Urethral Bulking Agents for the Minimally Invasive Treatment of Stress Urinary Incontinence
Workshop 33
Tuesday 24 August 2010, 09:00 – 12:00

Time	Time	Topic	Speaker
09:00	09:05	Introduction	Linda Cardozo
09:05	09:20	Cure from the patient perspective	Dudley Robinson
09:20	09:45	Urethral bulking agents used in the USA	Gamal Ghoniem
09:45	10:00	Coaptite and Durasphere	Roger Dmochowski
10:00	10:20	Bulkamid	Karl Tamussino
10:20	10:30	Round Table Discussion	All
10:30	11:00	Coffee Break	
11:00	11:20	Complications of Bulking Agents	Sender Herschorn
11:20	12:00	Hands on Training	All

Aims of course/workshop

Urethral Bulking Agents remain an important component of the treatment armamentarium for women with Stress Urinary Incontinence (SUI). This workshop aims to explore the use of bulking agents in the treatment of SUI by particularly focusing on the patient orientated approach.

The clinicians, all of whom are experienced in the use of bulking agents, will share the latest clinical data and evidence for the currently available products. The workshop will also cover treatment specific complications related to bulking agents and the management of those complications.

In addition there will be the opportunity for hands on training and demonstrations.

Educational Objectives

Urethral bulking agents continue to have an important role in the management of women with stress urinary incontinence and, whilst having lower efficacy than mid-urethral tapes, are associated with lower morbidity and may be performed in the office setting. This 'trade off' may explain why women often choose a bulking agent in preference to more invasive surgery.

The workshop will begin with a presentation suggesting that "cure" from the patient's perspective is not necessarily identical to cure from the perspective of the clinician and focus primarily on the use of bulking agents.

An overview of the clinical role of bulking agents will also cover indications and the advantages of urethral bulking in specific patient groups. The use of bulking agents under

local anaesthesia in the ambulatory setting will also be covered with advice and guidelines for developing an outpatient service.
The success rate of the procedure depends largely upon the nature of the injection material and operator expertise. Each member of the faculty will present the evidence supporting the use of the various bulking agents that are on the market including the most recent publications and safety data. The potential advantages, and disadvantages of each product will also be covered including personal experience with 'tips and tricks' to maximise the success rates as well as complications.

The workshop is planned to be highly interactive and a free open discussion with the audience will be encouraged throughout. Ample opportunity will be given at the end of the workshop for 'hands on' experience using each of the products with the use of clinical training models. This which will be completely interactive and allow demonstrations by the 'experts' with regard to techniques and patient selection.

An Minimally Invasive Approach to Stress Urinary Incontinence: Urethral Bulking Agents

Urethral bulking agents are a minimally invasive surgical procedure for the treatment of urodynamic stress incontinence and may be useful in the elderly and those women who have undergone previous operations and have a fixed, scarred and fibrosed urethra with poor bladder neck mobility.

Although the actual substance which is injected may differ the principle is the same. It is injected either periurethrally or transurethrally on either side of the bladder neck under cystoscopic control and is intended to 'bulk' the bladder neck, in order to stop premature bladder neck opening, without causing out-flow obstruction. They may be performed under local, regional or general anaesthesia. There are now several different products available **[Table 1]**. The use of minimally invasive implantation systems has also allowed some of these procedures to be performed under local anaesthesia, in the office setting, and without the need for cystoscopy.

Urethral Bulking Agent	**Application technique**
Gluteraldehyde cross linked bovine collagen **(Contigen)**	Cystoscopic
Polydimethylsiloxane **(Macroplastique)**	Cystoscopic MIS Implantation System.
Pyrolytic carbon coated zirconium oxide beads in β Glucan gel **(Durasphere)**	Cystoscopic
Ethylene vinyl co-polymer in dimethyl sulfoxide (DMSO) gel **(Tegress, Uryx)**	Cystoscopic
Calcium Hydroxylapatite in carboxymethylcellulose gel **(Coaptite)**	Cystoscopic
Polyacrylamide hydrogel **(Bulkamid)**	Cystoscopic

Table 1: Urethral Bulking Agents

In the first reported series 81% of 68 women were dry following two injections with collagen (Appell 1990)[1]. There have been longer term follow-up studies most of which give a less than 50% objective cure rate at 2 years but a subjective improvement rate of about 70% (Harris *et al.* 1996[2]; Khullar *et al.* 1997[3]; Stanton & Monga 1997[4]). Macroplastique has

recently been compared to Contigen in a recent North American study of 248 women with urodynamic stress incontinence. Outcome was assessed objectively using pad tests and subjectively at 12 months. Overall objective cure and improvement rates favoured Macroplastique over Contigen (74% vs 65%; p=0.13). Whilst this difference was not significant subjective cure rates were higher in the Macroplastique group (41% vs 29%; p=0.07). (Ghoniem et al, 2005)[5] A 12 month open label European study of 142 women with urodynamic stress incontinence treated with Zuidex has reported cure and improvement rates of 78% at 12 weeks and 77% at 12 months (Chapple et al, 2005)[6] although this product has now been withdrawn due to concerns regarding safety.

Whilst success rates with urethral bulking agents are generally lower than those with conventional continence surgery they are minimally invasive and have lower complication rates meaning that they remain a useful alternative in selected women. The recent introduction of minimally invasive implantation systems also allows these procedures to be performed under local anaesthesia in the clinic setting.

This presentation will examine the concept of 'cure' as well as providing a brief overview of the techniques available

REFERENCES

[1] Appell RA (1990) New developments: injectables for urethral incompetence in women. Int Urogynaecol 1, 117-19.

[2] Harris DR, Iacovou JW & Lemberger RJ (1996) Peri-urethral silicone micro implants (Macroplastique) for the treatment of genuine stress incontinence. Br J Urol 78, 722-8.

[3]Khullar V, Cardozo LD, Abbot D & Anders K (1997) GAX collagen in the treatment of urinary incontinence in elderly women: a 2 year follow-up. Br J Obstet Gynaecol 104.

[4] Stanton SL & Monga AK (1997) Incontinence in elderly women: is periurethral collagen an advance? Br J Obstet Gynaecol 104, 154-7.

[5] Ghoniem G, Bernhard P, Corcos J, Comiter C, Tomera K, Westney O, Herschorn S, Lucente V, Smith J, Wahle G, Mulcahy J. Multicentre randomised controlled trial to evaluate Macroplastique urethral bulking agent for the treatment of female stress urinary incontinence. Int Urogynaecol J 2005; 16(2): S129-130.

[6] Chapple CR, Haab F, Cervigni M, Dannecker C, Fianu-Jonasson A, Sultan AH. An open, multicentre study of NASHA/Dx Gel (Zuidex) for the treatment of stress urinary incontinence. Eur Urol 2005; 48: 488-494.

ICS/IUGA 2010 Workshop 33 (W33)

Tuesday, August 24, 2010
09:00 - 12:00

Urethral Bulking Agents for the Minimally Invasive Treatment of Stress Urinary Incontinence

Chair: Linda Cardozo, United Kingdom
Speakers: Gamal Ghoniem, United States; Karl Tamussino, Austria; Roger Dmochowski, United States; Sender Herschorn, Canada

"Experience with UBAs: Macroplastique®"

Gamal M. Ghoniem, MD, FACS
Head, section of Female Urology & Voiding Dysfunction
Clinical Professor of Urology/surgery Nova NSU, USF, OSU
Cleveland Clinic Florida

INTRODUCTION:
Urethral Bulking Agents (UBAs) injection represents minimally invasive, office-based approach to SUI. Women with urinary incontinence have realistic expectations from treatment and accept less effective modality; providing it is minimally invasive. In our study of 100 women with stress urinary incontinence (SUI), the majority of them (71%) found a minor surgery, like a transobturator tape, or a clinical procedure, like UBA, most desirable.

The Implant:
The unique nature of the Macroplastique implants is created via a proprietary process rendering a highly textured, soft implant that easily agglomerates with other implants.

It is believed this agglomeration property allows for firm anchoring within the submucosal area of the urethra because of the rapid tissue response around and through the open matrix of the material.
The open matrix of an individual Macroplastique implant can be most easily described as being similar to a natural sea sponge with a flexible, three-dimensional structure (note scanning electron micrographs of an individual implant and an agglomeration of implants below). This characteristic allows for the rapid formation of a fibrin net around the implanted material (referred to as a "bolus") with subsequent robust collagen deposition. The size of an individual, non-agglomerated implant is approximately 150 microns in diameter, and can be as large as 400+ microns.
The large size and compression of the soft, textured implants is the reason for the high resistance of the suspension during delivery, thus requiring a special Administration Device designed to deliver the material in a slow, precise manner.

Figure 1 SEM of Individual Macroplastique Implant

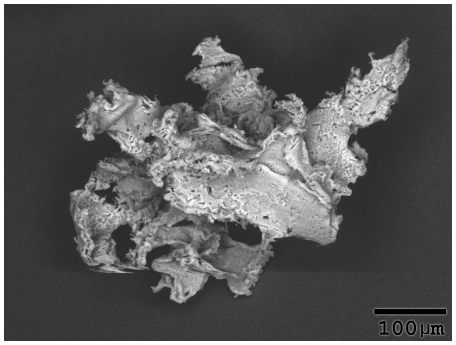


Figure 2 SEM of Agglomerated Macroplastique Implants

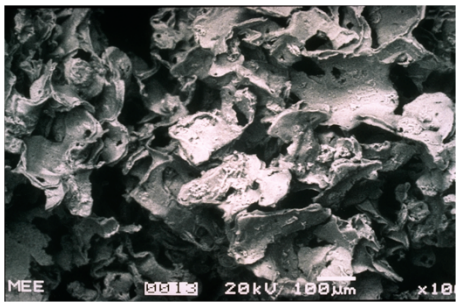
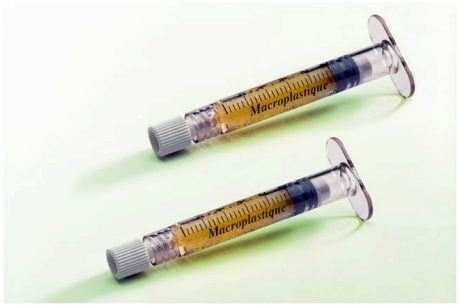


