Oncothermia Journal 5:11-22 (2012)

AndroTherm application for Peyronie disease (Phase I/II study)

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Abstract

A pilot study is performed for Peyronie's disease by oncothermia principle with a specially developed so called androthermia device. The case-studies and the preliminary efficacy results are promising, and show the feasibility of the new method to treat Peyronie's disease in various stages.

Keywords: Peyronie's disease, electric field, plaque, heat, androthermia

Introduction

Peyronie's Disease, (*Induratio Penis Plastica*) is a plaque forming disease on the penis, deforming it mostly during erection [1], [2]. It is painful, and frequently blocks the normal intercourse. One of the first authoritative descriptions of the disease was made as early as 1561 by Fallopius, and almost 200 years later was rediscovered Peyronie, in 1743, [3]. The Peyronie's disease is mostly observable at men of their middle ages (50-60 y) in Caucasian race, [4]. Earlier its morbidity was measured less than one percentage, [5]; but nowadays it is apparently more common. [6]: 1.5% in man at ages 30 and 6 % for those who older than 70. Men in their 40-60 are affected by Peyronie disease in 2-3% [7]. It is shown in general, Other study showed 9% morbidity among American men, [8], and by autopsy statistics may be that the Peyronie disease is present over 20% of men, [9]. There are large variety of penile deformations and presence of the disease in young men patients [10].

The abrupt penis deformation during sex may disrupt small blood vessels within the tunica albuginea, which process could trap blood between layers of the tunica. The actual trauma could lead to inflammation Bleeding and trauma are accompanied by the release of a number of chemicals that lead to inflammation, [11]. The closed, layered structure of the tunica may limit the ability to drain the produced inflammatory mediators away from the site of injury, leading to prolonged inflammation there. Inflammation is usually a good process helping of healing, however when it became chronic it could block the healing process, [12], [13]. This could change the elastin and collagen fibers, reducing the adaptability of stretch of the penis [14] and deforming it.

In fact there is no effective therapy exists for this disease. There are many non-surgical treatments for Peyronie's disease like Vitamin E, Carnitine, Colchicine, Pentoxifylline, and various herbal and complementary remedies like Acetyl L-Carnitine (ALC) and dimethyl Sulfoxide (DMSO), or the "Thacker formula"; enzymes like Wobenzym, Fibrozym, Vitalzym, and Neprinol; as well as the minimally invasive (local in-situ injection) treatments of Verapamil, Interferon, Collagenase, and various steroids (e.g. Glucocorticoids) could be applied. All of the treatments applied have no or poor efficacy. There are various surgical options to solve this problem, [15]. There are huge interet to treat this disease worldwide [16] and also comprehensive books published in the topic [17], [18].

The transdermal electrophoresis [19] could be effective for the treatment combined with definite drug-therapy called "transdermal electromotive drug therapy" (EMDA) [20]. This placebo controlled, double-blind study used Orgotein (8mg), Dexamethasone (8 mg), Lydocain (120 mg) for 20 min three times a weak in three weeks duration. The plaque reduction was 79%, the curvature improvement 62% and the pain reduction 100%. Others had also used EMDA with Dexamethasone + Verapamil combination [21], also compared to Lidocain effect alone [22]. EMDA application with Verapramil alone [23] also was effective.

Contrary the new review of non-surgical solutions to treat Peyronie's disease [24], hyperthermia also was applied with success for Peyronie disease [25]. They studied 60 patients with Peyronie's disease,

having a comparison between application of Verapamil and hyperthermia. The chosen cohort groups were identical in their main relevant parameters (see Figure 1.)

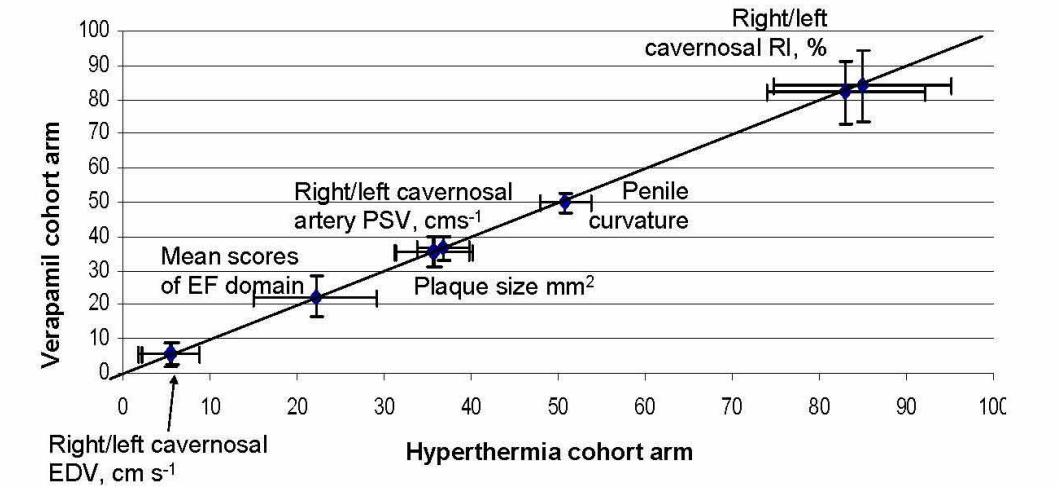

Figure 1. Comparison of the groups involved in the study [25]

Hyperthermia was applied for 20 minutes, twice a week for 5 weeks. A 2nd cycle was made after a 1 month having 10 treatments. The control group received 10mg injection of Verapamil once a week for 3 months. The Verapamil group had no real benefit of the treatment, (see Figure 2.). It was significant relief of both subjective and objective symptoms in hyperthermia treated group, without any adverse side effects (see Figure 3.). The penile curvature decreased by 55.9% with hyperthermia, while only 3.8 % with Verapamil, and the plaque-size decreased 42.1% and 2.2% with hyperthermia and Verapamil, respectively. Similar controlled clinical study is in progress to repeat the results, [26]. The clinical trial compare the only heat treatment and the treatment group is receiving a combination of Vitamin D and testosterone injections additional to heat by infrared heating.

