NUMERICAL AND MATERIAL MODELLING FOR THE DEVELOPMENT OF A NEW DEVICE FOR THE TREATMENT OF INDURATIO PENIS PLASTICA

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ABSTRACT

The aim of the work is numerical and material modelling for the development of a new device for the treatment of Induratio penis plastica (IPP) also known as Morbus Peyronie, where it is necessary to specify the parameters of the new device for its production in cooperation on a project of the Czech Technical University in Prague and the company Medipo-ZT,s.r.o. Shock wave method was applied for patients. Evaluation and study on models created from cement mixtures with different degrees of hardness was also included, because of waiting for a real sample taken after the plaque operation. The approximate material properties of collagen are taken into account in the models. An integral part of the work is the evaluation of individual important indicators, such as plaque size, penile angulation, the international questionnaire of erectile dysfunction and the age of patients before and after treatment. At the same time, the intention is to develop a relationship between the individual indicators. Applied shock wave therapy was used for the solution, which is used in urology in the treatment of urinary stones. In physiotherapy and orthopaedics, it is used in the treatment of calcification and non-calcification diseases, such as plantar fasciitis, tennis or golf elbow, heel spur and humeroscapular periarthritis. The project is further developing software to help doctors outline the success and scope of treatment for a particular patient of a given age.

Keywords: Morbus Peyronie, Peyronie's disease, shock wave, dorsal angulation, size plate, numerical model, material model, new device, developed software.

1 INTRODUCTION

Induratio penis plastica (IPP) was described in 1561 by Fallopius and Vesalius as fibrous cavernousitis. This disease was also dealt with more thoroughly by the personal physician of King Louis XIV of France, Francois de la Peyronie, who conducted a study on plastic induration of the penis and recommended therapeutic approaches in the treatment of this disease (1743) [1]. Since then, the term induratio penis plastica or Morbus Peyronie has been used. In the past, a number of physicians and scholars (Bishop of Theodoric, Bologna – 13th century) dealt with the treatment of this deformity. Older authors considered induratio penis plastica to be a rare disease with a high tendency to regression, but recent studies report only exceptionally spontaneous disappearance (up to 2–3%)

Epidemiological data are limited, the prevalence of IPP has been rising in recent decades. Today it is in the range of 6–9% of men in Europe [1], in the USA it is slightly higher and in the range of 7–11%. Nevertheless, a number of studies suggest that the disease is often overlooked and underdiagnosed and its prevalence is even higher. The prevalence is mainly increased by the current incidence of erectile dysfunction, diabetes, high blood pressure, hyperlipoproteinemia, smoking and alcohol consumption. A typical patient is a man between 55 and 60 years old. IPP is a disease that locally affects the tunica albuginea, most commonly on the dorsum and flank of corpus cavernosum.

The aetiology of this disease is not fully understood. Recently, a disorder of wound healing (so-called microvascular injuries and traumas caused during sexual intercourse) is being considered. Prolonged healing and abacterial inflammation lead to the formation of a

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scarred fibrotic plaque, which loses the elasticity of the tunic of the albuginea [2], [3]. As part of the healing, calcium salts also begin to fall into this plate, which further potentiates the rigidity of the plaque. The fact that this disease is one of the autoimmune diseases with impaired healing is also indicated by the high incidence of patients who are also affected by other autoimmune diseases of connective tissue (Dupuytren's contracture). The prevalence is 9–39%.

The disease manifests itself in several ways. Some patients report a sudden onset of penile angulation without ever having a painful erection. In others, a painful erection first appears, which is accompanied by a curvature of the penis after a few months. Most patients complain of penile shortening. From the acute phase, Peyronie's disease passes to a resting stage, which is characterized by the permanent presence of deformity. Pain persists at rest in 35–45% [4]. Deformation is expressed by the curvature and shortening of the penis during erection. The formation of a solid scar (plaque) results in the development of penile dysfunctions. In more than 50% of men, the penis is deformed during erection and thus difficulties during sexual intercourse, which negatively affects the quality of life not only of affected men, but also of their partners.