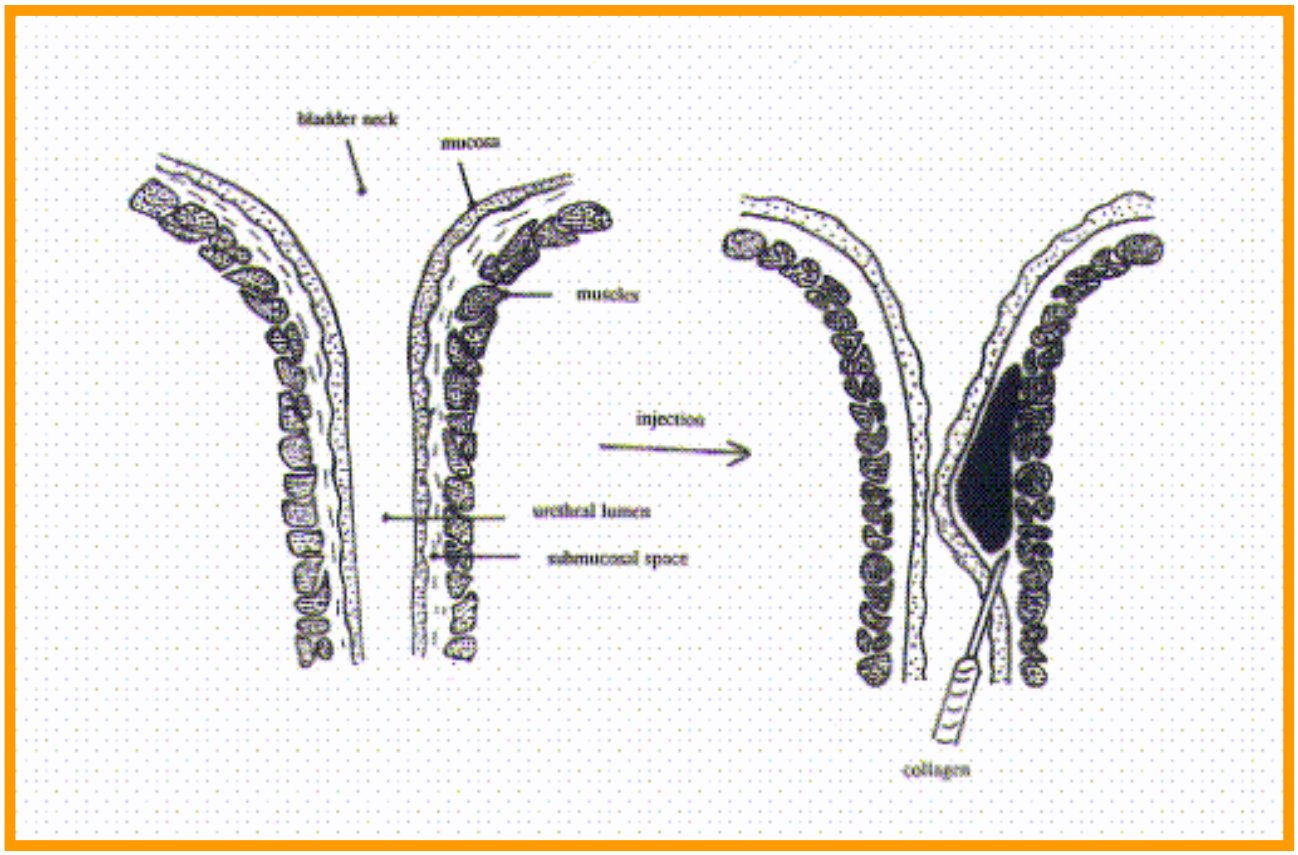
Figure 3 Macroplastique Administration Device

Figure 4 Macroplastique 2.5cc Syringes



The Transurethral Technique:

To get good results, the deposition of Macroplastique should be distal to Bladder neck and into the proximal urethra. The tunneling technique is important to trap the implant. To achieve both criteria, the puncture (entry) should be just above the external sphincter level. Visual coaptation of the mucosa is important.



Before Procedure:

Patients with ISD
Urine clear
Premarin cream for 2-3 weeks
Antibiotics, start the morning before
Pre-medicated orally with diazepam 2-5mg and tramadol 50mg on arrival to office
Patient to void

During Procedure:

Intra-urethral lidocaine
Minimize manipulations
May need to drain the bladder with 10 F catheter

After Procedure:

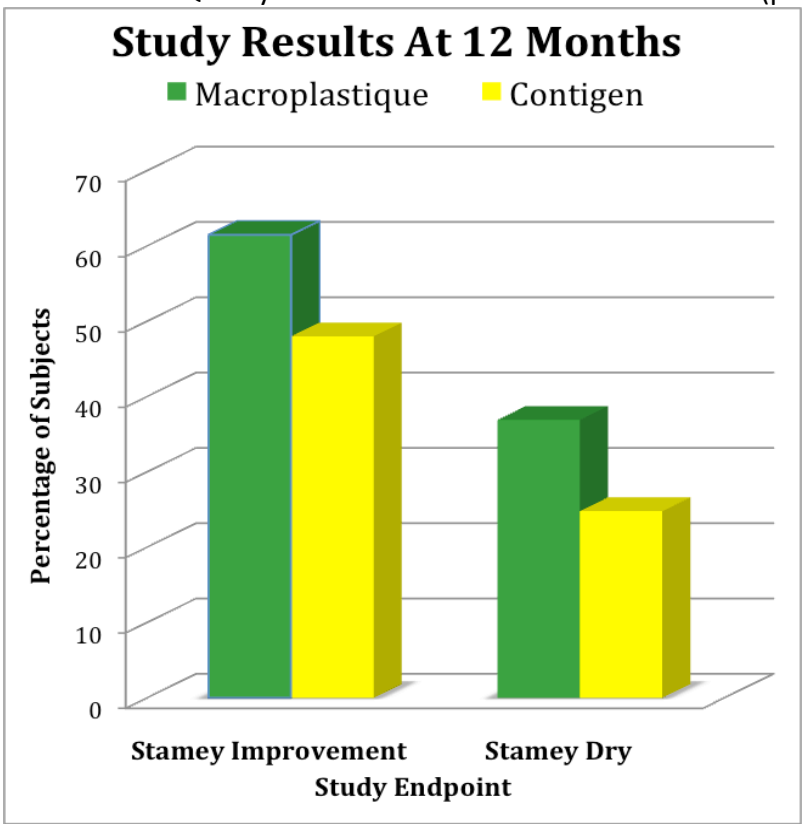
Check residual urine
Continue antibiotics x 3 days
Phenazopyridine 200 mg tid

Cross-linked polydimethylsiloxane injection for female stress urinary incontinence: results of a multicenter, randomized, controlled, single-blind study. J Urol 2009 Jan; 181(1): 204-10

SUMMARY:

Macroplastique® was compared to Contigen® in a non-inferiority study design in 247 women (122 vs. 125 respectively) with intrinsic sphincter deficiency. Only one repeat treatment was allowed at 3 months. At 12 months after treatment **61.5%** of patients who received Macroplastique and **48%** of controls had improved 1 Stamey grade. In the Macroplastique group the dry/cure rate was **36.9%** compared to **24.8%** in the control group ($p < 0.05$). In the Macroplastique and control groups the 1-hour pad weight decrease was 25.4 and 22.8 ml from baseline ($p = 0.64$), and the mean improvement in Urinary

Incontinence Quality of Life Scale score was 28.7 and 26.4 (p 0.49),respectively.



This study is different from older Macroplastique studies in many ways: first North American, included large number of patients from different centers, blinded to patients, used control (Contigen), used strict criteria for analysis. It also classified and analyzed all genitourinary adverse events that occurred at any time during the study as treatment related whether they were determined by investigating physicians to be treatment-related or not.

Study limitations include the intent-to-treat analysis where all drop outs were analyzed as failures rather than using last value carried forward; which would have given a higher success and cure rate. This is unique to this study (not used in other UBA studies) and the strictest test. Other bulking agents approved by FDA (Coaptite and Durasphere) used last value carried forward for failures. Secondly, the subjects were retreated at only the 3-month point and were not able to get a retreatment at any other time during their 1 year follow up. In reality, a patient can have a retreatment anytime after 3-months. Lastly, from this study there may be patients who still had an OAB urge component remaining after their SUI is resolved, but those patients are not included in the dry group.

Durability of Urethral Bulking Agent Injection for Female Stress Urinary Incontinence: 2-Year Multicenter Study Results

Gamal Ghoniem,*,† Jacques Corcos,‡ Craig Comiter,§ O. Lenaine Westney¶ and Sender Herschorn‖

From the Cleveland Clinic Florida (GG), Weston, Florida, McGill Urology Associates (JC), Montreal, Quebec and University of Toronto (SH), Toronto, Canada, University of Arizona (CC), Tucson, Arizona, and University of Texas (OLW), Houston, Texas