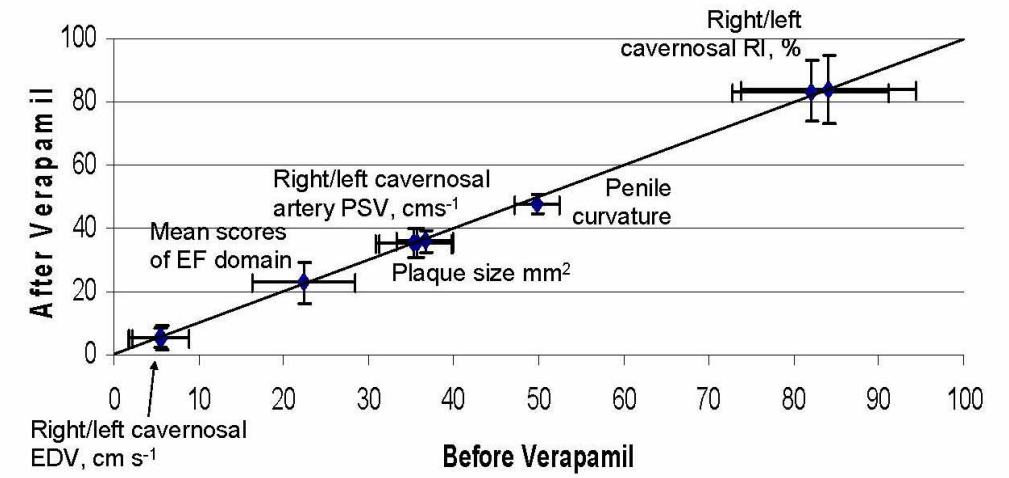

Figure 2. The group treated by Verapamil had no benefit from the therapy

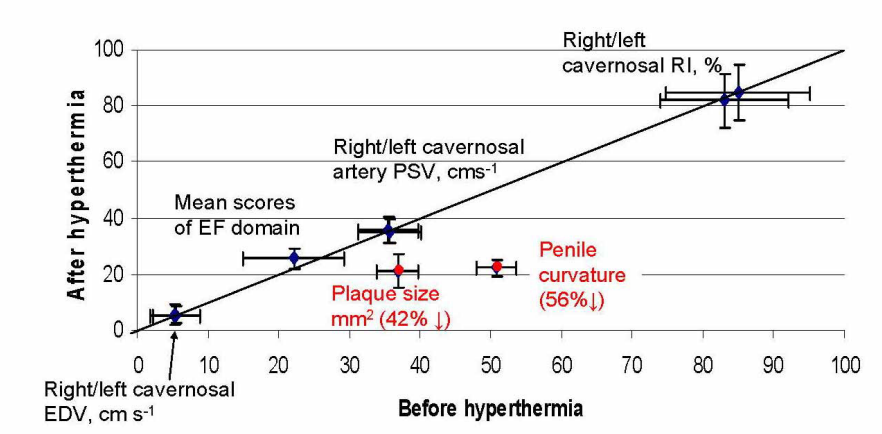

Figure 3. Hyperthermia had shown definite benefit for the patients

Learning the failures of many applied conventional treatments and seeing the possible applicability of the heat and the electric field, we had developed a new device for treatment of the penile disorders, including Peyronie's disease. The collected evidence based research data indicate inflammation processes. On this basis the Peyronie disease more similar to keloids than to scars. It is a benign tumor [27], which is

1. plaque fibroblasts are immortalized cells;
2. plaques and normal tunica albuginea have chromosomal differences;
3. induces immune response by the plaque fibroblasts and their products;
4. mitochondrial dysfunction is observed in plaque fibroblasts.

In coherence of the above conditions it is not a surprise that the apoptotic processes can play definite role in plaque formation and its elimination. There is a finding that apoptosis activation [28] in tunica albuginea plaques occurs. This, at least in part, is realized via the extrinsic pathway [29]. Probable the stem-cell activity has also role in the plaque formation in Peyronie diseases [30].

Peyronie's disease is known to be associated with Dupuytren's disease [31]. Main characteristic of the Dupuytren's disease is palmar aponeurosis hyperplasy and contract which lead to finger flexion contracture [32]. Peyronie's and Dupuytren's diseases have common pathophysiology, [33]. The imbalance between proliferation and apoptosis, producing malignant growth was thus confirmed for fibrosarcoma, but not the same form for Dupuytren's disease, [34], becase that is benign as well, similarly to Peyronie's. However both can be regarded as system's disease, [35], because the immune system is involved. It was hypothesize that periostin, secreted by Dupuytren's disease cord myofibroblasts into the extra-cellular matrix, promotes the transition of resident fibroblasts in the palmar fascia toward a myofibroblast phenotype, thereby promoting disease progression, [36]. The periostin can interact with other ECM proteins such as fibronectin and collagen I and may affect fibroblastic migration, [37].

The induced extrinsic pathway of apoptotic is involved in the novel hyperthermia method in oncology (oncothermia [38]). This is the reason, why the new development based on the oncothermia technology inducing apoptosis, is applied in the AndroTherm studies.

Method

The traditional hyperthermia had good benefit in the treatments of Peyronie disease, however it is controlled the only single thermodynamic intensive parameter, with the temperature.

Oncothermia is a special hyperthermia [38], working on the action of the modulated electric field in the locally treated lesion. It has long experience in the oncology [39]. Its idea to use the benefit of electric field makes feasible applying it for Peyronie disease, unifying the effect of EMDA and heat in a specialized treatment. Our objective is to perform a pilot study with application of special (adaptively modified) kind of oncothermia for Peyronie disease, called androthermia.

The method is based on the paradigm of the energy-dose control, replacing the single temperature concept [40], [41], [42]. With this approach oncothermia returned to the gold standards of the dose concepts in medicine: instead of the parameter, which can not regarded as dose (the temperature does not depend on the volume or mass), oncothermia uses the energy (kJ/kg [=Gy]), like the radiation oncology uses the same (Gy) to characterize the dosing of the treatment.

