + \sum_{i=1}^{n_{mv}}\left[U_m^\infty(I_3) - \frac{1}{2}\mathbf{q}_{mv}^i : \mathbf{C}\right], \tag{7}$$

$$\psi_{mi}(\tilde{I}_1, \tilde{I}_2, \mathbf{q}_{mi}^i) = \tilde{W}_m^\infty(\tilde{I}_1, \tilde{I}_2) + \sum_{i=1}^{n_{mi}}\left[\tilde{W}_m^i(\tilde{I}_1, \tilde{I}_2) - \frac{1}{2}\mathbf{q}_{mi}^i : \mathbf{C}\right], \tag{8}$$

and

$$\psi_f(I_4, \mathbf{q}_f^i) = W_f^\infty(I_4) + \sum_{i=1}^{n_{nf}}\left[W_f^i(I_4) - \frac{1}{2}\mathbf{q}_f^i : \mathbf{C}\right]. \tag{9}$$

The constitutive model defined by equations (6) to (9) corresponds to the assumption of the rheological model of Zener, with n_{mv}, n_{mi} and n_f viscous processes related to volumetric and iso-volumetric response of the ground matrix and elongation of the collagen fibers, respectively. The strain energy functions included in the summations of equation (7) to (9) are expressed as a function of the corresponding terms (3) to (5), through the use of relative stiffness parameters.

Finally, the possibility to develop damage phenomena is included in the constitutive model by considering further internal variables and defining a more general Helmoltz free-energy function of the type:

$$\psi(\tilde{I}_1, \tilde{I}_2, I_3, I_4, \mathbf{q}_\alpha^i, d_\alpha^i, d_\alpha^\infty) = \Gamma_m(d_m^i, d_m^\infty) \cdot \left[\psi_{mv}(I_3, \mathbf{q}_{mv}^i) + \psi_{mi}(\tilde{I}_1, \tilde{I}_2, \mathbf{q}_{mi}^i)\right] + \Gamma_f(d_f^i, d_f^\infty) \cdot \psi_f(I_4, \mathbf{q}_f^i), \tag{10}$$

where Γ_m, Γ_f are global damage functions for the ground matrix and collagen fibers, respectively. These scalar functions are adopted to account for a possible decrease of strength/stiffness of the tissue as a function of the damage accumulation, which is given by internal variables related to the ground matrix d_m^i, d_m^∞ and to the collagen fibers d_f^i, d_f^∞.

Instead of the previous formulation, which is developed to describe the mechanical behavior of transversally isotropic materials, it is possible to define the constitutive model including more families of fibers, according to possible more complex conformations of the tissues. This modification is quite simple from numerical point of view, while it needs larger amount of experimental data. Further, because of the multi-modal behavior of the functions describing the mechanical response, specific procedure must be adopted for the fitting of the models to the experimental data [12].

IV. Results and Discussion

In this section some results are reported, aiming to show the capabilities of the constitutive models developed to describe the mechanical behavior of soft connective tissues. Figure 2 shows the hysteresis for a tensile loading-unloading cycle in young and aged tissues subjected to elongation in the direction of the collagen fibers. The same level of stress is obtained in the two cases with a different level of strain. In addition, the loading-unloading cycle of the young tissue reveals a larger amount of dissipated energy (the area enclosed between loading and unloading curves of each cycle) in comparison to the case of the aged tissue.

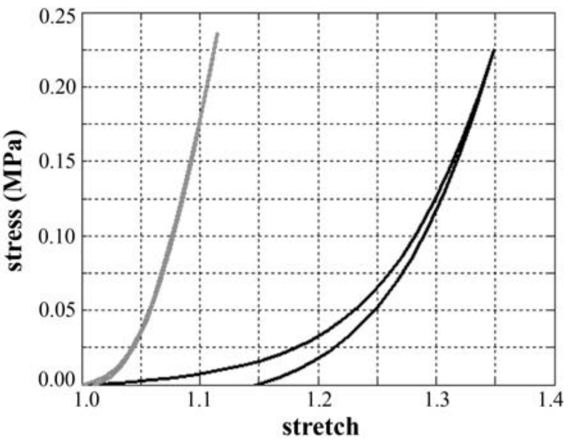

Fig. 2. Hysteresis for young (black line) and aged (grey line) viscoelastic tissues for a tensile loading-unloading cycle. The dissipated energy is represented by the area in between loading and unloading curve.

The behavior of the tissue up to the total failure in the case of elongation in the direction of the collagen fibers is represented in Figure 3 in terms of stress versus stretch. The different conformation of the collagen fibers (especially, the initial crimp), which is assumed to be different for young and aged tissue, results in a different capability of energy adsorbing capability. The latter is decreased in the aged tissue and, in addition, lower stress and strain values at failure with respect to the young tissue. The stiffness of the aged tissue increases in a small range of strain, while the young tissue show an initial 'toe' region characterized by high compliance.

