Experimental and computational analysis of soft tissue mechanical response under negative pressure in forearm

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Background: Instrumentation, relying on the use of negative pressure (suction), has been introduced to reduce pathological tissue swelling. Then, relative contribution of skin, adipose tissue and muscle, to the overall mechanical response is not known.

Methods: Under suction, stretch of soft tissues in the forearm of human subjects (N = 11) was experimentally measured at rest and under venous occlusion. Three dimensional, fibril-reinforced hyperelastic finite element (FE) model was constructed, the model response was matched with the experimental measurement and the mechanical characteristics of each tissue were derived. Parametric analyses were conducted to evaluate the impact of different tissues on the total stretch.

Results: The model suggested that, at large strains, the stretch response was more sensitive to changes in the elastic modulus of skin than those in adipose tissue. During venous occlusion, reduction of the stretch of forearm tissues was related to stiffening of the skin and adipose tissue, as evidenced by increased modulus of 27 ± 21% and 35 ± 26%, respectively.

Conclusion: The method based on suction may be used to diagnose and monitor changes in properties of soft tissues, especially those of skin, as well as tissue swelling typical to pathological conditions such as oedema.

Key words: skin – adipose tissue – muscle – collagen – suction treatment device – finite element analysis – oedema

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Several pathologies, most typically soft tissue oedema, induce variations in the mechanical properties of soft tissues. Therefore, pathological development may be diagnosed by monitoring the tissue mechanical properties (1, 2). Mechanical measurements of soft tissues may rely on the use of positive or negative external stress, such as mechanical indentation or suction, respectively, and subsequent recording of tissue load and deformation. In experimental measurements, typically, different soft tissues such as skin, adipose tissue and skeletal muscle, contribute to the overall mechanical response. Unfortunately, we lack mostly the knowledge about the relative effects of different soft tissues on the measured response.

Mechanical properties of skin have been investigated using negative pressure loading in several previous studies (3–8). However, most of these studies have not taken into account the effect of underlying tissues on the measured mechanical response (3, 6). Mechanical properties of the adipose tissue (mainly fat) have been characterized by using compression tests of human breast (9–12), human heel (13, 14) or porcine tissues (15). Anisotropic mechanical properties of passive skeletal muscles have also been investigated using compression tests (16–19). In modeling studies, skin (3, 7, 8, 13), adipose tissue (20–22) and muscle (17, 23, 24) tissues are usually considered as hyperelastic. However, human skin is a heterogeneous material composed mostly of collagen and elastin fibres (3, 25). Collagenous soft tissues are often modeled as fibril-reinforced materials (26–29). There are no 3D models of human forearm to which the fibril-reinforced hyperelastic skin, and hyperelastic adipose tissue and muscle have been implemented to mimic the measured tissue stretches under negative pressure.

Instrumentation, relying on the use of negative pressure, has been introduced to stimulate...
the lymph flow in order to reduce pathological tissue swelling. The instrumentation measures the degree of deformation of human soft tissues under suction. In the present study, we conducted experimental measurements to investigate soft tissue deformation of human forearm and effects of tissue swelling on the recorded mechanical response. By using a finite element (FE) model with realistic geometries of major soft tissues of human forearm (skin, adipose tissue and muscle) we simulated the experimental measurements, evaluated the effect of swelling on tissue properties, and estimated the impact of different tissues on the biomechanical response. In the model, the adipose and muscle tissue were considered to be hyperelastic material and the skin was fibril reinforced hyperelastic material. The study was established to provide answers to the specific questions, such as (1) to which degree different soft tissues control the forearm deformation under suction?; (2) how and which tissue properties change during manipulated tissue swelling? The findings of the present study can help to evaluate the diagnostic feasibility of in vivo suction measurements.

Materials and Methods

Study protocol
First, mechanical suction measurements were performed before and after manipulated tissue swelling in the forearm of each subject. Then, peripheral quantitative computed tomography (pQCT) images were taken to determine the dimensions of tissues at the site of mechanical measurements. The FE model geometry and mesh were based on those dimensions. The FE model was fitted to experimental measurements by optimizing the model parameters of each tissue. Finally, sensitivity of the mechanical response to changes in the mechanical properties of different tissues was evaluated by using the FE model.

