Computational tools in rehabilitation of erectile dysfunction

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Abstract

Erectile dysfunction (ED) is defined as the inability to achieve and maintain an erection adequate for satisfactory intercourse. It is a common problem among approximately 50% of men between the ages of 40 and 70. Erectile dysfunction is not only stressful to both the affected individual and his partner, but it can also negatively affect self-esteem. Biomechanical models have recently been developed to study both the structural and hemodynamic factors involved in normal and pathological erectile conditions. These computational models, which are reviewed in the present paper, allow for better understanding of the mechanisms acting in ED and provide a suitable basis for development of state-of-the-art interdisciplinary treatment approaches aimed to improve the quality of life for these men. © 2001 IPEM. Published by Elsevier Science Ltd. All rights reserved.

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1. Introduction

The human penis contains erectile tissue that enables changes of its dimensions and level of rigidity. Penile erection is required for achieving sexual intercourse and for delivering the sperm near the cervical entrance of the uterus in the process of reproduction. Sperm transfer requires that the erect penis reach a sufficient degree of rigidity and axial strength. Erectile dysfunction (ED) is defined as the inability to achieve and maintain an erection adequate for satisfactory sexual intercourse [1]. Recent observations suggested that it is a problem common to about 50% of men over 40 yr of age [2]. Erectile dysfunction is often stressful to both the affected individual and his partner, and may also negatively affect self-esteem. Biomechanical computational tools have recently been developed to study both the structural and hemodynamic factors involved in normal and pathological erectile conditions. These computational models, which are reviewed in the present paper, allow for better understanding of the mechanisms involved in ED and provide a suitable basis for development of state-of-the-art interdisciplinary treatment approaches aimed to improve the quality of life for these patients.

2. Physiological and clinical background

2.1. Anatomical basis of erection

The human penis [Fig. 1(a)] consists of three cavernosal bodies: two dorsally located corpora cavernosa which share a perforated septum, and a ventral corpus spongiosum that surrounds the urethra and extends to the glans penis distally. A thick fibrous sheath, called the tunica albuginea, surrounds each of the corpora cavernosa and the corpus spongiosum. The corpora cavernosa and the corpus spongiosum contain numerous cavernous spaces separated by trabeculae composed of smooth muscle, fibroblasts, collagen and elastin fibers. The corpus spongiosum consists of larger cavernous spaces and smaller trabeculae with fewer smooth muscle cells than the ones found in the corpora cavernosa [3–6].

The erectile process is initiated in the brain where signals of arousal originate and are sent via the hypothalamicus down the spinal cord to autonomic nerves in the penis [Fig. 1(b)]. Erection results from smooth muscle relaxation mediated by parasympathetic penile nerves, including relaxation of the arterioles (Fig. 2). This causes an increased blood flow through the penis and engorgement of the corpora. Detumescence occurs following completion of the sexual act causing activation of the sympathetic fibers, which reduces blood flow after the contraction of the cavernosal smooth muscle [7–9]. The contractility of corporal smooth musculature plays a critical role in the entire erectile process. Moreover, in the absence of severe vascular disease or congenital or other structural abnormalities/malformations, relaxation of the corporal smooth muscle is both necessary and sufficient to elicit a sustained erection [10,11].

The tunica albuginea of the corpora cavernosa is a multilayered structure, containing mostly collagen and some elastin fibers [5]. Around the corpora cavernosa, the tunica has a thickness of 2–3 mm in the flaccid state and 0.25–0.5 mm in the erect state [12]. The tunica albuginea of the corpus spongiosum is thinner, and contains more elastic fibers [13,14]. The proximal part of the penis (the penile base) is anchored to the pelvic bone. In its distal part (the penile tip), the glans of the penis is constructed differently from its shaft. It is covered...
with very thin and firmly adherent skin, it has no fibrous sheath, and it contains abundant fibrous connective tissue. The glans has a sponge-like appearance due to a very rich venous network. The dimensions of the penis vary widely in the normal population. Chen et al. [15] studied 55 caucasian men aged 21–78 yr and found that the average length of the penis was 7.4±1.6 cm in the erect state.

### 2.2. Hemodynamics of erection

The circulation of the penis mainly involves several large vessels. Most of the flow is perfused via the internal pudendal artery that becomes the penile artery and then divides into four arteries, i.e., dorsal, urethral, deep (cavernosal), and bulbar (Fig. 1). These arteries terminate in the sponge-like corporal tissue. There are also large draining veins running along the entire length of the penis [16]. During erection, the penis increases in volume by the accumulation of blood, and an angle between 0 and 45° from the horizontal plane is created in an upright position. In this state, the shaft of the penis is rigid, and intracavernous pressure is close to the mean arterial blood pressure. The process of erection and detumescence has been summarized and divided into several different phases by various investigators [8,16,17]:

- **Phase 0** is the flaccid phase. When the penis is in the flaccid state, there is a dominant sympathetic influence and the terminal arterioles and cavernosal smooth muscles are contracted. Blood flow through the cavernous artery is minimal (about 5 ml/min) and there is a free outflow of blood from the sub tunical venules to the emissary veins [18].

