CHARALAMPOS K. MAMOULAKIS

ASSISTANT PROFESSOR OF UROLOGY

UNIVERSITY OF CRETE - FACULTY OF MEDICINE

CURRICULUM VITAE

MAY 2014

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Dr. Charalampos Mamoulakis, MD, MSc, PhD, FEBU, Assistant Professor of Urology, University of Crete, Medical School, Heraklion, Crete, Greece

Dr. Charalampos Mamoulakis is a distinguished graduate of the National & Kapodistrian University of Athens Medical School. After accomplishing his urological residency in Athens, Greece (2006), he acquired the FEBU title (same year), and has been working as certificated urologist in Greece, and the Netherlands (MSRC) since that time. He holds Master's degree in Biostatistics (MSc; University of Athens Medical School, Department of Hygiene & Epidemiology, Faculty of Mathematics; University of Ioannina, Faculty of Mathematics, Ioannina, Greece) and PhD on molecular analyses of genetic factors in cryptorchidism (University of Ioannina, Medical School, Ioannina, Greece). He worked for two years as a NHS Staff Member at the Department of Urology, General Hospital "Aghios Georgios", Chania, Crete, Greece. Between February 2008 and March 2010 he worked as a Staff Member at the Department of Urology, AMC University Hospital, Amsterdam, the Netherlands and he was awarded the title of the first European Association of Urology (EAU) Section of Urotechnology (ESUT) Fellow in Endourology & Laparoscopy (2010). He has been working with pioneers in the field of Endourology and emerging technologies in many projects. His research and clinical activity focuses on Endourolgy and Minimal Invasive Techniques including applications to stones and BPH management, which has resulted in several publications in scientific journals of highest impact. He acquired an academic post (Lecturer of Urology) at the University of Crete, Medical School (2009), and works since January 2011 at the University Hospital of Heraklion, Heraklion, Crete, Greece. In July 2014 he has been nominated Assistant Professor of Urology at the same University. He holds a PhD researcher position at the Department of Urology, Academic Medical Centre, University of Amsterdam, Amsterdam the Netherlands, focusing on bipolar electrosurgery in patients with BPH. He has been honored with distinctions, awards and grants by the Hellenic Urological Association (HUA, 2004 & 2006), Public Benefit Foundation "Alexander S. Onassis" (2008-2009) and EAU (EUSP, 2009). He was proposed by HUA as the most suitable candidate among young Greek urologists for EAU Crystal Matula Award 2011. Since 2011 he is a member of the EAU BPH/Male LUTS/BOO Guidelines Office Panel. Since 2013 he is a member of the International Consultation on Urological Diseases (ICUD) (3rd International Consultation on Stone Disease; Société Internationale d'Urologie). He is a member of several associations including ASA, AUA, EAU, Endourological Society, ESUT, International Biometric Society and SIU having contributed to their activities as presenter, member of the organizing committees or invited faculty.

1. PERSONAL INFORMATION

Name:	Charalampos K. Mamoulakis
Date of birth:	17 May 1970
Place of birth:	Athens
Nationality:	Hellenic
Marital Status:	Married; three children
Διεύθυνση οικίας:	P.O. Box: 1031
	71001 Heraklion, Crete
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2. UNDERGRADUATE-POSTGRADUATE EDUCATION-DEGREES

I. Basic Education-Foreign languages

- 1985-1988: 2nd Lyceum of Heraklion, Crete-"Apolytirion"[1]: grade "Excellent"
- July 1988: National & Kapodistrian University of Athens, Medical School, Athens, Greece after succeeding in the National "Panhellenic Examinations"
- Foreign languages:

  English: Certificate of Proficiency in English-Cambridge University

  German: Zeugnis Zertifikat Zentrale Mittelstufenprüfung-Goethe Institute

  Spanish: Certificado Básico de Salamanca

II. Undergraduate Education

- 1988-1996: National & Kapodistrian University of Athens, Medical School, Athens, Greece. "Ptychio Iatrikes"[2]: grade "Excellent". Date of graduation 26-04-1996. Hellenic Medical License: 17982/09-10-1996

III. Postgraduate Education-Degrees

1. Specialization in Urology (see: 3. Medical Experience, relevant section)

- ✓ July 2006: Certificated Urologist in Greece; Decision 5456/24-7-2006
- ✓ September 2008: Certificated Urologist in the Netherlands (MSRC)

2. PhDs in Urology

- ✓ National PhD holder, University of Ioannina, Medical School, Ioannina, Greece (18-03-2008)

  Subject: "Spermatologic alterations & genetic factors in cryptorchidism"
  Supervisor: Prof. N. Sofikitis, Chairman of the Department of Urology, University of Ioannina, Medical School, Ioannina, Greece

- ✓ International PhD candidate, University of Amsterdam, The Netherlands

[1] The Greek equivalent degree to the A-level

[2] The Greek medical qualification

Subject: “The position of bipolar technology in transurethral resection of the prostate for benign prostatic obstruction: An evidence-based approach”. Promoters: J.J.M.C.H de la Rosette & J.J. Rassweiler

The Thesis is expected to be defended within the year 2013

3. **MSc in Biostatistics (23-05-2005)**

   He followed a two-year-duration, multi-institutional postgraduate programe in “Biostatistics” that led to MSc title (23-05-2005):

   Participating institutions: 1. University of Athens, Athens, Greece: A. Faculty of Medicine (Department of Hygiene & Epidemiology), B. Faculty of Mathematics; 2. University of Ioannina, Ioannina, Greece: Faculty of Mathematics); Academic period: September 2002-September 2004

   Supervisor: Prof. A. Tzonou, Department of Hygiene, Epidemiology & Medical Statistics, Athens University Medical School, Athens, Greece

   Thesis entitled: “Seasonal variation of hypospadias in Greek population”

4. **Fellow of the European Board of Urology (FEBU; 10-06-2006)**
5. **EUSP/EAU-ESUT Fellow of Endourology and Laparoscopy**

   He followed a two-year Clinical Fellowship programme under the auspices of the European Urology Scholarship Programme & the European Association of Urology Section of Uro-Technology.

   Host institution: Department of Urology, Academic Medical Center (AMC) University Hospital, Amsterdam, the Netherlands; Supervisor: Prof. J.J.M.C.H. de la Rosette; Period: February 2008 – March 2010.

6. **Clinical Fellow in Urology with emphasis on Endourology & Laparoscopy (Sabbatical Leave)** February 2014-August 2014, Department of Urology, Saifee Hospital; MUHS (Maharashtra University of Health Sciences), Mumbai, India; Supervisor: Prof. Dr Gaurang Shah; Period: February 2014 – August 2014 .

3. MEDICAL EXPERIENCE

- **Fellowship:** June-September 1996: Department of Neurosurgery, "St-Luc" University Hospital, UCL, Brussels, Belgium (supervisor: Prof. Ch. Raftopoulos, Chairman of the Department)
- **Military Service:** January-September 1997 Medical Officer of the Hellenic Air force at "251" General Hospital of the Hellenic Air force, Athens, Greece and the Air force Base of Heraklion, Crete, Greece
- **Rural Medical Service**[1]**:** October 1997 - October 1998, "Tzermiades" Health Centre, Lassithi, Crete, Greece.
- **Specialization in Urology:** May 1999 - May 2006: "Aghia Sophia" General Children's Hospital, [2] & "Evangelismos" General Hospital[3] (16 months Surgery, 48 months Urology in total). From November 2001 to May 2003, he entered a "between-hospitals waiting list period". During this period of time he participated in the activities at the First Department of Paediatric Surgery, "Aghia Sophia" General Children's Hospital focusing on his PhD research.
- **NHS Staff Member (non-academic) in Greece:** November 2006 – November 2007: Department of Urology, General Hospital "Aghios Georgios", Chania, Crete, Greece

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[1] One-year general medical practice in terms of the compulsory medical rural service in Greece

[2] "Aghia Sophia" General Children's Hospital is a 750-bed hospital in Athens, the biggest national paediatric center in Greece. It is a university hospital, which involves the whole range of paediatric specialties and offers complete training in Paediatric Surgery in Greece. Aproximately 40 beds are used for General Paediatric Surgery and 10 for Paediatric Urology. He participated fully in all clinical and educational activities of the department: emergency duties, inpatient care, outpatient clinics, operating theatre, on-call rota 1:4

[3] "Evangelismos" General Hospital of Athens is a 900-bed university hospital. It is the biggest hospital in Greece. It involves the whole range of specialties and offers complete training in urology. Approximately 40 beds belong to the Department of Urology. He participated fully in all clinical and educational activities of the Department: emergency duties, inpatient care, outpatient clinics, operating theatre, on-call rota 1:4

- **Clinical Fellow in Endourology and Laparoscopy:** February 2008 – March 2010 at the Department of Urology, AMC University Hospital, Amsterdam, the Netherlands. From September 2008 to March 2010 he was appointed as a Staff member of this department (overlap with section 2-III.5)
- **NHS Staff Member (non-academic) in Greece:** May 2010 - January 2011: Department of Urology, General Hospital "Aghios Georgios", Chania, Crete, Greece
- **Lecturer of Urology** (election: 26/5/09, appointed by Decision 1254-31/12/2010): University of Crete, Faculty of Medicine, Department of Urology, University General Hospital of Heraklion, Heraklion, Crete, Greece, 25/01/2011- 19/12/2013
- **Assistant Professor of Urology** (election: 15/7/2013, appointed by Decision: 1464-16/12/2013): University of Crete, Faculty of Medicine, Department of Urology, University General Hospital of Heraklion, Heraklion, Crete, Greece, 20/12/2013- Today)
- **Clinical Fellow in Urology with emphasis on Endourology & Laparoscopy (Sabbatical Leave):** February 2014-August 2014, Department of Urology, Saifee Hospital; MUHS (Maharashtra University of Health Sciences), Mumbai, India.

4. CLINICAL ACTIVITY

During the period of service as Lecturer of Urology at the University of Crete, he has performed clinical work fully and exclusively at the Department of Urology, University Hospital of Heraklion.

This clinical activity may be summarized as follows:

- ✓ Endourology & SWL – Endoscopic Urology Unit (responsible staff member)
- ✓ Operation theater: On a regular (one day per week on average) and emergency base
- ✓ On call: Twice per week on average
- ✓ Outpatient clinic (focused on urinary stone management): once per week
- ✓ Outpatient clinic (General Urology): twice per week
- ✓ Urodynamic unit: once per week (responsible staff member)
- ✓ SWL: twice per week
- ✓ Regular ward rounds – Regular Inter- & Intra-clinical mettings – Scientigic regular Meetings of the University Surgical Sector

He has developed Endoourology in the University General Hospital of Heraklion. He trained manpower (urological residents and a specific group of operation theater nurses) to support the execution of various interventions. He has organized the provision of modern equipment needed (full range of consumable material, specialized endourological high definition tower, Holmium Laser system for stone management, system for percutaneous renal access, flexible ureteroscopes, etc.) for scripting and digital recording of endourological interventions, which are executed systematically by him since the beginning of 2012.

(http://www.imop.gr/uro-e-learning-65; http://www.imop.gr/uro-e-learning/rirs)

Recently, he has been appointed due to his certified special education and experience, the responsible physician of the newly formed Endourology – Endoscopic Urology - Urolithiasis Unit (EEUU) of the Department of Urology, University General Hospital of Heraklion. The EEUU deals with the study of Endourology - Minimally Invasive Urology; and the application of modern urotechnology in the diagnosis, treatment and

monitoring of patients with diseases such as urolithiasis, benign prostatic hyperplasia, urinary tract tumors etc., which require sophisticated and specialized treatment based on the international guidelines and standards. Examples of such applications include: intracorporeal lithotripsy using Laser-flexible ureterorenoscopes, percutaneous nephrolithotripsy, extracorporeal shock wave lithotripsy , diagnosis - monitoring and treatment of tumors of the urinary tract using specific light sources - flexible fiberoptic and digital cyctoscopes/ureterorenoscopes, transurethral resection/vaporization of the prostate and tumors with the use of safer energy sources such as bipolar electrosurgery, Lasers etc.). One of the EEUU main purposes includes, among others, investigation of the epidemiology/pathogenesis of urolithiasis in terms of study, treatment/monitoring of relevant patients, which will be held in the existing Special Urolithiasis Oupatient Clinic that supports it. In the EEUU also belongs fully the Extracorporeal Lithotripter at the University General Hospital of Heraklion. The EEUU will collaborate with the University of Crete, other domestic and foreign universities, certified National and International bodies of Endoourology and other departments of the University General Hospital of Heraklion and other hospitals in Greece and abroad in relevant educational, research and clinical issues (training of urology residents and medical students, execution of basic and clinical research protocols, clinical problems addressing).