The requested job is to change the structure of the target, for what a definite energy dose is necessary [43]. The historical energy-dose-like control (temperature multiplied by its application time), is physically incorrect, and operates with an overall energy average in the area, instead of a directed and well measurable energy-dose (measured in kJ).

So these points are realized, and called this procedure modulated electro-hyperthermia or oncothermia [44], and specialized now for andrology. Of course many theoretical considerations were done to make this idea working. The membrane effects by the outside electromagnetic field are shown against the old theories [45]. Also the modern fluctuation analysis (fractal-physiology) supports the method [46], [47]; as well as the resonance phenomenon is studied and used in the light of a new theory [48]. The hypoxia study [49] and special vector-potential theory [50] helps to complete the method. We also study the possible side-effects of the scattered radiation, [51], reduce the risk, and make the method as safe as possible. The acceptance of the new paradigm is a clear demand of the theory and the practice as well [52].

The presently applied radiative hyperthermia devices, operating one order of magnitudes higher frequency than oncothermia, are in fact also capacitive-coupled, because the applicators are definitely in the near-filed arrangements. However, these are far not optimally coupled and their frequency is also too high to be able to provide the desired effects. No artificial focusing needed for selectivity in the applied androthermia method, and no isotherms in space and time has to be controlled. Both effects are solved in oncothermia with a directed electric field. It is a well designed capacitive coupling on 13.56 MHz free-frequency, [53]. The process is controlled by the changes of the impedance, and by the absorbed energy, which both are accurately measured. In this meaning oncothermia is very similar to the RF-ablation hyperthermia, where the temperature is not measured, the effects is controlled by the measured impedance of the tissue. The power is ranging form 30 W to 150 W, which is far enough for heating up the tumor over 42 ºC in a well controlled focusing. (You may touch a working 12 W halogen lamp to be sure on its burning efficacy. Less than 20 W is enough to heat up a 5 cm diameter tumor from 36 ºC to 44 ºC at 3 minutes! The only clue is the focusing.)

The advantage of this method was clearly shown: the electric field has significantly higher effect as the temperature. Furthermore the temperature and electric field act synergistically, [54]. We expect that androthermia with modulated electric field effect works in synergy with the classical temperature- based hyperthermia concept. In preclinical conditions (in vivo and in vitro) many measurements were done in animals for oncology applications. The actual temperature development by the method would be too problematic to control in depth by the necessary invasive measurement approach. We worked out the energy-controlled dose. When necessary the temperature also could be measured, as we had shown in a sophisticated, well-controlled clinical temperature measurement [55]. The CT-guided fluoroptic sensor was positioned by interventional radiologist, and the patient (suffering with advanced sarcoma) was treated with the medium applicator. The maximal temperature in the tumor was 44 ºC, while the surface temperature

remained around 32 ºC.

Androtherm© device (Treat-therm® trade-mark), is the product of Oncotherm GmbH, Troisdorf, Germany) (see Figure 4.). It was developed for Peyronie disease, concentrating the plaque dissolution, using all the experiences and achievements from the past 20 years.

Figure 4. The front look of Androtherm device (Treat-therm ® trade-mark)

A set of special electrodes were developed for best performance (see Figure 5.)

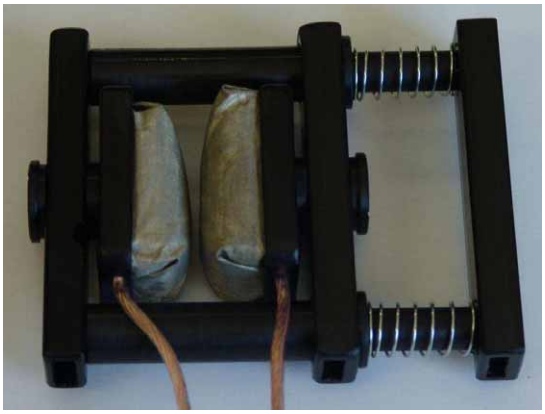

Figure 5. The electrode setup for penile treatment of plaques

The proposed and tested protocol of treatment was made 30 min two times a week, overall treatment number was 30 treatments/case in 3 cycles (10 sessions in each). One of the actual treatment setups is shown in (see Figure 6.).

Figure 6. Actual treatment setup, shows the fit of the electrode on the penis

The treatments was used only as monotherapy, studying first the effect of the new method alone. All the patients were advanced stages, and their symptoms were measured in standard methods. The practical parameters to observe the expected changes were:

Size of the plaque
Curvature of the penis
Pain-reduction at erection
Erection function

Results

16 patients were studied till now. One of them was withdrawn (the patient subjectively evaluated no change). The age distribution was far from the normal (see Figure 7.) shifted to the elderly categories, which agrees with the epidemiological data **[4]**

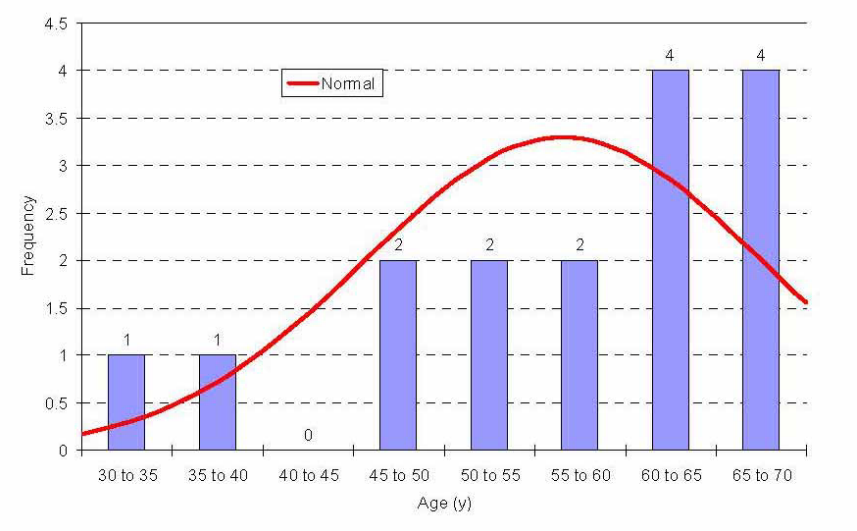

Figure 7. Age distribution of the patients involved in the study

The body-mass index (BMI) data follows the normal (Gaussian), distribution (see Figure 8.), which indicates the unbiased patient collection. Patients are dominantly overweighed.