- **Phase 1** is the filling phase. Following sexual stimulation, parasympathetic nervous activity dominates, and there is an increased blood flow (about 20 ml/min) through the cavernosal arteries without any change in the systemic blood pressure [18]. The peripheral resistance is decreased due to dilatation of the cavernosal arteries. As a result, the penis elongates but the intracavernous pressure still remains unchanged.

- **Phase 2** is the tumescence phase. Due to relaxation of the trabecular smooth muscle, lacunar intracavernosal spaces increase as they are filled by blood. The pressure created by the inflow of blood stretches and compresses the sub tunical venules, creating effective venous outflow resistance (Fig. 2). As a result, the intracavernous pressure increases rapidly, and compliance of the cavernosal bodies rises substantially, causing penile engorgement and erection. The arterial flow rate decreases at the end of this phase.

- **Phase 3** is the full erection phase. The relaxed trabecular muscle expands and, together with the increased blood volume, compresses the network of venules against the tunic albuginea, thereby reducing venous outflow, in the manner of a ‘venoocclusive mechanism’. At this point, the intracavernous pressure reaches about 100 mmHg (1 KPa equals 7.5 mmHg), while venous flow is only slightly higher than it is during the flaccid state [19].

- **Phase 4** is the rigid erection phase. The intracavernous pressure rises above the systolic pressure as a result of contraction of the ischiocavernous muscle (surrounding the corpus cavernosa). There is no flow through the cavernous artery at this stage.

- **Phase 5** is the transition phase. Increased activity in the sympathetic nervous system leads to contraction of the trabecular smooth muscle. Arterial flow is renewed at a low level, but the venoocclusive mechanism is still activated.

- **Phase 6** is the initial detumescence phase. There is a moderate decline of intracavernous pressure, indicating the reopening of the venous outflow channels and the decreasing of arterial flow.

- **Phase 7** is the rapid detumescence phase. The intracavernous pressure declines rapidly, the venoocclusive
mechanism becomes inactivated, the arterial flow decreases to its prestimulation level and the penis returns to its flaccid state.

2.3. Impotence and its causes

Penile erection normally follows sexual stimulation of visual, tactile, auditory or olfactory origin. Normal erections therefore depend on the central nervous system as well as the integrity of the autonomic nerves and blood supply of the penis. While erectile dysfunction can generally be associated with psychogenic or organic factors, it is difficult to differentiate between them (e.g., an originally organic lesion may often acquire psychological significance). Organic impotence can be caused by lesions in the central nervous system as a result of accidents, tumors or diseases (e.g., multiple sclerosis) which may be congenital or develop during life. Older individuals undergo degeneration in the nervous and circulatory systems which may be accelerated by diseases, such as diabetes, as well as by alcoholism and drug abuse [7]. Some characteristic pathophysiologicals of erectile dysfunction deserve mention.

Venous impotence is the failure to adequately restrict blood outflow during erection. The inability to trap arterial blood flow into the penis may result from any macroanatomical, cellular or biochemical abnormalities that reduce restricted corporal expansion. Venocclusive dysfunction seems to result from a defect within the penis rather than within the veins themselves. Structural alterations in the intracavernous smooth musculature or in the fibroelastic components of the trabeculae are predominant factors involved in inducing this condition [20]. These modifications also appear to be correlated with adverse influences of chronic ischemia [21,22].

Diabetes is a well-documented risk factor for erectile dysfunction. Diabetic patients become impotent at an earlier age and with a significantly higher prevalence, ranging as high as 75%, compared to other populations of impotent men [2]. Both neurogenic and vascular factors are important in the pathogenesis of erectile dysfunction in diabetes. Venous leakage in these patients is probably produced by autonomic dysfunction of the penile vascular innervation or degeneration of penile smooth muscles [23]. There is also some evidence for a reduction in the number of nerves to the penis in patients with diabetes compared with ‘non-naturopathic’ impotent men [24,25].

Peyronie’s disease is a pathological condition of the penis characterized by an alteration in the appearance and cellularity of the collagen that comprises the tunica albuginea. This change occurs in single or multiple plaque formation sites. As the disease progresses, the dorsal and middle parts of the tunica albuginea gradually become fibrotic or ossified [26–29]. Although the disease involves only the tunica albuginea and does not extend into the erectile tissue in the early acute stage, secondary nerve damage and ischemia in the chronic stage may induce further fibrosis of the cavernosal erectile tissue [30]. Painful erections during the acute stage and penile deformities during the chronic stage are common symptoms of the disease, which is also accompanied by erectile dysfunction in about 20% of the cases [31]. The prevalence of Peyronie’s disease is approximately 0.4–1% [32,33].

Blunt trauma to the erect penis may occur during intercourse, when the penis slips out of the vagina and is subsequently thrust against the partner’s perineum or pubic bone, or due to self-inflicted abnormal bending of the penis, e.g., during masturbation. Blunt injury to the erect penis may induce impotence in the long-term, due to venocclusive dysfunction. Penile fracture involving tunical rupture and associated intercavernous bleeding and hematoma is the classical representation of the most dramatic example of blunt injury to the penis in its erect state. It is a relatively uncommon injury, with less than 300 reported cases [34]. The focally damaged tunica fails to provide an adequate structural resistance for subcutaneous venule compression, thereby contributing to the development of site-specific leaks [12].