We divide the therapy of induratio penis plastica into conservative and surgical. We prefer conservative therapy in patients early after the transition from the acute to the chronic phase. In the acute stage, we recommend antiphlogistic and analgesic treatment with non-steroidal analgesics. We divide conservative treatment into oral and injectable directly into the plate.

Conservative therapy involves the oral administration of vitamin E, colchicine, L-arginine, injection of steroids, verapamil or interferon directly into the plaque. The most effective methods include the application of shock waves (SWT) [4] and the injection of Clostridial collagenase (CCH). Surgical treatment is recommended after failure of conservative therapy (surgery according to Nesbit 1965, according to Yaschia 1993) [5]. Today, only a minimum of patients undergo surgical treatment. The reason is the success of conservative therapy (especially SWT and CCH), the risk of recurrence and possible postoperative complications, including erectile dysfunction. Often, surgery is also associated with shortening of the penis during erection, as a result of surgical techniques.

2 THE DEVICE DEVELOPMENT PROCESS

The aim of the present project is industrial research on a new medical device for the treatment of Morbus Peyronie patient using new diagnostic techniques in active collaboration with a potential customer (the Central Military Hospital in Prague, hereinafter UVN).The new facility will involve a wider range of generations effect of shock waves through the applicator applied to the tissue being treated and will include patient comfort (seat attachment etc.). The new facility will be equipped with software, which will help doctors determine the intensity of the shock energy, including the number of shock waves, as well as the length of treatment. The software is based on a database of 150 patients, where the treatment is evaluated depending on the size of the plaque, the curvature of the penis, the intensity of treatment and its success.

For the new device facility, it was necessary to address several construction details, in particular:

1. Functional sample control unit
2. Keyboard
3. Power part of the shock wave generator
4. Generator control unit

5. Shock wave applicator with aiming and fixing device
6. Adjustable spark gap with motor and motor mechanism for spark gap replacement
7. Applicator positioning motors
8. Water treatment plant
9. Development of an ellipsoid with marking of foci
10. Patient's chair
11. Source part
12. Fixation and orientation of the affected area
13. Software.

Fig. 1 shows shock wave applicator-ellipsoid with marked foci; Focus F1-spark gap in the aquatic environment; and Focus F2-therapeutic focus approx. Ø9 × 38 mm. Fig. 2 shows pressure profile in focus.

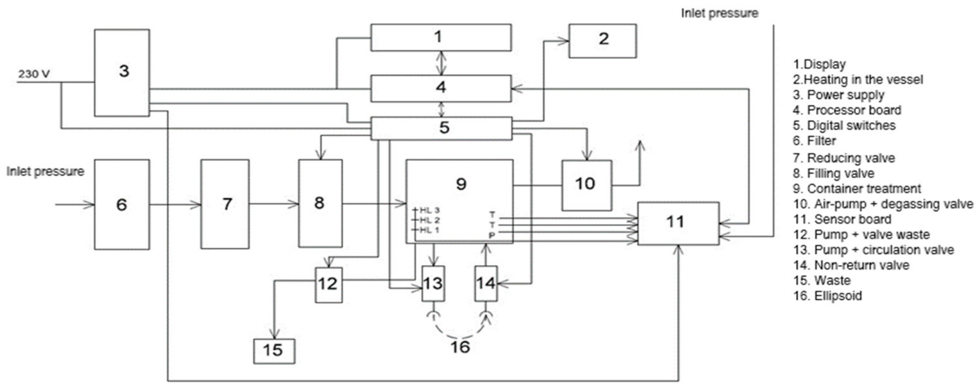


Figure 1: Shock wave applicator-ellipsoid with marked foci.