5. EDUCATIONAL EXPERIENCE

1. Medical students (4th & 5th year):

During the period of service at the University of Crete, he organized the curriculum; he undertook the bulk of the amphitheater teaching of the compulsory subject “Urology” and conducted progress/final examinations. He actively participated in organizing, teaching/conducting the examinations of the elective course "Andrology" and in the supervision, training and evaluation of the students in terms of their clinical practice in Urology.

2. Urological Residents:

He contributed to the guidance, supervision and evaluation of theoretical training (annual program of intra-clinical courses), clinical training (endourological interventions-SWL, urodynamics) and academic activities (assignments, lectures, courses, clinical studies) of the urological residents at the Department. In addition, he has participated in the training of the urological residents at the AMC, and other Urology departments in Greece and abroad, in collaboration with the responsible Professors serving as an examiner, instructor or invited speaker:

- ✓ Member of the FEBU Board of Examiners
- ✓ Invited instructor of Endourology with the use of simulators
- ✓ Invited speaker for seminars organized by the HUA section of Endourology – Laparoscopic/Robotic Urology and Urotechnology
- ✓ Invited speaker for the seminars given during the annual training weeks for Greek Urological residents organized by the HUA

3. Nursing Staff:

Instructor in training programs for nurses acquiring the surgical specialty at “Evangelismos” General Hospital of Athens and University Hospital of Heraklion. He has been participating with lectures on the subject of “Urology”. In addition he has trained a specific group of operation theater nurses to support

the execution of various endourological interventions including RIRS and PCNL.

6. DISTINCTIONS - AWARDS

1. Mamoulakis C, Sofikitis N, Tsounapi P, Vlachopoulou E, Chatzikyriakidou A, Antypas S, Tzortzakakis D, Sofras F, Takenaka A, Georgiou I. **The (TAAAA)(n) polymorphism of sex hormone-binding globulin gene is not associated with testicular maldescent. Andrologia. 2013;45:40-5.2 (Invited for the Royan International Research Award)** [1]

   http://www.royanaward.com/index.aspx

2. Mamoulakis C. Skolarikos A. Schulze M. Scoffone CM, Jens J. Rassweiler JJ, Alivizatos G. Scarpa RM, de la Rosette JJMCH. **Bipolar versus monopolar transurethral resection of the prostate: Evaluation of the impact on overall sexual function in an international randomized controlled trial setting. BJU Int 2013;112:109-20.** [2] **(Article of the week**)

3. Mamoulakis C, Schulze M, Skolarikos A, Alivizatos G, Scarpa RM, Rassweiler JJ, de la Rosette JJ, Scoffone CM. **Midterm Results from an International Multicenter Randomised Controlled Trial Comparing Bipolar with Monopolar Transurethral Resection of the Prostate. Eur Urol. 2013;63:667-76.**[2] **(Platinum Priority**)

3. C. Mamoulakis, A. Skolarikos, M. Schulze, C. Scoffone, J. Rassweiler, G. Alivizatos, R. Scarpa, J. De La Rosette. **Bipolar vs monopolar TURP: Impact on the overall sexual function and midterm safety-efficacy results of an international multicenter randomized controlled trial Eur Urol Suppl 2013; 12(1):e521-e522.** 28th Annual EAU Congress, 15-19 March 2013; Milan, Italy[2] (prized work)

4. Proposed for his overall research activity by the Hellenic Urological Association as the most suitable young Greek urologist to represent Greece in claiming the EAU Crystal Matula Award, 2011

5. C. Mamoulakis, D. Ubbink, M. Laguna, J. De la rosette. **Bipolar versus monopolar transurethral resection of the prostate: a meta-analysis of**

[1] Publication from the National PhD research project

[2] Publication from the International PhD research project

randomized clinical trials. J Endourol 2009;23 (s1):A264. 27th WCE, 6-10 October 2009, Munich, Germany[1] (prized work)

6. C. Mamoulakis, P. Beemster, S. Mehmedovic, H. Wijkstra, J. de la Rosette, M. Laguna. **Intermediate follow-up of renal masses treated by laparoscopic cryoablation. J Endourol 2009;23 (s1):A294.** 27th WCE. 6-10 October 2009, Munich, Germany (prized work)
7. Scholar of the Public Benefit Foundation "Alexander S. Onassis" for a Clinical Fellowship Programme at the AMC
8. EAU Scholar (European Urological Scholarship Programme, EUSP) for a Clinical Fellowship Programme at the AMC
9. HUA Distinction (2006): Highest performance at the examinations in terms of the 1st Educational Week for Greek Urological Residents
10. HUA Award (2004): Ranked first among the Greek Urological Residents at the annual written examinations
11. Tuition waivers (MSc in Biostatistics; 2002): Excelled during the selection process of candidates
12. Lycopoulou L, Bounatsou M, Hantzi E, Mamoulakis C, Antypas S, Demetriadis D, Bakoula C, Pagali A, Papassotiriou I. **Reduced prognostic value of procalcitonin in the diagnosis of acute appendicitis.** 20th National Congress of Microbiology – 2nd Panhellenic Congress of Medical Biopathology, 13-16 March, 2002; Athens, Greece (prized work)

[1] Publication from the International PhD research project

7. PUBLICATIONS & PRESENTATIONS

7.1. h-index - Citations

h-index - Αναφορές (ISI): 11 – 363 (19 May 2014)

h-index - Αναφορές (Scopus): 12 – 461 (15 April 2014)

7.2. Full publications in international scientific journals

1. Chondros K, Karpathakis N, Tsetis D, Sofras F, Mamoulakis C. **Systemic thrombolysis with the use of tenecteplase for segmental acute renal infarction associated with multiple thrombophilic gene polymorphisms. Hippokratia. 2014;18:67-70**

2. Oelke M, Weiss JP, Mamoulakis C, Cox D, Ruff D, Viktrup L. **Effects of tadalafil on night-time voiding (nocturia) in men with lower urinary tract symptoms suggestive of benign prostatic hyperplasia: a post-hoc analysis of pooled data from four randomized, placebo-controlled clinical studies World J Urol. 2014 Feb 7. [Epub ahead of print]**

3. Mamoulakis C. **Re: A plea for higher quality data for GreenLight laser technology in the context of surgical benign prostatic obstruction trials: The GOLIATH study - Fact or fiction in the era of evidence based urology? Eur Urol. 2014;65:943-6**

4. Mamoulakis C, Georgiou I, Dimitriadis F, Tsounapi P, Giannakis I, Chatzikyriakidou A, Antypas S, Sofras F, Takenaka A, Sofikitis N. **Genetic analysis of the human Insulin-like 3 gene: Absence of mutations in a Greek paediatric cohort with testicular maldescent. Andrologia. 2014 (Accepted: 12/09/2013)**[1]

5. Mamoulakis C, Sofras F, de la Rosette J, Omar MI, Lam TBL, N'Dow JMO, Ubbink DT. **Bipolar versus monopolar transurethral resection of the prostate for lower urinary tract symptoms secondary to benign prostatic obstruction. Cochrane Database of Systematic Reviews 2014(1): CD009629.**

[1] Publication from the national PhD research project

6. Omar MI, Lam TBL, Cameron A, Graham J, Mamoulakis C, Imamura M, Maclennan S, Stewart F, N'Dow JMO. **Systematic review and meta-analysis of the clinical effectiveness of bipolar compared to monopolar transurethral resection of the prostate. BJU Int. 2014 Jan;113:24-35.**

7. Mamoulakis C, Ubbink DT, Sofras F, N'Dow JM, de la Rosette JJ. **Letter to the Editor referring to the article: Huang X, Wang L, Wang XH, Shi HB, Zhang XJ, Yu ZY. Bipolar transurethral resection of the prostate causes deeper coagulation depth and less bleeding than monopolar transurethral prostatectomy. Urology. 2012;80:1116-20. Urology 2013;81:1113-5.**

8. Mamoulakis C. Skolarikos A. Schulze M. Scoffone CM, Jens J. Rassweiler JJ, Alivizatos G. Scarpa RM, de la Rosette JJMCH. **Bipolar versus monopolar transurethral resection of the prostate: Evaluation of the impact on overall sexual function in an international randomized controlled trial setting. BJU Int 2013;112:109-20.** [1]

9. Mamoulakis C, Georgiou I, Dimitriadis F, Tsounapi P, Koukos S, Antypas S, Tzortzakakis D, Sofras F, Takenaka A, Sofikitis N. **Screening for Y chromosome microdeletions in childhood: lack of evidence for a direct association with testicular maldescent. Andrologia. 2013;45:409-16.**[2]

10. Mamoulakis C, Schulze M, Skolarikos A, Alivizatos G, Scarpa RM, Rassweiler JJ, de la Rosette JJ, Scoffone CM. **Midterm Results from an International Multicenter Randomised Controlled Trial Comparing Bipolar with Monopolar Transurethral Resection of the Prostate. Eur Urol. 2013;63: 667-76.**[1]

11. Mamoulakis C, Schulze M, Skolarikos A, Alivizatos G, Scarpa RM, Rassweiler JJ, de la Rosette JJ, Scoffone CM. **Reply from Authors re: Alexander Bachmann, Gordon H. Muir, Stephen F. Wyler, Malte Rieken. Surgical benign prostatic hyperplasia trials: The future is now! Eur Urol.**

[1] Publication from the international PhD research project

[2] Publication from the national PhD research project

2013;63:677-9. Best available evidence in 2012 on bipolar versus monopolar transurethral resection of the prostate for benign prostatic obstruction: It's about time to decide! Eur Urol. 2013;63:677-680.[1]

12. Mamoulakis C, Sofikitis N, Tsounapi P, Vlachopoulou E, Chatzikyriakidou A, Antypas S, Tzortzakakis D, Sofras F, Takenaka A, Georgiou I. **The (TAAAA)(n) polymorphism of sex hormone-binding globulin gene is not associated with testicular maldescent. Andrologia. 2013;45:40-5.**[2]

13. Rassweiler MC, Mamoulakis C, Kenngott HG, Rassweiler J, de la Rosette J, Laguna MP. **Classification and detection of errors in minimally invasive surgery. J Endourol. 2011;25:1713-21.**

14. Mamoulakis C, Skolarikos A, Schulze M, Scoffone CM, Rassweiler JJ, Alivizatos G, Scarpa RM, de la Rosette JJ. **Results from an international multicenter double-blind randomized controlled trial on the perioperative efficacy and safety of bipolar vs. monopolar transurethral resection of the prostate. BJU Int. 2012;109:240-8.**[1]

15. Mamoulakis C, Skolarikos A, Schulze M, Scoffone CM, Rassweiler JJ, Alivizatos G, Scarpa RM, de la Rosette JJ. **Letter to the Editor (Reply), Re: Results from an international multicenter double-blind randomized controlled trial on the perioperative efficacy and safety of bipolar vs. monopolar transurethral resection of the prostate. BJU Int. 2012;109: E22-E4.**[1]

16. Mamoulakis C, Skolarikos A, Schulze M, Scoffone CM, Rassweiler JJ, Alivizatos G, Scarpa RM, de la Rosette JJ. **Letter to the Editor (Reply), Re: Results from an international multicenter double-blind randomized controlled trial on the perioperative efficacy and safety of bipolar vs.**

[1] Publication from the international PhD research project

[2] Publication from the national PhD research project

monopolar transurethral resection of the prostate. BJU Int. 2012;109: E38-E40. [1]