It is beyond the scope of this review to discuss the clinical assessment and pharmaceutical treatments of impotence. We refer the reader to several recent comprehensive reviews on this subject [35–37].

2.4. Prosthetic treatments of impotence

Successful pharmaceutical treatment of impotence, e.g., intracavernosal injections or sildenafil citrate (more commonly known by its brand name, Viagra), is dependent upon normal penile blood flow, intact nerves and sufficient capacity to produce nitric oxide which causes relaxation of the smooth muscle cells of the penis. When pharmaceutical and other conservative treatments fail to restore the erectile function, a penile prosthesis can be implanted to create artificial erections. Since the early 1950s, various penile prostheses for restoration of the erectile function have been used. All currently available penile prostheses are designed to be placed in the corporal bodies of the penis (Fig. 1) and they successfully provide sufficient rigidity to allow penetration. They differ markedly in how they produce the erection and how well they allow concealment of the penis during everyday activities [3,38–40]. Until recently, there were four basic types of prostheses available: rods, bistable, inflatable and self-contained erectile devices. Only rods and inflatable prostheses are in current clinical use [41,42].

It is generally accepted that an inflatable penile prosthesis (IPP) provides the best physiological results since its mechanism of operation mimics the normal erectile process by approximating the way blood enters the
corpora cavernosa. It consists of three components: a silicone reservoir that is located in the perivesical space, two inflatable silicone cylinders that are surgically inserted along the erectile bodies of the penis, and a small pump that is inserted within the scrotum (Fig. 3). When erection is desired, the penis can be distended to a near normal configuration by repeatedly squeezing the pump, thereby transferring fluid from the reservoir to inflate the cylinders within the penis. Manual release of the valve at the lower portion of the pump will return the fluid into the reservoir, and the penis will then become flaccid. One of their drawbacks is that IPPs are more complex and require additional surgical effort to implant than non-inflatable models [43].

Numerous successful procedures involving multi-component IPPs have been performed over the last 15 yr. However, a variety of complications have been encountered, including mechanical faults or failure of the prosthesis, intra- and post-operative complications, infections and patient dissatisfaction [43,44].

3. Computational models of erection

Knowledge of the mechanical behavior of the penis during erection, including both structural and fluid mechanics aspects, is a key to understanding its normal sexual function and allows better comprehension of various conditions of ED. Existing technology is limiting direct measurements of mechanical properties and behavior of the penis in vivo, e.g., it is not currently feasible to measure the internal stress distribution within and between the penile tissues during erection [45]. Hence, computer simulations that allow the development of biomechanical models of the human penis are the only practical alternatives to carry out such investigations and open new approaches for treatment of conditions that cause ED. Recent progress in modeling the structural and hemodynamic behavior of the penis during erection is reviewed in the following sections.

3.1. Structural analysis

Erectile function is dependant upon penile rigidity [46]. ‘Buckling’ is the term used in structural engineering to describe the curving of an otherwise straight column due to the action of large axial compressive loading. The same term can also be used to describe the curving of an erect penis with insufficient rigidity under the loads associated with initial vaginal penetration or when it is subjected to the constraining forces from contact with the vaginal sidewalls during intercourse.

Axial penile rigidity during erection is measured by penile buckling forces which are dependent on intracavernosal pressure, penile geometry and the penile tissue’s material properties. Udelson et al. [47] developed a biomechanical model for penile buckling which is based on these constitutents of penile rigidity during erection and initial coital penetration. Utilizing Euler’s formula, the critical load \( F_{\text{buc}} \) that induces a column’s buckling is related to the elasticity modulus \( E \), the length \( L \) and the second moment of cross-sectional area \( I \),

\[
F_{\text{buc}} = \frac{\pi^2 EI}{L^2}
\]

The penile shaft is modeled as a circular cylinder made of a homogenous, isotropic and linearly elastic material. Using Eq. (1) and standard engineering definitions of compliance, capacitance and volumetric stiffness, Udelson et al. [47] derived the following theoretical equation for prediction of the critical buckling force

\[
F_{\text{buc}} = \frac{3\pi^4}{64(2\nu_e-1)} \left( \frac{D}{L} \right)^2 \frac{D}{\rho} \left( \frac{V_E}{V_{E/F}} \right) \left( \frac{V_E}{V_{F/P}} \right) \left( 1 - \frac{V_E}{V_{F/P}} \right) + 1
\]

where \( \nu_e \) is the Poisson’s ratio of the corpora, \( X \) is the cavernosal expandability, \( \Delta P \) is the increase of intracav-
ernosal pressure above the flaccid state, and $D$, $L$ and $V$ are the diameter, length and volume of the pendulous penis, respectively. The subscripts $F$ and $E$ stand for the flaccid and erect states, respectively. Intracavernosal pressure, geometrical and tissue characteristics obtained during erectile function tests have been shown to theoretically predict the magnitude of clinically measured penile buckling forces according to the above relation [Eq. (2)].