Subjects and measurements
Eleven healthy volunteers (nine males, two females, age = 31 ± 7 years, height = 179 ± 9 cm, weight = 84 ± 9 kg and length of ulna bone = 29 ± 2 cm) participated in this study. Nine subjects were right-handed and two left-handed. All subjects gave their informed consent for the study. The study was approved by the Kuopio University Hospital Committee on Research Ethics (diary number 7/2010).

The treatment apparatus in use (Lymphatouch, HLD Healthy Life Devices, Espoo, Finland) is a hand held device for treatment of post-surgical or post-traumatic oedema and lymphoedema. Using infrared light sensor, it also measures the skin rise (stretch or deformation) caused by the negative suction pressure (Fig. 1). The minor and major axes of ellipse shaped suction head are 28.0 and 43.5 mm, respectively. In treatment, the suction head, made of thermoplastic elastomer SEBS (Thermolast K, Kraiburg TPE GmbH & Co. KG, Waldkraiburg, Germany), makes a tight contact with the skin. The pressure and skin deformation were measured through the experiment with accuracies of ± 0.01 mmHg and ± 10 μm, respectively, at the sampling frequency of 40 Hz. The data was analyzed offline using Matlab (version 7.8.0, Mathworks Inc., Natick, MA, USA). Statistical analysis was performed using Wilcoxon’s paired, two-sided signed rank test.

In mechanical tests, the dominant forearm of the subject was positioned to lay on a mechanical support during testing, similarly as presented earlier (30). In all the measurements, the test site was localized in the mid ulna (proximal-distal direction), centrally between the ulna and radius on the dorsal forearm. For measurements at rest (FR: forearm at rest), the test subject relaxed the forearm muscles. Subsequently, after a 5 min break, venous occlusion (VO) was created by using a pressure cuff at 8 kPa (60 mmHg) for 12 min to induce swelling of the forearm soft tissues. During each protocol, 20 repeated measurements were conducted, and the mean responses (deformation vs. suction...
pQCT measurements
The pQCT imaging of the forearm was performed at the sites of mechanical testing (Stratec XCT 2000, Stratec Medizintechnik GmbH, Pforzheim, Germany). One image slice (thickness = 2.3 mm, pixel size = 0.2 mm × 0.2 mm) was taken from each subject [Fig. 2(a)]. Different tissue layers were manually segmented from the images, and the tissue areas were calculated using Matlab. The location of tissue midpoint was also based on pQCT measurements.

FE model and simulations
Using the pQCT images the model geometry was constructed by first simplifying each tissue cross-section to be of circular shape [Fig. 2(b)]. Then, a circular shaped cross-section area, defined by the circle radius, of each tissue in the model was matched with the measured cross-section area (Table 1). Finally, the 2D geometry was extruded to 3D, achieving a cylindrical shape for the model geometry [Fig. 2(c)].

Three different models were created; one was based on the mean experimental results of all subjects (N = 11), while two were based on measurement results of two individuals with clearly different (maximum, minimum) tissue responses. The FE model (Fig. 3) was created and simulations were conducted using ABAQUS 6.9 (SIMULIA, Dassault Systemes, Providence, RI, USA). In the model geometry, the forearm was 30 cm in length, long enough to exclude any edge effects. The suction head consisted of 3063–6774 rigid 4-node surface elements (R3D4) and the tissues of 24860–32976 hexahedral 8-node elements with reduced integration points (C3D8R). The mesh at the areas of interest (in close proximity of the suction area) was made denser to obtain smoother stress/strain distributions. Optimal density for the FE mesh was found after running a convergence study. Contact between the suction head and the skin was assumed to be frictionless. The ulna and radius bones in the model were considered to be rigid and static by restricting the movement of the muscle nodes in contact with the bones. As the perimeter of the bones was fixed to be stationary, there was no need to use elements inside the bones. The movement of the nodes at the edge of the muscle was restricted. The suction pressure field was modeled to be shaped as a portion of a sphere (5), exposed on the skin surface within the suction area.

