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Review

The role of tissue biomechanics in the implantation and performance of inflatable penile prostheses: current state of the art and future perspective

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Abstract

Introduction: Erectile dysfunction (ED) affects to some degree approximately 52% of the male population aged 40–70 years. Many men do not respond to, or are precluded from using, pharmaceutical treatments for ED and are therefore advised to consider penile prostheses. Different types of penile prosthesis are available, such as inflatable penile prostheses (IPPs). IPPs consist of a pair of inflatable cylinders inserted into the corpora cavernosa (CC). During inflation/deflation of these cylinders, the CC and other surrounding tissues such as the tunica albuginea (TA) are highly impacted. Therefore, it is critical to understand the mechanics of penile tissues for successful implantation of IPPs and to reduce tissue damage induced by IPPs.
Objectives: We explored the importance of the biomechanics of penile tissues for successful IPP function and reviewed and summarized the most significant studies on penile biomechanics that have been reported to date.
Methods: We performed an extensive literature review of publications on penile biomechanics and IPP implantation.
Results: Indenters have been used to characterize the mechanical behavior of whole penile tissue; however, this technique applied only local deformation, which limited insights into individual tissue components. Although one reported study addressed the mechanical behavior of TA, this investigation did not consider anisotropy, and there is a notable absence of biomechanical studies on CC and CS. This lack of understanding of penile tissue biomechanics has resulted in computational models that use linear-elastic materials, despite soft tissues generally exhibiting hyperelastic behavior. Furthermore, available benchtop/synthetic models do not have tissue properties matched to those of the human penis, limiting the scope of these models for use as preclinical testbeds for IPP testing.
Conclusion: Improved understanding of penile tissue biomechanics would assist the development of realistic benchtop/synthetic and computational models enabling the long-term performance of IPPs to be better assessed.

Keywords: erectile dysfunction; inflatable penile prostheses; penile biomechanics; animal models; benchtop/synthetic models; computational model; IPP complications.

Introduction

Erectile dysfunction (ED) is a commonly undiagnosed and undertreated male disease whereby the patient suffers from the inability to achieve or maintain a satisfactory penile erection during intercourse.[1] Approximately 52% of men in the age range of 40 to 70 years suffer from some degree of ED,[2] while for men older than 70 years the rate of ED ranges from 50% to 100%.[3] Erectile dysfunction may lead to mental anguish and depression in patients, with reduced quality of life for both the patients and their partners. Several treatments exist, including oral pharmacotherapy, intracavernous injection (intraurethral pellets and cream), low-intensity shock-wave therapy and vacuum erection devices, among others.[4] However, patients with underlying diseases (such as diabetes, vascular disease, or previous pelvic trauma/injury) might not respond to pharmacotherapies, necessitating the option of permanent surgical implantation.[4] Different types of penile implants are available; namely malleable penile prostheses (MPPs) and 2- and 3-piece inflatable penile prostheses (IPPs). All of these implants consist of a pair of cylinders inserted into the corpora cavernosa, while the 2- and 3-piece IPPs are composed of additional elements: a pump and both a pump and reservoir, respectively.

Penile anatomy

The penis is composed of 3 cylindrical shafts: a pair of corpora cavernosa (CC) and a corpus spongiosum (CS) along the dorsal and ventral penis, respectively. The CS originates from

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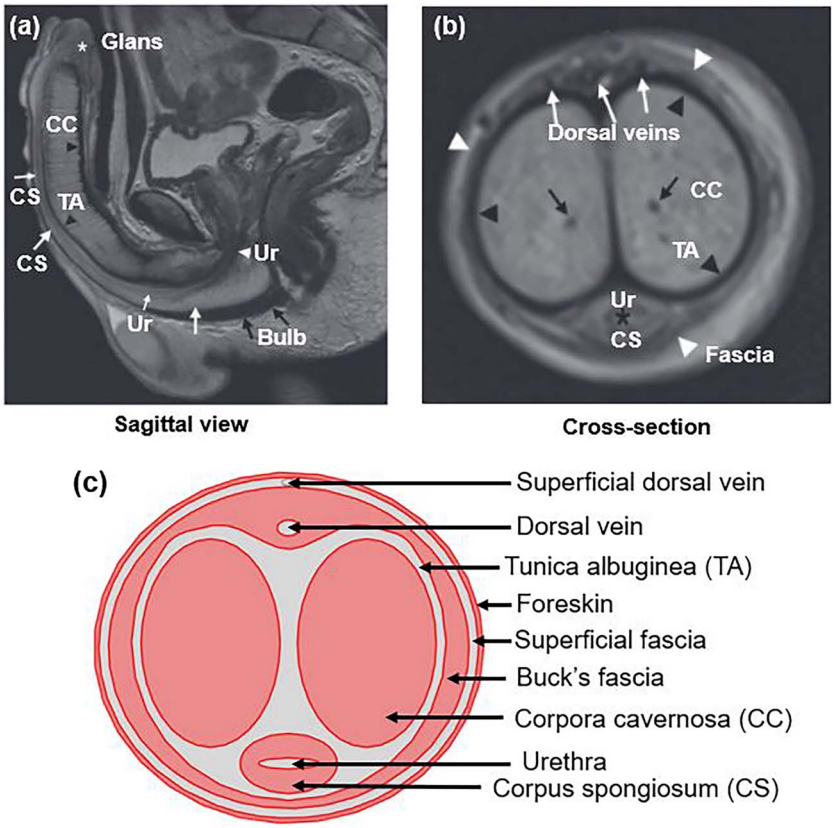

Figure 1. Penile anatomy: Sagittal (a) and cross-sectional (b) views (where).[5] (c) Schematic of the cross-section of the penis. CC, corpora cavernosa; CS, corpus spongiosum; TA, tunica albuginea; Ur, urethra.

the penile bulb (proximal penis) and runs along the midline of the penis to the distal penis or glans (Figure 1a).[5–7] Corpus spongiosum is a spongy tissue that encompasses the urethra. The cavernosa diverge at the penile root to form the crura, which adhere to the ischial tuberosities.[8] Corpus spongiosum and CC contribute to the erection,[9] with the latter being partially entrapped by the skeletal muscles.[7]

The cross-sectional view of the penis (Figure 1b and 1c) shows CC being surrounded by the fibrous TA layer,[5,8] which contains a high percentage of collagen fibers.[10] A superficial and less dense fibrous sheath (Buck's fascia) envelops the TA,[8] which resembles the superficial and deep fascia of the extracellular matrix. The glans is covered by the prepuce (also known as the foreskin), which is rich in free nerve endings. The urethral tissues are surrounded by a spongy mass of CS.[5]

The assessment of penile dimensions is important for andrological evaluation and penile reconstruction. The most relevant dimensions during the treatment of erectile dysfunction (ED) include penile length and girth. Previous studies have investigated the changes in these penile dimensions which can affect the quality of life in diabetic patients.[11] The measurements (length and girth/circumference) of penis are performed in the flaccid, stretched, and erect stages.[11-13]

History and development of IPPs

The first attempt in the development of a penile prosthesis was made by Borgoras in 1936 using rib cartilage, which was resorbed into the body over time.[14] The first artificial acrylic penile prosthesis was developed in 1952 by Goodwin and Scott and was later (in 1964) modified to a silicone-based penile implant by Lash and colleagues.[15] These early inventions in the field of erectile restoration paved the way for the later evolution of the IPPs. The history of the evolution of the IPPs is illustrated in Figure 2a.