A simplified structural model of the penis as a blood-filled circular cylinder with walls made of a homogenous material was also developed by Chen et al. [15] in order to predict penile elongation during erection. Evaluation of penile dimensions is a routine clinical procedure during the diagnosis of impotence and in the planning process of reconstructive penile surgery, such as Nesbit’s procedure, Peyronie’s plaque removal, penile augmentation and penile prosthesis implantation [48]. The cylinder walls of the model represented the tunica albuginea (Fig. 4), which is the main load-bearing structure [14]. The axial stress, $\sigma$, in a unit volume of the cylinder wall during erection was determined from the relation

$$\sigma = \frac{\pi P r^2}{\pi (R^2-r^2)}$$

where $P$ is the internal cavernosal blood pressure and $r$ and $R$ are the inner and outer radii of the cylinder, respectively. Similarly to Udelson et al. [47], the penile tissues were assumed to be isotropic and linear elastic. Accordingly, the mechanical stress–deformation relationship yields

$$\sigma = E \frac{L_e-L_f}{L_f} = E (\lambda_e-1)$$

where, $E$ is the penile elasticity, $L_f$ and $L_e$ are the lengths of the penis in the flaccid and erect states, respectively, and $\lambda_e=L_e/L_f$ is the stretch ratio. Using Eqs. (3) and (4), one can predict the length of the penis in the erect state from its flaccid length as well as the intracavernous pressure during erection,

$$L_e = \frac{L_f}{E (R^2-r^2)} [P r^2 + E (R^2-r^2)]$$

The predicted penile length during erection is an important factor in the pre-surgical evaluation for the establishment of surgical guidelines and for consultation with the patient about realistic postoperative expectations. A demonstration of penile length in its erect state can be achieved in the clinical setting by means of intracavernos injections, however, this procedure may cause priapism [49] while the modeling approach aims to be a safe alternative. The above model was therefore tested by comparing the predicted erect penile length [Eq. (5)] with the actual erect length, measured during pharmacologically induced erection. The theoretical and experimental results showed good agreement. The differences that were found between the length of the penis during pharmacologically induced erection and its stretched length, as measured during gentle stretching for pre-surgical evaluation, could also be explained by the modeling approach [15].

Models incorporating the real cross-sectional anatomy of the penis necessarily yield a more realistic representation of its structural behavior and further provide information on the internal stress distribution within its different tissue components. A realistic model that considers the different characteristics of the tunica albuginea and skin, dorsal blood vessels and the urethral channel, was developed by Gefen et al. [45] to study stress distributions in the normal penis during erection [Fig. 5(a)]. The symmetrical two-dimensional (2D) geometry of the model was extracted from an anatomical schematic section through the middle of the penis and scaled to con-
form to averaged dimensions. The model was solved for the structural stress distribution by using commercial finite element software.

The boundary conditions included four constraints on the lateral and dorsal–plantar aspects of the penis, allowing its expansion as a result of inflation by an equivalent erectile pressure \( P_e = P_a - \sigma_{cc} \). The erectile pressure, \( P_a \), reflected the resistance stress \( \sigma_{cc} \) of the spongy corpus cavernosa tissue to inflation pressure \( P_a = 100 \) mmHg caused by arterial blood flow into the cavities of the penis. As the penis becomes erect, blood is supplied to the corpus cavernosa until the full erection corporal volume reaches \( V_0 \) which is the total corporal capacity (TCC). When blood drains and the penis becomes flaccid, the corporal volume reduces up to \( V_f = 35\% \) TCC [50]. Assuming that the corpus cavernosal tissue is unstressed at \( V_f \), the characteristic stretch ratio \( \lambda_{\text{max}} \) from flaccid to full erection is given by the generally accepted relationship \( \lambda = (V_f/V_0)^{1/3} \) and equals 1.42. In the absence of literature data describing the constitutive law of the corpus cavernosal tissue, it was assumed that \( \sigma_{cc} = 7 \) KPa at \( \lambda_{\text{max}} = 1.42 \) from the mechanical characteristics of similar microstructures, such as the lung parenchyma. The penile soft tissues were assumed to be homogenous, isotropic, and linear elastic materials [45].

The simulation of stress distribution in the normal penis indicated that most of the load bearing during inflation is carried by the dorsal part of the tunica albuginea, where stresses are in the range of 5–30 KPa [Fig. 5(b)]. Since this site contains several nerves, it is most vulnerable to intensified mechanical stresses. The skin appeared to bear a negligible load. Inflation of the neutral, elliptical cross-sectional shape of the cavernosum during erection yielded a more circular corporal profile as well as lateral expansion of the cross-sectional shape of the penis (Fig. 5). This modeling approach allows simulation of stress distributions in various pathologic conditions of the penis (e.g., diabetes, Peyronie’s disease) by altering the geometry and material properties of its components [29,45,51].

3.2. Hemodynamic analysis

Penile rigidity is variable and achieved by the blood pressures acting within the organ’s soft tissues. Accordingly, the most widely studied physical parameters of penile rigidity have been intracavernosal blood pressure and flow [52]. In general, penile rigidity occurs with pressures approaching 90 mmHg. However, in some individuals, rigidity may develop at pressures as low as 40–50 mmHg or, in others, not until pressure exceeds 100–120 mmHg. These differences result from variability in the cavernosal compliance and capacitance [46].