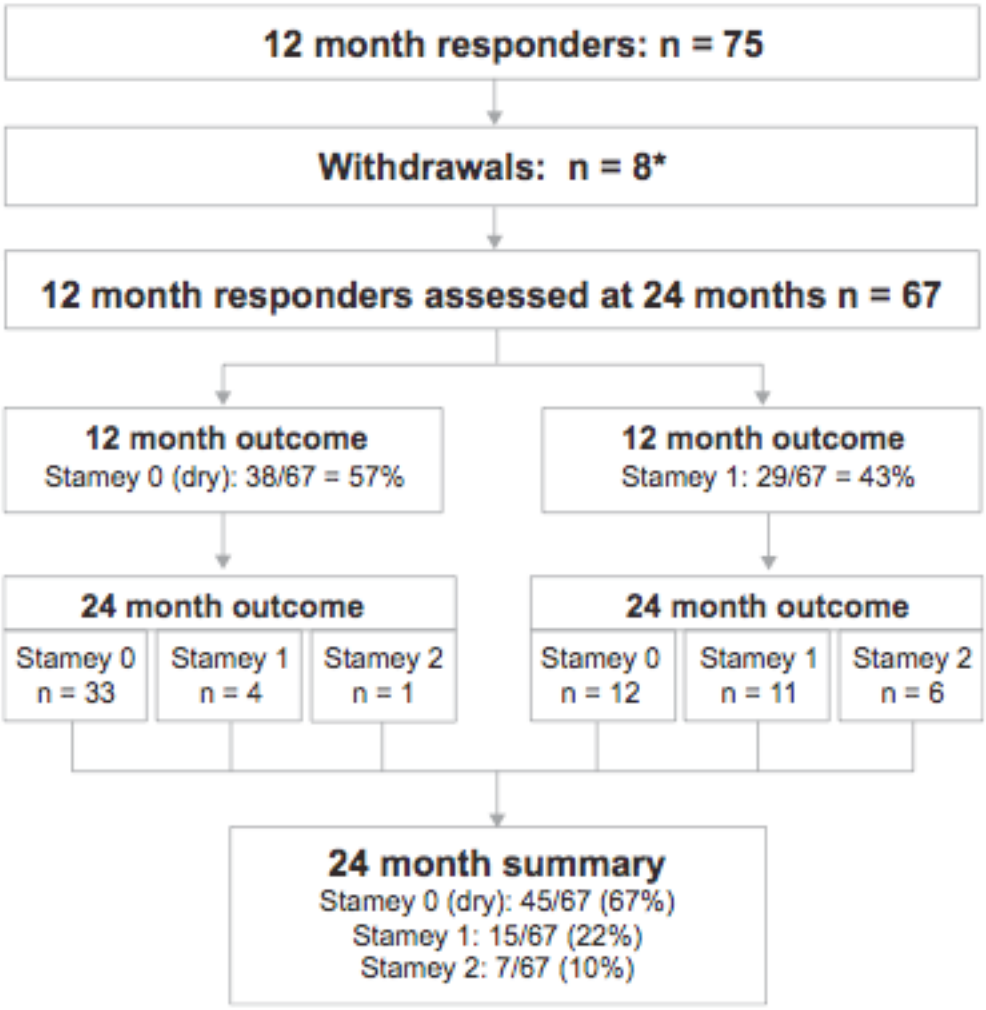


Figure 3. Study flow shows Stamey grade by visit. Asterisk indicates reason for study withdrawal and 12-month Stamey grade, including unknown reason (Stamey 0) and no response to followup communication (Stamey 0) in 2 patients each, and changed contact information and unavailable (Stamey 0), did not attend multiple appointments (Stamey 0), withdrew due to investigator move (Stamey 0) and did not want to return for followup due to age 85 years (Stamey 1) in 1 each.

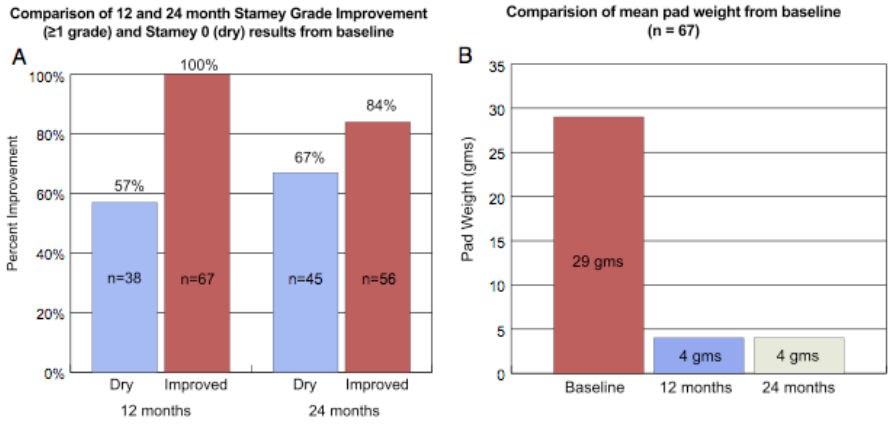


Figure 4. *A*, 12 and 24-month Stamey grade 0 (dry) and 1 or greater (improved). At 12 months all patients reported improvement from baseline for study eligibility. *B*, mean pad weight in 67 patients at baseline, and at 12 and 24 months.

Table 1. *Global Impression of Improvement in 67 patients*

	No. Pt (%)	No. Physician (%)
12 Mos:*		
Cured	29 (43)	37 (55)
Marked improvement	32 (48)	28 (42)
Slight improvement	6 (9)	2 (3)
24 Mos:		
Cured	28 (42)	44 (66)
Marked improvement	28 (42)	13 (19)
Slight improvement	5 (8)	8 (12)
No change	5 (8)	2 (3)

* No patient had no change.

Conclusions: Substantial, durable results were sustained during 2 years with 84% of patients maintaining significant Stamey grade improvement from the 12-month assessment. Two-thirds of patients were dry at 24 months. The dura- bility of Macroplastique shows its effectiveness as a viable long-term therapy for female stress urinary incontinence primarily due to intrinsic sphincter deficiency.

ID	Title	Score
655	Urinary Incontinence Treatment Preferences of Geriatric Patients: A Study in Hospitalized Cognitively Competent Older Adults 80 Years and Older	12.25
34	Effects of Mesenchymal Stem Cells on Leak Point Pressure and Closing Pressure in Rats with Transected Pudendal Nerves	12
576	Valsalva Leak Point Pressure and Detrusor Overactivity Do Not Predict, but Urodynamic Stress Incontinence Does Predict, Continence Outcomes after Burch or Pubovaginal Sling Procedures	12
57	DIFFERENCES IN THE FUNCTION OF THE PREFRONTAL CORTEX BETWEEN WOMEN WITH URGE URINARY INCONTINENCE AND CONTINENT COHORTS	11.8
71	INCREASED ACTIVITY OF a1-ADRENOCEPTORS AFTER HUMAN MUSCLE-DERIVED STEM CELLS INJECTION INTO THE DENERVATED RAT URETHRA	11.8
73	Somatic injury induces de novo expression of chemokines and their receptors in bladder primary afferent neurons	11.8
762	URODYNAMIC ASSESSMENT IN SPINAL CORD INJURIED MALE AFTER VARDENAFIL ADMINISTRATION	11.75
586	CORRELATION BETWEEN THE EXPRESSION LEVEL OF ALPHA1-ADRENOCEPTOR SUBTYPE MRNA AND PATIENT AGE OR PROSTATE VOLUME IN BENIGN PROSTATIC HYPERPLASIA PATIENTS	11.67
317	The Colpopexy and Urinary Reduction Efforts Trial: Two Year Outcomes	11.5
363	A randomised controlled trial of a progressive protocol for neurogenic bowel management	11.4
611	EVIDENCE FOR CENTRAL HYPEREXITABILITY IN PATIENTS WITH INTERSTITIAL CYSTITIS	11.4
278	Aetiology of urinary storage symptom syndromes: evaluation of a diet and lifestyle model involving diabetes and obesity in women	11.25
341	Study design as the main predictor for good outcome in a randomised placebo-controlled multicentre trial in children suffering from overactive bladder and urinary incontinence	11.25
238	DOES PELVIC FLOOR MUSCLE TRAINING DURING PREGNANCY NEGATIVELY AFFECT LABOUR AND BIRTH?	11.2
515	Is injury to the levator ani nerve preventable in rectal surgery?	11.2
718	The heritable contribution to lower urinary tract symptoms in women	11.2
60	Urinary dysfunction and right frontal hypoperfusion in idiopathic normal pressure hydrocephalus; an [123I]-IMP SPECT study	11
304	Performance and cost-effectiveness of absorbent products for women with light urinary incontinence: a randomized cross-over clinical trial	11
308	Gender differences in performance of and preferences for absorbent products for men and women with moderate-heavy urinary incontinence: a randomized cross-over clinical trial	11
365	The mechanism of atropine resistance in human detrusor muscle	11
458	Does the bladder have a memory? Is Childhood Dysfunctional Voiding related to bladder and pelvic floor dysfunction in adult women?	11

450	Risk factors associated with failure of surgical treatment for stress urinary incontinence at 24 months follow-up	10.83
579	Combining Behavior and Drug Therapy to Improve Drug Withdrawal in the Treatment of Urge Incontinence: a Randomized Trial	10.8
784	PROSPECTIVE RANDOMIZED CONTROLLED STUDY BETWEEN TWO DIFFERENT PROCEDURES TO SUSPEND THE VAGINAL VAULT: HIGH LEVATOR MYORRAPHY AND UTEROSACRAL VAGINAL VAULT SUSPENSION.	10.8
491	Mitochondrially-Targeted Drugs for the Prevention of Radiation Cystitis	10.67
206	How do incontinence status in pregnancy and delivery mode affect urinary incontinence 6 months post partum?	10.6
251	Results of Retropubic and Transobturator placement of sub-mid urethral tapes (M.U.T.) in First International Registry: Results on 984 patients at 3 and 12 months	10.6
290	REPEATED INTRADETRUSOR INJECTIONS OF BOTOLINUM TOXIN-A IN NEUROGENIC OVERACTIVE BLADDER: URODYNAMIC, UDI-6 AND QUALITY OF LIFE DATA	10.6
380	Evaluation of non-invasive bladder pressure and urine flow measurement systems for routine clinical use: Assessment of interpreter and test-retest variability	10.6
489	Interstitial Cells Drive Overactivity in Pathological Bladders—Determined Using Optical Imaging	10.6
78	SUPPRESSION OF DETRUSOR OVERACTIVITY AND DETRUSOR-SPHINCTER DYSSYNERGIA BY GABA-RECEPTOR ACTIVATION AT THE LUMBOSACRAL SPINAL CORD IN SPINAL CORD INJURY RATS	10.5
118	Urodynamic Function and Expression of Neurotrophins after a Maternal Childbirth Injury Model of Vaginal Distension and Pudendal Nerve Crush in Rats	10.5
142	Causes of Failed Urethral Botulinum Toxin A Treatment for Voiding Dysfunction	10.5
186	Overactive bladder symptoms are not related to Detrusor Overactivity	10.5
431	Dose response relationship of fesoterodine 4 mg vs 8 mg and onset of action in subjects with overactive bladder: results from a pooled analysis of 2 randomized trials	10.5
379	Randomised controlled trial of the clinical effectiveness of services for urinary symptoms: six year follow-up	10.4
472	Nerve preservation in tension free vaginal mesh procedures for pelvic organ prolapses: a cadaveric study using fresh and fixed cadavers.	10.4
670	Pelvic floor muscle training or bladder training to treat stress urinary incontinence in elderly women: a single blind randomised controlled trial	10.4
464	Normal values of frequency volume parameters in 788 asymptomatic volunteers compared to volunteers with elevated I-PSS.	10.33
653	The role of smooth muscle in the pathogenesis of pelvic organ prolapse – an	10.33