In 1973, Scott et al, succeeded in fabricating the 3-piece IPP, offering functional similarity during both the erect and flaccid state.[19] This type of IPP consists of a pair of cylinders, a pump (for inflation and deflation of the cylinder), and a reservoir (to store the saline fluid), which are implanted in the penile corporal bodies, the scrotum, and the abdomen or abdominal wall, respectively (see Figure 2b). A 2-piece "self-contained" IPP, manufactured by American Medical Systems (AMS) in 1985, consisted of a pair of cylinders (placed in the corporal bodies) and a pump (placed in the scrotum, Figure 2b) and was especially useful for patients who had undergone multiple abdominal surgeries.[16] Another relevant type of penile implant is the malleable penile prosthesis (MPP) which consists of 2 semi-rigid cylinders which are inserted in the corpora cavernosa. First developed in 1975, the early MPPs were composed of a semirigid rod,[20] while Jonas and Jacobi were the first to introduce silicone cylinders with a twisted core.[21] This device showed a satisfactory result and was operated manually to provide an erection (similar to a "goose-neck" device). In 2003, AMS improved the MPP by adding segmented articulating polyethylene rods (Dura II) for better range of motion and rigidity.[22] Further developments included increased distal shafts and customized products with various cylinder lengths and diameters (Coloplast). Later, in 2009, AMS introduced MPPs with alternating titanium

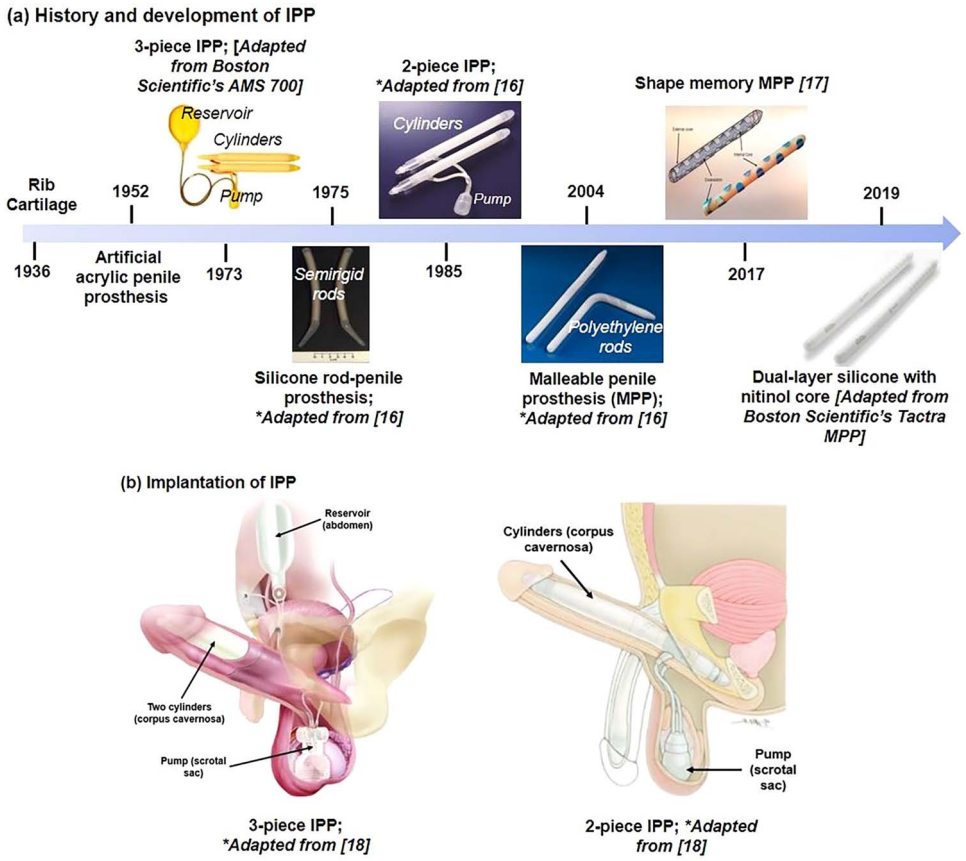

Figure 2. (a) Development of IPPs over the years[16,17] and (b) positioning of the 3- and 2-piece IPP in the pelvis.[18]

and polyethylene segments for enhanced concealment. The Tactra MPP was launched by Boston Scientific in 2019 and consists of a dual–silicone layer cylinder with nitinol core for better durability. Recently, researchers have been trying to develop shape-memory "touchless" malleable penile prostheses (from nickel-titanium), which uses temperatures above normal physiological temperature (42°C)[17] or magnetic induction[23] for activation. Shape-memory alloys can change their shapes when they are subjected to temperature or magnetic field effects and come back to their original form when these environmental factors are removed. Therefore, the shape-memory penile prosthesis can imitate the flaccid and erect state of the human penis.

Several advancements have been introduced to innovate the design of the different components of the IPPs and MPPs over the years. The world-leading manufacturers of IPPs, Coloplast and AMS/Boston Scientific, have reported overall patient satisfaction of about 90% to 95%,[24] while still striving to further improve IPP components.

Post-IPP implantation complications

IPP implantation is generally a safe procedure having high success rates for both user and partner satisfaction. Post-implantation complication rates are usually low, with 0.46%–5.3% of cases due to infection,[25] 0.2%–3.6% of patients presenting with bleeding/hematoma,[26] and 0.8%–3.1% of outcomes resulting in mechanical failure.[27]

Infections occurring from medical devices are a major issue causing medical complications and physiological trauma.[28] Computed tomography (CT) scans have exhibited severe skin thickening (irregularity and ulceration), tissue swelling, and fat stranding,[18] most often requiring surgical removal of the device. As such, antibiotic-coated IPPs were developed which reduced the transmission of infections compared to non-coated IPPs.[29] Postoperative hematomas (accumulation of blood with fat stranding, which are usually mild and generally settle spontaneously) have been observed in patients within 2 weeks post-surgery.[18,30] Hematoma formation can be prevented by use of drains post-operatively and compression dressings.

Cylinder complications may lead to buckling within intact TA, whereas perforation/erosion results in herniation, disrupting the TA.[31] Migration of cylinders can occur in medial and anterior-posterior directions, the latter being associated with the asymmetric position of the rear tip extenders.[18] Similar complications of erosion, migration/malposition, and hematomas have been observed in patients using pumps and reservoirs.[18,31,32] Another type of failure – system leakage—is generally observed years after device implantation and might occur due to cracking, rupturing, or failure of the connector tubes.[18] The complications related to post-IPP implantation are shown in Figure 3.

Better understanding of the complications of post-IPP implantation from a biomechanics perspective would be highly beneficial for engineers and would enable design changes to reduce tissue damage over time. Despite the fact that post-IPP complications have been reported by several clinicians, as yet, no computational or benchtop model exists which would be capable of capturing the tissue damage mechanics responsible for these complications or failures.