An analog model of electrical components for analysis of penile hemodynamics was suggested by Venegas et al. [19] in order to relate penile compliance and capacitance with steady-state intracavernosal pressure. The model represented the arterial pressure by a voltage source, blood infusion by an electrical current, arterial and venous resistances by resistance elements and cavernosal and tunical compliance by capacitive elements (Fig. 6). The model predicted a relation for the cavernosal blood pressure–volume with two phases: an initial phase characterized by a gradual slope up to a critical flow, and a second phase characterized by a much steeper slope after limitation of the subtunical venular flow. These predictions were validated with experimental data obtained during pharmacologically induced erections and, accordingly, the multi-compartment modeling approach was shown as being capable of interpreting and characterizing penile hemodynamic data.

Barnea [53] developed a multi-compartmental analog model for representation of the hemodynamics of erection that incorporates a ‘valve-like’ action of the partially collapsed venous vessels during erection. This model includes an inlet arterial vessel, a corpus cavernosa compliant chamber and a venous draining vessel [Fig. 7(a)]. The pressure at the arterial vessel inlet of the model is the systemic arterial pressure, while the outlet pressure of the artery and inlet pressure of the vein equal the corporal pressure. The corporal pressure, \( P_C \), and volume, \( V_C \), are assumed to be non-linearly related by

\[
P_C = a_1 \ln(a_2 V_C) + a_3 e^{a_4 V_C}
\]

where \( a_1, a_2, a_3 \) are constants. The inlet flow \( Q_{in} \) and outlet flow \( Q_{out} \) are then solved to be

![Figure 5](image-url)
Fig. 6. The analog model of electrical components for analysis of penile hemodynamics [19]: (a) model configuration, where \( P_{\text{art}} \) is arterial pressure, \( R_c \) is capillary bed resistance, \( R_a \) is resistance of helicine arterioles, \( P_{\text{cm}} \) is cavernosal pressure, \( Q_i \) is infusion flow, \( P_{\text{sm}} \) is pressure developed by smooth muscle tone, \( R_{\text{st}} \) is resistance of uncollapsed subtunical venules, \( C_c \) is cavernosal compliance, \( C_t \) is tunical compliance, \( P_{\text{st}} \) is subtunical pressure, \( P_{\text{cc}} \) is pressure across \( C_c \), \( R_{\text{leak}} \) is resistance of fixed leak path, \( R_{vp} \) is peripheral venous resistance; (b) simulation results for the model’s dynamic behavior in response to a series of step changes in the infusion flow. Smooth muscle pressure was taken as \( P_{\text{sm}} = 0, 0.1, 0.2 \) and \( 0.5 \) mmHg. Resistance of the collapsed subtunical venules was kept constant at \( 0.4 \) mmHg/ml/min. It was demonstrated that pressure increased for a given value of smooth muscle tone, reaching a steady state after only a few seconds. This behavior continued until a critical flow rate was exceeded, at which point the pressure rapidly increased, reflecting the onset of flow limitation.

\[
Q_m = \frac{E_A}{C_A} (e^{2(E_c-P_{\text{cm}})/E_A} - 1) \tag{7}
\]

\[
Q_{\text{out}} = \frac{E_v}{C_v} (1-e^{2(E_c-P_{\text{cm}})/E_v}) \tag{8}
\]

where \( E \) is an elasticity factor of the vessel, \( C \) is constant and the subscripts ‘A’ and ‘V’ denote artery and vein, respectively. For \( Q_m = Q_{\text{out}} \), Eqs. (6)–(8) allow for a graphical identification of the steady state pressure–flow curve during transition from a flaccid to an erect state [Fig. 7(b)]. The observation that flow is continuous during erection supports experimental observations concerning blood oxygenation: the ‘valve-like’ mechanism of the partially collapsed venous vessels never closes completely and, therefore, blood flow maintains the required level of oxygen concentration [20]. For the steady states, i.e., flaccid or erect, flow is limited to a small range, but it increases dramatically during transition from flaccid to erect to fill the corporal spaces.

A recent model of the hemodynamics of erection by Udelson et al. [46] further incorporated the material properties of the cavernosa in terms of its compliance and stiffness. Cavernosal compliance is determined by the properties of the erectile tissue it contains and the stiffness of the surrounding tunic. The cavernosal compliance, \( C_{\text{comp}} \), is varied as a function of the intracavernosal pressure, \( P_c \), at a given time, \( t \), in the erectile process according to the relation

\[
C_{\text{comp}} = \frac{-t(Q_{m0})}{(P_0-P_v)\ln\left(\frac{P-P_v}{P_0-P_v}\right)} \tag{9}
\]

where \( (Q_{m0}) \) is the initial inflow, \( P_0 \) is the initial intracavernosal pressure and \( P_v \) is the venous pressure. Using
the above relation, the cavernosal compliance can be determined for the whole erectile process assuming that the pressure–volume–flow relations are known, for instance, by using Eqs. 6–8 of Barnea. Further analysis of the non-linear material behavior of the penile tissues during erection can be obtained using the tunical distensibility and cavernosal expandability parameters [46]. The tunical distensibility parameter (TD) represents the elastic characteristics of the tunica and is calculated by

$$TD = \frac{V_E}{V_F}$$

(10)

where $V_E$ is the fully erect cavernosal volume and $V_F$ is the flaccid volume. The cavernosal expandability parameter (CE) describes the cavernosal tissue’s expansive behavior at lower cavernosal volumes, $V$, in which the confining effect of the tunica during full erection is not yet active,

$$CE = \frac{1}{P_V - P} \ln \left( \frac{V - V_E}{V_F - V_E} \right)$$

(11)

A common clinical problem is comparing the erectile function of individual patients in terms of penile tumescence and rigidity during erection, in order to describe how their pathology differs from the ‘normal’ condition. However, at the present stage, clinical diagnostic methodologies are lacking standardization procedures and comparative databases for classification of patients with erectile dysfunction. The above-reviewed engineering relations (e.g., those characterizing cavernosal compliance, tunical distensibility and cavernosal expandability) seem to be applicable in clinical research and practice and can be used to produce standard databases for patient evaluation.