Muscle and adipose tissue were modeled as Neo-Hookean hyperelastic material. The Neo-Hookean material can imitate closely the mechanical behaviour of biological soft tissues, especially skin and adipose tissue, under short-term loading (9, 30–35). As the Neo-Hookean material is defined with only two parameters, optimization of the material parameters is straightforward. The strain energy potential function of the Neo-Hookean model is expressed in the form

Table 1. Radius of different tissue layers (circular approximation) used in the finite element models. Mean of the group (N = 11) and separately for subjects 1 (s1) and 2 (s2).

<table>
<thead>
<tr>
<th>Subject(s)</th>
<th>Tissue layer radius (mm)</th>
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<tbody>
<tr>
<td></td>
<td>Skin</td>
</tr>
<tr>
<td>Group (N = 11)</td>
<td></td>
</tr>
<tr>
<td>s1</td>
<td>38.9</td>
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<tr>
<td>s2</td>
<td>40.0</td>
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Fig. 2. (a) pQCT image of the forearm of a single subject. The image was used to measure areas of different tissues. Pixel size was 0.2 mm × 0.2 mm. (b) Image after tissue segmentations with arm support removed and (c) the simplified geometry used for FE simulations.
\[ U = C_{10}(I_1 - 3) + \frac{1}{D_1}(J_{el} - 1)^2 \] (1)

where \( I_1 \) is the first deviatoric strain invariant, \( J_{el} \) the elastic volume ratio and \( C_{10} \) and \( D_1 \) are parameters defining the shear behaviour

\[ C_{10} = \frac{G_0}{2} = \frac{E}{4(1 + \nu)} \] (2)

and the bulk behaviour

\[ D_1 = \frac{2}{B_0} = \frac{6(1 - 2\nu)}{E} \] (3)

In Eqs (2) and (3), \( G_0 \) is the initial shear modulus, \( B_0 \) the initial bulk modulus, \( E \) the elastic modulus and \( \nu \) the Poisson’s ratio. Therefore, both \( C_{10} \) and \( D_1 \) can be expressed with \( E \) and \( \nu \). The Poisson’s ratio for each tissue was fixed to 0.4, similarly to previous studies (2, 17, 19, 30, 36, 37).

Hyperelastic material was not considered to describe skin behavior realistically (3), as revealed by our preliminary and validation simulations. Therefore, fibril-reinforcement was added to the skin properties. This was realized by using nonlinear springs (SPRINGA element type in Abaqus), which were aligned length-wise along tension axis. Properties of the collagen fibers could then be described by the fibril network modulus \( E_f = \Delta \sigma / \Delta e \) [Fig. 4(a)]. We also added \( \varepsilon_0 \), the toe limit strain, in the model to describe the possible effect of fibril straightening; larger \( \varepsilon_0 \) indicates longer tissue elongation before collagen fibers have been straightened. The initial properties of the fibril-reinforced hyperelastic (FRHE) model were obtained by capturing the mechanical tensional response of skin presented experimentally in (38). The FRHE material was, while simple neo-Hookean hyperelastic (HE) material was not, able to capture the mechanical response [Fig. 4(b)]. In these simulations, the optimized properties of the FRHE skin were: \( E_{\text{skin}} = 115 \text{ MPa}, \varepsilon_0 = 3.6\% \) and \( E_f = 0.43 \text{ GPa} \). The mean absolute error between the experimental measurements and simulations was less than 0.3%.

As the mechanical role of the muscles was found minimal in the model, the elastic modulus of the muscle was fixed to 100 kPa (17, 30, 36, 39, 40). The fibril network modulus values of over 50 MPa produced similar tissue stretches (see below, Fig. 9), thus, it was fixed to a literature value of 4.4 GPa (41). Optimization of the material properties was conducted for the elastic modulus of skin, toe limit strain of skin fibrils and elastic modulus of adipose tissue by minimizing the mean squared error (MSE) between the simulated and experimental responses using a multidimensional unconstrained nonlinear minimization routine, utilizing Nelder-Mead method available in Matlab.

Sensitivity of the tissue stretch in the forearm to the mechanical parameters of different tissues was investigated. In the FE model the values of the elastic modulus for skin, adipose tissue and muscle were altered independently from 50\% to 200\% of the optimized reference values, and the effects on the mechanical response were analyzed. Similarly, significance of the fibril network modulus and the toe limit strain of skin was analyzed.