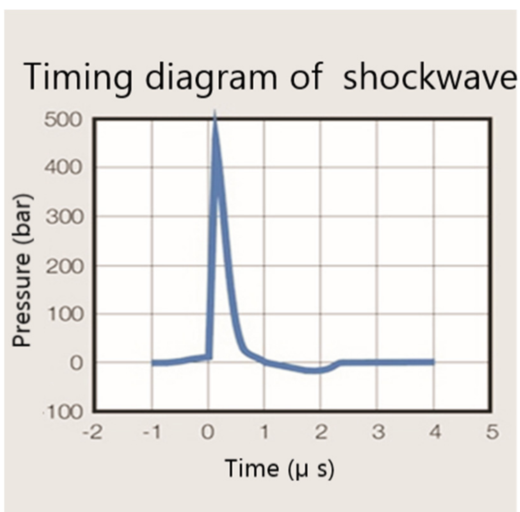


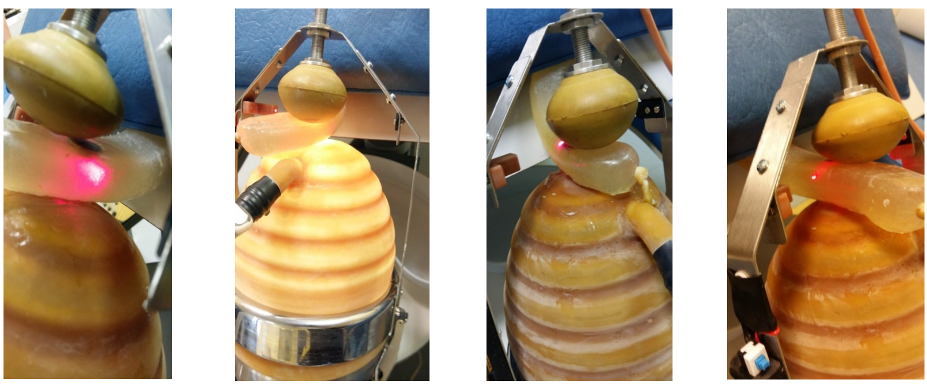
Figure 2: Pressure profile in focus.

3 SPECIFICATION OF MATERIAL MODELS

The project managed to obtain a database of approximately 150 patients suffering from the disease and which underwent shock wave therapy on devices that did not serve directly to treat the disease, so the success rate of treatment was about 75%. The database contained data on plaque size, patient age, penile curvature, the number of sessions and the total amount of energy used in the operation, and the database contained data on whether the patient was cured or not. Material models served primarily as a feedback analysis to create a new device, i.e. focus adjustment, attachment, application of energy, as current devices do not allow this. The current existing devices are primarily manufactured for other purposes and thus create inaccuracy in targeting, including very uncomfortable patient, who often has to assist doctors with attachment throughout the procedure.

In the context of this project, 43 models of penises with plaques were produced, the material was designed according to the experience of surgeons from Military University Hospital Prague (UVN). The models were tested on the Litotryptor MEDILIT device, a standard loading procedure of 3,000 cycles. The models were manufactured to test the accuracy of the shock wave impact and alignment, including the proposed mount and foci of the new device. The outputs were tested on a Phenom XL microscope, which is owned by CTU in Prague, and were compared with unloaded samples.

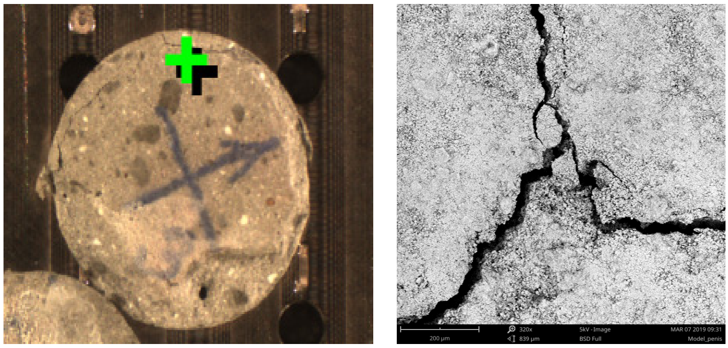
The material samples are composed of collagen bags with cement plaque models from C25/30 to C35/45. Fig. 3(a) shows samples of the cement plaques produced from collagen models (Fig. 3(b)) and detail of model focus to focus (Fig. 3(c)) including partial destruction after surgery (Fig. 3(d)). In the experiment, it was evident that the accuracy of focusing on the focus of the plaque and the attachment of the penis model plays an extremely important role in making the procedure more successful. That is why the team members have already designed a laser focus and an inflatable penis fixation element.