4. Computational treatment planning

With the introduction of Viagra, the first effective oral medication for the treatment of erectile dysfunction, many experts predicted a dramatic reduction in the number of surgeries for repairing conditions associated with ED. While it is apparent that less-invasive therapies (e.g., oral, vacuum tumescence devices, etc.) can rectify most of the milder cases of ED, the number of ED cases continues to increase with the aging of the population. Accordingly, the number of surgical interventions aimed to restore erectile function has increased considerably in the last decade [54]. Objective information is frequently needed to evaluate the likelihood of success of a planned surgical intervention. Realistic computational models of the penis are able to provide such a pre-operative evaluation by simulating the structural or hemodynamic effects of the intended surgical treatment. Possible utilizations of models of the penis in the planning process of clinical and surgical interventions for ED are discussed in the following sections.

4.1. Biomechanical evaluation of pathologic erectile conditions

The biomechanical models described in this section provide objective tools for analyzing the dependency of penile erection on the relative contributions of underlying mechanical factors. For example, the resistance to buckling of the erect penis [Eq. (2)] was shown to be dependent upon high values of intracavernosal pressure, high values of the penile aspect ratio, a large flaccid diameter and high cavernosal expandability [Eq. (11)]. Tunical distensibility [Eq. (10)], however, has only a small effect on the axial rigidity of the penis [47]. Inadequate penile rigidity and impotence may occur in some patients solely on the basis of abnormal tissue mechanical properties and/or geometric factors, despite adequate intracavernosal blood pressure values and sufficient blood perfusion. For instance, patients undergoing microvascular arterial bypass surgery may not reach sufficient penile rigidity during erection because of some abnormalities in their penile tissues despite improved blood perfusion. Thus, erectile function of these patients will not be improved by the vascular reconstructive procedure [55]. Bearing this in mind, the development of computational models capable of identifying and isolating the effect of specific mechanical factors that act in erectile dysfunction (i.e., decreased tunical compliance, low intracavernosal pressures etc.) is of major clinical importance.

The analogy of electrical circuits and penile hemodynamics allows different simulations of the hemodynamic effects present in the abnormal alterations of the mechanical characteristics of the penile tissues. For example, the model of Venegas et al. [19] predicted that the primary venocclusive mechanism could still function in pathological conditions of decreased cavernosal compliance, although it will require much higher flow rates to be activated. In these cases, the surgical reduction of certain venous pathways will result in an increase in blood flow through the remaining open paths. If such an increase in flow is strong enough to bring flow through the individual open pathways to levels that exceed a critical flow rate, the venocclusive mechanism will be triggered and the surgical procedure can be considered successful. Conversely, the model predicted that if the venocclusive mechanism is completely non-functioning (e.g., by formation of scar tissue that decreases cavernosal compliance until obstructing any venular collapse), the surgical removal of venous outlet pathways will result in an increased outlet resistance but will still not induce sufficient rigidity such as that obtainable through the flow-limitation mechanism of venocclusion.
Accordingly, when integrated with Doppler ultrasound measurements of penile blood flow, hemodynamic modeling of the penis may be used in the future to predict the amount of closures needed in order to achieve a critical flow rate for activation of the venocclusive mechanism. For the quantitative determination of the penile tissue’s material characteristics which are needed for accurate modeling, new measurement methods will have to be developed. Tissue elastography techniques which employ an ultrasound imaging method to visualize soft tissue’s viscoelastic properties [56] may be of potential use for this purpose.

In addition to tunical/cavernosal compliance, the elastic properties of the supplying and draining blood vessels is also of critical importance for the development of an adequate erection. The model of Barnea [53] shows that corporal pressure is sensitive to both arterial and venous muscle tones during the transition from flaccid to erect states. These findings explain the pathological mechanisms wherein tumescence is obtained without adequate rigidity when the blood vessels are sclerotic and cannot fully relax.

The above findings demonstrate the major role of the vasculature system in achieving and maintaining an adequate erection. An additional critical factor for adequate erection is smooth muscle relaxation which is controlled by the nerves located at the dorsal aspect of the penis [8,9]. Interference of neural activity or obstruction of blood vessels due to structural or functional damage in the dorsal/middle parts of the tunica albuginea, such as in Peyronie’s disease, decreases the capability to achieve and/or maintain a normal erection [57,58]. The mechanisms by which Peyronie’s disease progresses are not well known, and this invariably affects patient management [59]. In order to better understand the development of Peyronie’s disease, Gefen et al. [29] employed their computational model of the penis for analysis of the stresses within its tissues during erection.