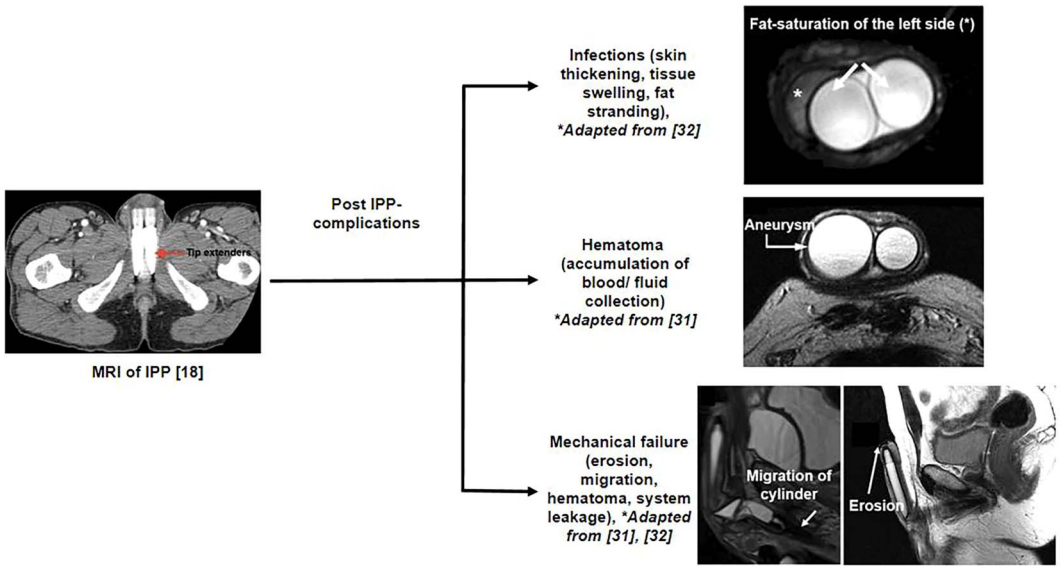

Figure 3. Post-operative complications.[18,31,32]

Such models would clearly aid manufacturers and clinicians in minimizing the associated tissue damage, likely reducing the effect of hematomas and erosion from implantation and device failures.

Biomechanics of penile tissues

Biomechanics is the study of the movement or structure of biological tissues from a mechanical perspective. In other words, biomechanics employs mechanical theories/approaches to describe the responses of biological tissues to mechanical loading or any kind of structural stimulation. Having knowledge of the mechanics of biological tissues can provide key insights into the interactions between different components inside organs, the interpretation of pathological studies, the relationships between structures and their functions, and better predictions of tissue strength, lifetime, etc. This section focuses on the biomechanics of penile tissue, including various measuring techniques and quantitative values that were obtained during whole-penis testing and its segregated tissue components (CC, CS, TA, fascial layers, urethra, and foreskin) which are impacted by IPP implantation.

Limited work is reported on the biomechanics of the whole penis and its different tissue components. The biomechanics (axial rigidity) of an erect penis during vaginal intromission was investigated with different commercially available IPPs.[33] The circumferential expansion of IPPs creates higher resistance during biomechanical testing, which is important when choosing a penile implant for a patient.[34] Another study showed the pressure-dependent rigidity of different IPPs during expansion and their overall longitudinal and horizontal resistance.[35] Ex vivo experimentation on different commercially available IPP cylinders under different loading conditions is essential for a physician and patient to decide on the type of cylinders.[36] However, all these studies did not consider the individual tissue mechanics, or the tissue damage linked to the usage of these devices but were limited to exploring the levels of stress/pressure generated to the IPP cylinders during expansions. Timm et al.,[37] designed a penile external fixator with four indenter tips to record the applied force along with the respective displacements. The applied force and displacement on the tissue varied in the range 0.7–1.1 N and 7–10 mm, respectively, assisting in the development of a finite element model (FEM) for urinary incontinence. The stiffness of the whole penis was estimated at 0.014 MPa from the experiments and use of an inverse finite-element technique. While this is the first mechanical characterization of the whole penis, the indenter tips created very localized tissue deformation and hence generated only limited knowledge regarding the whole organ tissue characterization. A finite-element (FE) study by Levy et al.,[38] investigated tissue deformation in the whole penis to explore the effect of various urinary incontinence device designs during urethral compression. The study focused on developing incontinence devices to prevent urine leakage in males.

Corpus cavernosa, a pair of cylindrical spongy erectile tissues, are a major part of penile tissue that is affected during IPP implantation. Histological analysis has shown the presence of trabeculae separated by collagen, connective tissues and smooth muscle cells (SMCs).[39,40] Some researchers used shear wave elastography (SWE) to determine the stiffness of corpora cavernosa.[41,42] The same technology also demonstrated an increase in the stiffness of CC with increasing age.[43] The study by Zhang et al., showed no significant differences between the stiffness of the left and right CC.[44] Recently, researchers developed a 2D penile ultrasound vibro-elastography system to quantify the stiffness of penile tissues and the associated cardiovascular risks for patients with ED or Peyronie's disease (PD).[45] The stiffness of the cavernosum for healthy participants ranged from 18.5–25.2 kPa[43,44] while a much lower stiffness (approximately 2–12 kPa) was observed in case of patients suffering from ED/PD.[45] CS is a spongy tissue composed of collagen, elastin, and muscle cells, which encompasses the urethral tissue.[46] Ultrasound vibro-elastography has also been used to quantify the stiffness of CS, but elastography does not provide the force-displacement curves needed to extract the full range of material properties.[41] Although these techniques have been used to measure the stiffness of CC and CS, full characterization of the mechanical behavior of the tissues is still lacking for the range of deformations for IPP implantation.

Surrounding the corpora cavernosa and spongiosum is a thick bilayered fibrous layer (ranging from 1.7 to 3.3 mm

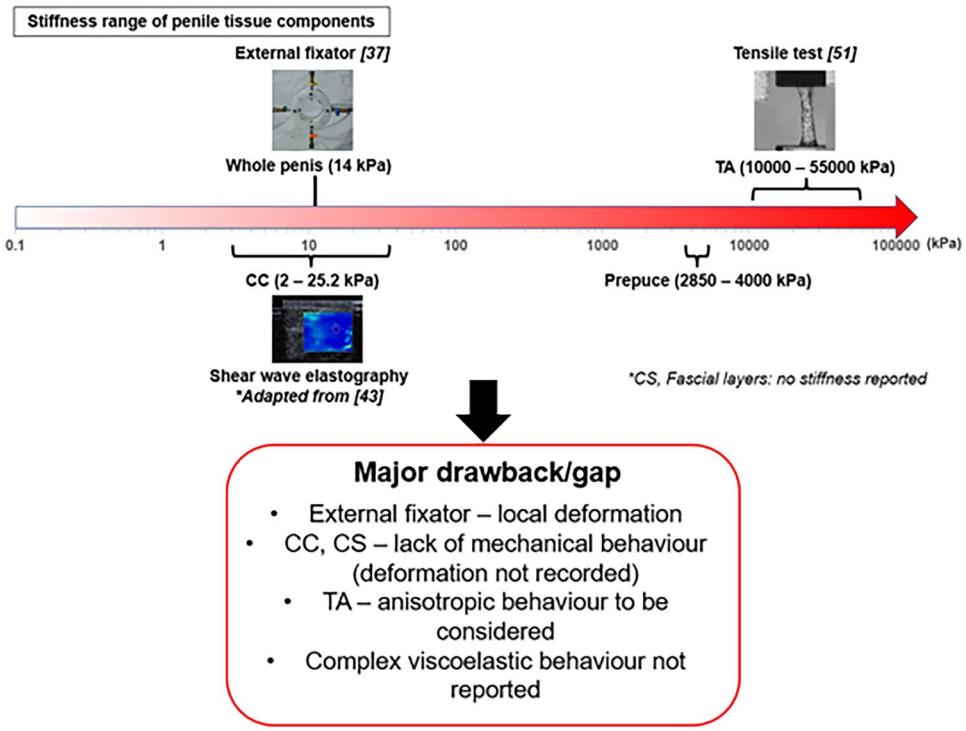

Figure 4. The range of stiffness of penile tissues.[37,43,51] The tensile/compressive strength and strain generation are important parameters to fully understand penile mechanics, yet these are not reported in most studies. The major drawbacks are also highlighted.