(a) (b) (c) (d)

Figure 3: Parts (a)–(d) show a laser aiming test and an inflatable pad for measurement on an artificial penis sample with plaque according to the actual dimensions.

Twelve samples of class C25/30 and C35/45 were examined with a microscope. All tested samples showed cracks after loading with shock waves; in some they were visible to the eye. The results from two samples of Class C25/30 are illustrated in Fig. 4. Samples was subjected to shock waves. For accuracy, three places in the micro level were focused

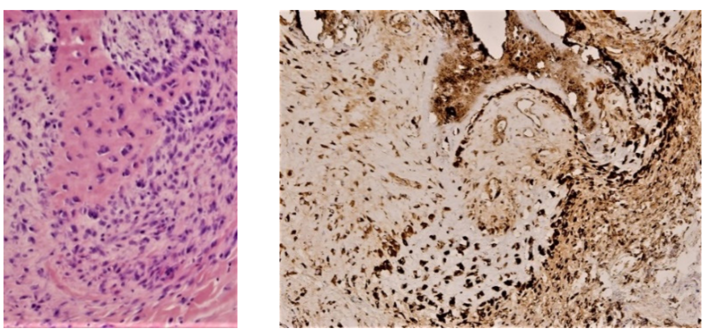


(a) (b)

Figure 4: Parts (a) and (b) of the sample show places in the micro level were focused under a microscope which were subjected to shock wave.

under a microscope; in sample number one there is a noticeable decay, with sharp cracks across the whole sample, which is caused by shock waves. However, the samples served rather to accurately determine and specify the focus of the instrument.

A numerical model was established for the treatment of patients and the dosing of the amount of energy, which was based on the actual material values measured by the pathologist and mechanical tests of the plaque removed during surgery. In this respect, the data used in the article are unique, because due to the risks of the operation, the number of procedures is negligible. The results from the histology of plaque, namely the population of spindle fibroblasts in the phase of chaotic orientations and in the phases of oriented fibroblasts in the directions of main stresses/strains and bone beam structure lined with fibroblasts, copying the boundaries between beam and fibrous scar are illustrated in Fig. 5. From pathological examination with the cooperation of bioengineers which was carried out by Prague's Institute of Pathology" it was determined that the modulus of elasticity of the plasma is between 15–20 MPa and the Poisson's ratio is 0.4. Further mechanical tests were performed in a specialized laboratory of CVUT in Prague, which are described below.



(a) (b)

Figure 5: Parts (a) and (b) show the results from the histology of plaque, namely the population of spindle fibroblasts in the phase of chaotic orientations and in the phases of oriented fibroblasts in the directions of main stresses/strains and bone.

4 ASSESSING OF MATERIAL PROPERTIES FROM EXPERIMENTAL ACTIVITIES

The aim of the tests was to evaluate the mechanical properties of the supplied biological plaque samples during pressure tests. Two samples were delivered for the implementation of experiments. The evaluation parameters were the elastic stress gradient (direction of the tangent in the relief phase) and the absorbed energy up to 50% deformation. A methodology developed, verified and validated in the mechanical testing laboratory was used for testing.

The tested plaque samples were supplied from the Institute of Pathology of the 1st Faculty of Medicine, Charles University and the General Hospital.

The MTS Mini Bionix 858.02 system (metrological designation PM 00, accuracy class 1, see Fig. 6) with a fitted force transducer (PM 00/18) with a range of 0 ÷ 500 N was used for testing. Special jigs for pressure tests were also used (see Fig. 7). A program created in FlexTest GT software called: Pressure modul.000 was used to control the test.

Figure 6: Testing system MTS Mini Bionix.

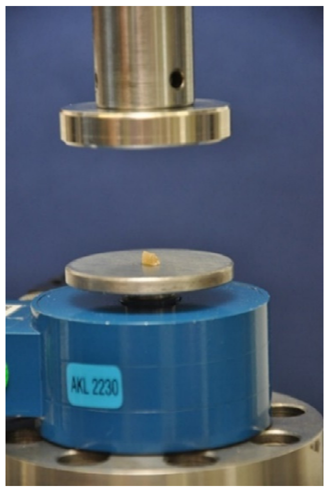


Figure 7: Image close-up shot of a sample save.