The model simulations demonstrated that Peyronie’s plaques may induce intensified stresses around the penile nerves and blood vessels, up to double those in the normal penis (Fig. 8). These elevated stresses may cause a painful sensation of neural origin or ischemia in regions of compressed vascular tissue. Severe penile deformities have been shown to develop even if Peyronie’s plaques develop only around one of the corpora cavernosa, due to the non-homogeneous resistance of the tunica to expansion during erection. By identifying the etiology of ED in Peyronie’s disease and providing the prognosis as related to the plaque tissue’s characteristics and location, this model can be applied clinically as an aid in the planning process of reconstructive surgeries or the insertion of prostheses.

Biomechanical modeling can further be used for presurgical evaluations of specific treatments of ED in patients with different penile pathologies. The model of

![Biomechanical modeling of Peyronie’s disease](image)

Gefen et al. [45] was used to simulate the stress distribution in penile cross-sections following IPP implantation, in order to analyze the contribution of tissue characteristics in normal and diabetic patients, and to gain better understanding of soft tissue loading during IPP-aided erection. Several clinical studies have indicated that severe penile pain following IPP-aided artificial erection is a complication among as many as 20% of the patients who suffer from diabetic neuropathy. This phenomenon may be related to metabolic and microstructural changes observed in diabetic patients (i.e., nonenzymatic glycosylation of several proteins and increased content of collagen fibers) which increase soft tissue stiffness [2,58,60–62]. The computational model was successfully used to analyze the effect of soft tissue stiffening in the progression of diabetes on the structural stresses within the penis during IPP-aided erection.

During IPP-aided erection, structural stresses in the tunica albuginea increase by a factor of ten compared to
the natural erectile stresses (Fig. 9). In diabetic patients following IPP-implantation, structural stresses in the tunica albuginea are further magnified by a factor of two, due to pathologic tissue stiffening. These elevated stresses may irritate the nerves of the tunica albuginea as well as the dorsal nerves, and impose an abnormally large pressure on the vascular bed [45]. Thus, it is reasonable to assume that intensified stresses around the nerves, especially near their roots, may lead to discomfort or even sensations of pain during IPP-obtained erection in diabetic patients. Elevated mechanical stresses may also obstruct blood supply to the penile tissues and cause ischemic pain. Therefore, when implantation of an inflatable device is considered, the effects of the prosthesis–tissue mechanical interaction can be modeled and taken into account in clinical decision-making by considering the simulation results with respect to advantages and disadvantages of other prostheses and pharmaceutical (e.g., Viagra) options.

For example, based on these model predictions, it can be concluded that a semi-rigid implant which transfers less load to the stiffened penile soft tissues may be preferable in diabetic patients.

4.2. Optimization of the design parameters of implantable prostheses

The mechanical interaction between the artificially inflated prosthetic cylinders and the surrounding penile tissues induces mechanical stresses within the penis, which may include sites of localized, highly elevated stresses. Destruction of some penile tissues during a surgical procedure exposes nerve endings on the internal surfaces surrounding the cylinders. Many researchers now agree that under such conditions, these nerve endings develop hypersensitivity (alodynia) and, therefore, their being stimulated by excessive stretching and/or compression of adjacent tissue are perceived by the patient as painful sensations [63,64]. These effects of local intensified stresses could be the underlying causes for penile pain during inflation of the prosthetic cylinders, which was clinically observed to be the most common cause for dissatisfaction with the device [65]. Therefore, the ‘biomechanical compatibility’ of an IPP can be characterized by the stresses developing around primary nerve roots and blood vessels while inflating the IPP cylinders.

Gefen et al. [51] utilized their computational model to analyze penile stresses post-implantation of different IPP types in order to optimize prosthesis design by enabling minimal stress transfer to dorsal blood vessels and nerves. The results (Fig. 10) suggested that intraluminal pressures should be maintained at low levels (about 80 KPa) while cylinder thickness and stiffness should be kept just high enough (approximately 15% of the radius and 1000 MPa, respectively) to eliminate deleterious cylinder–tissue contact stresses. Smaller prosthetic cylinders, i.e., occupying about 45% of the cavernosal space, may be advantageous in terms of reducing dorsal stresses, but lower penile rigidity should be expected. These computational predictions also indicated that circular cylinders may allow greater biomechanical compatibility of the IPP with the structure of the penis than elliptic ones.

4.3. Optimization of surgical positioning of implantable prostheses

An optimizing analysis of the biomechanical compatibility of prosthetic cylinders can be helpful to avoid deleterious physical pressure on the dorsal nerve roots and blood vessels during IPP-aided erection. For this purpose, Gefen et al. [51] analyzed cases of large and small cylinders positioned upwards (toward the dorsal aspect) and downwards (toward the ventral aspect) within the...