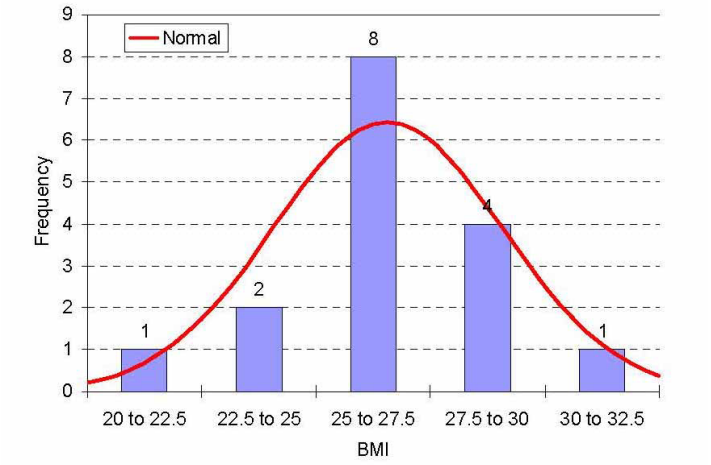

Figure 8. Distribution on the body-mass index

The age (y), weight (kg) height (cm) and the BMI (kg/m^2) is shown in Figure 9.

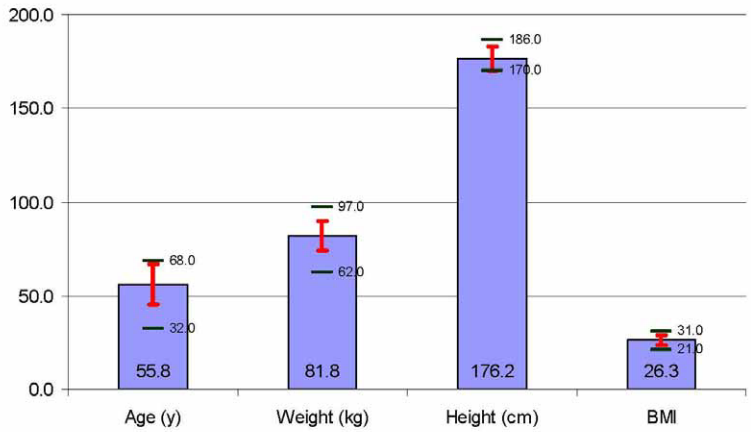

Figure 9. Descriptive values of the patients showing the averages (at bottom of the columns) the standard deviations (red intervals), and the minimal and maximal values in the given set of patients are shown by green lines

Typical cases are shown demonstrating the effect on curvature of the penis. The photos of the result before and after the treatment shows spectacular improvement (see Figures 10. and 11.)

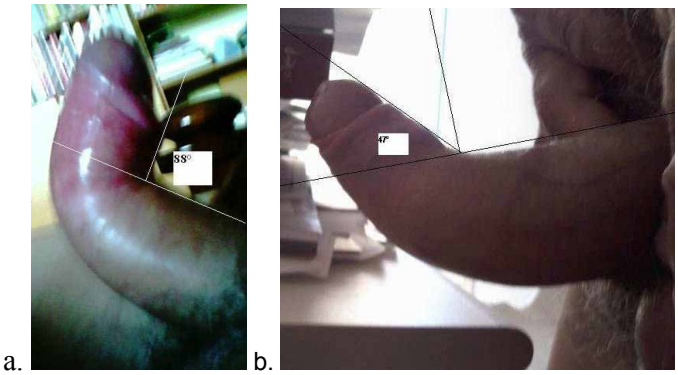

Figure 10. Patient #4 before (a) and after (b) the androthermia treatment sessions (Extreme penile curvature)

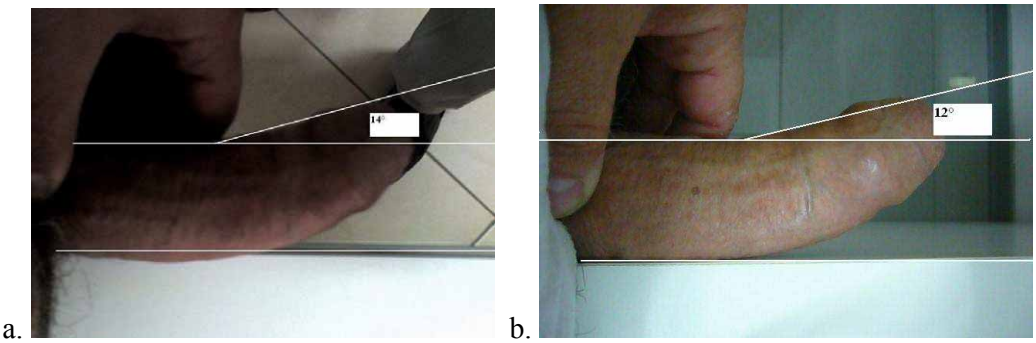

Figure 11.The penile curvature of the patient #16 before (a) and after (b) the androthermia treatment sessions (minor penile curvature)

The treatments were dominantly successful. All patient had benefit, improvement at least one of the investigated four (curvature, plaque, erection, pain) parameters. The plaque size before and after the Androtherm treatment decreased (see Figure 12.) except one case (#7), but the consistence of the plaque here also was softer after the therapy.