243	Modulation of sub-urothelial myofibroblast responses to sensory modulators	10.25
757	The interaction of cortico-spinal pathways and sacral reflexes following spinal cord injury	10.25
198	Analysis of the prognostic factors for overactive bladder syndrome following surgical treatment in patients with symptomatic benign prostatic enlargement	10.2
295	BOTULINUM TOXIN A: INTRADETRUSOR RE-INJECTIONS IN IDIOPATHIC OVERACTIVE BLADDER EVERY 6 MONTHS – 3 YEARS FOLLOW UP	10.2
342	Title	10.2
343	Cost-effectiveness of transanal irrigation versus conservative bowel management for spinal cord injury patients	10.2
294	Prevalence of Defecatory Dysfunction in Women With and Without Pelvic Floor Disorders	10.17
742	Does pregnancy and delivery affect pelvic organ support? Pregnancy And Prolapse Assessment [PAPA] Study	10.17
49	Which screening test is best for my clinic? A comparison study of the Bladder self-assessment questionnaire (B-SAQ) and OAB-V8 questionnaire.	10
72	BLADDER OVERACTIVITY INDUCED BY CHRONIC PUDENDAL NERVE LIGATION INJURY IS ASSOCATED WITH INCERASED EXPRESSION OF NERVE GROWTH FACTER AND ACTIVATION OF a1-ADRENOCEPTORS IN THE RAT BLADDER	10
86	A RANDOMIZED CONTROLLED TRIAL OF BACILLUS CALMETTE-GUERIN AND BOTULINUM TOXIN-A FOR THE TREATMENT OF REFRACTORY INERSTITIAL CYSTITIS	10
93	ANTIOXIDANT AND PHYTOSTEROL TREATMENT OF PROSTATE CANCER	10
117	Premenstrual Syndrome and Premenstrual Dysphoric Disorder: Are women at increased risk for pelvic floor disorders?	10
151	Effects of electrical stimulation of the striatum on bladder contraction in cats	10
194	Pelvic organ prolapse symptoms in relation to POP-Q, ICS ordinal stages and ultrasound stages	10
204	Do women with early anatomical recurrences of anterior vaginal wall prolapse after anterior vaginal repair have lower vaginal tissue collagen content?	10
205	GABAergic mechanism mediated via D1 receptors in the rat periaqueductal grey participates in micturition reflex: an in vivo microdialysis study	10
226	Planned cesarean versus planned vaginal delivery : a comparison of lower urinary tract symptoms.	10
229	The increase in 24-hr urine production/weight causes nocturnal polyuria due to impaired function of antidiuretic hormone in elderly men	10
235	Prazosin improves detrusor overactivity secondary to bladder outlet obstruction through the inhibition of the afferent activation in the rat.	10
263	[illegible]	10

269	Urinary incontinence in Dutch Health Care Organizations	10
298	WEAR OFF TIME IN IDIOPATHIC OVERACTIVE BLADDER PATIENTS TREATED WITH BOTULINUM NEUROTOXIN-A. DOES IT CHANGE WITH REPEATED INJECTIONS?	10
316	Refractory Urge Urinary Incontinence and Botulinum A toxin Injection Trial	10
366	Urethral injection therapy. What is the mechanisme of action?	10
368	The detrusor glycogen content of a de-obstructed bladder reflects the functional history of that bladder during PBOO	10
394	Potential for recovery in bladder function after removing a urethral obstruction.	10
410	No difference in urinary incontinence between training and control group six years after cessation of a randomized controlled trial, but improved sexual satisfaction in the training group	10
422	ONCE-DAILY TROSPIUM CHLORIDE EXTENDED RELEASE IS EFFECTIVE AND WELL TOLERATED FOR THE TREATMENT OF OVERACTIVE BLADDER: RESULTS FROM A MULTICENTER, PHASE III TRIAL	10
445	ALFUZOSIN, BUT NOT TAMSULOSIN, RELIEVES BLADDER HYPERTROPHY IN RATS DESPITE A PERSISTENT BLADDER OUTLET OBSTRUCTION	10
510	TESTING ACCURACY OF THE ICIQ-LUTS-C: A NEW INSTRUMENT TO SCREEN LOWER URINARY TRACT SYMPTOMS IN CHILDREN	10
527	Urethral Motion Profile: A Novel Method To Study Urethral Mobillity	10
561	RELATIONSHIP BETWEEN DETRUSOR OVERACTIVITY, AGE AND BLADDER OUTLET OBSTRUCTION IN MEN WITH BENIGN PROSTATIC HYPERPLASIA	10
594	Inter-rater reliability of puborectalis and the anal sphincter muscles imaging abnormalities with the three-dimensional ultrasound	10
595	Inhibitory effects of ß-adrenoceptor agonists on detrusor contraction involve the ß3-adrenoceptor in pig bladder dome	10
604	Trigonal injection of botulinum toxin type A does not cause vesicoureteral reflux in patients with refractory neurogenic detrusor overactivity	10
663	Defining surgical cure: do surgical goals meet patient expectations?	10
666	Botulinum toxin into the trigone in neurogenic overactive bladder non responder to detrusor injection	10
673	Urinary white cells and the symptoms of the overactive bladder	10
841	MRI anatomy of Lysyl Oxidase Like-1 deficient (LOXL1 KO) mice with and without pelvic organ prolapse (POP): A Pilot Study	10
857	Does Diet Coke cause overactive bladder? A 4-way crossover trial, investigating the effect of carbonated soft drinks on overactive bladder symptoms in normal volunteers.	10
--	EFFECTS OF DULOXETINE, NOREPINEPHRINE AND SEROTONIN REUPTAKE	

433	Preoperative urodynamics in women with pure stress urinary incontinence: A study following a recent recommendation from NICE	9.83
99	PDE5 inhibitor (vardenafil) protects rat bladder from partial outlet obstruction-induced contractile dysfunction	9.8
201	Reduced Type I Collagen of vaginal tissue in women with symptomatic anterior vaginal compartment prolapse (Cystocoele): A cause or a result of worsening prolapse?	9.8
221	Diabetes-related risk factors for urinary incontinence in women with diabetes	9.8
225	The role of the urothelium and suburothelium in spontaneous contractions of pig bladder dome strips	9.8
265	The Natural History of Nocturia 10 years long-term follow-up in male patients aged 40 years and above	9.8
288	BOTULINUM TOXIN A 100 vs 150 UNITS IN IDIOPATHIC OVERACTIVE BLADDER PATIENTS: IS THERE ANY DIFFERENCE?	9.8
359	Assessing interventions for neurogenic bowel management using anorectal manometry	9.8
369	Non-drug lifestyle measures for the management of nocturia	9.8
409	COMPARISON OF THE EFFECTS OF BESIPIRDINE, ITS MAIN METABOLITE AND DULOXETINE ON URETHRAL PRESSURE IN ANESTHETIZED FEMALE RATS	9.8
449	Sexual function and vaginal anatomy in women before and after surgery for pelvic organ prolapse	9.8
487	Irradiation Induces Detrusor Overactivity - Studied Acutely Using a Mouse Model of Radiation Cystitis	9.8
488	Stretch Dependent Activation of Urothelial Muscarinic Receptors Promotes Detrusor Overactivity following Spinal Cord Injury—Revealed Using Optical Imaging	9.8
549	Anatomical distribution of prostatic peripheral nerve tissue – A notable portion located on the dorsal surface of the apex	9.8
634	A qualitative study of patients' experience during non-invasive urodynamics	9.8
731	Combination of alfuzosin and tadalafil exerts additive relaxant effect on human prostate	9.8
68	THE EXPRESSION AND THE ROLE OF BK CHANNELS IN THE URINARY BLADDER: THE ALTERNATION OF SUBUNIT EXPRESSION PROFILE IN ASSOCIATION WITH BLADDER OUTLET OBSTRUCTION, AND THE AFFECT OF BK CHANNEL ON AFFERENT PATHWAY IN LOWER URINART TRACT	9.75
149	EXPRESSION LEVEL AND ROLE IN URETERAL CONTRACTION OF ALPHA1-ADRENOCEPTOR SUBTYPES IN HUMAN URETER	9.75
154	The effects of L-arginine and L-NAME on the response to chronic partial bladder outlet obstruction in the rabbit	9.75
318	MEASURING PATIENT SATISFACTION WITH CONTINENCE TREATMENT: A TALE OF GUTSS AND SAPS	9.75

490	Increased Gap Junction Connectivity in the Suburothelial Region Enhances Overactivity in Pathological Bladders—Measured Using Optical Imaging	9.75
654	The impact of spinal anaesthesia on urinary bladder sensation following elective Caesarean Section.	9.75
828	EVALUATION OF MEDIAN AND LONG TERM OUTCOMES OF STRIATED URETHRAL SPHINTER BALLOON DILATATION	9.75
831	Transcutaneous Mechanical Nerve Stimulation (TMNS) Using Perineal Vibration — A Novel Method for the Treatment of Females with Detrusor Overactivity Incontinence.	9.75
70	Hysterectomy is associated with an increased risk for subsequent stress urinary incontinence surgery	9.71
38	Beneficial effect of preconditioning on ischemia-reperfusion injury in the rat bladder in vivo	9.67
124	The Status of the Anal Sphincter in Patients with Post-Obstetrical Vesicovaginal Fistulas.	9.67
321	Screening of Un-noticed Urinary Retention in an Extended Care Hospital	9.67
323	Comparative study of pelvic floor function in nulliparous women using 4D ultrasound and Magnetic Resonance Imaging	9.67
362	Synergy between neurotransmitter actions in trigonal smooth muscle	9.67
460	Extending the life of long term indwelling catheters: An RCT of catheter flush with saline or acidic solution vs standard care	9.67
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678	The effect of a physiotherapy exercise program on pelvic floor muscle strength in women undergoing prolapse surgery.	9.67
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132	THERAPEUTIC EFFECTS OF ENDOTHELIN RECEPTOR ON BLADDER OVERACTIVITY IN RATS WITH CHRONIC SPINAL CORD INJURY	9.6
224	The puborectalis muscle anatomy and function in women with fecal incontinence versus parous controls: a case-control study.	9.6
391	A NEW NOMOGRAM FOR THE PENILE CUFF STUDY	9.6
509	Long-term follow-up of refractory neurogenic detrusor overactivity patients with English botulinum toxin A: one single centre experience.	9.6
533	THE PROGRESSION OF OVERACTIVE BLADDER SYMPTOMS: A PROSPECTIVE LONGITUDINAL STUDY IN MEN AGED 45 TO 103 YEARS	9.6
713	A multi-center randomized trial comparing the transobturator tape with tension-free vaginal tape for the surgical treatment of stress urinary incontinence	9.6
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452	Tolterodine Extended Release and Sexual Quality of Life, Anxiety, and Depression Among Women With Overactive Bladder and Urgency Urinary Incontinence	9.5
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562	NEUROPHYSIOLOGIC STUDIES OF THE SACRAL REFLEX IN WOMEN	9.5
622	In vivo analysis of brain muscarinic receptor occupancy after oral oxybutynin in conscious rhesus monkey by using positron emission tomography (PET)	9.5
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494	The Urothelium in FIC (feline interstitial cystitis) Cat Bladders Exhibits Altered Responses to UTP—Elucidated Using Optical Imaging	9.4
525	The effect of Botulinum toxin A on autonomous contractions differs between normal and spinalised rat bladders.	9.4
529	Ballooning: How to define abnormal distensibility of the levator hiatus	9.4
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619	A Randomized Sham Controlled Study of Lidocaine EMDA for Bladder Anaesthesia	9.25
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179	Role of spinal glutamatergic mechanisms in sneeze-induced urethral continence reflex in rats	9.2
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612	Visual Analogue Scale Questionnaire to Assess QOL Specific to Each Symptom of IPSS Identified the Symptom to Be Treated for Leading Patient Satisfaction	9.2
626	Transobturator tape ARIS for Female Stress Urinary Incontinence: A multicentric tracker study	9.2
664	OAB: Are we giving women what they want?	9.2
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43	Reversal of voiding dysfunction in the diabetic rat by a 5 HT1A serotonin receptor agonist	9
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143	A molecular biological and functional analysis of ß-adrenoceptors in human detrusor smooth muscle and urothelium	9
197	The long-term relationship between a real change in prostate volume and a significant change in lower urinary tract symptom severity in individual men: 4.2 years follow-up data from a population-based study of men aged 50–78 years	9
202	Overactive bladder in diabetes: a peripheral or central mechanism?	9
214	Urinary HB-EGF variation with symptom severity and menstrual cycle in patients with painful bladder syndrome	9
306	KRP-204, a selective beta3-adrenoceptor agonist, suppresses licking behavior induced by intravesical instillation of capsaicin in rats	9
347	The time of nocturia in patients with LUTS: an important factor in Quality of Life.	9
401	The Impact of Variation in Symptoms of Overactive Bladder on Change in Adaptive Behavior in a Population Based Longitudinal Study	9
429	TROSPIUM CHLORIDE 60 MG ONCE DAILY IMPROVES QUALITY OF LIFE IN SUBJECTS WITH OVERACTIVE BLADDER SYNDROME	9
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444	CARDIAC ION CHANNEL EFFECTS OF PROPIVERINE	9
447	FUNCTIONAL IMPORTANCE OF CHOLINERGIC AND PURINERGIC NEUROTRANSMISSIONS FOR MICTURITION REFLEX IN ANESTHETIZED MICE.	9
453	Characterization of Sexual Function in Women With Overactive Bladder and Urgency Urinary Incontinence at Baseline and After Treatment With Tolterodine Extended Release	9
471	Pelvic floor involuntary response during coughing in continent and stress urinary incontinent postmenopausal women	9