in thickness) called tunica albuginea.[8,10] It contains a very high percentage of collagen fibers and a low level of elastin,[10] significantly contributing to the load-bearing component of the penis.[47]

Most of studies on TA have focused on molecular pathologies such as PD.[48-50] Although some studies quantified the biomechanical properties of TA (stiffness: 100 MPa and tensile strength: 0.001–0.01 MPa), these studies were performed with tensiometers which did not report the levels of strain generation.[10] Recently, Brady et al. [51] estimated the mechanical properties (tensile strength (2–4.5 MPa) and strain at ultimate tensile strength (20%–25%) of TA specimens with a calcification of 0–28% volume ratio. A dramatic difference in the properties, especially modulus (11.8–55.3 MPa) and failure mechanism (measured using digital image correlation), was observed which was attributed to the level of calcification and irregular mineralization of the specimens, respectively. This study provided considerable new insights into the tissue mechanics of the TA, yet, the tissue anisotropy was not considered. Furthermore, the irregular specimen geometry (neither dog-bone nor rectangular strips) used during the tensile tests might have resulted in a wide variation in the results reported.

Other tissue components include fascial layers and prepuce (foreskin). Fascia is a soft connective tissue enveloping the organs, bones and muscles, thus forming a connective network throughout the body. Fascia is subdivided into 3 different categories—superficial, deep and epimysium—of which the latter is not present in the penis.[8] Several studies have quantified the mechanics of fascial layers of different organs; however, the mechanics of penile fascia has not yet been reported. A wide variation in the mechanical behavior of fascia from different organs exists. While nasal fascia is soft with stiffness of approximately 1 MPa,[52] thigh fascia is highly anisotropic with stiffness ranges from 3.2–41.9 MPa to 71.6–275.9 MPa depending on the fibrillar orientation.[53] Considering the high variability of the stiffness of fascial layers based on their anatomical position, it is important to investigate the mechanical behavior of penile fascial layers for a better understanding of the whole penile tissue response to mechanical loading.[52]

The prepuce is a highly vascularized and densely innervated bilayer tissue occupying the distal end of the skin of the penis. Despite the rigorous biomechanical forces it experiences during intercourse, mechanical characterization of this tissue is rather limited. The mean (±SD) values of Young's modulus of fresh and decellularized human foreskin have been reported to be approximately 2.85 (±0.28) MPa and 3.01 (±1.26) MPa, respectively.[54] This study did not consider the effect of anisotropy or strain rate which may have a profound effect on human skin.[55,56]

It is evident that there is generally a lack of knowledge on the mechanics of the penile tissues. Indentation has been used to predict the mechanical response of the whole penis, with a view to ascertaining the stiffness of the different penile tissues and their interaction, but the highly localized deformation of the tissue precludes this. In addition, the degree of tissue anisotropy in CS, CC, and TA has been completely overlooked. Furthermore, the complex viscoelastic response of penile tissues needs to be quantified to better understand the tissue mechanics relevant to the design of preclinical testbeds for IPPs/MPPs. In addition, understanding penile mechanics would aid in detection of penile pathologies. The range of stiffness of penile tissues is presented in Figure 4. The mechanical response of the major tissues—CC, CS and TA—are either estimated by direct measurements (tensile test, external fixator) or imaging techniques (SWE). The gap in the knowledge of penile mechanics severely limits the development of both computational and benchtop models which can be used as pre-clinical testbeds for future generation IPPs.

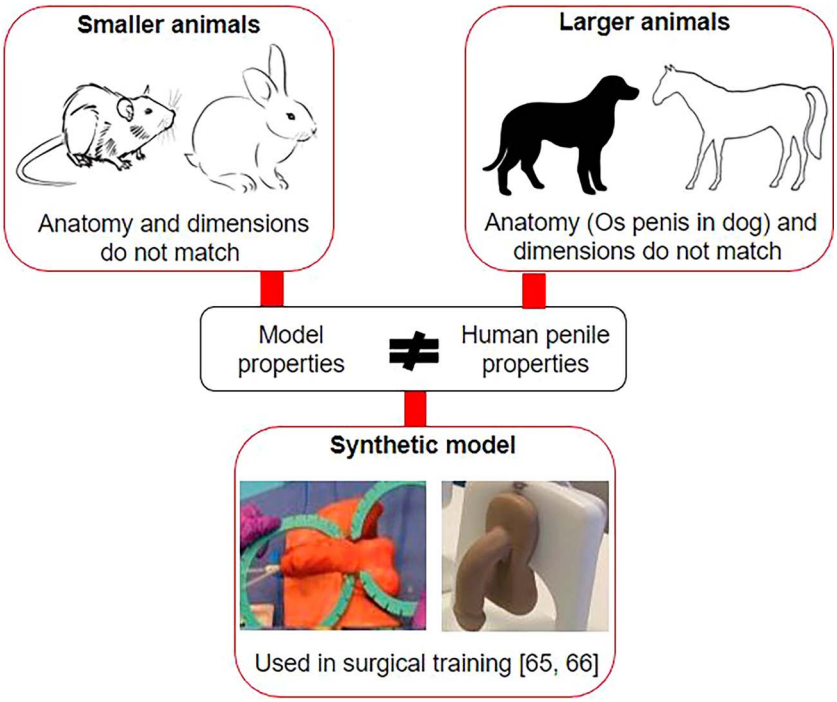

Figure 5. The available animal and synthetic models do not have mechanical properties equivalent to the human penis. Therefore, these models are not ideal for preclinical testbeds for IPPs to understand the impact of the pressure generated during inflation/deflation.[65,66]

Progress in modelling

Animal/synthetic model

Animal models used as benchtop models provide a good estimation about the operation of a medical device in vivo and are also useful for surgical training. It is worth noting, however, that the assessment of ED in any model has generally been limited to the recording of the intracavernosal pressure (ICP). Therefore, the effects of both electrical stimulation and pharmacological drugs on ICP have been studied, especially on freely moving animals,[57,58] yet any associated tissue damage has been overlooked. Some of the animals widely used for the treatment of ED include rats, mice, and rabbits.[59] However, due to the mismatch in the anatomical features and dimensions of the penis in these animals compared to human beings, these animals are unsuitable for biomechanical preclinical testbeds of IPPs.