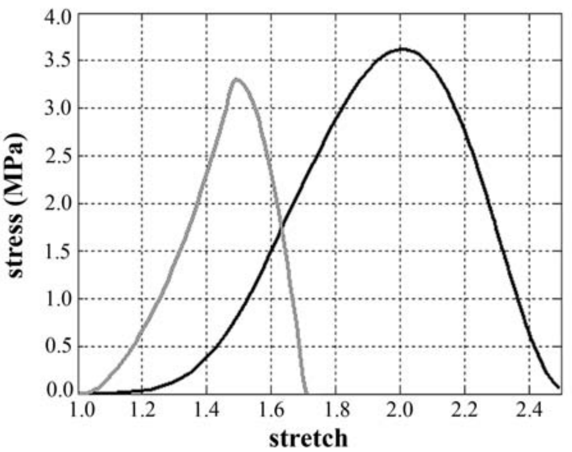

Fig. 3. Monotic tensile behavior for young (black line) and aged (grey line) tissues up to the total failure. The dissipated energy is represented by the area under the stress-strain curve.

The high compliance of a soft connective tissue for relative small strains is considered a positive factor to ensure its mechanical functionality. Further, the capability of adsorbing a large amount of energy at failure is a safety factor against possible injuries determined by overuse. In this sense an aged tissue has large predisposition to injury.

V. CONCLUSION

The constitutive model proposed shows a good capability to describe the mechanical behavior of soft connective tissues. The numerical formulation can be easily adapted to account for the mechanical behavior of tissues having microstructural conformation slightly different from the one considered in the examples presented. In this way the effects of a different number of collagen fibers groups or their particular mutual orientation can be described coherently with the experimental evidence. This fact confirms the general validity of the constitutive formulation proposed and, in particular, the possibility to describe a change in the mechanical response of the tissue due to a change occurring in its structure as typical in the aging process.

The identification of the constitutive parameters needs a lot of experimental data that are difficult to be obtained, since the required experimental testing is particularly complex. This problem is faced with the complexity of the mechanical behavior of such tissues, where different non-linear phenomena, such as elastic response, viscosity and damage are coupled with anisotropic characteristics. While the numerical formulation is sufficiently developed, further efforts are therefore required on the experimental front.

REFERENCES

[1] M.R. Dressler, D.L. Butler, R. Wenstrup, H.A. Awad, F. Smith and G.P. Boivin, "A potential mechanism for age-related declines in patellar tendon biomechanics", Journal of Orthopaedic Research, vol. 20, pp. 1315-1322, 2002.

[2] Bailey A.J., Paul R.G. and L. Knott, "Mechanisms of maturation and ageing of collagen", Mechanisms of Ageing and Development, vol. 106, pp. 1-56, 1998.

[3] N. Maffulli, V. Barrass and S.W.B. Ewen, "Light microscopic histology of Achilles tendon ruptures: a comparison with unruptured tendons", American Journal of Sports Medicine, vol. 28, pp. 857-863, 2000.

[4] A. Viidik, "Age-related changes in connective tissues", in Lectures on Gerontology Biology of Ageing - part A 1, A. Viidik (Editor), London: Academic Press, London, 1982, pp. 173-211.

[5] F.H. Silver, J.W. Freeman and G.P. Seehra "Collagen self-assembly and the development of tendon mechanical properties", Journal of Biomechanics, vol. 36, pp. 1529-1553, 2003.

[6] N. Sasaki and S. Odajima, "Stress-strain curve and Young's modulus of a collagen molecule as determined by the X-ray diffraction technique", Journal of Biomechanics, vol. 29, pp. 655-658, 1996.

[7] M.V. Narici, C.N. Maganaris and N.D. Reeves, "Myotendinous alterations and effects of resistive loading in old age", Scandinavian Journal of Medicine and Science in Sports, vol. 15, pp. 392-401, 2005.

[8] K. Komatsu, M. Kanazashi, A. Shimada, T. Shibata, A. Viidik and M. Chiba, "Effects of age on the stress–strain and stress–relaxation properties of the rat molar periodontal ligament", Archives of Oral Biology, vol. 49, pp. 817-824, 2004.

[9] W.Y. Gu, X.G. Ma, R.J. Foster, M. Weidenbaum, V.C. Mow and B.A. Rawlins, "The anisotropic hydraulic permeability of human lumbar anulus fibrosus. Influence of age, degeneration, direction, and water content", Spine, vol. 24(23), pp. 2449-2455, 1999.

[10] A.N. Natali, P.G. Pavan, E.L. Carniel, C. Dorow, "Visco-elastic response of the periodontal ligament: an experimental-numerical approach", Journal of Connective Tissue Research, vol. 45, pp. 222-230, 2004.

[11] A.N. Natali, P.G. Pavan, E.L. Carniel, M.E. Lucisano and G. Taglialavoro "Anisotropic elasto-damage constitutive model for the biomechanical analysis of tendons", Medical Engineering and Physic, vol. 27, pp. 209-214, 2005.

[12] A.N. Natali, E.L. Carniel, P.G. Pavan, F.G. Sander, C. Dorow, M. Geiger, "A constitutive model for the analysis of the biomechanical response of the periodontal ligament", Journal of Biomechanical Engineering – Trans. of ASME, vol. 130(3), 031004 1-8, 2008.