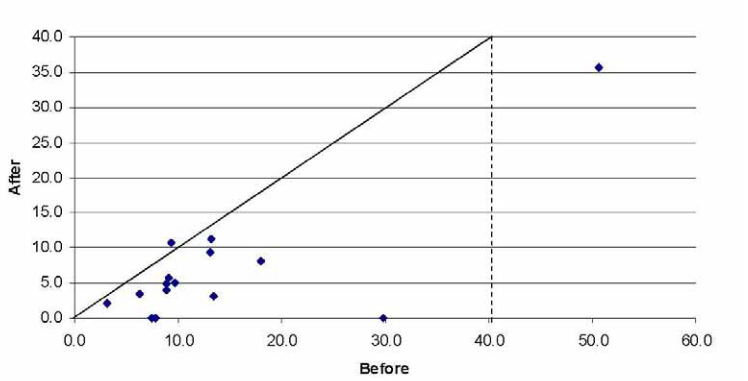

Figure 12. The plaque size before and after androthermia treapy. Except one case, all points are below the equal line, which means that after was the plaque size less than before (The equal-line is given to guide of the eye)

The change in percentages is shown in Figure 13.

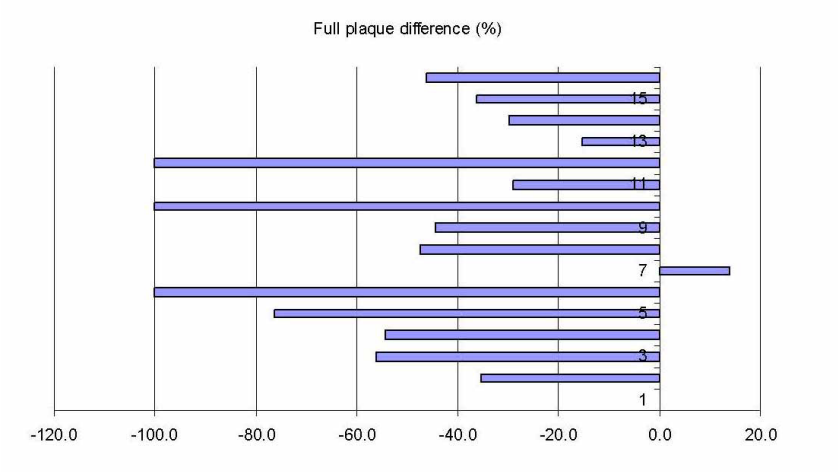

Figure 13. The plaques are reduced by considerable percentages

The average of the plaque size decreased by more than 50% (see Figure 14.).

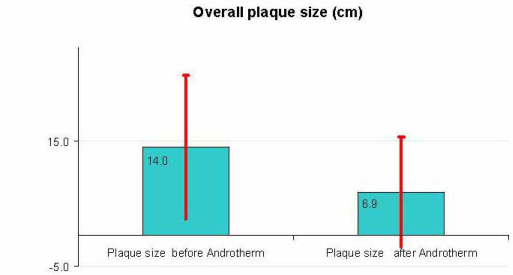

Figure 14. The average of the plaque size before and after androthermia. The red lines are the standard deviations

The curvature is also definitely improved, (see Figure 15. and Figure 16.), only in one case was unchanged (#11), but the curvature was originally small. One patient (#3) had no curvature and it was not changed.

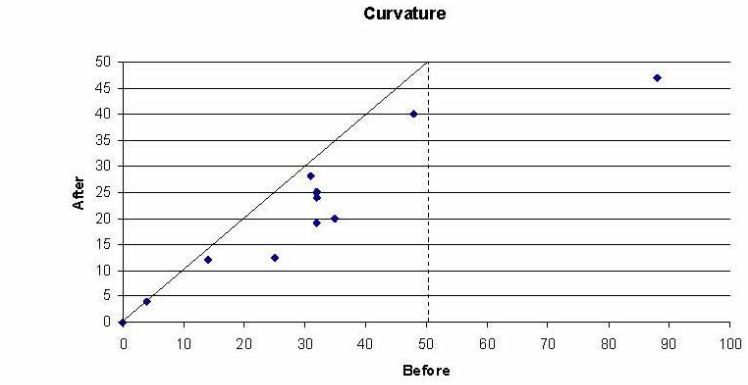

Figure 15. The penile curvature (degrees) before and after androthermia therapy (The equal-line is given to guide of the eye)

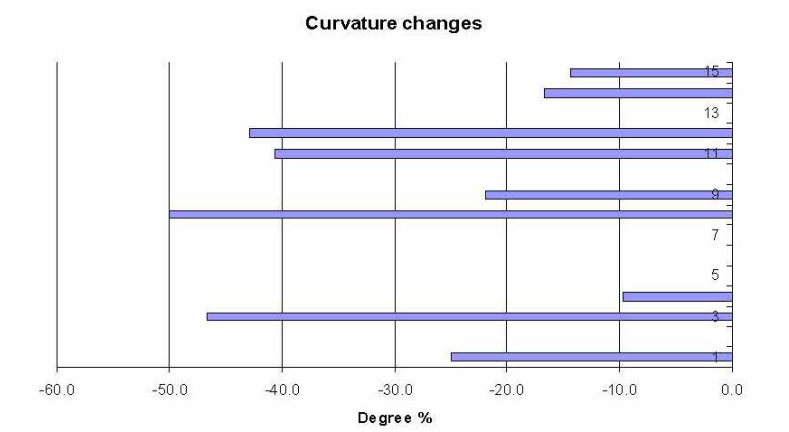

Figure 16. Change of curvature in percentages by androtherm therapy

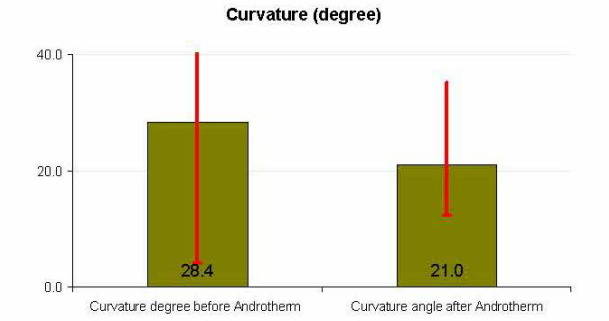

Figure 17. The average of curvatures (degrees in columns) and their standard deviations (red lines)

The IIF scores are also improved in general. In case of IIF5 [56] the results were not so significant (see Figure 18.) (only four patients reported better scores after the treatment) but the IIF15 [57] (see Figure 19.) was more successful, only slight worsening was in fourth cases but all the others had definite benefit for their IIF15 scores.