Some limited studies have considered larger animals such as the dog and bull for urological treatments. The dog model was employed for penile girth[60] and urethral[61] augmentation, which showed promising post-operative outcomes. Nevertheless, a significantly different penile anatomy (presence of bony or "os penis") limits the use of IPP implantation in the dog model. Interestingly, a bullock cadaver model has been used for intracavernosal (IC) therapies for ED treatment via needle-free injection.[62] Still, large domestic animal models such as horse and bullock would not be suitable as an IPP implantation model, as the penile dimensions do not match the human penis. As such, it is evident that no current animal model exists having anatomical features and dimensions analogous to the human penis.

In the light of the limited suitability of animal models, cadaveric or synthetic models should be employed. Some researchers used cadaveric models to demonstrate the treatments of ED[62,63]; however, their high cost, availability, ethical concerns, and the risk of transferable disease limits their applicability. Commercially available synthetic models have often been used to understand the key pinch strength involved in inflation/deflation of IPP devices for older patients.[64,65] Recently, Renterghem and Ghazi designed a penile model from polyvinyl alcohol (PVA) polymer by varying the viscosity of the powder mix and freeze–thaw cycles. This model was processed to create a male genital structure which was layered around a 3D-printed pelvic bone.[66] This model is suitable as a surgical tool, but it still does not replicate the biomechanical properties of the various penile tissues. The absence of matched tissue properties in the model would limit the accuracy of any results obtained during inflation/deflation (pressure-related) of IPPs.

Consequently, there is a clear lack of availability of a penile model which has biomechanical properties similar to human penile tissues. The currently used animal and synthetic models (Figure 5) would not be the best for understanding the tissue stress or damage developed during the IPP cycling process. The growing interest in improved outcomes with male urological devices for treating ED demands the development of benchtop models capable of replicating human penile properties.

Computational modeling

Experimental analysis can determine tissue properties; however, a proper understanding of the tissue mechanics on implantation of medical devices is crucial to estimate potential tissue damage. A biomechanical computational model can be used to estimate tissue damage under the influence of various loading conditions. In this section, the progress on computational modelling of the penis and relevant devices is reviewed.

Udelson and team compared the structural rigidity of the penis to straight columns,[67] according to which they modeled

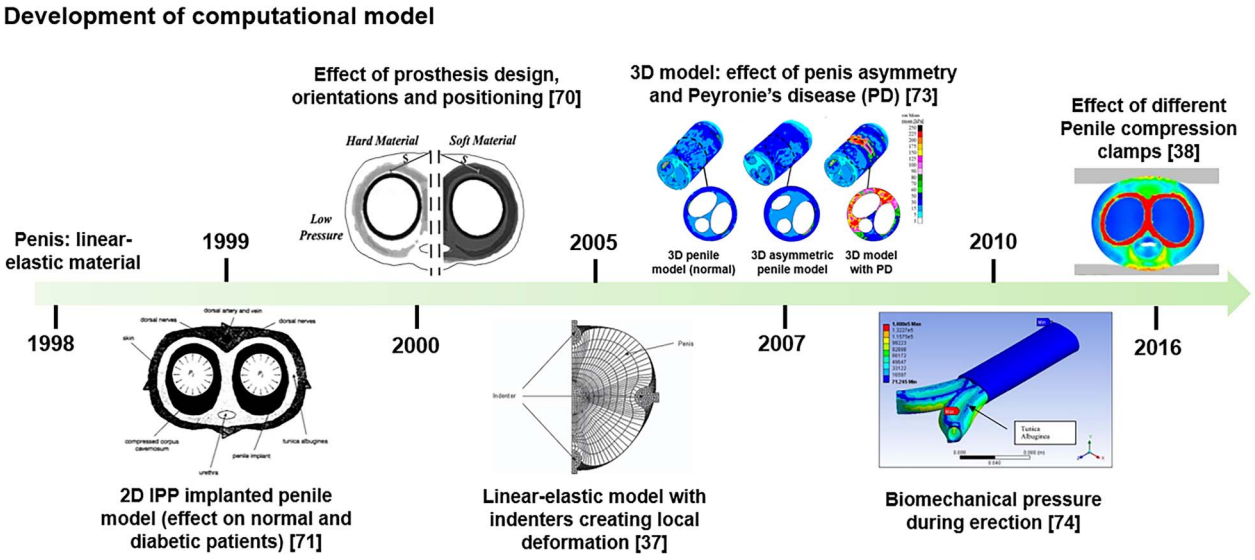

Figure 6. The state-of-the-art penile models. 2D and 3D penile models developed to date use linear-elastic tissue properties. Initial 2D models were developed for both the healthy and diseased penis with and without IPPs[71] while others demonstrated the effect of soft and hard IPP materials.[70] The later 3D models showed the generation of von Mises stress of different penile models during erection.[73,74]

it as a cylinder composed of an isotropic, homogenous, and linear elastic material.[68] Following this study, Chen et al. developed a penis model with "blood-filled circular cylinders" where TA (represented as cylindrical walls) contributed to the load-bearing of the organ.[69] In that study the authors also considered the penile tissues to be isotropic and linear-elastic. Another study developed penile models beneficial for understanding biomechanical compatibility and surgical decisions while selecting IPP cylinders for implantation (i.e. cylinder positioning and alignment).[70] An isotropic, homogenous, and linear-elastic 2D penile model with an idealized anatomical geometry was modelled by Gefen et al., which showed the various different penile tissue components.[71] Furthermore, that study also demonstrated the impact of IPPs on the internal stresses generated in normal and diabetic patients. In Zhu et al., tissue characterization data obtained from various participants was used to develop a penis model to better understand the effect of geometry for urinary continence,[37] and again, linear elasticity was assumed for the soft tissues. Another study by Levy et al. also focused on the different device designs for treatment of urinary incontinence, considering the TA and skin as orthotropic materials, and the fat, CC, and CS as isotropic materials, and all as linear elastic.[38] Orthotropy in TA was discussed by Kelly in 1999, where the presence of longitudinal and transverse collagen fiber directions supports TA being an orthotropic material,[72] and skin is well known to be anisotropic.[55] The results in the Levy et al. study suggest that a minor misalignment in the penile compression clamps (PCCs) would generate increased tissue strains and skin stresses due to misuse of the device and asymmetries of the human penis. A 3D-penile model with similar material properties (TA and skin as orthotropic-elastic materials; CC and CS as isotropic-elastic materials) was developed to predict the stress distribution within various penile tissue components for asymmetric and PD cases.[73] A study of a 2- versus 1-compartment 3D penile model showed that the former is better for use in understanding the biomechanical properties of the penis during erection due to lateral forces acting on the TA.[74]

In summary, the literature presents several studies focused on developing a realistic penile model (see Figure 6), yet none have included consideration the penile tissues as hyperelastic anisotropic materials (despite soft tissues generally being considered hyperelastic). To date, penile components have been modeled as isotropic-linear-elastic or orthotropic-linear-elastic materials. In addition, these studies have generally considered idealized geometrical models and not used medical imaging, such as magnetic resonance imaging (MRI) or computing technology (CT)-based images to establish the best anatomical geometry of the organ. Furthermore, the complex viscoelastic properties of penile tissue have not been measured experimentally, and thus it has not been possible to implement them into computational models.