VAR	Category	MM	OR	SM	CR	DC	R	NC	I	F
4.25	Gerontology	4	4	3	3	0	0	0	4	0
0	Neurourology: basic science	1	4	4	4	0	1	0	1	0
4	Urodynamics	7	3	3	3	0	0	0	5	0
4.7	Neurourology: clinical	5	4	3	2	0	0	1	3	0
5.2	Neurourology: basic science	5	3	3	3	0	0	1	4	0
0.2	Neurourology: basic science	5	4	3	4	0	0	1	4	0
0.92	Neurourology: clinical	4	3	3	4	0	0	0	2	0
6.33	LUTS in men	3	3	3	3	0	0	0	1	0
3	Urogenital prolapse	4	3	3	3	0	0	1	1	0
10.3	Lower Bowel Dysfunction	5	3	2	2	0	0	2	2	0
2.3	Painful bladder syndromes	5	3	3	3	0	0	1	2	0
8.25	Epidemiology & Outcomes Research	4	3	3	3	0	0	1	1	0
3.58	Pediatrics	4	3	3	2	0	0	1	3	0
2.7	Pelvic floor	5	3	3	3	0	0	0	1	0
0.7	Anatomy	5	3	3	3	0	0	1	1	0
6.7	LUTS in women	5	3	2	3	0	0	0	4	0
10	Neurourology: clinical	6	2	2	2	0	0	1	4	0
3	QoL	3	3	4	3	0	0	0	1	0
3.5	QoL	5	3	3	3	0	0	0	1	0
4	Cellular physiology	4	2	3	3	0	0	0	1	0
1	Pelvic floor	5	4	3	3	0	0	2	2	0

5.37	Surgery for stress incontinence	6	2	2	3	0	0	1	2	0
2.2	Rehabilitation and conservative treatments	5	3	3	3	0	0	0	1	0
4.7	Reconstructive Surgery. Pelvic floor	5	3	2	2	0	0	2	0	0
2.33	Pharmacology: Basic science	3	3	3	3	0	0	0	1	0
8.8	Pregnancy	5	2	3	2	0	0	1	2	0
10.3	Surgery for stress incontinence	5	3	3	2	0	0	1	2	0
3.8	Neurourology: clinical	5	3	2	3	0	0	0	2	0
1.8	Urodynamics	5	3	3	3	0	0	1	2	0
3.3	Pharmacology: Basic science	5	3	3	3	0	0	0	2	0
3	LUT Physiology	4	3	3	3	1	0	1	2	0
3	Pelvic floor	4	3	3	3	0	0	0	2	0
3	Pharmacology: Clinical	4	3	3	3	0	0	0	1	0
6.7	Detrusor overactivity	6	2	2	2	0	0	1	1	0
4.5	Pharmacology: Clinical	2	3	3	3	0	0	0	1	0
6.8	Epidemiology & Outcomes Research	5	2	2	2	0	0	0	2	0
10.3	Reconstructive Surgery. Pelvic floor	5	2	2	2	0	0	1	0	0
4.8	Rehabilitation and conservative treatments	5	3	2	2	0	0	0	1	0
2.33	LUTS in men	3	3	3	3	0	0	1	2	0
8.33	Urogenital prolapse	3	3	2	2	0	0	0	1	0

0.92	Cellular physiology	4	3	3	3	0	0	0	1	0
0.92	Neurourology: basic science	4	3	3	3	0	0	0	1	0
2.2	LUTS in men	5	2	3	3	0	0	0	2	0
1.7	LUTS in women	5	3	3	3	1	0	1	2	0
0.7	Detrusor overactivity	5	3	3	3	0	0	2	2	0
3.2	Lower Bowel Dysfunction	5	3	2	3	0	0	1	0	0
1.77	Lower Bowel Dysfunction	6	3	3	3	0	0	0	1	0
2.97	Pregnancy	6	2	2	3	0	0	1	3	0
0	LUTS in women	1	3	3	4	0	1	0	1	0
5	Detrusor overactivity	5	3	2	2	0	0	0	3	0
2.4	Painful bladder syndromes	6	3	2	3	0	0	1	3	0
0	Pharmacology: Clinical	1	3	3	4	0	1	1	0	0
0.5	Pelvic floor	5	3	3	3	0	0	0	0	0
2	Neurourology: basic science	5	3	2	3	0	0	1	1	0
4.5	Urogenital prolapse	5	3	2	2	0	0	0	2	0
4	Urogenital prolapse	5	2	3	2	0	0	0	1	0
4	Pharmacology: Basic science	5	3	3	2	0	0	0	1	0
7.2	LUTS in women	6	1	3	1	1	0	0	1	0
2	LUTS in men	4	3	3	3	0	0	1	1	0
2	Neurourology: basic science	5	3	3	3	0	0	0	1	0

3.33	Epidemiology & Outcomes Research	4	3	3	2	0	0	0	1	0
2	Pharmacology: Clinical	5	3	3	3	0	0	0	2	0
1.5	LUTS in women	5	3	3	3	0	0	2	0	0
4.67	Surgery for stress incontinence	4	2	3	2	0	0	1	1	0
1	Pediatrics	3	3	3	3	0	0	0	1	0
2.8	Pediatrics	6	2	3	2	0	0	0	2	0
3.33	Pelvic floor	4	3	2	3	0	0	1	1	0
3	Pharmacology: Clinical	3	3	3	3	0	0	1	1	0
2	LUTS in men	4	3	3	3	0	0	1	1	0
1	Pediatrics	5	3	3	3	0	0	0	2	0
2.5	Anatomy	5	3	2	2	0	0	1	1	0
0.5	Detrusor overactivity	5	3	3	3	0	0	0	2	0
5	Imaging techniques	5	2	3	2	0	0	0	1	0
1.33	Pharmacology: Basic science	4	3	3	3	0	0	1	0	0
2	Detrusor overactivity	5	3	3	2	0	0	0	1	0
4.4	Pelvic floor	6	2	3	2	0	0	0	0	0
1	Neurourology: clinical	5	3	3	2	0	0	1	1	0
3.33	Detrusor overactivity	4	3	2	3	0	1	1	2	0
8	Imaging techniques	4	2	2	2	0	0	1	1	0
6	LUTS in women	4	3	1	3	0	0	3	2	0
	Neurourology: basic									

3.77	Urodynamics	6	3	2	2	0	0	0	1	0
10.7	Neurourology: basic science	5	2	1	2	1	0	1	2	0
3.7	Urogenital prolapse	5	3	2	2	0	0	0	1	0
3.7	Epidemiology & Outcomes Research	5	2	3	3	0	0	0	1	0
5.2	LUT Physiology	5	3	2	2	0	0	0	1	0
1.7	LUTS in men	5	3	2	2	0	2	2	2	0
2.7	Pharmacology: Clinical	5	3	2	2	0	0	1	2	0
1.7	Lower Bowel Dysfunction	5	3	3	3	0	0	1	1	0
3.7	QoL	5	3	2	2	0	0	0	2	0
0.7	Pharmacology: Basic science	5	3	3	3	0	0	0	0	0
1.7	Reconstructive Surgery. Pelvic floor	5	3	3	3	0	0	1	0	0
7.7	Detrusor overactivity	5	3	1	2	0	0	1	0	0
0.7	Pharmacology: Basic science	5	3	3	3	0	0	1	0	0
0.7	Neurourology: basic science	5	3	3	3	0	0	2	0	0
8.7	Urodynamics	5	3	2	2	0	0	1	1	0
1.7	Pharmacology: Basic science	5	3	3	3	0	0	1	1	0
2.92	Neurourology: basic science	4	3	3	2	0	0	0	2	0
0.92	Pharmacology: Basic science	4	3	3	3	0	0	0	1	0
0.92	LUTS in men	4	3	3	3	0	0	1	1	0
4.92	Epidemiology & Outcomes Research	4	3	2	3	0	0	0	1	0