Fig. 9. Predicted von Mises stress distribution following IPP implantation [45]: (a) in a non-diabetic versus a diabetic penile cross-section during IPP-aided erection. The indices MX and MN mark the locations of the maximal and minimal stress values, respectively; (b) stresses along dorsal nerves and blood vessels (section A–A) during normal erection in a healthy penis (○) and a diabetic penis (■), and during IPP-aided erection in a normal penis (●) and a diabetic penis (■). IPP=inflatable penile prosthesis.
Fig. 10. Distribution of von Mises stresses during IPP-aided erection [51] for representative cases of dorsally positioned circular cylinders with (a) thick walls (15% of radius) subjected to low intralumenal pressure (600 mmHg); (b) thick walls subjected to high intralumenal pressure (1300 mmHg); (c) thin walls (5% of radius) subjected to low intralumenal pressure; (d) thin walls subjected to high intralumenal pressure. For each of the above cases, three diagrams are shown: the left one is the stress distribution for the hard cylinders ($E=1000$ MPa), the middle one is for the soft cylinders ($E=10$ MPa) and the right one presents curves of stresses (logarithmic scale) along the dorsal vessels and nerves (line $S$) for both the hard (---) and soft (- - -) cylinders. IPP = inflatable penile prosthesis.

corpora cavernosa. The resultant stress distributions due to inflation of the large cylinders showed that positioning of the cylinders close to the ventral aspect of the corpora (only about 4 mm lower than in Fig. 10) reduced stresses at the vicinity of the dorsal nerves by as much as 20–40%. Such positioning, however, also increased the stresses around the urethra. Use of cylinders with a smaller diameter not only effectively eliminated this problem but also minimized the dorsal stresses to negligible levels. It should be borne in mind that small-diameter cylinders will also have relatively less penile rigidity during IPP-aided erection. Insofar as this trade-off relation may have little negative effect on sexual satisfaction while it may be highly efficacious in avoiding the development of penile pains during prosthetic-aided erection, further clinical investigation is warranted.

Current surgical techniques do not allow for highly accurate manipulation of cylinder positioning, mainly because the dilatators used to clear the intracavernosal space to make room for the cylinders during the operation are not designed to provide precise control of the dilatation positioning. However, based on the above simulation results, the surgeon should aim toward the ventral aspect, considering that even minimal lowering of the cylinder’s position would be highly advantageous in terms of decreasing the stresses within the dorsal penile tissues. This and other possible implications of computational modeling of the penis on the surgical techniques and tools for IPP implantation should be experimentally evaluated in animal models in order to test their validity in vivo.

4.4. Toward custom-designed surgical treatment of erectile dysfunction

Surgical applications of computational anatomy reconstruction and biomechanical modeling have been growing rapidly over the last decade thanks to the development of sophisticated and user-friendly systems that allow the clinician to obtain digital imaging data more easily, and to use them for surgical planning. There are now vast opportunities to make use of this advanced technology in the field of urology by employing it to select the most effective surgical intervention for restoring erectile function. Further development of the methodologies reviewed in this paper toward adaptation of structural and hemodynamic models of the penis to anatomical characteristics of specific patients show promise to accomplish the above aims. Indeed, in current clinical practice, geometric reconstructions of numerical models of the penis specifically made for pre-surgical assessment of individual patients are not practically feasible, mainly due to the complexity and excessive consumption of time needed for the development and simulation process. A possible approach to overcome these difficulties of structural modeling (e.g., using the finite element method) involves the use of parametric solid modeling. With this approach, a limited set of anthropometric parameters (e.g., penile length, circumference, cavernosal cross-sectional area, tunical thickness, etc.) will be acquired through medical imaging techniques (e.g., ultrasound or MRI) and then used to generate a custom-made solid model based on a predefined parametric general-purpose model. Subsequently, hemodynamic measurements will be used to adjust the loading system of the model, i.e., the characteristic erectile pressure, and the material characteristics of its components, i.e., tunical/cavernosal compliance.

Successful application of computational tools to assist in the rehabilitation of ED is highly dependent upon acquisition of experimental data that characterize the nonlinear biomechanical properties of the penile biological components, including the viscoelastic behavior of...
the penile skin, tunica albuginea and erectile tissue. After these data become available, a quasi-linear viscoelastic approach could be useful to obtain an even more accurate representation of the structural behavior of the penis. It is believed that in the future, with the progress in the development of computational modeling methods as well as computer hardware and software platforms, the structural and hemodynamic behavior of the penis of will be modeled in specific patients as a routine pre-treatment procedure in the clinical setting, using designated software packages and by applying a systematic adaptation approach.

5. Summary

The study of the erectile process is complex and is based on a wide range of knowledge from a number of different disciplines (e.g., anatomy, physiology, neurology, psychology, structural engineering and fluid mechanics). The following features were studied using biomechanical models: (i) penile rigidity as related to its geometry and tissue characteristics, (ii) hemodynamics of the normal and abnormal penis, (iii) stress–strain distributions in the normal penis as well as in some pathologic erectile conditions (e.g., diabetes and Peyronie’s disease) and (iv) the mechanical interaction between the penile tissues and penile prostheses. Until recently, studies of the erectile function were limited to animal models and clinical observations. The future, however, seems to be very promising for the availability of computer models that will make use of current progress in computational capabilities to allow highly realistic simulations of both the structural and hemodynamic aspects of penile erection. Our understanding of normal erectile function as well as of ED conditions and treatment alternatives can be expected to increase significantly. Finally, computational modeling tools developed for studying conditions of ED should expand clinical and research opportunities by delineating what are the experimental studies required for the establishment of guidelines for specific medical/surgical recommendations.

References