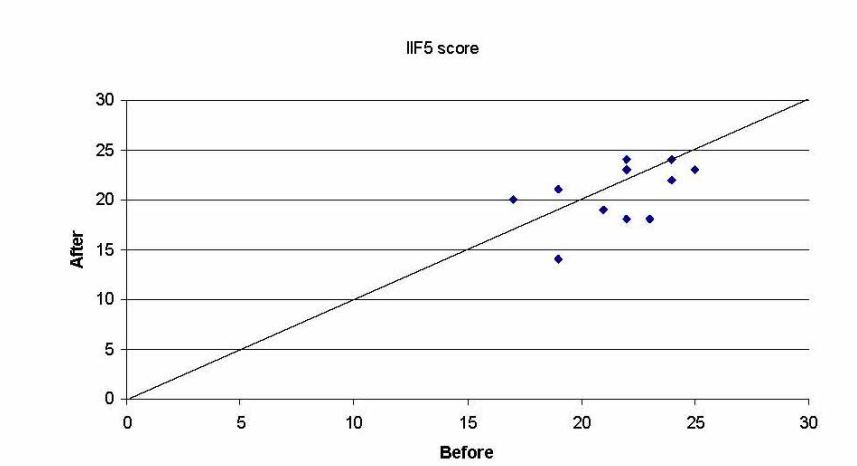

Figure 18. The IIF5 score before and after androthermia therapy. (The equal-line is given to guide of the eye.)

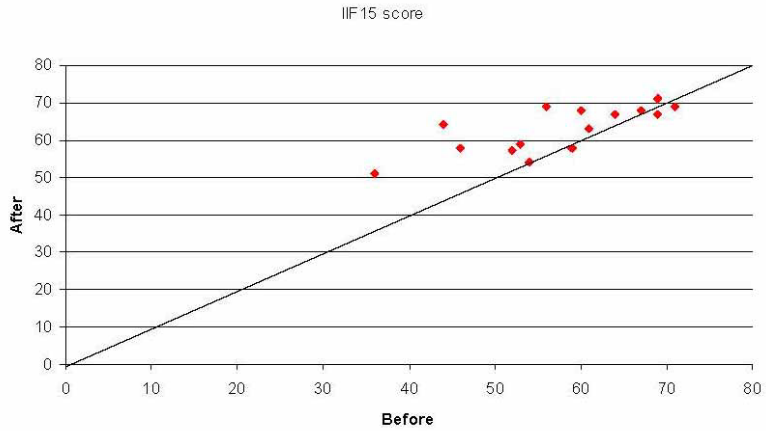

Figure 19. The IIF5 score before and after androthermia therapy. (The equal-line is given to guide of the eye.)

The averages of the IIF5 (see Figure 20.) and IIF15 (see Figure 21.) scores have no dramatic change, even the IIF5 slightly decreased, while IIF15 increased more than 9%.

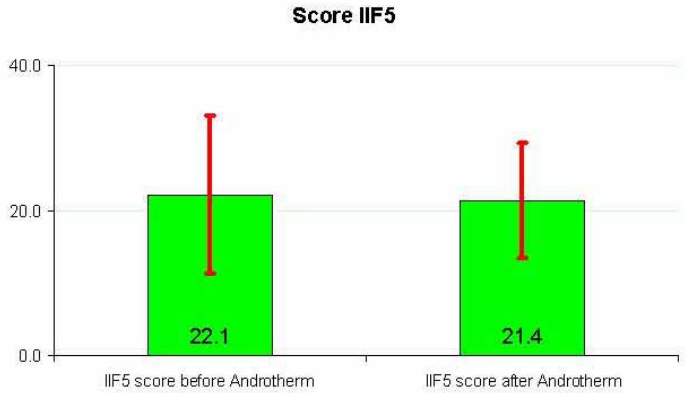

Figure 20. The IIF5 scores before and after androthermia therapy

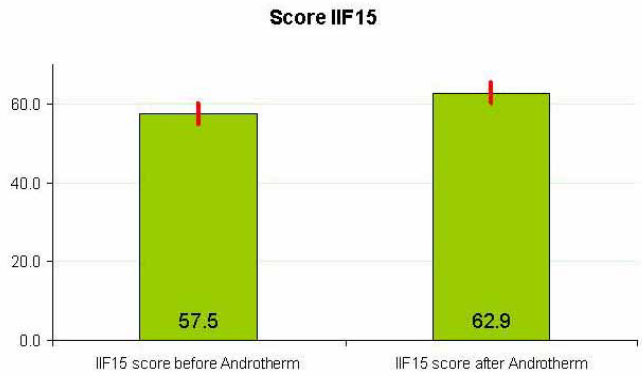

Figure 21. The IIF15 scores before and after androthermia therapy

In cases of the patients who had pain at erection, the pain was vastly reduced. The pain in most of the cases had disappeared at the end of therapy. The cases of erectile dysfunctions had functioning erection after the treatment.

Patients (except one) were subjectively satisfied, no adverse side effects were observed.

Conclusion

Androthermia is feasible and promising treatment modality for Peyronie disease. It is able to reduce most of the symptoms (see Figure 22) in most of the cases, and except one, no case was reported as non- effective.

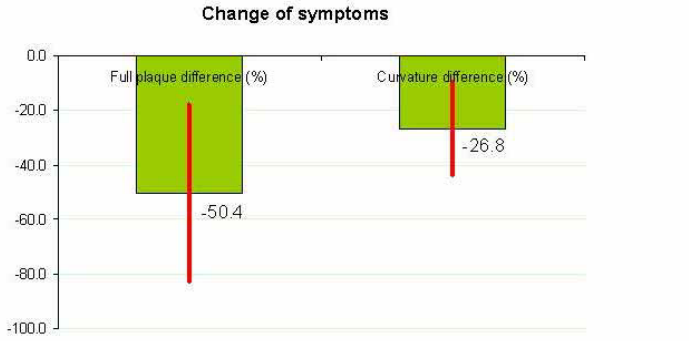

Figure 22. Change (percentages) of the main symptoms by androthermia therapy

Larger number of patients and more experience is necessary to make any conclusion. The further study is in progress.