0.92	Detrusor overactivity	4	3	3	3	0	0	1	0	0
6.92	Pregnancy	4	2	2	2	0	0	0	0	0
8.25	Neurourology: clinical	4	2	2	2	0	0	0	1	0
0.25	Detrusor overactivity	4	4	2	3	0	0	1	2	0
7.9	Epidemiology & Outcomes Research	7	2	1	2	0	1	1	4	0
1.87	Pharmacology: Basic science	6	3	3	1	0	0	1	3	0
3.47	Fistulas	6	2	2	3	0	0	0	1	0
1.47	Gerontology	6	3	2	3	0	0	0	1	0
2.27	Pelvic floor	6	2	3	3	0	0	1	1	0
0.33	LUT Physiology	3	3	3	3	0	0	0	1	0
0.33	Rehabilitation and conservative treatments	3	3	2	3	0	0	1	1	0
13.47	LUTS in women	6	2	2	2	0	0	0	1	0
2.27	Rehabilitation and conservative treatments	6	3	2	2	0	0	1	1	0
2.3	Epidemiology & Outcomes Research	5	3	2	3	0	0	0	1	0
1.3	Pharmacology: Basic science	5	3	3	2	0	0	1	1	0
1.8	Lower Bowel Dysfunction	5	3	3	2	0	0	0	1	0
0.8	Urodynamics	5	3	3	3	0	0	0	2	0
3.8	Neurourology: clinical	5	2	3	3	0	0	0	1	0
3.3	Gerontology	5	3	2	2	1	0	0	2	0
6.3	Surgery for stress incontinence	5	2	2	2	0	0	1	1	0
6.33	LUTS in men	4	3	3	1	2	0	2	3	0
	Neurourology:									

0.5	Epidemiology & Outcomes Research	2	3	3	3	0	0	0	1	0
0.5	Detrusor overactivity	2	3	3	2	0	0	0	1	0
0.5	Detrusor overactivity	2	3	3	3	0	0	0	0	0
0.33	LUTS in women	4	3	3	3	0	0	0	0	0
4.33	Neurourology: basic science	4	3	2	2	0	0	0	0	0
1.1	Neurourology: clinical	6	2	3	3	0	0	1	2	0
0.33	Imaging techniques	4	3	3	3	0	0	0	1	0
7	Neurourology: clinical	4	2	2	2	0	0	1	1	0
1	Pharmacology: Clinical	4	3	3	3	0	0	0	1	0
3.1	Imaging techniques	6	3	2	2	0	0	0	2	0
1.3	Pharmacology: Basic science	5	2	3	3	0	0	0	1	0
2.8	Neurourology: basic science	5	2	2	3	0	0	0	1	0
0.8	LUTS in women	5	3	3	2	0	0	0	2	0
0.8	Neurourology: basic science	5	3	3	3	0	0	0	1	0
14.3	LUTS in men	5	2	1	1	0	1	1	1	0
0.3	Urogenital prolapse	5	3	3	3	0	0	0	1	0
3.3	Painful bladder syndromes	5	2	3	2	0	0	0	0	0
0.3	Pharmacology: Basic science	5	3	3	3	0	0	0	1	0
2.3	Pelvic floor	5	2	2	2	0	0	0	0	0
	Epidemiology &									

0.3	Lower Bowel Dysfunction	5	3	3	3	0	0	1	2	0
7.8	Urodynamics	5	2	2	2	0	0	0	3	0
2.3	Neurourology: basic science	5	2	3	3	0	0	1	0	0
3.47	Neurourology: basic science	6	2	3	2	0	0	0	2	0
3.87	Imaging techniques	6	2	2	2	0	0	1	0	0
2.33	Biochemistry and Molecular Biology	3	3	3	2	0	0	0	0	0
8.67	Urodynamics	6	1	1	2	0	0	0	2	0
2.33	Pharmacology: Basic science	3	3	3	2	0	0	0	0	0
5.87	Reconstructive Surgery. Pelvic floor	6	2	2	2	0	0	0	0	0
1.07	Lower Bowel Dysfunction	6	2	3	3	0	0	0	0	0
6.27	Surgery for stress incontinence	6	2	2	2	0	0	1	2	0
1.33	Neurourology: basic science	3	3	3	2	0	0	1	0	0
1.33	LUT Physiology	3	3	3	2	0	0	0	0	0
3.07	Painful bladder syndromes	6	3	2	2	0	0	1	1	0
10.9	Surgery for stress incontinence	7	1	1	1	0	1	1	2	0
17.58	Neurourology: basic science	4	1	1	1	0	0	1	0	0
4.92	Epidemiology & Outcomes Research	4	2	2	2	0	0	0	1	0
6.25	LUTS in women	4	3	1	2	0	0	1	1	0
6.25	Epidemiology & Outcomes Research	4	2	2	2	0	0	0	1	0
2.92	Pediatrics	4	2	2	3	0	1	1	0	0

4.92	Pregnancy	4	2	2	2	0	0	0	1	0
20.25	Pharmacology: Basic science	4	2	1	1	0	0	1	1	0
4.92	Painful bladder syndromes	4	2	2	3	0	0	0	1	0
0.92	Detrusor overactivity	4	2	2	3	0	0	2	0	0
3.7	Pharmacology: Basic science	5	2	2	2	0	0	1	2	0
1.7	LUTS in men	5	3	2	2	0	0	2	0	0
0.7	Neurourology: basic science	5	3	3	2	0	0	0	1	0
4.7	Urodynamics	5	2	2	2	0	0	0	0	0
1.7	Rehabilitation and conservative treatments	5	2	3	2	0	0	1	1	0
0.2	LUTS in men	5	3	3	3	0	0	0	1	0
5.2	Surgery for stress incontinence	5	2	3	2	0	0	1	0	0
4.2	LUTS in women	5	2	2	2	0	0	0	2	0
0.7	Pharmacology: Basic science	5	3	3	2	0	0	0	1	0
1.2	Imaging techniques	5	3	3	2	0	0	0	0	0
1.77	Neurourology: basic science	6	2	3	2	0	0	0	2	0
5.37	Detrusor overactivity	6	2	2	2	1	0	2	1	0
3.77	Urodynamics	6	2	2	2	0	0	1	2	0
2.57	Neurourology: clinical	6	2	3	2	0	0	1	0	0
2.57	Pelvic floor	6	3	2	2	0	0	0	0	0
6.17	Urodynamics	6	2	2	2	0	0	0	2	0
0	Neurourology: basic science	1	3	3	3	0	1	0	0	0
2.8	Gerontology	6	2	2	2	0	0	2	1	0

1	Pharmacology: Basic science	3	3	3	2	0	0	0	0	0
0.67	LUTS in men	4	3	3	2	0	0	0	0	0
0	Neurourology: clinical	4	3	3	3	0	0	0	1	0
4.67	Painful bladder syndromes	4	2	2	2	0	0	0	1	0
0.67	Neurourology: basic science	4	3	3	2	0	0	0	0	0
0.8	LUTS in men	6	3	2	2	0	0	0	1	0
2.4	Epidemiology & Outcomes Research	6	1	2	3	0	0	0	1	0
4	QoL	3	2	3	2	0	0	1	0	0
7	Pediatrics	3	2	3	2	0	0	1	0	0
2	Pharmacology: Basic science	2	3	3	2	0	0	0	1	0
0.67	Pharmacology: Basic science	4	3	3	2	0	0	0	0	0
0.67	LUTS in women	4	3	3	2	0	0	0	0	0
4.5	Pelvic floor	5	2	2	2	0	0	1	0	0

Comments
Craggs: A very detailed psychological study with an interesting outcome
Michel: data only partly support conclusions
Schick: Important observation to better understand PBS/IC.
Vierhout: rct
Schick: Rarely studied topic! van Kampen: power calculation: 175pp, study: 68pp
Schick: Interesting concept and study.
Craggs: Admit to poor understanding of epidemiological modelling
Vierhout: title is not supported
Schick: Is this an ICS or a colorectal surgery paper? Review.
Craggs: Few evaluable data. Relationship does not infer causality
Ghoniem: Bladder memory is a misnomer Schick: Weakness of the study: relies on memory for childhood voiding dysfunction

Schick: F-V chart = 3 days for No of UI episodes. 24-h pad test > 15 gms. Review.
van Kampen: no power calculation Vierhout: RCT!//table 3point C very unlikely
Vierhout: not new
Schick: F/U only 1 y. First International Database.
Schick: 1 line on 3rd page!
Craggs: Better in Neurourology: Basic Science
Van der Weide: this bring on a nice discussion
Craggs: Descriptive abstract with coloured figure!
Schick: We are missing studies defining normal parameters!

Vierhout: long term!
Craggs: Cause or effect or exacerbation? Ghoniem: stopped short of linking antimuscaric therapy to cardiovascular events
Craggs: No variability shown in Table 1. Cost differences marginal!
Vierhout: potential important long data but now poorly presented
Michel: comparing two experimental treatments against each other without a proper control group has limited value
Dmochowski: Does this belong at the ICS?
Craggs: No evaluable results
Schick: Some difficulty to understand and follow the description.

Craggs: Does Botox cause more retention in IDO than is commonly acknowledged? Vierhout: rct
Schick: Power calculation done. Interpretation of results questionable. Review.
van Kampen: no validated questionnaires
Artibani: duplicate?
Schick: Interesting study!
Schick: Valsalva not quantified. SD very large.
Craggs: Obviously a new novel drug in development!
Schick: Preliminary results 6/240 patients. F/U=???
Craggs: Names in the cited references.
Craggs: Few evaluable results on 4 animals
Craggs: Not a blinded RCT. Also not clear whether controlled for volume intake? Van der Weide: Inadequate proof to convince food industry that their products are bad for the consumers health Vierhout: how about volumes?
Craggs: Unfortunately anonymity lost by reference to ref 3 in

Craggs: Poor results. Category Pharmacology: Basic Sci
Schick: "Interpretation of results" is not an interpretation. Not on ICS template. Review. van Kampen: not ICS template, from 608 pp till 51
Vierhout: no power calc
Craggs: Raises controversial issues
Vierhout: which questionn?
Craggs: Few evaluable results based on >5 animals in each group
Craggs: Coloured figures!
Artibani: not really suitable for ICS Schick: Already published??? Review.
Schaefer: "We" is not anonymous
Schick: Same as # 727. Review.
Schick: Change category for Pharmacology, Review.

Craggs: Coloured figures!
Van der Weide: nice to discus with the audience
Craggs: Few evaluable data. Surgery or hormones?
Craggs: No n=, reference name Loprenzi in Aims
Ghoniem: no hypothesis
Ghoniem: incomplete analysis
van Kampen: wrong power calculation
Ghoniem: the title is too strong for the experiment
Schick: F/U >1 year. 15% difference (TOT<TVT). Review.
Ghoniem: basicscience, what's corpus cavernosus has to do with BOO? Schick: This is a pharmacologic paper,

Vierhout: control group?
Craggs: CPT in the bladder is questionable - how many different sites measured, repeatability at each site? Correlation does not infer causality?
Schick: Difficult to understand. Only 20 patients. Not ICS layout, 2006 template.