17. Rioja J, Mamoulakis C, Sodha H, Suwijn S, Laguna P, de la Rosette J. **A plea for centralized care for ureteroscopy: results from a comparative study under different conditions within the same center. J Endourol. 2011;25:425-9.**

18. Cauberg EC, Mamoulakis C, de la Rosette JJ, de Reijke TM. **Narrow band imaging-assisted transurethral resection for non-muscle invasive bladder cancer significantly reduces residual tumor rate. World J Urol. 2011;29:503-9.**

19. Mamoulakis C, Herrmann TR, Höfner K, Oelke M. **The fish-hook configuration of the distal ureter indicates bladder outlet obstruction due to benign prostatic hyperplasia. World J Urol. 2011;29:199-204.**

20. Beemster PW, Barwari K, Mamoulakis C, Wijkstra H, de La Rosette JJ, Laguna MP. **Laparoscopic renal cryoablation using ultrathin 17-gauge cryoprobes: mid-term oncological and functional results. BJU Int. 2011; 108:577-82.**

21. Zilberman DE, Lipkin ME, de la Rosette JJ, Ferrandino MN, Mamoulakis C, Laguna MP, Preminger GM. **Tubeless percutaneous nephrolithotomy-the new standard of care? J Urol. 2010;184:1261-6.**

22. Heretis I, Mamoulakis C, Papadimitriou V, Sofras F. **Strategic lithotripsy using the Doli S EMSE 220 F-XP for the management of staghorn renal calculi. Int Urol Nephrol. 2011;43:61-5.**

23. Rioja J, Tzortzis V, Mamoulakis C, Laguna MP. **Cryotherapy for renal tumors: current status and contemporary developments. Actas Urol Esp. 2010;34:309-17.**

24. Mamoulakis C, Efthimiou I, Kazoulis S, Christoulakis I, Sofras F. **The modified Clavien classification system: a standardized platform for**

[1] Publication from the international PhD research project

reporting complications in transurethral resection of the prostate. World J Urol. 2011;29:205-10.[1]

25. Mamoulakis C, Ubbink DT, de la Rosette JJMCH. **Re: Burke et al.: systematic review and meta-analysis of transurethral resection of the prostate versus minimally invasive procedures for the treatment of benign prostatic obstruction (Urology 2010;75:1015-1022). Urology. 2010;75:1235-6.** [1]

26. Meissner A, Mamoulakis C, Laube N. **Urinary tract infections and urolithiasis. Urologe A. 2010;49:623-8.**

27. Meissner A, Mamoulakis C, de la Rosette JJMCH, Laguna Pes MP. **Clinical update on testicular microlithiasis. Curr Opin Urol. 2009; 19:615-8.**

28. Mamoulakis C, Ubbink DT, de la Rosette JJMCH. **Bipolar versus monopolar transurethral resection of the prostate: a systematic review and meta-analysis of randomized controlled trials. Eur Urol. 2009; 56: 798-809.**[1]

29. Oelke M, Mamoulakis C. **MiniArc™ single incision sling system to treat stress urinary incontinence in women: Implantation technique and early clinical results. BJU Int. 2009 June (Surgical Atlas) [Epub: http://www.bjui.org/Restricted.aspx].**

30. de la Rosette JJMCH, Wink MH, Mamoulakis C, Wondergem N, ten Kate FJC, Zwinderman K, de Reijke TM, Wijkstra H. **Optimizing prostate cancer detection: 8 versus 12-core biopsy protocol. J Urol. 2009;182: 1329-36.**

31. Wezel F, Mamoulakis C, Rioja J, Michel MS, de la Rosette J, Alken P. **Two contemporary series of percutaneous tract dilation for PNL. J Endourol. 2009;23: 1655-61.**

32. Laguna MP, Beemster P, Kumar V, Klingler C, Wyler S, Anderson C, Keeley FX, Bachman A, Rioja J, Mamoulakis C, Marberger M, de la Rosette JJ. **Perioperative morbidity of laparoscopic cryoablation of small renal masses**

[1] Publication from the international PhD research project

with ultrathin probes-a European multicenter experience. Eur Urol. 2009; 56:355-61.

33. Tzortzis V, Mitrakas L, Gravas S, Mamoulakis C, Meissner A, Kyriakou D, Melekos MD. **Oral phosphodiesterase type 5 inhibitors alleviate recurrent priapism complicating thalassemia intermedia: a case report. J Sex Med 2009;6:2068-71**

34. Gravas S, Mamoulakis C, Rioja J, Tzortzis V, de Reijke TM, Wijkstra H, J.de la Rosette JJMCH. **Advances in ultrasound technology in oncologic urology. Urol Clin N Am 2009;36:133-45.**

35. Tzortzis V, Mamoulakis C, Rioja J, Gravas S, Michel MC, de la Rosette JJMCH. **Medical expulsive therapy for distal ureteral stones. Drugs 2009; 69:677-92.**

36. Efthimiou I, Mamoulakis C, Papageorgiou G, Kazoulis S, Prevedorou D, Kontogiorgos G, Christoulakis I. **Unilateral malignant leydig cell tumor of testis in a patient with contralateral cryptorchidism. Urol J. 2009; 6:60-2.**

37. Oelke M,[1] Mamoulakis C,[1] Ubbink DT, de la Rosette JJ, Wijkstra H. **Manual versus automatic bladder wall thickness measurements: a method comparison study. World J Urol. 2009;27:747-53.**

38. Mamoulakis C, Trompetter M, de la Rosette JJMCH. **Bipolar transurethral resection of the prostate-"the golden standard" reclaims its leading position. Curr Opin Urol 2009;19:26-32.**[2]

39. Efthimiou I, Mamoulakis C, Kazoulis S, Xirakis S, Vernadakis S, Christoulakis I. **Urachal carcinoma presenting with chronic mucusuria: a case report. Cases J. 2008 Oct 30;1(1):288.**

40. Chimona T, Proimos E, Mamoulakis C, Tzanakakis M, Skoulakis CE, Papadakis CE. **Multiparametric comparison of cold knife tonsillectomy,**

[1] Equal contribution of authors

[2] Publication from the international PhD research project

radiofrequency excision and thermal welding tonsillectomy in children. Int J Pediatr Otorhinolaryngol 2008;72:1431-6.[1]

41. Efthimiou I, Mamoulakis C, Petraki K, Zorzos I. **Renal actinomycosis presenting as a suppurated solitary cyst. Indian J Urol 2008;24(3):416-8.**

42. Kostopoulos C, Koutsikos J, Toubanakis C, Moulopoulos LA, Mamoulakis C, Gialafos E, Sfikakis PP, Zerva C, Mavrikakis M, Leondi A. **Lung scintigraphy with nonspecific human immunoglobulin G ((99m)Tc-HIG) in the evaluation of pulmonary involvement in connective tissue diseases: correlation with pulmonary function tests (PFTs) and high-resolution computed tomography (HRCT). Eur J Nucl Med Mol Imaging 2008;35: 345-51.**[1]

43. Koutsikos J, Grigoraki V, Athanasoulis T, Velidaki A, Mamoulakis C, Zomas A, Anagnostopoulos N, Georgiou E, Dimopoulos MA, Zerva Ch. **Scintigraphy with technetium-99m methoxy-iso-butyl-isonitrile in multiple myeloma patients; correlation with the International Staging System. Hell J Nucl Med 2006;9(3):177-80.**[1]

44. Lycopoulou L Mamoulakis C, Hantzi E, Demetriadis D, Antypas S, Giannaki M, Bakoula C, Chrousos G, Papassotiriou I. **Serum amyloid A protein levels as a possible aid in the diagnosis of acute appendicitis in children. Clin Chem Lab Med 2005;43:49-53.**

45. Gardikis S, Antypas S, Mamoulakis C, Demetriades D, Dolatzas T, Tsalkidis A, Chatzimicael A, Polychronidis A, Simopoulos C. **Colostomy type in anorectal malformations: 10-years experience. Minerva Pediatr 2004;56:425-9.**

46. Mirilas P, Mamoulakis C, de Almeida M. **Puberty does not induce serum antisperm surface antibodies in patients with previously operated cryptorchidism. J Urol 2003:170:2432-5.**

47. Yamamoto Y, Sofikitis N, Kaponis A, Georgiou J, Yannakis D, Mamoulakis C, Loutradis D, Giannakopoulos X, Mio Y, Miyagawa I. **The use of a highly**

[1] He contributed also in the statistical analysis

sensitive quantitative telomerase assay in intracytoplasmic sperm injection programmes for the treatment of 47, XXY non-mosaic Klineferter men. Andrologia 2002;34:218-26.

48. Mamoulakis C, Antypas S, Stamatiadou A, Demetriadis D, Kanakas N, Loutradis D, Miyagawa I, Yannakis D, Kaponis A, Tzonou A, Giannakopoulos X, Sofikitis N. **Cryptorchidism: seasonal variations in Greece do not support the theory of light. Andrologia 2002;34:194-203.**

7.3. Full publications in Greek scientific journals

1. Karpathakis N, Mamoulakis C. **Results of the first 41 flexible ureterorenoscopies in the management of urolithiasis in the Deprtment of Urology of the University Hospital of Heraklion. Sihroni Ourologia (Contemporary Urology) 2013;37:34-37.** [1]

2. Volonakis I, Mamoulakis C. Risk calculators in oncology**: Kidney cancer – Bladder cancer. Sihroni Ourologia (Contemporary Urology) 2012;34: 28-34.**[1]

3. Tsifetakis S, Mamoulakis C. **Validation of the revised Epstein criteria for insignificant prostate cancer in the population of Crete. Sihroni Ourologia (Contemporary Urology) 2012;33:22-27.**[1]

4. Georgopoulos I, Stamatiadis G, X. Manolaraki H, Mamoulakis C. **Trifecta outcome after retropubic radical prostatectomy. Sihroni Ourologia (Contemporary Urology) 2012;31:14-15.**[1]

5. Tzortzakakis D, Mamoulakis C. **Cryptorchidism Κρυψορχία. Sihroni Ourologia (Contemporary Urology) 2011;28: 24-26.**[1]

6. Mamoulakis C, Glaritis D. **Duplication of the lower urinary tract. Sihroni Ourologia (Contemporary Urology) 2010;26: 16-18.**[1]

7. Bafaloukos P, Lonis M, Chrisanthakopoulos G, Kazoulis S, Christoulakis I, Mamoulakis C. Penile fractures: **The experience of the Department of**

[1] Journal published by the department of Urology, University of Crete, Medical School (link)

Urology in Chania, Crete. Sihroni Ourologia (Contemporary Urology) 2010;25: 16-18.[1]

8. Paterakis P, Mamoulakis C. **Molecular markers for the diagnosis of bladder cancer. Sihroni Ourologia (Contemporary Urology) 2010;25: 20-24.**[1]
9. Mamoulakis C. **Cryotherapy and radiofrequency ablation for the treatment of small renal masses. Sihroni Ourologia (Contemporary Urology) 2009;22:24-31.**[1]
10. Mamoulakis C. **Bipolar technology reinforces transurethral resection of the prostate leading position in benign prostatic hyperplasia. Sihroni Ourologia (Contemporary Urology) 2009;21:28-33.**[1]
11. Efthimiou I, Mamoulakis C, Sofras F. **Evidence based medicine: Basic principles and application in Urology. Hellenic Urology 2008;20:192-201.**[2]
12. Mamoulakis C, Zarifis G, Kalaitzakis M, Skordilaki A, Efthimiou I, Dimitriadis A, Kazoulis S, Giannou S, Christoulakis I, Sofras F. **Segmental acute renal infarction associated with multiple thrombophilic gene polymorphisms treated with tenecteplase in terms of systematic thrombolysis. Sihroni Ourologia (Contemporary Urology) 2008;15:38-45.**[1]
13. Giotitsas N, Baltogiannis D, Tsounapi P, Gratsia S, Baltogiannis N, Pardalidis N, Kalampoki V, Giannakis D, Mamoulakis C, Faviou E, Kanakas N, Sofikitis N. **Genetic mechanisms regulating testicular descent in the scrotum.**[3] **Anir (Male) 2007;9:155-64.**[4]