The MAHR 16EX digital caliper and the KINEX caliper were used to measure the samples. The environmental conditions were recorded by a digital thermometer-hygrometer COMET (PM 07). All used meters are registered in the quality management system of the laboratory and are metrologically linked to standards. Calibrations take place at regular intervals at accredited calibration laboratories.

4.1 Experimental methodology

The methodology of the experiment was based on the determination of the elastic stress gradient in the relief phase and the absorbed energy. For this type of material, the elastic stress gradient can be considered comparable to the Young's modulus. The principle of the test was loading the test specimen inserted between two metal plates at a constant feed rate to F1, unloading to the level F0 and repeating the loading to the forces F2, F3, F4, F5 and always subsequent unloading to F0. The loading speed was set at 2.0 mm/min and was the same for the unloading speed. The sampling frequency of the quantities (time, force, displacement) of the experimental test system MTS Mini Bionix 858.02 was 30 Hz.

4.2 Measured values

The samples were approximately cuboid in shape. Table 1 below summarizes the determined dimensions of the individual samples together with the selected levels of loading forces. Sample No. 1 was only for calibration purposes and was made of a different material, so it is not listed below.

Table 1: Dimensions of samples.

Number of samples	Dimensions of samples			Levels of loading forces				
	Width (mm)	Length (mm)	Height (mm)	F1 (N)	F2 (N)	F3 (N)	F4 (N)	F5 (N)
2	2.53	5.50	1.85	15	30	45	60	75
3	3.27	5.62	2.77	15	30	45	60	100

4.3 Evaluation

A contractual diagram (stress-strain curve) was prepared for each sample loaded by the pressure test according to the above methodology. By evaluating this diagram, the tangent guidelines in each relief-load cycle and the absorbed energy were determined. The stress result for sample numbers 2 and 3 are shown below in Figs 8 and 9.

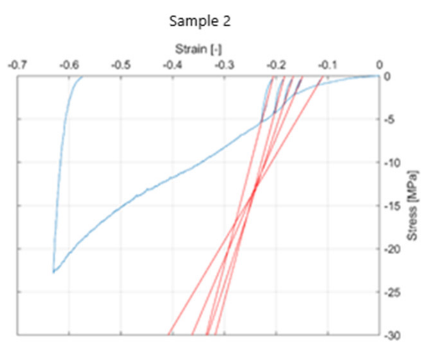


Figure 8: Diagram of sample 2 for stress–strain curve.

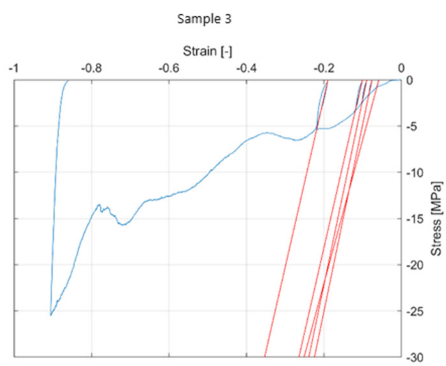


Figure 9: Diagram of sample 2 for stress–strain curve.

The points through which the secant (line) is intersected are shown in the graph as the maximum value of the stress in the relief phase and as the first point from which the relief phase began. The linear line in the form $y = a \cdot x + b$ is led by the points found in this way, where the parameter a corresponds to the elastic stress gradient.

The absorbed energy is proportional to the area under the stress–strain curve up to 50% of the strain (see Figs 10 and 11).

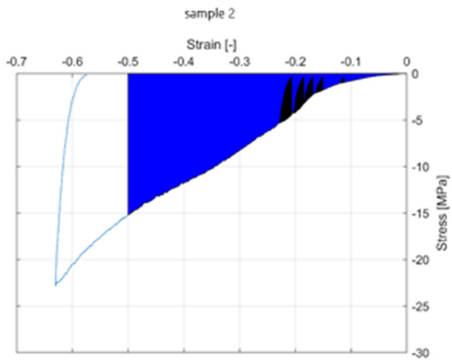


Figure 10: Diagram of energy – sample 2.