Ghoniem: I like for cost effectiveness, but it is more theortical, I wish they have actual patients in these two pathways to support their analysis.
Ghoniem: what kind of NGB in those 6 patients?
Craggs: Comparisons with other methods of evaluating the anal sphincter?
Schick: Outcome at 6 months.
Ghoniem: looks like collagen in BOO
Schick: Last paragraph of "Hypothesis" not true! Review.
Craggs: Names in text & references - non-compliance with rules
Schick: Not qualified. Review.
van Kampen: no ICS template
Schick: Not on ICS template.

Craggs: No controls, no evaluable results
Craggs: No controls Vierhout: high withdrawal rate
Craggs: Poor presentation of results
Ghoniem: should be with #52 Schick: Results only on graphs. Interpretation of results are the results and no interpretation of results. Review.
Vierhout: poor agreement in very selcted hads only!
Schick: Only 11/510 patients have F/U>2 years. Ongoing study. Just another tape?? Review.
Ghoniem: poorley written Vierhout: gerontolgy
Schick: F/U 12 m.
Schick: Retrospective study.
Schick: Nos too small (17). No randomization. van Kampen: 16 patients

Schick: Same comment as # 427,
Ghoniem: PNE looks like percutaneous nerve evaluation!
Schaefer: some misconceptions

Urethral Bulking Agents: Calcium Hydroxylapatite

Roger R. Dmochowski, MD, FACS
Department of Urologic Surgery
Vanderbilt University School of Medicine
Nashville, Tennessee

Calcium Hydroxylapatite

Cost

Durability

Biocompatible

Ease of Use

No Additional Technical Equipage

No Need for special Handling

- refrigeration
- admixing

Agent Characteristics

Wound healing characteristics

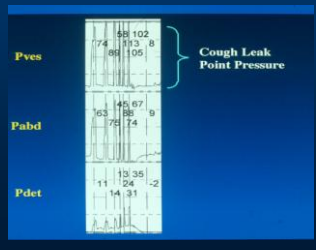
- Minimal fibrotic ingrowth
- Minimal extra-capsular inflammation
- Minimal or no migration

Biocompatible

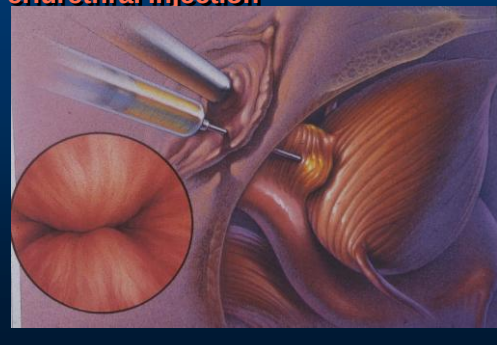
Rheologic characteristics

- Conformation to and with tissue

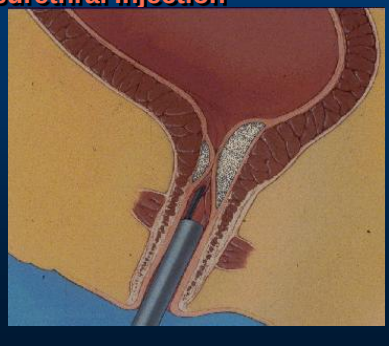
Leak Pressures



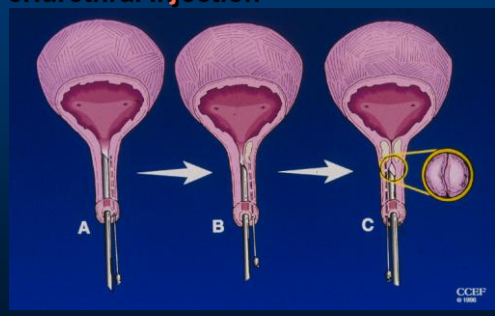
Periurethral Injection

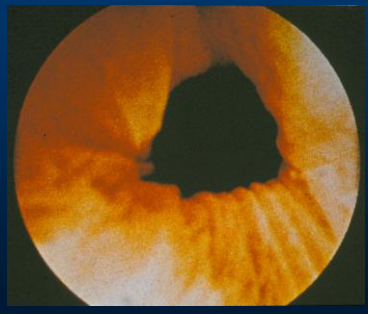


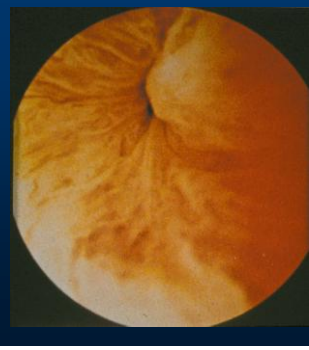
Transurethral Injection



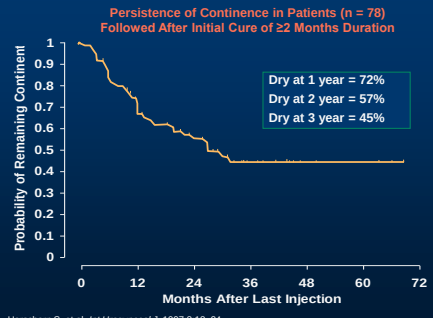
Periurethral Injection







Collagen Durability



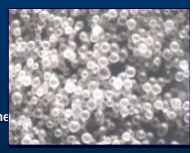
Herschorn S, et al. *Int Urogynecol J.* 1997;8:18–24.

Calcium Hydroxylapatite

- *Hydoxylapatite spheres in carboxylmethylcellulose carrier*
- *Indicated in dental restoration / orthopedics*
- *Biocompatible / non-encapsulated / adheres to tissue*
- *Ease of injection / radiographic correlation*
- *Maintains volume*

Coaptite (Calcium hydroxylapatite)

- *Bioform (California)*
- *Composed of:*
  - CaHA spheres
    - Calcium hydroxylapatite (CaHA)
      - Synthetic form of the major component of bone
  - Gel suspension
    - glycerine and water gel
    - polysaccharide support (sodium carboxymethylcellulose)
- *Approved in EU for SUI, VUR and radiographic marking*
- *FDA approved for SUI, marking, and Filler*



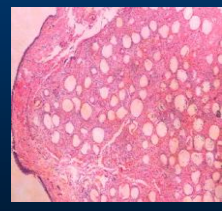
75-125 microns

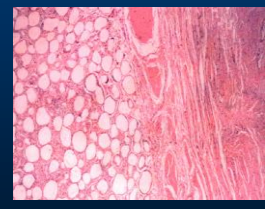
Current BioForm European CE Clearance Coaptite®

- *Stress Urinary Incontinence Treatment*
- *Vesicoureteral Reflux*
- *Fecal Incontinence*
- *Vocal Cord Augmentation*
- *Plastic and Reconstructive Surgery*
  - Subdermal Augmentation

Particulate Composition

Histologic Interactions





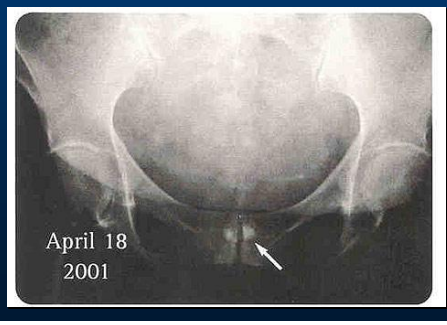
Coaptite

- *CaHA remains soft and pliable over time*
  - Tissue ingrowth with time
    - Some resorption but replaced by tissue ingrowth
  - No heterotopic bone formation
  - 75µm to 125µm spheres
- *Biocompatible*
  - No immunogenic components
    - Natural to the body
    - No tissue reaction or inflammation with injection
    - No sensitivity testing required
- *No special storage/handling requirements*
- *No special equipment required for injection*

Coaptite

- *No migration with time*
- *No capsule formation*
- *Applied with 21 Gauge needle*
  - No burning with injection
- *Radioopaque*
- *Tissue ingrowth with time*
  - Dissolution to Ca and PO4 ions
- *Does NOT induce bone formation with time*

Coaptite



Coaptite: Clinical Studies

- *Mayer et al**
- *10 patients with transurethral injection*
- *F/u 1 year*
  - 3 dry (no pads)
  - 4 substantial improved
  - 2 somewhat improved
  - 1 failure
- *5/10 with transient urinary retention*

*Mayer, et al, Urology 57: 434-438, 2001

Coaptite: Clinical Studies

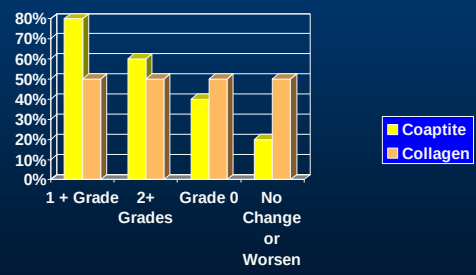
- *ICS 2002 (Dmochowski et al)*
- *Coaptite vs. Contigen*
  - 29 patients
  - 12 month interim analysis
  - Dry rates (24 hour pad test)
    - Coaptite: 33%
    - Contigen: 21%

Coaptite: Clinical Studies

- *AUGS 2004*
- *Sand et al*
- *Coaptite vs. Contigen*
  - 61 patients for 12 months
  - Stamey grade improvement ≥ 1
  - Coaptite: 80%
  - Contigen: 57%

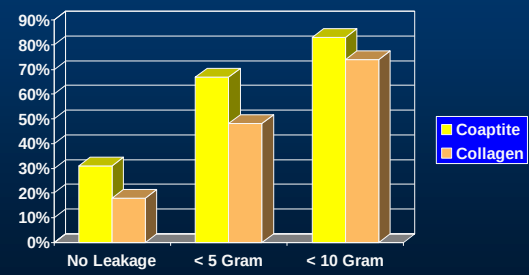
Treatment Outcome

Stamey Grade Improvement - 12 Month



Treatment Outcome

24 Hour Pad Weight Reduction - 6 Month
% Patients with Leakage



Conclusion

- *Evolving technologies*
- *Collagen soon to be historical only*
- *Better understanding of host / material interactions*
- *Probable emergence of better synthetic*

Complications of Injectable Agents

Sender Herschorn, MD, FRCSC
Division of Urology

University of Toronto

History

- 1900: Gersuny – periurethral paraffin injection for SUI
- 1914: Kelly and Dumm – showed temporary improvement but warned about embolism
- 1938: Murless – injected sodium morrhuate (sclerosing agent from cod liver oil) into anterior vaginal wall; vaginal sloughing
- 1963: Sachse – injected granuginol oil (Dondren) a sclerosing agent
  - Cured 12/24 men and 4/7 women
  - Urethral sloughing and pulmonary emboli

PTFE (polytetrafluoroethylene)

- Injectable paste : .74 gm PTFE, .74 gm glycerine, polysorbate
- 50% of bulk (glycerine) absorbed in first several days
- Minimal inflammatory response, ingrowth of fibroblasts and multinucleated giant cells, build up of tissue around particles
- Never obtained approved for clinical use in the U.S.