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[1] Journal published by the department of Urology, University of Crete, Medical School (link)

[2] The official journal of HUA; authorized by IATROTEK (a Greek-English database representing the Greek equivelant to MEDLINE)

[3] Publication from the national PhD research project

[4] The official journal of the Hellenic Society of Andrology

14. Malovrouvas D, Karantzos D, Mamoulakis C, Petraki K, Syrmos C. **Endometriosis of the ureter: Description of a rare clinical entity. Hellenic Urology 2004;16:284-8.**[2]

15. Mamoulakis C, Markakis I. **Calcium homeostasis in the nerve cell Iattriki, 1997;72: 360-7.**[1]

16. Mamoulakis C, Markakis I, Armaganidis A. **Delayed cerebral ischaemia in aneurismal subarachnoid haemorrage: pathophysiology and management with calcium antagonists Hippocrates, 1997;5:103-17.** [2]

17. Markakis I, Mamoulakis C, Armaganidis A. **Calcium antagonists in the central nervous system: principles of physiology and pharmacology. Hippocrates 1996;4:73-84.**[1]

7.4. Book Chapters

1. Lotan Y, Mamoulakis C, Miyazawa K, Rogers A, Talati J. **Epidemiology of Stone Disease. In: Stone Disease. 3rd International Consultation on Stone Disease.**
2. Gravas S, Bachmann A, Descazeaud A, Marcus Drake M, Gratzke C, Madersbacher S, Mamoulakis C, Oelke M, Tikkinen KAO; members of the European Association of Urology (EAU) Guidelines Office. Guidelines on **non-neurogenic male lower urinary tract symptoms (LUTS), including benign prostatic obstruction (BPO). In: EAU Guidelines, edition presented at the 29th EAU Annual Congress, Stockholm 2014**
3. Mamoulakis C, Tzortzakakis D, Sofras F. **Cryptorchidism. In: Essentials in Pediatric Urology. Sakellaris G (ed.), Research Signpost, 2012.**
4. Meißner A, Mamoulakis C, Veldink A,. de la Rosette JJC.H. **Sexual problems in patients with cancer. In: The MASCC textbook of cancer**

[1] Greek Scientific Journal authorized by IATROTEK (a Greek-English database, which represents the Greek equivelant to MEDLINE)

[2] Quarterly publication by Athens University, Medical School, Athens, Greece

supportive care and survivorship MSCC. Olver IN (ed.), Springer, 2011.

5. Rioja J, Mamoulakis C, Gravas S, de la Rosette J. **Imaging in diagnosis and staging of urological cancers: ultrasound, CT and PET. In: Interventional Techniques in Uro-Oncology. Ahmed HU, Arya M, Scardino PT, Emberton M (eds.), Wiley-Blackwell Science, 2011.**
6. Mamoulakis C, Tzortzis V, Rioja J, Gravas S, Wijkstra H, de la Rosette JJMCH. **Advances in diagnostic and therapeutic ultrasonography. In: New Technologies in Urology. Dasgupta P, Fitzpatrick J, Kirby R, Gill S (eds.), Springer, 2010.**
7. Mamoulakis C, Kaponis A, Georgiou J, Giannakis D, Antypas S, Tsambalas S, Giannakopoulos X, Miyagawa I, Sofikitis N. **Mammalian testicular descent and maldescent; implications in fertility potential.**[1] **In: Male infertility today. Colpi GM (ed). Italian Andrological Society, Milan, Italy, 2004 (4);63-137**

7.5. Selected presentations in international congresses

7.5.1. Abstracts published in international scientific journals

1. N. Karpathakis, K. Fasoulakis, I. Georgopoulos, I. Bolonakis, F. Sofras, C. Mamoulakis. **Completely standardized flexible ureterorenoscopy for treating renal calculi: A single-center experience. J Endourol 2013;27 (s1): A407.** 31th WCE & SWL, 22-26 October 2013, New Orleans, LA, United States.
2. Mamoulakis C, Skolarikos A, Schulze M, Scoffone C, Rassweiler J, Alivizatos G, Scarpa R, De La Rosette J. **Bipolar vs. monopolar TURP: Impact on the overall sexual function and midterm safety-efficacy results of an international multicenter randomized controlled trial Eur Urol Suppl 2013; 12(1):e521-e522.** 28th Annual EAU Congress, 15-19 March 2013; Milan, Italy[2]

[1] Publication from the national PhD research project

[2] From the international PhD research project

3. Omar MI, Lam T, Alexander CE, Graham J, Mamoulakis C, Imamura M, MacLennan S, Stewart F, N' Dow J. **Systematic review and meta-analysis of the clinical effectiveness of bipolar compared to monopolar transurethral resection of the prostate. Eur Urol Suppl 2013; 12(1): e523-e524.** 28th Annual EAU Congress, 15-19 March 2013; Milan, Italy
4. Mamoulakis C, Skolarikos A, Schulze M, Scoffone CM, Rassweiler JJ, Alivizatos G, Scarpa RM, de la Rosette JJM.H. **Results from a randomized double-blind controlled trial on perioperative efficacy and safety of bipolar versus monopolar transurethral resection of the prostate. Eur Urol Suppl 2011; 10(2):62.** 26th Annual EAU Congress, 28-22 March 2011; Vienna, Austria.[1]
5. Cauberg ECC, Mamoulakis C, de la Rosette JJ, de Reijke T. **Narrow band imaging-assisted transurethral resection for non-muscle invasive bladder cancer significantly reduces early tumour recurrence rate. J Endourol 2010;24 (s1): A115.** 28th WCE, 1-4 September 2010, Chicago, IL, United States
6. Barwari K, Mamoulakis C, Beemster P, Wijkstra H,. de la Rosette JJMCH,. Laguna MP. **Midterm oncological follow up of Laparoscopic Renal Cryoablation (LRC) with third generation cryoprobes in 100 small renal masses (SRM). Eur Urol Suppl 2010;9(2):246.** 25th Annual EAU Congress, 16-20 April 2010; Barcelona, Spain
7. Mamoulakis C, Ubbink D, Laguna M, de la Rosette J. **Bipolar versus monopolar transurethral resection of the prostate: a meta-analysis of randomized clinical trials. J Endourol 2009;23 (s1):A264.** 27th WCE, 6-10 October 2009, Munich, Germany[1]
8. Mamoulakis C, Beemster P, Mehmedovic S, Wijkstra H, de la Rosette J, Laguna M. **Intermediate follow-up of renal masses treated by laparoscopic cryoablation. J Endourol 2009;23 (s1):A294.** 27th WCE. 6-10 October 2009, Munich, Germany
9. C. Mamoulakis C, Rioja J, Wezel F, Michel M, Alken P, de la Rosette J. **Two contemporary series of percutaneous tract dilation for PNL. J**

Endourol 2009;23 (s1):A44. 27th WCE, 6-10 October 2009, Munich, Germany

10. Mamoulakis C, de la Rosette JJ, Laguna MP, Wink MH, Wondergem N, ten Kate FJC, Zwinderman K, de Reijke TM, Wijkstra H. **8 and 12 core TRUS guided PBPs achieve similar PCa detection. J Endourol 2009;23(11):A-23.** 2nd International Workshop on «Focal therapy and imaging in prostate and kidney cancer». 10-13 June 2009, Nordwijk, Amsterdam

11. M.P. Laguna, P. Beemster, V. Kumar, C. Klingler, S. Wyler, C. Anderson, F. X. Keeley, A. Bachmann, J. Rioja, C. Mamoulakis, M. Marberger, J.J. de la Rosette. **Perioperative morbidity of laparoscopic renal cryoablation: a multicentre experience. J Endourol 2009;23(11):A-14.** 2nd International Workshop on «Focal therapy and imaging in prostate and kidney cancer». 10-13 June 2009, Nordwijk, Amsterdam

12. M. Schulze, C. Mamoulakis, J. Rioja, A. Skolarikos, J. J. Rassweiler, G. Alivizatios, J.J.M.C.H. de la Rosette. **Preliminary results from an international multicenter blinded randomized clinical trial comparing bipolar with monopolar transurethral resection of the prostate. J Urol 2009;181(Suppl 1):699.** Annual AUA Meeting, 25-30 April 2009; Chicago, IL, USA.[1]

13. M. Oelke, C. Mamoulakis, H. Wijkstra, D.T. Ubbink, J.J. de La Rosette. **Bladder wall thickness measurements by conventional ultrasound and bladder scan BVM 6500: A method comparison study. Eur Urol Suppl 2009;8(4):133.** 24th Annual EAU Congress, 17-21 March 2009; Stockholm, Sweden

14. C. Mamoulakis, H. Wijkstra, T.M. de Reijke, M.P. Laguna, J.J.M.C.H. de La Rosette. **Is there a difference in prostate cancer detection rates between 8- versus 12-core transrectal ultrasound-guided biopsy protocols? Results from a randomized clinical trial. Eur Urol Suppl 2009;8(4):217.** 24th Annual EAU Congress, 17-21 March 2009; Stockholm, Sweden.

[1] From the international PhD research project

15. J. Rioja, C. Mamoulakis, A Skolarikos, G. Alivizatos, M. Schulze, J. Rassweiler, C.M. Scoffone, R.M. Scarpa, J.J. de La Rosette. **Bipolar versus monopolar transurethral resection of the prostate: Results of an international multicenter blinded randomized clinical trial. Eur Urol Suppl 2009;8(4):266.** 24th Annual EAU Congress, 17-21 March 2009; Stockholm, Sweden.[1]

16. C. Mamoulakis, H. Wijkstra, L. Kuilman, M. Visser, M.P. Laguna, T.M. de Reijke, J.J.M.C.H. de La Rosette. **Does neoadjuvant sorafenib treatment affect microvessel density count in prostate cancer? Eur Urol Suppl 2009;8(4):277.** 24th Annual EAU Congress, 17-21 March 2009; Stockholm, Sweden

17. C. Mamoulakis, L. Kuilman, H.G. van der Poel, J.J.M.C.H. de la Rosette, P. Laguna, T.M. de Reijke, H. Wijkstra. **Is ultrasound imaging helpful in predicting extracapsular penetration in prostate cancer? J Endourol 2009;23(6):1041.** 24th Annual Meeting of the Engineering and Urology Society, 25 April 2009; Chicago, IL, USA

18. A. Leondi, J. Koutsikos, C.A. Rapidi, H. Fotinaki, C. Mamoulakis, A. Daramaras, E. Kandilakis, V. Valotasiou, E. Karava, C. Petropoulou, C. Zerva. **Detection of urological and/or nephrological complications in patients with spinal cord injury and neuropathic bladder by diuretic renogram (Tc-99m MAG-3). Correlation with urodynamics and classification by American Spinal Injury Association (ASIA) impair. Eur J Nucl Med Mol Imaging 2007;34(Suppl 2):S369.** Annual EANM Congress, 13-17 October 2007; Copenhagen, Denmark

19. I. Efthimiou, C. Mamoulakis, S. Kazoulis, A. Fildisis, E. Chrisafis, I. Christoulakis. **Medical expulsive therapy using extended-release alfuzosin for symptomatic distal ureter stones: a single-centre experience.** 1st Eastern Mediterranean EAU Meeting, 19-20 October, 2007; Antalya, Turkey

20. A. Hatzikyriakidou, C. Mamoulakis, D. Baltogiannis, N. Sofikitis, I. Georgiou. **No evidence for a correlation of genetic variants of the**

insulin-like factor with the development of cryptorchidism. Eur Urol Suppl 2005;4(3):100. 20th Annual EAU Congress, 16-19 March 2005; Istanbul, Turkey.[1]

21. C. Mamoulakis, N. Sofikitis, D. Baltogiannis, D. Giannakis, A. Chatzikyriakidou, I**.** Georgiou. **Evidence against a contribution of $(TAAAA)_n$ repeat polymorphism within the human sex hormone-binding globulin (SHBG) gene promoter region to testicular maldescent (TMD) phenotype: absence of association/genetic linkage in a family-based study. Eur Urol Suppl 2004;3(2):183.** 19th EAU Congress, 24-27 March 2004; Vienna, Austria.[1]