Conclusions and future perspective

IPPs have been used by patients suffering from ED for decades, with only limited improvement in the design and mechanism of operation since their original launch. Designing an ideal IPP with good long-term performance requires preclinical testing of these devices in both ex vivo and in silico environments. Testing in these environments would help to predict levels of the internal tissue stresses and strains (during inflation/deflation of IPPs), and help to predict the degree of tissue remodeling likely in the penile tissues post implantation. Understanding the various penile tissue properties is important but even more so is the way they work in concert with one another as the penis transitions between the flaccid and erect state, both the natural penis and those with an IPP implanted. Focus on these properties is important as to-date very little knowledge exists on the biomechanics of penile tissues, especially with an IPP in place.

Creating multiple test bed approaches, such as benchtop and in silico models, can enable an understanding of the role various penile tissues play in the erect and flaccid behavior of the penis. Benchtop models can enable evaluation of a given solution in a physical manner, while the computer modeling

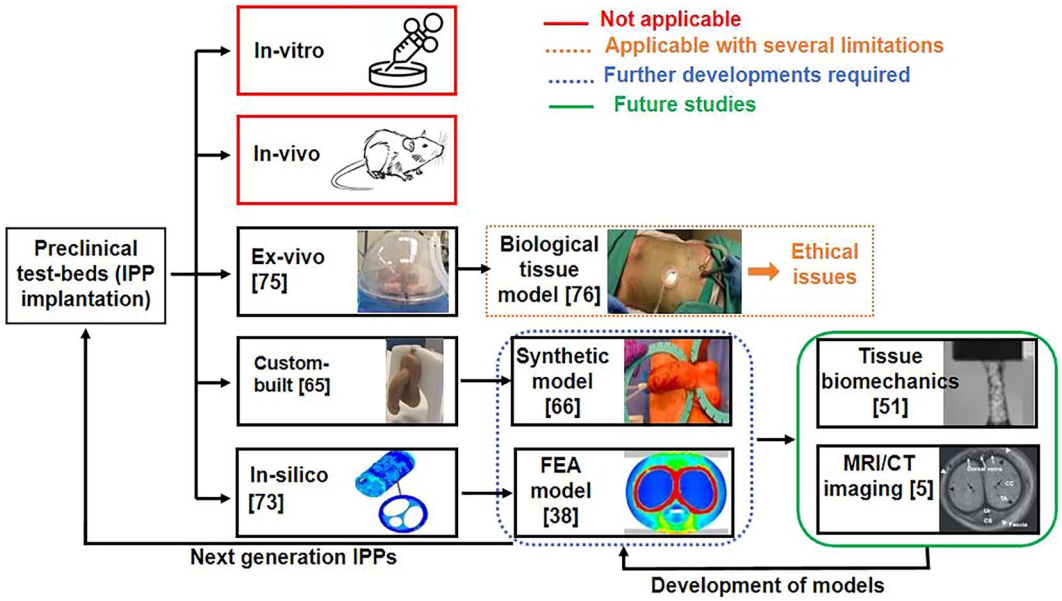

Figure 7. Future directions that would assist in improving IPPs for next-generation applications.[5,38,51,66,73,75,76]

can enable hypothesis testing and/or parameter variation studies of the tissues or devices to quickly evaluate a large range of parameters (device or anatomical).

To build both the benchtop and computational models, a clear understanding of the experimental tissue mechanics is required. Using unrealistic material parameters to develop these models does not help in estimating the mechanical performance of IPP during implantation. Therefore, knowledge and understanding of penile tissue properties in important for creating these models. Interestingly, the experimental mechanics of penile tissues are relatively unexplored—to our knowledge no deformation analysis has been performed for the CC, CS, prepuce, or fascial layers. Using indentation techniques to measure the mechanics of the whole penis has produced only local tissue deformation, hence, a more suitable testing protocol should be considered. While the material properties of TA were recently studied, the study did not explore the effects of tissue anisotropy or strain rate. The determination of tissue damage during IPP implantation using computational models, however, requires analysis of the time-dependent viscoelastic properties of these tissues.

As discussed, animal models used for treatment of ED do not replicate the dimensions (geometries) and anatomy of human penis. Few attempts have been made to develop synthetic/benchtop penile models that match penile tissue properties, while some simplified models do exist which match the anatomy. One of the best ways to detect the damage in the tissues from the implantation of a medical device is the use of FE (computational) models. To date, researchers have developed penile models considering the tissues to be either linear-elastic or transverse-orthotropic elastic materials, which do not fully replicate the soft tissue behavior. The clear lack of experimental penile tissue properties to inform the computational models severely limits their implementation. Additionally, none of the existing models are based on medical imaging data.

Future research focused on exploring experimental penile tissue mechanics needs the development of accurate preclinical test beds. Generally, medical devices are tested on in-vitro, in-vivo, ex-vivo, custom-built, and in silico models (Figure 7). However, in-vitro and in vivo preclinical testing of IPPs would not be possible due to their dimensions and the unsuitable anatomy of animal models. Ex vivo models produced from biological tissues generally offer several restrictions, such as ethical issues and storage and transfer of infectious disease to avoid mishandling. Therefore, custom-built and in silico (computational) models are the best preclinical testbeds for IPP testing. Successful implementation of these models requires knowledge of tissue mechanics (from experiments) and medical imaging (from MRI/CT scans) from human IPP patients. This would enable the creation of benchtop and computational models with mechanical properties and anatomy similar to that of the human penis, delivering a platform for design improvements of IPPs.

These realistic preclinical test beds could offer a means to evaluate IPPs and other implantable solutions for patients suffering from ED by providing a platform (1) to test the safety and efficacy of the devices, i.e., to ascertain if the devices cause acute or chronic damage to the surrounding penile tissues in the short- or long term, and (2) to develop device solutions that better mimic the healthy human penis, both flaccid and erect. These steps would generate safer implants that would be developed to reflect native biomechanical behavior, as well as providing an implant with more natural performance and feeling, ultimately improving both clinical outcomes and patient satisfaction.