References

[1] Gingell JC, Desai KM (1989) Peyronie's disease. Br J Urol. 63:223–226
[2] Gholami SS, Gonzalez-Cadavid NF, Lin CS (2003) Peyronie's disease: A review. J Urol. 169:1234-41
[3] Dunsmuir WD, Kirby RS (1996) Francois de La Peyronie (1678 –1747): the man and the disease he described. Br J Urol. 78:613-22
[4] Shaw K, PUri K, Ruiz-Deya G, Hellstrom WJG (2001) Racial consideration in the evaluation of Peyronie's disease. J Urol. 165:170;687A
[5] Lindsay MB, Schain DM, Grambsch P, Benson RC, Beard CM, Kurkland LT (1991) The incidence of Peyronie's disease in Rochester, Minnesota, 1950 through 1984. J Urol. 146:1007-9
[6] Schwarzer U, Sommer F, Klotz T, Braun M, Reifenrath B, Engelmann U (2001) The prevalence of Peyronie's disease: results of a large survey. BJU Int. 88:727-30
[7] Rhoden EL, Teloken C, Ting HY, Lucas ML, Teodósio da Ros C, Ary Vargas Souto C (2001) Prevalence of Peyronie's disease in men over 50 years old. J Urol 165:200
[8] Mulhall JP, Creech SD, Boorjian SA, Ghaly S, Kim ED, Moty A, Davis R, Hellstrom W (2004) Subjective and objective analysis of the prevalence of Peyronie's disease in a population of men presenting for prostate cancer screening. J Urol. 171(6 Pt 1):2350-2353
[9] Smith BH (1969) Subclinical Peyronie's disease. Am J Clin Pathol. 52:385-90
[10] Levine LA, Estrada CR, Storm DW Matkov TG (2003) Peyronie disease in younger men: characteristics and treatment results. Journal of Andorology 24:27-32