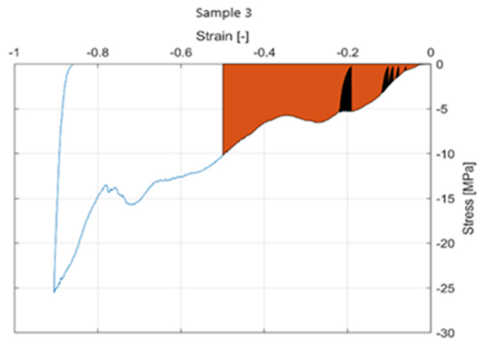


Figure 11: Diagram of energy – sample 3.

4.4 Results

The summary results of the elastic stress gradient and the absorbed energy for both samples are given in the following Table 2 and resulting values of absorbed energy are given in the Table 3.

Table 2: Elastic stress gradient.

Elastic stress gradient (MPa)		
Cycle	Sample 2	Sample 3
F1 – F0	100	155
F2 – F0	140	202
F3 – F0	181	201
F4 – F0	224	183
F5 – F0	231	183
Arithmetic mean	175	185
SD	55	19
Median	181	183
LQ (lower values)	140	183
UQ (upper values)	224	201

Table 3: Resulting values of absorbed energy.

Results of absorbed energy (MJ.m^{-3})	
Sample 2	Sample. 3
3.24	2.58

5 NUMERICAL MODELING OF PENIS DEFORMATION IN INDURATIO PENIS PLASTICA

For numerical modelling, program ATENA (Advanced Tool for Engineering Nonlinear Analysis) [6] was used. It's based on finite element method and fracture mechanics, which is very suitable for solving this problem. Several models were created in longitudinal and transverse section of the penis (Fig. 12). The supports correspond to the designed device for attaching the penis and only prevent movement in the normal direction. The load is continuous, perpendicular to the horizontal projection of the element.

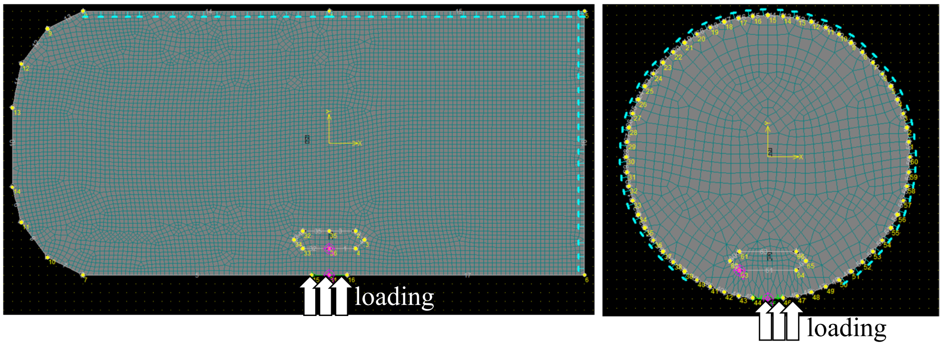


Figure 12: Models in longitudinal and transverse section of the penis.

The penis is not of a homogeneous material, but the material characteristics of its soft parts are quite similar. Therefore, only two types of material are used in the model. One homogenized for the penis where Young's modulus of elasticity was 30 kPa and Poisson's number was 0.48. The second was material of penile plaque. Here the material characteristics obtained from pathological examination was used. Young's modulus of elasticity was 80 kPa and Poisson's number was 0.46.

At first the results from model of the entire cross section of the penis is introduced. The triangular elements were used in this model (1716 elements, 905 nodes). It can be seen on them that only a small area around the plaque is affected by the load (see Figs 13 and 14). Therefore, only the section of this area is further modelled, which allows a more detailed network of elements. In Fig. 15, a cut-out from the longitudinal section of the model is depicted, with the variation of normal stress in horizontal direction σ_x. In this model were used quadrilateral elements (10,490 elements, 10,759 nodes). As well as in the cross-section model, only the variation of stress in a small area around plague is of interest. There were used 5,153 triangular elements with 2,842 nodes in this model. The crack development is depicted in Figs 16–18 together with normal stress in horizontal direction σ_x.