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Supplementary material

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References

1. Lizza EF, Rosen RC. Definition and classification of erectile dysfunction: report of the nomenclature committee of the international society of impotence research. *Int J Impot Res*. 1999;**11**:141–143.
2. Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and psychosocial correlates: results of the Massachusetts male aging study. *J Urol*. 1994;**151**(1):54–61.
3. Shamloul R, Ghanem H. Erectile dysfunction. *Lancet*. 2013;**381**(9861):153–165.
4. Salonia A, Bettocchi C, Boeri L, *et al*. European association of urology guidelines on sexual and reproductive health—2021 update: male sexual dysfunction. *Eur Urol*. 2021;**80**(3):333–357.
5. Kirkham A. MRI of the penis. *Br J Radiol*. 2012;**85**(1):S86–S93.
6. Goldstein AM, Padma-Nathan H. The microarchitecture of the intracavernosal smooth muscle and the cavernosal fibrous skeleton. *J Urol*. 1990;**144**(5):1144–1146.
7. Hsu GL, Hsieh CH, Wen HS, *et al*. Anatomy of the human penis: the relationship of the architecture between skeletal and smooth muscles. *J Androl*. 2004;**25**(3):426–431.
8. Tu LH, Spektor M, Ferrante M, Mathur M. MRI of the penis: indications, anatomy, and pathology. *Curr Probl Diagn Radiol*. 2020;**49**(1):54–63.
9. Hsu GL. Hypothesis of human penile anatomy, erection hemodynamics and their clinical applications. *Asian J Androl*. 2006;**8**(2):225–234.
10. Bitsch M, Kromann-Andersen B, Schou J, Sjøntoft E. The elasticity and the tensile strength of tunica albuginea of the corpora cavernosa. *J Urol*. 1990;**143**(3):642–645.
11. Salama N. Penile dimensions of diabetic and nondiabetic men with erectile dysfunction: a case-control study. *Am J Mens Health*. 2018;**12**(3):514–523.
12. Blecher GA, Vukina J, Ralph DJ. Penile dimensions: what are surgeons measuring? *Int J Impot Res*. 2019;**31**(6):444–450.
13. Chen XB, Li RX, Yang HN, Dai JC. A comprehensive, prospective study of penile dimensions in Chinese men of multiple ethnicities. *Int J Impot Res*. 2014;**26**(5):172–176.
14. Chung E. Penile prosthesis implant: scientific advances and technological innovations over the last four decades. *Transl Androl Urol*. 2017;**6**(1):37–45.
15. Gee WF. A history of surgical treatment of impotence. *Urol*. 1975;**5**(3):401–405.
16. Barnard JT, Cakir OO, Ralph D, Yafi FA. Technological advances in penile implant surgery. *J Sex Med*. 2021;**18**(7):1158–1166.
17. Le B, McVary K, McKenna K, Colombo A. A novel thermal-activated shape memory penile prosthesis: comparative mechanical testing. *Urol*. 2017;**99**:136–141.
18. Chou HL, Mohsen NA, Garber BB, Feldstein DC. CT imaging of inflatable penile prosthesis complications: a pictorial essay. *Abdom Radiol*. 2019;**44**(2):739–748.
19. Scott FB, Bradley WE, Timm GW. Management of erectile impotence use of implantable inflatable prosthesis. *Urol*. 1973;**2**(1):80–82.
20. Small MP. The Small-Carrion penile prosthesis: surgical implant for the management of impotence. *Sex Disabil*. 1978;**1**(4):282–291.
21. Rowe PH, Royle MG. Use of Jonas silicon-silver prosthesis in erectile impotence. *J R Soc Med*. 1983;**76**(12):1019–1022.
22. Sadeghi-Nejad H, Fam M. Penile prosthesis surgery in the management of erectile dysfunction. *Arab J Urol*. 2013;**11**(3):245–253.
23. Le BV, McVary KT, McKenna K, Colombo A. Use of magnetic induction to activate a 'touchless' shape memory alloy implantable penile prosthesis. *J Sex Med*. 2019;**16**(4):596–601.
24. Bernal RM, Henry GD. Contemporary patient satisfaction rates for three-piece inflatable penile prostheses. *Adv Urol*. 2012;**2012**:10–15.
25. Eid JF, Wilson SK, Cleves M, Salem EA. Coated implants and 'no touch' surgical technique decreases risk of infection in inflatable penile prosthesis implantation to 0.46%. *Urol*. 2012;**79**(6):1310–1316.
26. O'Rourke TK Jr, Erbella A, Zhang Y, Wosnitzer MS. Prevention, identification, and management of post-operative penile implant complications of infection, hematoma, and device malfunction. *Transl Androl Urol*. 2017;**6**(S5):S832.
27. Wilson SK, Cleves MA, Delk JR. Comparison of mechanical reliability of original and enhanced mentor∗ alpha I penile prosthesis. *J Urol*. 1999;**162**(3):715–718.
28. Weinstein RA, Darouiche RO. Device-associated infections: a macroproblem that starts with microadherence. *Clin Infect Dis*. 2001;**33**(9):1567–1572.
29. Wilson SK, Zumbe J, Henry GD, Salem EA, Delk JR, Cleves MA. Infection reduction using antibiotic-coated inflatable penile prosthesis. *Urol*. 2007;**70**(2):337–340.
30. Garber BB, Bickell M. Delayed postoperative hematoma formation after inflatable penile prosthesis implantation. *J Sex Med*. 2015;**12**(1):265–269.
31. Hartman RP, Kawashima A, Takahashi N, LeRoy AJ, King BF. Inflatable penile prosthesis (IPP): diagnosis of complication. *Abdom Radiol*. 2016;**41**(6):1187–1196.
32. Abualruz AR, O'Malley R, Ponnatapura J, *et al*. MRI of common penile pathologies and penile prostheses. *Abdom. Radiol*. 2020;**45**(9):2825–2839.
33. Madiraju SK, Wallen JJ, Rydelek SP, Carrion RE, Perito PE, Hakky TS. Biomechanical studies of the inflatable penile prosthesis: a review. *Sex Med Rev*. 2019;**7**(2):369–375.
34. Wallen JJ, Barrera EV, Ge L, *et al*. Biomechanical comparison of inflatable penile implants: a cadaveric pilot study. *J Sex Med*. 2018;**15**(7):1034–1040.
35. Scovell JM, Ge L, Barrera EV, Wilson SK, Carrion RE, Hakky TS. Longitudinal and horizontal load testing of inflatable penile implant cylinders of two manufacturers: an ex vivo demonstration of inflated rigidity. *J Sex Med*. 2016;**13**(11):1750–1757.
36. Barboglio Romo P, Chikkatur HP, Beldona S, Yi Y, Bruns TM, Malaeb BS. Comparative evaluation of physical characteristics of different inflatable penile prostheses. *Scand J Urol*. 2017;**51**(5):420–425.
37. Timm GW, Wulfman DR, Kim S, *et al*. Tissue characterization for improved external penile occlusive device design. *J Biomech Eng*. 2005;**127**(6):956–963.
38. Levy A, Fader M, Bader D, Gefen A. Penile compression clamps: a model of the internal mechanical state of penile soft tissues. *Neurourol Urodyn*. 2017;**36**(6):1645–1650.
39. Assaly R, Giuliano F, Clement P, *et al*. Extracorporeal shock waves therapy delivered by aries improves erectile dysfunction in spontaneously hypertensive rats through penile tissue remodeling and neovascularization. *Sex Med*. 2019;**7**(4):441–450.
40. Zhu D, Deng Y, Pan Y, *et al*. N-acetylcysteine ameliorates the erectile dysfunction caused by chronic intermittent hypoxia in rats: partly involvement of endoplasmic reticulum stress. *Urol*. 2015;**86**(4):844.e7–844.e14.
41. Camoglio FS, Bruno C, Zambaldo S, Zampieri N. Hypospadias anatomy: elastosonographic evaluation of the normal and hypospadic penis. *J Pediatr Urol*. 2016;**12**(4):199.e1–199.e5.
42. Riversi V, Tallis V, Trovatelli S, *et al*. Realtime-elastosonography of the penis in patients with Peyronie's disease. *Arch Ital Urol Androl*. 2012;**84**:174–177.
43. Inci E, Turkay R, Nalbant MO, Yenice MG, Tugcu V. The value of shear wave elastography in the quantification of corpus