**Results**

After the VO, the skin deformation was reduced by 7.9 ± 9.5\% (\( N = 11 \), Fig. 5). The measured differences in responses during FR and VO were statistically significant (\( P < 0.05 \)). Values of the elastic modulus of skin and adipose tissue, as obtained by fitting the model to the experimental data at rest, were 1.13 ± 0.21 MPa and 0.80 ± 0.36 kPa (mean ± SD), respectively (Fig. 6, Table 2). The fibril toe limit strain at rest was 2.8 ± 1.4\%. As a result of the VO, the
optimized modulus values of the skin and adipose tissue increased by $27 \pm 21\%$ and $35 \pm 26\%$, respectively. The difference between the experimental and the FE data was less than $1.0\%$ in all loading configurations.

The highest von Mises stress values were located in the skin layer, at the longitudinal edges of the instrument suction head (Fig. 7). The highest logarithmic strain values were present in the adipose tissue layer, and located under the center of the suction head. The maximum von Mises stress value under the FR/VO condition was $61.2 \pm 8.9 / 64.1 \pm 13.7$ kPa for the skin, $1.0 \pm 0.2 / 0.9 \pm 0.2$ kPa for the adipose tissue and $1.6 \pm 0.6 / 2.0 \pm 0.6$ kPa for the muscle. The maximum logarithmic strain value under the FR/VO condition was $0.04 \pm 0.01 / 0.04 \pm 0.00$ for the skin, $0.94 \pm 0.07 / 0.87 \pm 0.05$ for the adipose tissue and $0.02 \pm 0.01 / 0.02 \pm 0.01$ for the muscle.

Based on the parametric analyses, sensitivity of the deformation registered by the instrument to different tissue properties varied along the level of tissue deformation. Under small deformation (<2 mm), the model response was slightly more (up to 13%) sensitive to changes in the elastic modulus of the adipose tissue than to those of the skin. Under large deformation

Fig. 4. (a) Typical mechanical response of collagenous skin in tension (red curve) with the implemented response in the present skin model (blue curve). (b) Geometry for a tension measurement with the experimental response (38) to test the suitability of the hyperelastic (HE) and the fibril-reinforced hyperelastic (FRHE) skin models. The mean absolute error between the experimental measurements and the FRHE model was less than 0.3%.

Fig. 5. Experimental results (Mean ± SD) at rest (FR) and under venous occlusion (VO). (a) the mean response, (b) the response of subjects 1 ($s_1$) and 2 ($s_2$). Difference between the measured responses during FR and VO was statistically significant ($P < 0.05$).
(<3 mm), the model response was substantially more (up to 86%) sensitive to changes in the elastic modulus of the skin than to those of the adipose tissue (Fig. 8). Further, under large deformation, the modeled response was up to 54% more sensitive to changes in the fibril toe limit strain than in the elastic modulus of the adipose tissue. The modulus of muscle and the fibril network modulus of skin (when > 50 MPa) had only minor effects on the model response (Figs 8 and 9).

Discussion
Pathological tissue swelling, a characteristic condition related to post-surgical or post-traumatic oedema and lymphoedema, is characterized by impaired lymph flow. Therapeutic instrumentation (LymphaTouch, HLD Healthy Life Devices, Espoo, Finland), applying a negative pressure, i.e. suction, has been introduced to stimulate the lymph flow. The treatment instrumentation has been designed to simultaneously measure deformation of human soft tissues, sensitively altered by pathological tissue swelling. Ideally, the mechanical measurement could provide direct information on the effect of treatment protocol. However, under negative pressure, the relative contribution of each soft tissue component, i.e. skin, adipose tissue and muscle, to the overall measured mechanical response is not known. In the present study, mechanical responses of human forearm soft tissues were measured at rest and under venous occlusion using a LymphaTouch device. A FRHE model with the geometry obtained from pQCT imaging was created to determine the elastic modulus of skin and adipose tissue, as well as deformational behavior of the skin fibrils, in the forearm. We specifically found that: (1) the suction device in use observes sensitively the mechanical properties of the skin, especially under large tissue deformation, (2) during manipulated tissue swelling, the skin and the adipose tissue stiffen simultaneously.