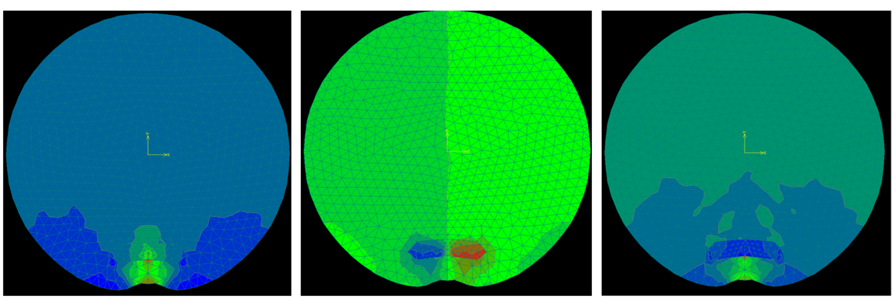


Figure 13: The variations of normal stress in horizontal direction σ_x, tangential stress τ_{xy} and normal stress in vertical direction σ_y.

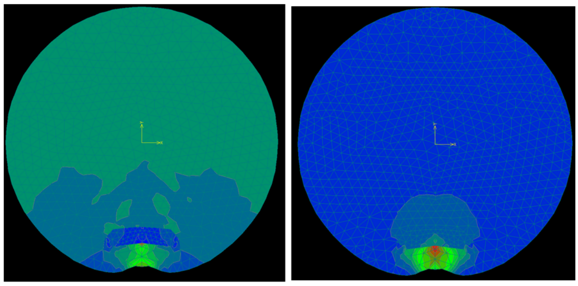


Figure 14: The variations of main stress σ_{max}, (left) and σ_{min} (right).

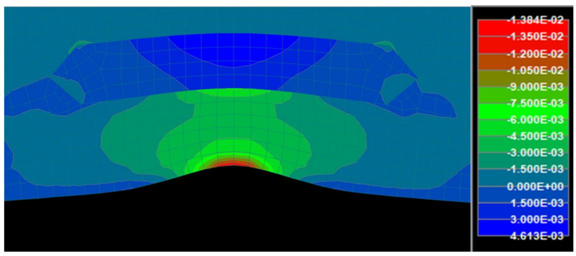


Figure 15: Cut-out from model of longitudinal section, with the variation of normal stress in horizontal direction σ_x.

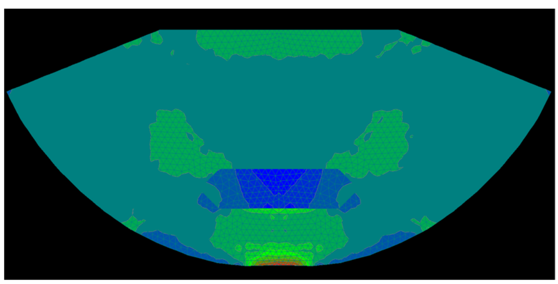


Figure 16: Model of section of area. Variation of normal stress σ_x, the state just before the formation of cracks.

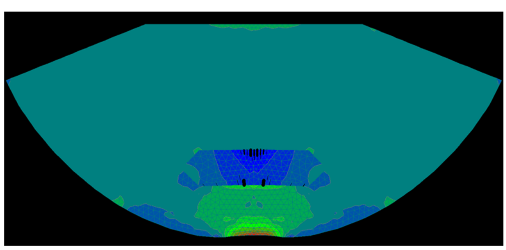


Figure 17: Initial stages of crack development.

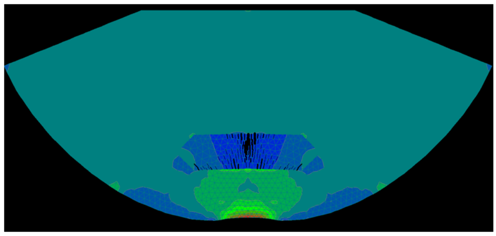


Figure 18: The final stage of crack development.