cavernosum penis rigidity and its alteration with age. *Eur J Radiol*. 2017;**89**:106–110.
44. Zhang JJ, Qiao XH, Gao F, *et al*. A new method of measuring the stiffness of corpus cavernosum penis with ShearWave™ Elastography. *Br J Radiol*. 2015;**88**(1048):20140671.
45. Zhang X, Zhou B, Kopecky SL, Trost LW. Two dimensional penile ultrasound vibro-elastography for measuring penile tissue viscoelasticity: a pilot patient study and its correlation with penile ultrasonography. *J Mech Behav Biomed Mater*. 2020;**103**:103570.
46. Cunnane EM, Davis NF, Cunnane CV, *et al*. Mechanical, compositional and morphological characterisation of the human male urethra for the development of a biomimetic tissue engineered urethral scaffold. *Biomaterials*. 2021;**269**:120651.
47. Kandabarow AM, Chuang E, McKenna K, Le B, McVary K, Colombo A. Tensile strength of penile tunica albuginea in a primate model. *J Urol*. 2021;**206**(Supplement 3):e1073–e1073.
48. Patel DP, Christensen MB, Hotaling JM, Pastuszak AW. A review of inflammation and fibrosis: implications for the pathogenesis of Peyronie's disease. *World J Urol*. 2020;**38**(2):253–261.
49. Rainer QC, Rodriguez AA, Bajic P, Galor A, Ramasamy R, Masterson TA. Implications of calcification in Peyronie's disease: a review of the literature. *Urol*. 2021;**152**:52–59.
50. Moreland RB, Nehra A. Pathophysiology of Peyronie's disease. *Int J Impot Res*. 2002;**14**(5):406–410.
51. Brady L, Stender CJ, Wang YN, *et al*. Mechanical characterization of fibrotic and mineralized tissue in Peyronie's disease. *Int J Impot Res*. 2021;**34**(5):477–486.
52. Findley T, Chaudhry H, Stecco A, Roman M. Fascia research–a narrative review. *J Bodyw Mov Ther*. 2012;**16**(1):67–75.
53. Otsuka S, Yakura T, Ohmichi Y, *et al*. Site specificity of mechanical and structural properties of human fascia lata and their gender differences: a cadaveric study. *J Biomech*. 2018;**77**:69–75.
54. Purpura V, Bondioli E, Cunningham EJ, *et al*. The development of a decellularized extracellular matrix–based biomaterial scaffold derived from human foreskin for the purpose of foreskin reconstruction in circumcised males. *J Tissue Eng*. 2018;**9**:2041731418812613.
55. Ottenio M, Tran D, Ní Annaidh A, Gilchrist MD, Bruyère K. Strain rate and anisotropy effects on the tensile failure characteristics of human skin. *J Mech Behav Biomed Mater*. 2015;**41**:241–250.
56. Pissarenko A, Yang W, Quan H, *et al*. Tensile behavior and structural characterization of pig dermis. *Acta Biomater*. 2019;**86**:77–95.
57. Giuliano F, Bernabé J, Rampin O, Courtois F, Benoit G, Rousseau JP. Telemetric monitoring of intracavernous pressure in freely moving rats during copulation. *J Urol*. 1994;**152**(4):1271–1274.
58. Sezen SF, Burnett AL. Intracavernosal pressure monitoring in mice: responses to electrical stimulation of the cavernous nerve and to intracavernosal drug administration. *J Androl*. 2000;**21**(2):311–315.
59. Williams JK, Andersson KE, Christ G. Animal models of erectile dysfunction (ED): potential utility of non-human primates as a model of atherosclerosis-induced vascular ED. *Int J Impot Res*. 2012;**24**(3):91–100.
60. Li X, Tao L, Cao C, *et al*. A new surgical method for penile girth enhancement. *Int J Clin Exp Med*. 2015;**8**(7):10753–10759.
61. Bertran J, Ham KM, Gibson JF, Litsky A, Kieves NR. Penile urethral resection and anastomosis augmentation with regional tissue tension relieving technique: a cadaveric mechanical study and clinical outcome in two dogs. *Vet Surg*. 2021;**50**(4):888–897.
62. O'Kane D, Gibson L, Du Plessis J, Davidson A, Bolton D, Lawrentschuk N. Delivery of intracavernosal therapies using needle-free injection devices. *Int J Impot Res*. 2017;**29**(6):225–228.
63. Regadas RP, Moraes ME, Mesquita FJ, Cerqueira JB, Gonzaga-Silva LF. Experimental model of human corpus cavernosum smooth muscle relaxation. *Int Brazilian J Urol*. 2010;**36**:490–496.
64. Masterson JM, Horodyski L, Patel R, Kineish O, Kohn TP, Ramasamy R. Impact of key pinch strength on patient preference for inflatable penile prosthesis: a prospective study comparing Coloplast™ and AMS™ models. *Int J Impot Res*. 2020;**32**(1):113–116.
65. Madhusoodanan V, Best J, Kalahasty K, *et al*. A prospective study analyzing both inflation and deflation preference for commonly available inflatable penile prostheses. *Int J Impot Res*. 2021;**33**(6):652–659.
66. van Renterghem K, Ghazi A. 3D pelvic cadaver model: a novel approach to surgical training for penile implant surgery. *Int J Impot Res*. 2020;**32**(3):261–263.
67. Udelson D, Nehra A, Hatzichristou DG, *et al*. Engineering analysis of penile hemodynamic and structural-dynamic relationships: part I—clinical implications of penile tissue mechanical properties. *Int J Impot Res*. 1998;**10**(1):15–24.
68. Udelson D, Nehra A, Hatzichristou DG, *et al*. Engineering analysis of penile hemodynamic and structural-dynamic relationships: part II—clinical implications of penile buckling. *Int J Impot Res*. 1998;**10**(1):25–35.
69. Chen J, Gefen A, Greenstein A, Matzkin H, Elad D. Predicting penile size during erection. *Int J Impot Res*. 2000;**12**(6):328–333.
70. Gefen A, Chen J, Elad D. Optimization of design and surgical positioning of inflatable penile prostheses. *Ann Biomed Eng*. 2000;**28**(6):619–628.
71. Gefen A, Chen J, Elad D. Stresses in the normal and diabetic human penis following implantation of an inflatable prosthesis. *Med Biol Eng Comput*. 1999;**37**(5):625–631.
72. Kelly DA. Expansion of the tunica albuginea during penile inflation in the nine-banded armadillo (Dasypus novemcinctus). *J Exp Biol*. 1999;**202**(3):253–265.
73. Linder-Ganz ERAN, Gefen A, Elad D, Chen J. A three-dimensional model of the penis for analysis of tissue stresses during normal and abnormal erection. *Ann N Y Acad Sci*. 2007;**1101**(1):464–476.
74. Mohamed AM, Erdman AG, Timm GW. The biomechanics of erections: two- versus one-compartment pressurized vessel modeling of the penis. *J Biomech Eng*. 2010;**132**(12):121004–121012.
75. Galasso M, Feld JJ, Watanabe Y, *et al*. Inactivating hepatitis C virus in donor lungs using light therapies during normothermic ex vivo lung perfusion. *Nat Commun*. 2019;**10**(1):1–12.
76. Kaouk JH, Autorino R, Laydner H, *et al*. Robotic single-site kidney surgery: evaluation of second-generation instruments in a cadaver model. *Urol*. 2012;**79**(5):975–979.