[11] Devine CJ, Somers KD, Ladaga LE (1991) Peyronie's disease: pathophysiology. Prog Clin Biol Clin Biol Res. 370:355–358
[12] Gonzalez-Cadavid NF, Rajfer J (2005) Mechanisms of disease: new insights into the cellular and molecular pathology of Peyronie's disease. Nat Clin Pract Urol. 2:291-297
[13] Lue TF (2002) Peyronie's disease: an anatomically based hypothesis and beyond. Int J Impot Res. 14:411-413
[14] Akkus E, Carrier S, Baba K (1997) Structural alterations in tunica albuginea of the penis: impact of Peyronie's disease, ageing, and impotence. Br J Urol. 79:47-53
[15] Hellstrom WG, Usta MF (2003) Surgical approaches for advanced Peyronie's disease patients. Int J Impot Res. 15 Suppl 5:S121-4
[16] Ji-Kan Ryu, Jun-Kyu Suh (2009) Peyronie's Disease: Current Medical Treatment and Future Perspectives. Korean Journal of Urology 50: 527-533
[17] Levine LA (2006) Peyronie's disease: Guide to Clinical management (Current clinical Urology), Humana Press
[18] Wellman R (2010) Peyronie's disease natural treatments and cures. Create Spaces
[19] Singh P, Maibach HI (1994) Transdermal iontophoresis. Clin Pharmacokinet 26:327–330
[20] Montorsi F, Salonia A, Guazzoni G, Barbieri L, Colombo R, Brausi M, Scattoni V, Rigatti P, Pizzini G (2000) Transdermal Electromotive Multi-Drug Administration for Peyronie's Disease: Preliminary Results. Journal of Andrology 21:85-90
[21] S.M. Di Stasi, A. Giannantoni, G. Capelli, E.A. Jannini, G. Virgili, L. Storti, G. Vespasiani (2003) Transdermal electromotive administration of verapamil and dexamethasone for Peyronie's disease, BJU International, 91:825–829
[22] Di Di Stasi SM, Giannantoni A, Robert L. Stephen, Capelli G, Giurioli A, Jannini EA, Vespasiani (2004) Prospective, randomized study using transdermal electromotive administration of verapamil and dexamethasone for Peyronie’s disease. J Urol 171:1605-1608
[23] Levine, LA (2003) Treatment of Peyronie's disease with intralesional verapamil. J Urol. 169:1775–1778
[24] Anthony J. Schaeffer, Arthur L. Burnett (2011) Non-surgical Interventions for Peyronie's Disease: 2011 Update, Journal of Andrology Feb.24
[25] Perugia G, Liberti M, Vicini P, Colistro F, Gentile V (2005) Role of hyperthermia in the treatment of Peyronie's disease: a preliminary study. Int. J. Hyperthermia, 21:367-374
[26] Cusmanich CC (2010) Treatment of Peyronie's disease with hyperthermia, vitamin D and testosterone: a pilot randomized controlled trial, running status, Curitiba, Brazil. (Ethics approval: ethics committee of Hospital de Clinicas da Universidade Federal do Parana (Brazil) on the 19th September 2007 (ref: CAAE: 01730208000-07; CEP/HC: 1489.154/2007-07).) (http://www controlled-trials com/ISRCTN82950322/, accessed: 16. Apr.2011)
[27] Giorgio Cavallini (2005) Towards an evidence-based understanding of Peyronie's disease; International Journal of STD & AIDS, 16:187-195
[28] Sang Kuk Yang, Bokyung Kim, Chang Kwan Lee, Hong Chung, Hong Sup Kim, Ji Kan Ryu, Kyung Jong Won, Seung Hwa Park, Hwan Myung Lee (2011) Differential Expression of Proteins Related with Penile Apoptosis in a Rat after Cavernous Nerve Resection. Korean J Androl. 29:111-126
[29] Carla Loreto, Guido Barbagli, Rados Djinovic, Giuseppe Vespasiani, Maria Luisa Carnazza, Roberto Miano, Giuseppe Musumeci, Salvatore Sansalone (2010) Tumor Necrosis Factor-Related Apoptosis-Inducing Ligand (TRAIL) and Its Death Receptor (DR5) in Peyronie's Disease. A Biomolecular Study of Apoptosis Activation. J Sex Med, 8:109-115
[30] Dolores Vernet, Gaby Nolazco, Liliana Cantini, Thomas R. Magee, Ansha Qian, Jacob Rajfer, Nestor F. Gonzalez- Cadavid (2005) Evidence That Osteogenic Progenitor Cells in the Human Tunica Albuginea May Originate from Stem Cells: Implications for Peyronie Disease. Biology of Reproduction 73:1199–1210
[31] H M Nugteren, J M Nijman, I J de Jong, M F van Driel (2011) The association between Peyronie's and Dupuytren's disease. International Journal of Impotence Research 23:142-145
[32] Morsi Khashan, Peter J. Smitham, Wasim S. Khan, Nicholas J. Goddard (2011) Dupuytren's Disease: Review of the Current Literature. The Open Orthopaedics Journal, 5-(Suppl 2-M9):283-288
[33] Qian A, Meals RA, Rajfer J, Gonzalez-Cadavid NF (2004) Comparison of gene expression profiles between Peyronie's disease and Dupuytren's contracture. Urology 64:399-404
[34] B. Jemec, A. O. Grobbelaar, G. D. Wilson, P. J. Smith, R. Sanders, D. A. McGrouther (1999) Is Dupuytren's Disease Caused by an Imbalance between Proliferation and Cell Death? J Hand Surg Eur 24:511-514
[35] Samrina Rehman, Royston Goodacre, Philip J Day, Ardeshir Bayat, Hans V Westerhoff (2011) Dupuytren's: a systems biology disease. Arthritis Research & Therapy, 13:238-249
[36] Vi L, Feng L, Zhu RD, Wu Y, Satish L, Gan BS, O'Gorman DB (2009) Periostin differentially induces proliferation, contraction and apoptosis of primary Dupuytren's disease and adjacent palmar fascia cells. Exp Cell Res. 315:3574-3586
[37] Kudo Y, Siriwardena BS, Hatano H, Ogawa I, Takata T (2007) Periostin: novel diagnostic and therapeutic target for cancer. Histol Histopathol 22:1167-1174
[38] Szasz A, Szasz N, Szasz O (2010) Oncothermia – Principles and Perspectives, Springer Science, Heidelberg
[39] Andocs G, Szasz O, Szasz A (2009) Oncothermia Treatment of Cancer: From the laboratory to clinic. Electromagnetic Biology and Medicine, 28:148-165
[40] Szasz A, Szasz O, Szasz N (2001) Electrohyperthermia: a new paradigm in cancer therapy. Wissenschaft & Forschung, Deutsche Zeitschrift für Onkologie, 33:91-99
[41] Szasz A (2008) Oncothermie, OM & Ernährung, Fachinformation, 123:F22-F23
[42] Szasz A (2008) Oncotherm, Traditionen und Reformen in der onkologischen Hyperthermie. Forum Hyperthermie, Forum Medizine, 1:22-23
[43] Szasz A, Vincze Gy (2007) Dose concept of oncological hyperthermia: heat-equation considering the cell destruction. Journal of Cancer Research and Therapeutics, 2:171-181
[44] Fiorentini G, Szasz A: Hyperthermia Today (2006) Electric energy, a new opportunity in cancer treatment. Journal of Cancer Research and Therapeutics, 2:41-46
[45] Vincze Gy, Szász A, Szasz N (2005) On the thermal noise limit of cellular membranes. Bioelectromagnetics, 26:28-35
[46] Szendrő P, Vincze G, Szász A (2001) Pink-noise behaviour of biosystems. Eur Biophysics J. 30:227-231
[47] Vincze G, Szasz A, Liboff A (2008) New theoretical treatment of inon resonance phenomana. Bioelectromagnetics, 29:380-386
[48] P. Szendrő, G. Vincze, A. Szász (2001) Bio-response to White Noise Excitation. Electro- and Magnetobiology 20:215-229
[49] Zaffaroni N, Fiorentini G, De Giorgi U (2001) Hyperthermia and hypoxia: new developments in anticancer chemotherapy. Eur J Surg Oncol. 27:340-342
[50] Hegyi G, Vincze G, Szasz A (2007) Axial-vector interaction with bio-systems. Electromagnetic Biology and Medicine, 26:107-118
[51] Joo E, Szasz A, Szendro P (2006) Metal-framed spectactesl and implants and specific absorption rate among adults and children using mobile phones at 900/1800/2100 MHz. Electromagnetic Biology and Medicine, 25:103-112
[52] Szasz A (2006) What is against the acceptance of hyperthermia? Die Naturheilkunde, Forum-Medizine, 83:3-7
[53] Szasz A (2003) Elektromagnetische Hyperthermieverfahren: die kapazitive Kopplung. Forum Komplementare Onkologie: Hyperthermie, 4:III-IX
[54] Andocs G. Renner H.Balogh L, Fonyad L, Jakab Cs, Szasz A (2009) Strong synergy of heat and modulated electromagnetic field in tumor cell killing, Study of HT29 xenograft tumors in a nude mice model. Accepted for publication in Radiology and Oncology [Strahlentherapie und Onkologie], 185:120-126
[55] Renner H (2008) Klinikum Nord, Nuernberg (Prof.Dr.Renner's Office)
[56] International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. Int J Impot Res. 1999 Dec;11(6):319-26. © 1999
[57] The international index of erectile function (IIEF) a multidimensional scale for assessment of erectile dysfunction. Urology. 1997 Jun; 49(6):822-30. Copyright 1997 by Elsevier Science, Inc)