CONCLUSION

The aim of the project was research on a new medical therapeutic agent for the treatment of Induratio Penis Plastica (i.e. Peyronie's disease, IPP), using new diagnostic and therapeutic methods, with the application of shock waves. In connection with the stated goals, the following were processed: histological analyses of plaques, numerical analyses and experimental verification of elasticity/stiffness of biomaterials and their correlation with the computational modulus of elasticity of plaques. The numerical model contributed to the demonstration of real therapeutic effects (such as tests on patients), which took place at the Central Military Hospital in Prague. The numerical model and experimental analyses proved the validity of the relevant biomechanical axiom: The angle of deviation of the penis axis in IPP is dominantly dependent (i.e. a function) of plaque stiffness, its 3D size and the hydraulic pressure of blood flow during erection.

Research proved that the early phase is histologically characterized by undirected, structurally disordered, type 1 collagen fibers. Early plaques are 3 to 5 mm in 3D size. In the central areas, they contain small districts of beginning ossification. In the early phase, there are no visually visible deviations of the penis median angle. However, mature plaques already contain longitudinally oriented fibroblasts and collagen fibers in the directions of dominant major tensile stresses. In the central parts they have fractal or compatible osteogenic islands (microlayers). The matured plaques are 6 to 15 mm in 3D size. In the early phase, the stiffness of the plaques is relatively small, the angular deviations of the penis median are not visually visible. In the mature phase, the plaque stiffness gradient clearly increases. The greater the dynamic modulus of elasticity of the plaques, the greater the deviation of the penis median angle. In clinical biomechanics, the more precisely the dynamic modulus of elasticity of plaques is verified, the more precisely the angle of the penis median is defined, in the mature phase of plaque genesis and subsequently the more effectively the therapeutic procedure is chosen. From the measurement of dynamic modulus of elasticity in modeled penises, it is clear that in fully inorganic (artificial) plaques, the dynamic modulus of elasticity reaches values in the order of GPa units and also the largest deviation of angles. Ultrasound measurements of dynamic modulus of elasticity in the hospital on patients have shown that the sizes of dynamic modulus of elasticity of plaques at the interface of their early and maturation phase of development have significantly lower values of dynamic modulus, which reach numerical sizes in tens of MPa. The higher the hydraulic pressure of the blood, the greater the hydraulic strengthening of the penis and the greater the gradient of the deviation of the deviation of the penis center angle. Direct ethical pressure measurements directly in the penis during erection could not be performed on patients for ethical reasons. However, direct measurement on the plates of many patients by ultrasound, sufficiently takes into account the dynamics of hydraulic loads and is sufficient for stress analysis of connective tissues and their transformation by FEM.

Currently, the work on the project is gradually being completed. Fig. 19 shows an example of a condensed function, enabling efficient control – software calibration. During the execution of the project, the above-mentioned author's team obtained a patent for the Czech Republic, which will be further extended for the USA and Germany. Next year, extensive clinical verifications will be performed on new devices, enabling effective therapy. We expect the therapeutic efficacy of IPP to increase by up to 85–90%.

Figure 19: Functional sample of a new device for the treatment of Peyronie's disease.

ACKNOWLEDGEMENT

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REFERENCES

[1] Muller, A. et al., The impact of shock wave therapy at varied energy and dose levels on functional and structural changes in erectile tissue. *European Urology*, **53**, pp. 635–643, 2008.

[2] La Peyronie, F.G., Sur quelques obstacles qui s'opposent á l'ejaculation naturele de la semence. *Mémoires de L'Académie Royale de Médecine*, **1**, pp. 337–342, 1743.

[3] Van de Water, L., Mechanisms by which fibrin and fibronectin appear in healing wounds: Implications for Peyronie's disease. *Journal of Urology*, **157**, pp. 306–310, 1997.

[4] Devine, C.J., Introduction to Peyronie's disease. *Journal of Urology*, **157**, pp. 272–275, 1997.

[5] Williams, G. & Green, N.A., The non-surgical treatment of Peyronie's disease. *British Journal of Urology*, **52**, pp. 392–395, 1980.

[6] Software ATENA 2D Verse 5.4.1.0, Cervenka Consulting: Manual users, Department of Mechanics.