22. A. Tasos, I. Pappas, D. Baltogiannis, K. Tsoukanelis, D. Giannakis, C. Mamoulakis, N. Sofikitis. **Effects of urinary incontinence on female sexual function. J Androl 2003;March/April Suppl:38.** 28th Annual ASA Meeting, 29 March-2 April, 2003; Phoenix, Arizona

23. C. Stefiadis, S. Tsabalas, A. Tasos, D. Tsalikis, D. Baltogiannis, C. Mamoulakis, I. Miyagawa, N. Sofikitis. **Testicular fluid dynamics indicate two distinct subpopulations of non-obstructed azoospermia (NOA) men. J Androl 2003; March/April Suppl:45.** 28th Annual ASA Meeting, 29 March-2 April 2003; Phoenix, Arizona

24. C. Mamoulakis, N. Sofikitis, A. Panagidis, I. Bouba, I. Alexandrou, D. Giannakis, I. Georgiou. **Lack of evidence for a direct aetiological relationship between Y chromosome microdeletions and testicular maldescent in childhood. J Androl 2003;March/April Suppl:62.** 28th Annual ASA Meeting, 29 March – 2 April 2003; Phoenix, Arizona

25. N. Sofikitis, S. Tsabalas, C. Mamoulakis, D. Baltogiannis, D. Tsalikis, D. Giannakis, I. Miyagawa. **Telomerase assay predicts the appearance of spermatozoa post-varicocelectomy in a large number of non-obstructed azoospermic men. J Androl 2003;March/April Suppl:74.** 28th Annual ASA Meeting, 29 March – 2 April, 2003, Phoenix, Arizona

[1] From the national PhD research project

26. E. Grammeniatis, I. Pappas, D. Tsalikis, C. Mamoulakis, A. Tasos, D. Giannakis, X. Giannakopoulos, N. Sofikitis **The role of sildenafil in premature ejaculation. J Androl 2003;March/April Suppl:75.** 28th Annual ASA Meeting, 29 March - 2 April, 2003; Phoenix, Arizona

27. C. Mamoulakis, N. Sofikitis, A. Chatzikyriakidou, I. Bouba, X. Giannakopoulos, I. Georgiou. **Screening for Y chromosome microdeletions in childhood: lack of evidence for a direct aetiological relationship with testicular maldescent.**[1] **BJU Int 2003;91 (s1):79.** 14th Annual ESPU Congress, 12-15 March 2003; Madrid, Spain

28. N. Kanakas, C. Mamoulakis, I. Miyagawa, A. Chatzilyriakidou, D. Yannakis, N. Sofikitis **Effects of sexual intercourse on testicular function. Fertil Steril 2002;76(3S):S266.** 58th Annual ASRM Meeting, 12-17 October 2002; Seattle WA

29. D. Tsalikis, N. Sofikitis, C. Mamoulakis, D. Yannakis, N. Kanakas, I. Miyagawa. **ICSI using hamster sperms generated in rat testes. Hum Reprod 2002;17:23.** 18th Annual ESHRE Meeting, 30 June - 3 July 2002, Vienna, Austria.

30. C. Mamoulakis, D. Dimitriadis, S. Antypas, N. Sofikitis. **Seasonality of cryptorchidism and hypospadias in Greece: Epidemiological relationships. J Androl March/April 2002 Suppl:36.** 27th Annual ASA Meeting, 24-27 April 2002; Seattle WA

31. S. Tsabalas, C. Mamoulakis, A. Kaponis, D. Baltogiannis, X. Giannakopoulos, I. Miyagawa, A. Tasos, N. Sofikitis. **Assisted reproduction using hamster spermatozoa generated into xenogeneic testes. J Androl March/April 2002 Suppl:45.** 27th Annual ASA Meeting, 24-27 April 2002; Seattle WA

32. A. Chatzilyriakidou, C. Mamoulakis, A. Kaponis, X. Giannakopoulos, I. Miyagawa, D. Tsalikis, D. Yiannakis, N. Sofikitis. **Effects of two techniques of left varicocelectomy (VRCL) on fertilization and**

[1] From the national PhD research project

embryonic capacity for implantation. J Androl March/April 2002 Suppl:57. 27th Annual ASA Meeting, 24-27 April 2002; Seattle WA

33. A. Rigas, D. Karamanolakis, C. Mamoulakis, A. Stefanidis, P.A. Androulakakis. **PUJ obstruction caused by crossing renal vessels: clinical and imaging features. BJU Int 2002;89 (Suppl 2):33.** 13th Annual ESPU Meeting, 11-13 April 2002; Budapest, Hungary

34. C. Mamoulakis, S. Antypas, A. Stamatiadou, D. Dimitriadis, A. Tzonou, N. Sofikitis **Cryptorchidism: seasonal variations in Greece. J Androl May/June 2001 Suppl:164.** 7th International Congress of Andrology, 15-19 June 2001; Montréal, Québec, Canada

35. C. Mamoulakis, L. Lycopoulou, E. Hantzi, S. Malamouli, M. Giannaki, D. Demetriadis, S. Antypas, I.Papassotiriou. **Comparative evaluation of serum amyloid A and C-reactive protein levels in pediatric patients with acute appendicitis. Clin Chem Lab Med 2001;39:S205.** 14th IFCC-FESCC European Congress of Clinical Chemistry and Laboratory Medicine, 5th Czeck National Congress of Clinical Biochemistry, May 26-31 2001 Prague, Czech Republic

7.5.2. Abstracts published in abstract books of congresses

1. F. Wezel, C. Mamoulakis, J. Rioja, P. Alken, J.J. de la Rosette, M.S. Michel. **Techniken der Traktdilatation bei der perkutanen Nephrolitholapaxie**. Swiss Urology Convention, 5 September 2009, Lausanne, Switzerland

3. C. Mamoulakis, M. Kalaitzakis, S. Kazoulis, G. Zarifis, A. Dimitriadis, A. Skordilaki, S. Giannou, M. Mamoulaki, I. Efthimiou, I. Christoulakis. **Systemic thrombolysis of acute renal infarction with the use of tenecteplase.** 10^{o} Symposium of Griechisch-Deutsche Gesselschaft fur Urologie, 27 June - 1 July 2007, Lübeck, Germany

4. C. Mamoulakis, S. Antypas, Ch. Damianou, Th. Dolatzas, A. Tzonou. **Seasonality of hypospadias: a common pathogenic environmental factor**

with cryptorchidism. [1] 52nd Annual International Congress of the British Association of Paediatric Surgeons, 12-15 July 2005, Dublin, Ireland

5. D. Malovrouvas, P. Dedeilias, P. Papadaniil, A. Grigorakis, V. Androutsopoulou, S. Karakaidos, C. Mamoulakis, A. Papadopoulos, E. Pantazis, C. Petraki, C. Syrmos. **Renal neoplasm invading the inferior vena cava. Our surgical technique.** 16th Video-Urology World Congress, 23-25 June 2005, Athens, Greece
6. S. Antypas, L. Lycopoulou, M. Vounatsou, C. Mamoulakis, E. Hantzi, I. Alexandrou, A. Panagidis, I. Papassotiriou. **Procalcitonin in children with acute appendicitis.** British Association of Paediatric Surgeons, 51st Annual International Congress, 27-30 July, 2004 Oxford, UK
7. A. Antoniou, C. Mamoulakis, K. Bratsas, A. Stefanidis, E.P. Diamandis, P.A. Androulakakis. **Serum prostate specific antigen (sPSA) levels in childhood.** IXth International Meeting of the European Society of Residents in Urology (ESRU), 23-26 February 2002, Birmingham, UK
8. K. Bratsas, A. Stefanidis, C. Mamoulakis, E. Spyropoulos, B.P. Zachariades, P.A. Androulakakis. **The role of hyperbaric oxygen in the treatment of chemotherapeutic agent-induced haemorrhagic cystitis in a child.** 9th International Meeting of the European Society of Residents in Urology (ESRU), 23-26 February 2002, Birmingham, UK
9. C. Mamoulakis, L. Lycopoulou, E. Hantzi, A. Stamatiadou, O. Moraloglou, D. Dimitriadis, S. Antypas, I. Papassotiriou. **Serum Amyloid A protein levels in the diagnosis and follow-up of acute appendicitis in paediatric patients.** British Association of Paediatric Surgeons, XLVIII Annual International Congress, 17-20 July, 2001 London, UK. Peter Paul Rickham Prize Session
10. M. Papadaki, Ch. Hadzigeorgi, K. Ioannidis, C. Mamoulakis, S. Antypas. **Ultrasonographic evaluation of testicular microlithiasis in paediatric patients.** 3rd Congress of Mediterranean Association of Paediatric Surgeons (MAPS), 12-15 October 2000, Corfu

[1] From the monography in terms of Master degree in Science (Biostatistics)

11. G. Harmanis, M. Ververidis, D. Dimitriadis, C. Mamoulakis, S. Antypas, T. Dolatzas. **Hypospadias combined with giant haemangioma of the lower half of the body and Kasabach-Merrit syndrome in a 4 year-old child.** 3rd Congress of Mediterranean Association of Paediatric Surgeons (MAPS) October 12-15, 2000 Corfu

12. S. Gardikis, S. Antypas, C. Mamoulakis, D. Dimitriadis, T. Dolatzas. **The influence of the colostomy type in the Peña procedure.** VII Pediatric Colorectal Club, 16-17 July, 2000 Rome, Italy

7.6. Full publications submitted in international scientific journals

1. Hatzidakis A, Glaritis I, Peteinarakis I, Kozana A, Mamoulakis C. Right-sided **Bochdalek hernia causing septic ureteric obstruction. Percutaneous treatment with placement of a nephro-ureteral double pigtail. (Cardiovasc Intervent Radiol; 18/05/2014)**

2. Kandasami SV, Mamoulakis C, El Nahas AR, Averch T, Tuncay OL, Rawandale-Patil A, Cormio L, de la Rosette JJ. **Impact of case volume on outcomes of ureteroscopy (URS) for ureteral stones: the Clinical Research Office of the Endourological Society (CROES) URS Global Study. (Eur Urol; 07/04/2014)**

3. Chondros K, Karpathakis N, Heretis I, Chondros N, Mavromanolakis E, Sofras F, Mamoulakis C. **Validation of revised Epstein's criteria for insignificant prostate cancer prediction in a Greek subpopulation. (Hippokratia Journal; 29/04/2014)**

4. Mamoulakis C, Karpathakis N, Antypas S, Sofras F, Tzonou A. **Seasonal trends in the incidence of hypospadias: Etiological implications.** [1] **(Hippokratia Journal; 28/02/2014)**

5. Hatzidakis A, Rossi M, Mamoulakis C, Kehagias E, Orgera G, Krokidis M, Karantanas A. **Management of renal arteriovenous malformations: A pictorial review. (Insights Imaging; 05/01/2014)**

[1] Από τη Διπλωματική εργασία του υποψηφίου στο πλαίσιο του Μεταπτυχιακού Προγράμματος Ειδίκευσης στην Βιοστατιστική

6. Oelke M, Speakman M, Desgrandchamps F, Mamoulakis C. **Urinary retention rates in the general male population and in patients with lower urinary tract symptoms participating in pharmacotherapy trials (Eur Urol; 16/07/2013)**

7. Gravas S, Bachmann A, Descazeaud A, Drake M, Gratzke C, Madersbacher S, Mamoulakis C, Oelke M, Tikkinen K. **Guidelines on the Assessment of Male Lower Urinary Tract Symptoms (LUTS), including Benign Prostatic Obstruction (BPO) (Eur Urol;)**

8. OTHER SCIENTIFIC ACTIVITIES

8.1. Member EAU BPH/Male LUTS/BOO Guidelines Office Panel

8.2. Member of the International Consultation on Urological Diseases (ICUD) (3rd International Consultation on Stone Disease; Société Internationale d'Urologie)

8.3. Selected invitations in scientific meetings

1. 1st International Congress on Clinical Topics in Urology: Lithiasis from A to Z , 5-6 July 2013, Athens, Greece