The present values for the skin elastic modulus (948–1364 kPa) are consistent with those reported earlier. In fact, the reported values show high variation, from 8 kPa up to 540 MPa (3–5, 30, 42). Also, the values of elastic modulus for the adipose tissue (0.45–1.17 kPa) agree with those reported in earlier studies, i.e., 0.5–5.6 kPa (36, 43, 44). Similar parameter, as the fibril toe limit strain in the present study, has been introduced for skin (3) and for human spine or rat tendon collagen using in vitro measurements (45, 46). This parameter is strongly affected by the initial stress/strain level of the skin, consistent with earlier studies. The present experimental method, combined with the computational analysis, was found to characterize skin and adipose tissue properties realistically.

According to parametric analyses, the modeled deformation was most sensitive to changes in the elastic modulus of the skin, although degree of tissue deformation significantly affected the sensitivity (Fig. 8). Under small deformation, the model response was sensitive to changes in the elastic modulus of the adipose tissue while, under large deformation, the response of the model was strongly affected by...
the changes in the elastic modulus of the skin and fibril toe limit strain. The effect of the muscle stiffness on the modeled suction response was minor. These results clearly highlight the importance of skin properties on the results obtained by using the present therapy instrument.

Variations (50%–200% of the reference value) in the values of the fibril network modulus had negligible effects on the model response. Only values lower than 50 MPa increased the error between the model and experiment (Fig. 9). This finding was related to rapid stiffening of the collagen after the fibril toe limit strain was exceeded. In fact, collagen has tensile strength comparable to steel (47) and the fibrils might swiftly turn nearly unstretchable (considering the forces present in the model).

The cuff pressure in use (60 mmHg) was considered to provide sufficient external pressure to keep the superficial veins occluded (48). The short-term venous occlusion prevents the veins from transporting the blood towards heart and causes the veins to swell, observed in this study mostly by local stiffening of skin and adipose tissue.

In the present study, friction between the skin and the suction head could not be measured. Therefore, this interface was assumed frictionless. Using the FE model, variations in the friction coefficient between 0.3 and 0.9 altered the mean skin deformation by 2.7%–6.7%, suggesting that the friction effects may not be negligible in the experimental suction measurements. When the suction head was modeled to be elastic (\( E = 2.83 \, \text{MPa}, \, v = 0.49 \)), instead of rigid material, 0.7% variation in the modeled response was demonstrated. This suggests that the assumption of a rigid suction head is an acceptable simplification.

There are limitations and simplifications in the material description of our FE model. Skin fibres were aligned parallel to the skin surface, making skin anisotropic. Due to simplicity required by the optimization process we could not differentiate between longitudinal and transversal fibres. The mechanical response of the collagenous fibril network in skin is usually considered to consist of three phases: low stiffness phase (crimped fibres), toe region (straightening of fibres) and elastic linear phase (straight fibres). This response was simplified by two phases [Fig. 4(a)] to minimize the number of parameters for optimization. The simplification was considered acceptable, as also suggested by the small error between the experimental test and the model prediction.

The realistic soft tissue geometry in the forearm is complex, and the amount and shape of each tissue alters from wrist to elbow. Fully realistic tissue geometry, reproduced from pQCT images, created many areas with distorted elements in the model. Therefore, in the present study, the 3D geometry of each tissue was simplified and modeled to be of cylindrical shape. This simplification may slightly change
the absolute values of the material parameters obtained from the optimization, but it should not influence the main conclusions of the study.

The present method could be applied to other body parts as well. The fluid-dependent viscoelasticity of the tissues could be incorporated in the model, especially if the time-dependent responses are analyzed. Fluid flow during short-term suction is minor or negligible, however, a more versatile model would be useful for investigating the time-dependent responses.

In conclusion, FE modeling provides a feasible method to evaluate factors affecting suction responses of inhomogeneous soft tissues. The present model was able to address the role and significance of different tissues (skin, adipose tissue, muscle) on the suction responses recorded by the experimental device. Based on the present results, the in vivo measurements with the device can be used to monitor changes in the mechanical properties of soft tissues,
especially those of the skin and adipose tissue. Therefore, the suction device can be useful when diagnosing and monitoring changes in soft tissue properties and tissue swelling, typical to pathological conditions such as oedema.

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Conflict of interest statement

Authors have no conflicts of interest.

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