2. 3rd International Meeting "Challenges in Endourology and Functional Urology", 26-28 June, 2013, Paris-France

3. 6th Interactive School of Urology, 26-29 April 2013, Portaria, Pelio, Greece

Interactive Seminar II: Extracorporeal Lithotripsy: from renal colic to full elimination of stone fragments

4. 8th Educational Week of Greek Residents in Urology, 26-30 March 2013, Athens, Greece

5. HUA Meeting, 20 March 2013, Athens, Greece. Sate of the Art Lecture: "Flexible Ureterorenoscopy for calyceal stones"

6. 4th International Urological Meeting of Central Greece, 2-3 February 2013, Larissa, Greece

7. HUA Section of Endourology & Laparoscopic/Robotic Urology-Urotechnology Meeting, 24 November 2012, Athens, Greece

8. 21th Pan-Hellenic Urological Congress, 11-14 October 2012, Athens, Greece. Member of the Scientific Committee and Moderator

9. 16th Medical Cretan Congress, 25-28 October 2012, St Nikolaos, Crete, Greece Round Table on "Urianry Stones and Minimaly Invasive Treatment of Urolithiasis"

10. 30th World Congress of Endourology 2012, 4-8 September, 2012, Istanbul, Turkey

11. 2nd International Meeting "Challenges in Endourology and Functional Urology", 27-29 June, 2012, Paris, France

12. 5th Interactive School of Urology, 26-29 April 2012, Portaria, Pelio, Greece

Problem Based Learning I: BPH: When the problems start

UroSwords I: Monotherapy or Combination Therapy in BPH

Risk Calculators in Urooncology

13. HUA Meeting, 18 January 2012, Athens, Greece. Sate of the Art Lecture: "Primary prevention on Prostate cancer"

14. 22nd Video World Congress Urology, 7-9 July 2011, Turin, Italy

15. Challenges in Endourology, 8-10 June 2011, Paris, Franc

16. 4th Interactive School of Urology, 26-29 May 2011, Portaria, Pelio, Greece

Tutorial III: Complications: How do we evaluate and how we report them

17. 6th Educational Week of Greek Residents in Urology, 4-8 April 2011 Athens, Greece

18. 3rd International Urological Meeting of Central Greece, 2-3 February 2013 Larissa, Greece

19. Training in Endourology, 20-22 April 2012, Athens, Greece:

20. Urologic Symposium "Evolutions and dillemas in the treatment of urologic cancer" 18-20 November 2010, Athens, Greece

21. 15th Medical Cretan Congress, 29-31 October 2010, Chania, Crete, Greece Clinical Tutorial on multidisciplinary management of severely injured patients: Lecture on "Renal Trauma"

22. 3rd Interactive School of Urology, 27-30 May 2010, Portaria, Pelio, Greece

Interactive Seminar: Urolithiasis from A to Z

23. 27th World Congress of Endourology. 6-10 October 2009, Munich, Germany. Hands-on training in ureteroscopy (HOT-URS2)

24. 2nd Aegean Urology Symposium "Office Urology" 1-4 October 2009, Heraklion-Crete, Greece

25. 2nd International Workshop on Focal therapy and imaging in prostate and kidney cancer. 12 June 2009, Nordwijk, Netherlands Workshop Planning Committee and Moderator

8.4. Reviewer in international scientific journals and congresses

8.4.1. International scientific journals

1. Andrologia
2. Asian Journal of Andrology
3. BMC Urology
4. British Journal of Urology International
5. Cochrane Database of Systematic Reviews
6. European Medical Journal – Urology
7. European Urology
8. Hippokratia
9. Histology and Histopathology
10. IEEE Transactions on Instrumentation & Measurement
11. Indian Journal of Urology
12. International Journal of Urology
13. Journal of Endourology
14. Joural of Urology
15. Urology
16. Urology Journal
17. World Journal of Urology
18. World Journal of Surgery
19. Yonsei Medical Journal

8.4.2. Congresses

1. Panhellenic Urological Congress 2012 (Section Endourology)
2. 29th Annual EAU Congress, 11-15 April 2014; Stockholm, Sweden. (Section: BPH: Intervention therapy)

8.5. Seminar attendance

1. Course in ultrasound-based bladder/detrusor wall thickness measurements, 8-12 Δεκεμβρίου 2008, Hannover, Germany

2. Urodynamic-Expert Course, Bristol Urological Institute, 22-23 Νοεμβρίου 2007, Bristol, UK

3. Urogynecology & Female Urology Operative Course, Bristol Urological Institute, 19-21 Νοεμβρίου 2007, Bristol, UK

4. Innovations & EBM in Urology 4-7 October 2007, Athens, Greece. Hands-on Training Workshop in Laparoscopy; Hands-on Training Workshop in Ureteroscopy

5. "Certificate in Urodynamics" Course, Bristol Urological Institute, 20-22 February 2006, Bristol,UK

8.6. Participation in research protocols

1. A Multinational, Phase 3, Randomized, Double Blind, Placebo Controlled, Efficacy and Safety Study of Enzalutamide in Patients With Nonmetastatic Castration Resistant Prostate Cancer
http://clinicaltrials.gov/show/NCT02003924

2. A randomized, double-blind, multi-centre study to evaluate the efficacy and safety of combining mirabegron treatment with solifenacin in incontinent OAB subjects who have received solifenacin 5mg for 4 weeks and require additional relief for their OAB symptoms.
http://clinicaltrials.gov/ct2/show/NCT01638000

3. A Double-Blind, Randomized, Parallel Group, Multi-Centre Study to Evaluate the Efficacy and Safety of Mirabegron Compared to Solifenacin in Subjects With Overactive Bladder (OAB) Treated With Antimuscarinics and Dissatisfied Due to Lack of Efficacy

http://clinicaltrials.gov/ct2/show/NCT01638000

4. A Phase 3b, Randomized, Double-blind, Placebo-controlled Parallel-design Study to Evaluate the Efficacy and Safety of Tadalafil Co-administered With Finasteride for 6 Months in Men With Lower Urinary Tract Symptoms and Prostatic Enlargement Secondary to Benign Prostatic Hyperplasia
   http://clinicaltrials.gov/show/NCT01139762
5. A Phase 2 Clinical Study to Evaluate Daily Oral Doses of LY500307 for 24 Weeks in Men With Lower Urinary Tract Symptoms (LUTS) and Prostatic Enlargement Secondary to Benign Prostatic Hyperplasia (BPH)
   http://clinicaltrials.gov/show/NCT01097707
6. Clinical Research Office of the Endourological Society (CROES):
   http://www.croesoffice.org/AboutCroes.aspx
   The Global Ureteroscopy observational study:
   URS-A prospective international observational study on indications and perioperative outcomes
   http://www.croesoffice.org/OngoingProjects/URSStudy.aspx
7. A prospective, randomized, double-blinded study to compare bipolar trans-urethral resection of the prostate (bipolar TURP) versus monopolar trans-urethral resection of the prostate (monopolar TURP) in terms of safety and efficacy
   (http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=703)
8. A single center open-label uncontrolled study to investigate the efficacy, safety and monitoring with different imaging modalities of neoadjuvant therapy with BAY 43-9006 single agent therapy in patients with operable prostate cancer/MDG00-0216a. (Phase II clinical trial)
   http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=577
9. Randomized, double-blind, placebo-controlled, parallel group study of vardenafil 10 mg twice daily to assess the effect on urodynamics in patients with Overactive Bladder (detrusor overactivity). (Multicenter Phase II clinical Trial)

Study number: BAY 38-9456/12392, EUDRACT-Number: 2006-005145-11
https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2006-005145-11

10. Prostate cancer: which patients need (repeated) prostate biopsies and how many biopsies do they need? (Multicenter International Phase III clinical trial).
http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=1368

8.7. Member in scientific associations

1. American Society of Andrology (ASA)
2. American Urological Association (AUA)
3. Endourological Society
4. European Association of Urology (EAU)
5. Hellenic Society of Andrology
6. Hellenic Urological Association (HUA)
7. International Biometric Society-East Mediterranean Region (IBS-EMR)
8. LUTforum (www.lutforum.org)
9. Société Internationale d'Urologie (SIU)

9. BRIEF PRESENTATION OF PhDs and MSc

9.1. PhD - National

Subject: **"Spermatologic alterations & genetic factors in cryptorchidism"** Supervisor: Prof. N. Sofikitis, Chairman of the Department of Urology, University of Ioannina, Medical School, Ioannina, Greece (18/3/2008)

The Thesis has resulted in the production of 4 publications (**see: 7.2. Full publications in international scientific journals: Publications 4, 9 & 12; 7.3. Full publications in Greek scientific journals: Publication 13; 7.4. Book Chapters: Publication 7**).

National PhD Summary

Objective: To investigate the hypothesis whether: a) Yq11 microdeletions are directly implicated in the pathogenesis of cryptorchidism, b) genetic alterations of the INSL3 gene are associated with cryptorchidism and c) the number of TAAAA repeats within the SHBG gene proximal promoter is associated with cryptorchidism.

Material and Methods: A total of 590 subjects participated in this family-based study: a) 180 cryptorchid children aged between 1-13 years (median age: 2.3 years) at the time of orchidopexy from 174 index families (groups A and B: patient population), b) 307 parents: 156 mothers-151 fathers, nine of whom were also cryptorchid (group P: parental population), c) three unrelated affected second degree relatives (group R: uncles: one father-sided, two mother-sided), and d) 100 normal controls (group C: control group). Patients were prospectively and retrospectively recruited from two different sources: a) all children that have been admitted to the 1st Paediatric Surgery Clinic, "Aghia Sophia" Childrens' Hospital, Athens, Greece as well as to the Department of Urology, University Hospital of Ioannina, Ioannina, Greece for surgical correction of cryptorchidism during the period December 1999–July 2002 (group A: prospective recruitment; n=109) and b) ex-cryptorchid children operated on, during the decade 1990–2000, at the 1st Paediatric Surgery Clinic, "Aghia Sophia" Childrens' Hospital, who were randomly selected from the archive (group B: retrospective recruitment; n=71). The control group consisted of unrelated males with normal external genitalia of respective age, recruited randomly from

the general paediatric population. Each individual was submitted to one blood sampling from a peripheral vein. Molecular analysis was performed at the Genetics Unit, Department of Obstetrics and Gynaecology, Medical School, Ioannina University, Ioannina, Greece. Genomic DNA was extracted from blood samples using standard salting out procedures. Yq11 microdeletion analysis was based on routine PCR amplification of genomic DNA from all individuals of groups A, B, R and C (n=283) with the use of two multiplex reactions (Multiplex A: sY86, sY127, sY254 sY238 to screen AZFa, AZFb, AZFc and ZFY regions, respectively; Multiplex B: sY14, sY84, sY134, sY255 to screen SRY, AZFa, AZFb and AZFc regions, respectively). Amplified reaction products were submitted to electrophoresis on 2% agarose gel containing ethidium bromide as intercalating DNA stain and visualized under ultraviolet light. INSL3 gene genetic alteration analysis was based on PCR–SSCP method. Genomic DNA from 170 unrelated individuals of groups A and B, including all cases with a documented family history (n=17), as well as from 50 individuals from group C was used. PCR-SSCP was used to examine both exons of the gene. Amplified reaction products were further processed and submitted to electrophoresis on 8% non-denaturing polyacrylamide gel under four different conditions. Bands were detected by silver staining. All different SSCP patterns were sequenced. Restriction assay was further employed using the restriction endonuclease Eag I, which recognizes the wild type G/G genotype at position 178 in exon 1 of the gene. Digested PCR products were analyzed on 2% agaroze gel containing ethidium bromide and restriction patterns were visualized under ultraviolet light. Pearson's/ Fisher's chi square test was performed to evaluate differences in the distribution of the alleles/genotypes for the detected genetic changes among: a) patients and controls b) familial and sporadic, c) bilateral and unilateral, and d) intra-abdominal and inguinal cryptorchid cases. TAAAA polymorphism genotype analysis was performed on genomic DNA of the total population of groups A, B and P (n=487). PCR products were electrophorized on 10% non-denaturating polyacrylamide gel and silver stained. The number of repeats (n) of each allele was detected by comparing the amplified products with samples of known number of repeats after sequencing, derived randomly from the general population. Data were separately analyzed for the whole population of parents-affected children as well as for the subpopulations of a) parents-affected children with intra-abdominal and b) parents-affected children with inguinal cryptorchidism.

Finally, the statistical analysis included data from 138 completely typed nuclear families (five of them included a second affected child, eight of them included cryptorchid fathers) as well as from five couples with one missing parent (429 subjects in total: 148 cryptorchid children, 156 cryptorchid cases in total). Statistical analysis was based on a) affected family-based control (AFBAC) method and b) logistic regression-based extension of the transmission disequilibrium test for multi-allelic loci (ETDT).

Results: No Yq11 microdeletions were detected in patients or controls. No genetic alterations of the INSL3 gene were detected exclusively in patients (mutations). However, three genetic alterations affecting exon 1 of the INSL3 gene were detected both in patients and controls (single nucleotide polymorphisms): 27G>A (A9A), 126G>A (L42L), 178G>A (A60T). Their frequency did not differ significantly between either a) patients and controls or b) sporadic and familial cases of cryptorchidism. As far as the non–synonymous polymorphism 178G>A is concerned, the wild type nucleotide was found in 55.9% and 55% of patient and control alleles, respectively (P=0.917). The non-wild type nucleotide 178A was detected in 52.9% and 42.3% of patient alleles with and without documented history of familial cryptorchidism, respectively (P=0.123). Finally, no association was detected with laterality (bilaterally-unilaterally: P=0.695) or with the testicular position (intra-abdomial-inguinal location: P=0,330). TAAAA polymorphism genotype analysis revealed five different alleles based on the number of their TAAAA repeats (n=6-10) in cryptorchid children. Both the AFBAC method (parental, paternal, maternal alleles transmitted vs. not transmitted to an affected child: P=0.921, P=0.979, and P=0.745, respectively; paternal vs. maternal alleles transmitted/not transmitted: P=0.690, P=0.877, respectively) and the ETDT (allele-wise and genotype analysis: P=0.883, P=0.615, respectively) failed to detect an association/genetic linkage between the number of repeats and cryptorchidism. Subgroup analysis in inguinal and inta-abdominal cases resulted in insignificant results as well.

Conclusions: The direct role of the Yq11 microdeletions in the pathogenesis of cryptorchidism is set under severe dispute and therefore their routine screening in children with testicular maldescent is not warranted in terms of preoperative evaluation or during the postoperative follow up. b) Genetic alterations of the INSL3 gene do not seem to be a common cause of cryptorchidism in the human. c) The polymorphic sequence (TAAAA)n

within the SHBG gene proximal promoter is not associated/genetically linked with cryptorchidism. Genetic predisposition that seems to affect a cryptorchid subpopulation should be further evaluated by investigating other candidate genetic factors.

9.2. PhD - International (link)

Subject: **"The position of bipolar technology in transurethral resection of the prostate for benign prostatic obstruction: An evidence-based approach"**
Promoters: J.J.M.C.H de la Rosette & J.J. Rassweiler

University of Amsterdam, the Netherlands

The Thesis is expected to be defended within the year 2013 has resulted in the production of 11 publications (**see: 7.2. Full publications in international scientific journals: Publications 8, 10, 11, 14-16, 24, 25, 28 and 38**), which are briefly presented in the form of an extended summary of the Thesis.

International PhD Extended Summary (brief presentation of respective publications)

This work was conducted with the scope to evaluate the position of bipolar technology in transurethral resection of the prostate (TURP) for treating patients with lower urinary tract symptoms (LUTS) secondary to benign prostatic obstruction (BPO), using an evidence-based approach. Seeking the best available evidence on a timely topic, this thesis presents the main results derived from the randomized controlled trials (RCTs) comparing efficacy and safety of bipolar TURP (B-TURP) with that of its predecessor, the current surgical "gold standard", namely monopolar TURP (M-TURP). *It provides unique clinical data from the first international, multicenter RCT in the field and has decisively contributed to the formulation of the basis for the 2014-updated European Association of Urology (EAU) Guidelines on B-TURP versus M-TURP.*

Part I (***Chapter 1): General Introduction.***

Part II (***Chapters 2-4): Current best available evidence in the field:***

Chapter 2 (see 7.2., Publication 38) presents an initial, exploratory, *narrative review* summarizing the knowledge accumulated from experimental studies/relevant RCTs with an

emphasis on morbidity, appearing in the international literature within 18 months prior to its publication. It is concluded that B-TURP shares similar and durable efficacy with M-TURP, with low complication rates. B-TURP has minimized bleeding risk and eliminated transurethral resection (TUR) syndrome. Urethral strictures (US)/bladder neck contracture (BNC) rates do not differ between the modalities. The potential advantages of B-TURP over M-TURP, warrant a further systematic evaluation. The importance of this review lies in that it serves as "gap-identifier"; notwithstanding the availability of a capable amount of RCTs–a focused, detailed systematic review (SR)/meta-analysis was never attempted before. Two previous SRs comparing newer methods (including B-TURP) against M-TURP, failed to provide precise estimates due to availability of few data/significant heterogeneity.

Chapter 3 (see 7.2., Publication 28) presents the results of a profound and focused *RCT-based SR/meta-analysis,* in an attempt to critically evaluate the available evidence. *This work provided for the first time sound and reliable conclusions for the short-term (up to 12 mo), based on level of evidence 1a.* Based on a detailed, unrestricted strategy, the literature was searched up to February 19, 2009, using Medline, Embase, Science Citation Index, and the Cochrane Library to detect all RCTs comparing B-TURP with M-TURP for patients with LUTS secondary to BPO. Methodological quality assessment of the RCTs was based on the Dutch Cochrane Collaboration checklist. Sixteen RCTs (1406 randomized patients) were included. Efficacy and safety were the primary outcomes. Efficacy was quantified by postoperative maximum flow rate (Q_{max}) and/or International Prostate Symptom Score (IPSS). Re-operation for residual adenoma was evaluated too. Safety was estimated by postoperative occurrence of at least one of the following parameters: (1) serum sodium level drop, (2) TUR syndrome, (3) hemoglobin level drop, (4) need for blood transfusion, (5) clot retention, (6) acute urinary retention after removal of the catheter, (7) meatal stenosis, (8) BNCs and (9) USs. Secondary outcomes included operation time, bladder irrigation duration, catheterization/hospitalization time. Overall trial quality was low (e.g., allocation concealment and blinding of outcome assessors were poorly reported). No clinically relevant differences in short-term (12-mo) efficacy were detected (Q_{max}: weighted mean difference [WMD]: 0.72 ml/s; 95% confidence interval [CI], 0.08–1.35; p = 0.03). Data on follow-up >12 mo are scarce for B-TURP, precluding long-term efficacy

evaluation. Treating 50 patients (95% CI, 33–111) and 20 patients (95% CI, 10–100) with B-TURP results in one fewer case of TUR syndrome (risk difference [RD]: 2.0%; 95% CI, 0.9–3.0%; p = 0.01) and one fewer case of clot retention (RD: 5.0%; 95% CI, 1.0–10%; p = 0.03), respectively. Operation times, blood transfusion rates, retention rates after removal of the catheter and urethral complications did not differ significantly. Irrigation and catheterization duration was significantly longer with M-TURP (WMD: 8.75 h; 95% CI, 6.8–10.7 and WMD: 21.77 h; 95% CI, 19.22–24.32; p < 0.00001, respectively). Inferences for hospitalization time could not be made due to heterogeneity. Subgroup analyses to check differences among different bipolar systems were also performed. PlasmaKinetic TURP showed a further improved safety profile regarding blood transfusions (RD: 3%; 95% CI, 1–6%; NNH: 33; 95% CI, 17–100; p = 0.02), and clot retentions (RD: 9%; 95% CI, 3–14%; NNH: 11; 95% CI, 7–33; p = 0.004) but the results were similar for the other outcomes to the results of the general meta-analysis. Data on TUR in saline (TURis) are not yet mature to permit safe conclusions. It is concluded that no clinically relevant differences in short-term efficacy exist, but B-TURP is preferable due to a more favorable safety profile (lower TUR syndrome/clot retention rates), shorter irrigation/catheterization time. Well-designed multicenter/international RCTs with long-term follow-up and cost analysis are still needed.

Following this publication, two additional SR/meta-analyses comparing M-TURP with minimal invasive procedures for BPO, including B-TURP, have been published. Based on a subset of RCTs, the original conclusions were supported. ***Chapter 4 (see 7.2. Publication 25)*** criticizes one of these papers on the terminology used and some methodological issues.

Part III *(Chapter 5): Standardized way of reporting TURP complications:*

Although results from several historical retrospective/prospective multicenter cohorts focusing on TURP morbidity/mortality have been reported, there is still no consensus on how to define its complications and grade their severity. This hampers reproducible and sound comparisons longitudinally within centers or among centers using similar or different technologies such as M-TURP versus B-TURP. Consequently, a standardized classification serving as a common platform for communication among urologists is necessary. The modified Clavien Classification System (CCS) has been proposed as a standard tool for this purpose to increase the quality of the related urological literature In

***Chapter 5 (see 7.2., Publication 24)**, the applicability of the modified CCS in grading TURP complications is evaluated for the first time.* Data on 198 men submitted to M-TURP during a two-year period at a non-academic center were evaluated for complications up to the end of the first postoperative month and were classified prospectively and independently by two urologists according to this system. Final decision was based on consensus. Forty-four complications were recorded in 31/198 patients (overall perioperative morbidity rate: 15.7%). Grading was generally easy, non-time-consuming and straightforward. Most of them were classified as grade I (59.1%) and II (29.5%). Higher grade complications were scarce (grade III: 2.3% and grade IV: 6.8%, respectively) There was one death (grade V: 2.3%) due to acute myocardial infarction (overall mortality: 0.5%). Negative outcomes such as mild dysuria during this early postoperative period or retrograde ejaculation were considered sequelae and were not recorded. Nobody was complicated with severe dysuria. There was one re-operation due to residual adenoma (0.5%). It is concluded that the modified CCS represents a straightforward and easily applicable tool that may help urologists to classify the complications of TURP in a more objective and detailed way, serving as a standardized platform of communication among clinicians that allows for sound comparisons.

Part IV *(Chapters 6-8): Results from the first international multicenter RCT in the field*

B-TURP is at present the most thoroughly investigated alternative to M-TURP in RCTs. Nevertheless, all these RCTs represent single-center experiences of relatively low quality ***Chapters 6-8 (see 7.2., Publications 8, 10, 11, 14, 15, 16)*** refer to the *first international, multicenter RCT* comparing efficacy and safety of B-TURP with that of M-TURP in patients with LUTS secondary to BPO (NTR703: http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=703). The trial was conducted with the *aim to fulfill established criteria of quality assessment for RCTs* (The Cochrane Collaboration).

Within a 3-year period, 295 consecutive patients with BPO were prospectively recruited in four academic urological centers (Center 1: Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands; Center 2: SLK Kliniken Heilbronn, University of Heidelberg, Heilbronn, Germany; Center 3: Sismanoglio Hospital, University of Athens Medical School, Athens, Greece; Center 4: San Luigi Hospital, University of Turin,

Orbassano, Turin, Italy) and randomized 1:1 into M-TURP/B-TURP after written informed consent was obtained. A medical ethics committee at each center approved the protocol. Randomization was performed blindly among centers through a central electronic system for data collection, to minimize potential selection bias/guarantee allocation concealment, using a stratified permuted computer algorithm based on prostate volume and age. 279 patients (M-TURP, n = 138; B-TURP, n = 141) received allocated intervention. Surgeons were not blinded due to the nature of the intervention. Outcome assessors (different from the surgeons), and patients were both blinded for the intervention type (double-blind RCT). *A true bipolar device not previously evaluated in RCTs* was used (AUTOCON® II 400 ESU; Karl Storz Endoscope, Tuttlingen, Germany). *Patients were evaluated at baseline and regularly (at 6 wk, 6 mo, 12 mo, 24 and/or 36 mo) followed up to 36 mo after surgery. This is one of the longest follow-up durations to date*. Primary outcome was safety throughout follow-up. Sample size determination was based on sodium level changes immediately after surgery. Efficacy quantified using Q_{max}, postvoid residual urine volume, IPSS; and re-intervention rates were also compared.

Chapter 6 (see 7.2., Publications 14, 15, 16) presents the *perioperative results* of this RCT. Safety was estimated using sodium and hemoglobin level drop immediately after surgery and complications occurring up to 6 wk after surgery. *Perioperative morbidity was standardized for the first time using the modified CCS, as previously proposed for TURP procedures* (Chapter 5). Secondary immediate perioperative outcomes included operation time, resection time, resection rate, capsular perforation, and catheterization-hospitalization time. No differences were detected in safety, efficacy or secondary immediate outcomes except that the sodium level drop was significantly greater after M-TURP (–2.5 vs. –0.8 mmol/L; p = 0.003). The lowest values were 131 and 106 mmol/L (the latter patient with TUR-syndrome) after B-TURP and M-TURP, respectively. The sodium values in nine patients were 125–130 mmol/L and in three patients < 125 mmol/L after M-TURP. Sodium levels decreased also after B-TURP (by 9 mmol/L maximum; two patients). In nine patients, in the M-TURP arm, the decrease was 9–34 mmol/L. These results were not translated into a significant difference in TUR-syndrome rates (1/138: 0.7% vs. 0/141: 0.0%, for M-TURP and B-TURP, respectively; p = 0.495). Hemoglobin levels decreased significantly but similarly in each arm. Fifty-five complications were recorded in 44

patients (morbidity: 15.8%). Two complications were fatal (myocardial infarction) in M-TURP arm vs. no complication in B-TURP arm (p = 0.244; overall mortality: 0.7%). Morbidities did not differ (26/138 vs. 18/141, for M-TURP and B-TURP, respectively; p = 0.220). No differences were detected in any specific complication rates, failures rates or Clavien grade between arms. In contrast to the previous evidence, no clinical advantage for B-TURP was shown. The potentially improved safety of B-TURP that is attributed to the elimination of dilutional hypernatremia risk, a risk still present with M-TURP, did not translate into a significant clinical benefit in experienced hands.

The effect of TURP on the overall sexual function (SF) and particularly on erectile function (EF) is controversial with conflicting results based on a low level of evidence. The effects of M-TURP/B-TURP on EF are similar, as shown in some non-focused RCTs. *Focused results of a comparative evaluation of these effects on SF quantified with the International Index of Erectile Function Questionnaire (IIEF-15) are published for the first time.* Short-term results (up to 12 mo) of this RCT are presented in ***Chapter*** 7 ***(see 7.2., Publication 8)***. It is concluded that there no differences exist between arms in any aspect of SF. Total IIEF/domain scores were calculated and EF score classified erectile dysfunction severity (EDS). Differences in EDS at each visit compared to baseline (EF evolution; EFE), classified patients into "improved", "stable" or "deteriorated". Pre-postoperative IIEF/domain scores and differences in EFE distribution were compared between arms throughout follow-up. 218/279 patients that received allocated intervention (78.1%) provided complete baseline IIEF-15 data and were considered in SF analysis. Complete pre-post data were available from 193/218 (88.5%), 186/218 (85.3%) and 179/ 218 (82.1%) patients at 6 wk, 6 mo and 12 mo, respectively. M-TURP insignificantly outperformed B-TURP, mainly in terms of IIEF/EF scores. After excluding patients with severe ED at baseline, the effect of resection type on SF scores remained insignificant. There were no differences in the distribution pattern of EDS/EFE at any time (M-TURP vs. B-TURP at 12 mo: improved, 23/87 [26.4%] vs. 18/92 [19.6%]; stable, 53/87 [60.9%] vs. 56/92 [60.8%]; deteriorated, 11/87 [12.7%] vs. 18/92 [19.6%]; p = 0.323). Some significant fluctuations were seen in the total population (two arms merged). Apart from an overall satisfaction improvement from 6 mo onwards, no other significant changes were detected at 12 mo. After excluding cases with severe ED at baseline, no alterations were seen. However, a

slight transient IIEF drop at 6 wk became significant, mainly driven by steep drops in EF, intercourse satisfaction and orgasmic function that remained low up to 6 mo. Sexual desire/overall satisfaction dropped at 6 wk but the overall fluctuation was insignificant compared to baseline. EFE distribution analysis showed stability in most cases with a trend towards relative improvement. Other baseline/ perioperative parameters potentially influencing EF after TURP were also investigated, including patient age, body mass index (BMI), prostate volume, baseline IIEF/EF scores, and capsular perforation. BMI and IIEF/EF scores at baseline were the only predictors of EFE. Patients with higher BMI had a higher probability of deteriorating opposed to patients with higher IIEF/EF scores at baseline. 7/27 patients with no ED at baseline presented with ED and 20/66 with severe ED improved at 12 mo. No variable tested predicted de novo ED appearance. However, in patients with severe ED at baseline, IIEF/EF baseline scores were the only predictors of EF improvement. Higher IIEF/EF scores at baseline predicted a higher chance of improvement.

Pooled data from RCTs with a short-term follow-up have shown a perioperative safety advantage for B-TURP compared with M-TURP (Chapter 3). However, RCTs with follow-up >12 mo are scarce. ***Chapter 8 (see 7.2., Publication 10)*** presents the short-term (up to 12 mo) and *midterm results (up to 24-36 mo)* of this RCT. Special emphasis was given on US and BNC rates, two potentially devastating complications of TURP typically occurring in the longer term. Midterm results from the first international/multicenter RCT show that the safety/efficacy of B-TURP is similar to M-TURP. The mean follow-up of the 279 treated patients was 28.8 mo. 186 patients (66.7%) completed the 36-mo follow-up. Post-treatment withdrawals did not differ significantly between arms. Primary outcome (safety) assessment was based on 230 patients (82.4%) at 24–36 mo (mean follow-up: 33.4 mo; 34.1 vs. 32.8 mo for M-TURP vs. B-TURP, respectively; $p = 0.077$). The only additional complications to those reported in the perioperative period (Chapter 6) were US and BNC. Ten US cases were seen in each arm (M-TURP vs. B-TURP: 9.3% vs. 8.2%; $p = 0.959$), and two versus eight BNC cases (M-TURP vs. B-TURP: 1.9% vs. 6.6%; $p = 0.108$) were collectively detected at midterm. No significant differences were detected between arms in the cumulative short- or midterm rates of either complication within centers or in the total population. Modeling of time-to-complication detection data confirmed that resection type

was not a predictor of US/BNC risk formation. Efficacy of methods was adequate, similar, and durable. 10/230 patients (4.3%) who completed the midterm follow-up experienced "failure to cure" and needed re-intervention (re-TURP for residual adenoma [n = 7], permanent intermittent catheterization [n = 2], bladder diverticulectomy [n = 1]. No difference was detected in re-intervention rates between arms. Considering all patients who needed re-intervention (including those with US/BNC), the difference remained insignificant (short term: 12/121 [9.9%] vs. 20/135 [14.8%]; p = 0.320; midterm: 16/108 [14.8%] vs. 23/122 [18.9%] for M-TURP vs. B-TURP, respectively; p = 0.523). High overall re-intervention rates, withdrawal rates, and sample size determination not based on US/BNC rates represent potential limitations of the trial.

Reply to comments received on this manuscript (Chapter 8) is presented in **Chapter 9**.

Limitations of the evidence are discussed within the general context of the quality of the existing surgical-urologic trials in several fields, including the surgical management of LUTS secondary to BPO. Potential solutions to improve the validity/ reduce uncertainty on risk of bias in urologic research are put in a future perspective. The value of the introduction of bipolar technology in TURP, in relation to M-TURP, for treating these patients is highlighted in the context of the current best available evidence.

In the general discussion of the thesis **(Part V)**, the main findings of the above-mentioned publications are wrapped up together in relation to the existing literature. Evidence and limitations defining the current position of B-TURP in the urological community and some practical considerations for daily practice are discussed such as economic issues, potential application of B-TURP in training and in special patient subpopulations, including those dependent on anticoagulation treatment, with severe comorbidities or "large" adenomas. Last but not least, future perspectives are discussed.

9.3. Master in Biostatistics (Monograph)

Subject: **"Seasonal variation of hypospadias in Greek population"**

Supervisor: Prof. A. Tzonou, Department of Hygiene, Epidemiology & Medical Statistics, Athens University Medical School, Athens, Greece (23/5/2005)

Participating institutions: 1. University of Athens, Athens, Greece: A. Faculty of Medicine (Department of Hygiene & Epidemiology), B. Faculty of Mathematics; 2. University of Ioannina, Ioannina, Greece: Faculty of Mathematics); Academic period: September 2002-September 2004

From this work, 1 paper has been produced, which has been submitted for consideration for publication in an international scientific journal.

Monograph Summary

Hypospadias represents the second commonest congenital abnormality of male external genitalia following cryptorchidism. Its etiology remains elusive. Seasonal variation of its incidence has been investigated in many countries, however results are contradictory. The aim of the current study is to examine seasonality of hypospadias in Greece, in an attempt to shed light on the complicated problem of the etiology.

All boys of Greek origin born among the years 1991-1998 who has been submitted to surgical correction of hypospadias at "Aghia Sophia" Children's Hospital in Athens (N=542) were included in the study. All newborns in Greece during the same period (M=421,175) served as controls (population at risk). Monthly mean sunlight, air temperature, and rainfall during the years 1990-1998 were also analyzed. Seasonality by month of birth was evaluated using specific statistical tests modified in order to take into account the magnitude of the population at risk as well as the exact duration of each month: a) Freedman's (F^*), b) Edwards' (E^*), c) Walter-Elwood's (WE^*), d) Roger's (R^*), e) Hewitt's (T) and f) X^2 goodness-of- fit test.

Monthly frequencies of hypospadiac births showed statistically significant departure from a uniform seasonal distribution (F^* =1,53-P<0,05), following a cyclic variation well

described by the equation of the simple harmonic oscillation with maximum-minimum incidence in October-April, respectively (Edwards: ϑ_{max} = 294,60°, ϑ_{min} =114,60°, α =0,171, E^* =7,92-P<0,02, X_{11}^2 = 13,24-P>0,20, Walter-Elwood: ϑ_{max} =288,40°, ϑ_{min} = 108,40°, α =0,168, WE^* = 8,85-P<0,02, X_{11}^2 = 13,64-P>0,20, Hewitt: August-January, T =55-P=0,048). The climatic parameters studied exhibit seasonal variation as well (maximal sunlight-temperature in the summer, minimal in the winter, maximal rainfall in the winter, minimal in the summer) and are strongly associated with each other.

Therefore, the first trimester (crucial embryonic period for the differentiation-development of male urethra) of hypospadiac gestations coincides statistically more frequently with the winter period. The relative seasonal pattern of a climatic factor (e.g. low environmental temperature) that acts either directly or indirectly might contribute to the pathophysiology of hypospadias.

It appears that the hypospadiac seasonal pattern observed is associated with the respective cryptorchid one, which has been previously detected in the Greek population (harmonic with maximum-minimum incidence in March-September, respectively). The coincidence of the first and third trimester (crucial embryonic period of the final phase of testicular descent) of a potentially genetically influenced gestation with the winter period, could lead to the phenotypic expression of hypospadias or cryptorchidism, respectively. Since the differentiation-development of male urethra as well as the final phase of testicular descent is both androgen-dependent procedures, the potential role of a cyclic-varied androgen-production stimulator seems plausible. The human chorionic gonadotrophin serves as an example of such a stimulator, since it exhibits a seasonal variation with lowest levels in winter. Seasonality of a common environmental factor, which acts either directly or indirectly via the above described mechanism, might contribute to the appearance of the observed seasonal patterns and possibly to a common pathogenesis of the congenital malformations in question.