PTFE Complications

- Particle size determines migration risk.
- Particles >50µm necessary to decrease risk
- Teflon particle size was determined 90% to be 4-40µm
- Experimental study with periurethral injection into 14 female dogs and 4 male monkeys
- Particles found at
  - 50-70 days in pelvic nodes in 6/7 animals and lungs in 4/7
  - 10.5 months in pelvic nodes, lungs, brain in 7/7, kidneys in 4/7, and spleen in 2/7
  - X-ray microanalysis confirmed teflon
  - Teflon granulomas were found at all injection sites and some distant migration sites

Malizia et al. JAMA 1984; 251:3277-3281

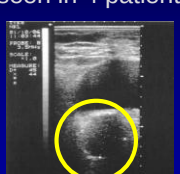
PTFE Complications

- Particle migration:
  - PTFE lung granuloma on postmortem (Mittleman and Marracini. Letter to the Editor, Arch Path Lab Med, 1983; 107:611)
  - Lymphocytic alveolitis (pulmonary inflammation) 3 years postinjection
    - Light microscopy showed Teflon particles in the lungs (Claes et al. J Urol 1989; 42:821)
- Granuloma: chronic foreign body reaction
- Transient retention
- Extrusion
- Perineal pain, infection, abscess
- Urethral diverticulum
- No neoplastic transformation reported clinically to date or experimentally (Dewan et al. 1996)

PTFE Complications

- 22 women and 8 men treated
- Complications seen in 4 patients

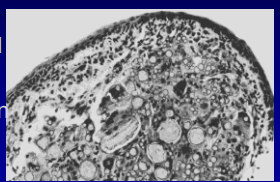
4.5 cm sterile anterior vaginal wall abscess



Kiilkoma et al. Neurourol Urodyn 1993; 12:131-131

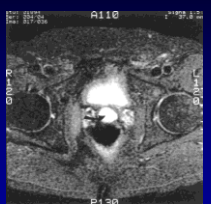
PTFE Complications

- Urethral diverticulum
  - Prolapsed urethral mucosa with a Teflon granuloma

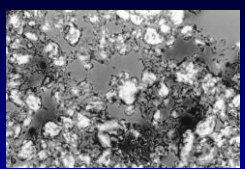


Kiilkoma et al. Neurourol Urodyn 1993; 12:131-131

PTFE Complications



Periurethral teflon cyst



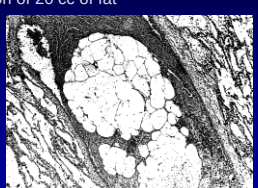
Teflon cyst fluid with birefringent foreign bodies

Kiilkoma et al. Neurourol Urodyn 1993; 12:131-131

Fat embolism

- 69 y.o. died of respiratory failure 5 days after periurethral injection of 20 cc of fat

Lung with adipose tissue embolus and fresh thrombus in pulmonary artery branch



Currie et al. Int Urogyn J. 1997; 6:377-80

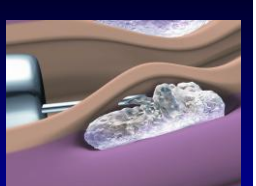
Tegress™ Implant

- EVOH copolymer in dimethyl sulfoxide (DMSO) carrier
  - DMSO rapidly dissipates and is exchanged for fluid in surrounding environment
  - EVOH precipitates; forms cohesive, hydrophilic, soft bulk within 60 seconds

Data on file. C. R. Bard, Inc., Murray Hill, New Jersey.

Tegress™ Implant: Volume-Constant

- Volume-constant bulk
  - Implant 1 mL fluid
  - Deliver 1 mL bulk
- Maintains volume and shape over time
  - Not subject to degradation, enzymatic breakdown, or absorption
- No migration from implant site



Data on file. C. R. Bard, Inc., Murray Hill, New Jersey.

Incidence of Adverse Events in >5% of Patients

Event, n (%)	Tegress™ Implant (n = 174)	Contigen® Implant (n = 79)
Urinary tract infection (UTI)	50 (29%)	15 (19%)
Delayed voiding	32 (18%)	10 (13%)
Dysuria	31 (18%)	11 (14%)
Exposed bulking material	28 (16%)	0 (0%)
Urinary urgency	24 (14%)	7 (9%)
Urinary frequency	22 (13%)	9 (11%)
Genitourinary infection	20 (11%)	10 (13%)
Hematuria	19 (11%)	5 (6%)
Urge incontinence	16 (9%)	4 (5%)
Worsening incontinence (urge)	14 (8%)	3 (4%)
Pain at implantation site	13 (7%)	4 (5%)
Pelvic pain	13 (7%)	7 (9%)
Outlet obstruction	13 (7%)	4 (5%)
Yeast infection	12 (7%)	3 (4%)

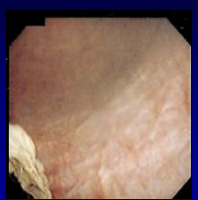
For Tegress™ Implant patients:

- Most treatment-related adverse events occurred within 24 hours of treatment and subsequently resolved within 30 days
- 97% of treatment-related adverse events were classified as mild or moderate

Data on file. C. R. Bard, Inc., Murray Hill, New Jersey.

EVOH (Tegress)

- 17/18 men completed follow-up
- 58.8% experienced complication of procedure
  - 41.8% urethral erosion of the material
  - 22% severe pain on injection
- 41.1% improved at least 50% after 4 months



Hurtado et al. Urology 2007; 71:662-5

Collagen

- Cross-linked bovine dermal collagen with glutaraldehyde results in a fibrillar structure with resistance to collagenases to enhance persistence
- No granulomas or migration
- GAX-collagen is a 35% suspension in a phosphate buffer containing 95% type I and 1% to 5% type II collagen.
  - Prepared by hydrolysing the carboxy and amino terminal segments to decrease antigenicity and increasing resistance to collagenases

Appell 2007, Campbell-Walsh Urology 2007

Collagen complications (350 pts.)

	Treatment-related		Non-treatment-related	
Adverse Event	*Events, No. (%)*	*Patients, No. (%)*	*Events, No. (%)*	*Patients, No. (%)*
Urinary retention	36 (15)	31 (8)	2 (1)	1 (<1)
Urinary tract infection	14 96)	14 (4)	92 (38)	63 (16)
Hematuria	8 (3)	8 (2)	0	0
Injection site injury	5 (2)	5 (1)	0	0
Urinary outlet obstruction	2 (1)	2 (<1)	5 (2)	4 (1)
Accidental injury, urinary	3 (1)	3 (1)	0	0
Pain at injection site	3 (1)	3 (1)	0	0
Balanitis	1 (<1)	1 (<1)	4 (2)	3 (1)
Urinary urgency	1 (<1)	1 (<1)	1 (<1)	1 (<1)
Urethritis	1 (<1)	1 (<1)	0	0
Epididymitis	1 (<1)	1 (<1)	0	0
Bladder spasm	1 (<1)	1 (<1)	0	0
Abscess injection site	1 (<1)	1 (<1)	0	0
Vaginitis	1 (<1)	1 (<1)	0	0
Application site reaction	0	0	1 (<1)	1 (<1)
Vesicovaginal fistula	0	0	1 (<1)	1 (<1)

Appell 2007, Campbell-Walsh Urology 2007

Common collagen complications

- Transient retention
  - 1-25%
- De novo urgency +/- UUI
  - US multicentre trial 1%
  - Other studies – 10[1]-50[2]%
- UTI 1-25%
- Extravasation resolves quickly
- Hematuria 2%

Herschorn J Urol 1992; 148:1797-1800
Winters UCNA 1995; 22:673-8
Appell Campbell's 7th ed. 1998

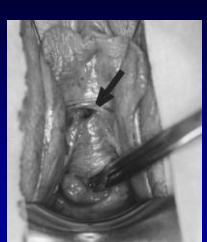
Rare collagen complications

- Periurethral abscess formation
- Vesicovaginal fistula following urethral injection after neobladder
- Delayed hypersensitivity at skin test site after negative skin test with and without arthralgias
  - Positive skin tests in 1-4%

Sweat J Urol 1999; 161:93-6
Pruthi J Urol 2000; 164:1638-9
Stothers J Urol 1998; 159:806-7

Rare collagen complications

- Urethrovaginal fistula in woman after injection
- ↑INR after warfarin stopped
- Periurethral hematoma



Carlin. J Urol 2000; 164:124

Silicone Microparticles

- microparticulate silicone rubber particles suspended in a non-silicone carrier gel
- 99% of the particles are 100 to 450 microns
  - low migration risk; encapsulated by fibrin

Harriss DR, et al. Brit J Urol 1996; 78:722-728

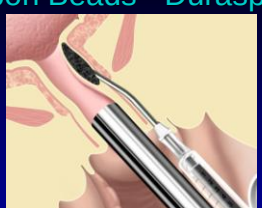
Injection sites

Macroplastique AEs (122 vs. 125 Collagen)

	No. Macroplastique (%)		No. Control (%)	
Urinary tract infection (0–365 days after implantation)	29	(23.8)	31	(24.8)
Dysuria	11	(9.0)	10	(8.0)
Urgency	11	(9.0)	9	(7.2)
Frequency	10	(8.2)	12	(9.6)
Urinary retention	8	(6.6)	4	(3.2)
Hesitancy	6	(4.9)	8	(6.4)
Urge incontinence	6	(4.9)	5	(4.0)
Slowed urine stream	5	(4.1)	10	(8.0)
Incomplete bladder emptying	5	(4.1)	5	(4.0)
Transient hematuria	5	(4.1)	5	(4.0)
Implantation site pain	4	(3.3)	5	(4.0)
Overactive bladder	3	(2.5)	0	(0.0)
Yeast infection	3	(2.5)	3	(2.4)
Bladder pain	2	(1.6)	2	(1.6)
Urine stream change	2	(1.6)	2	(1.6)
Increased/worsening nocturia	2	(1.6)	1	(0.8)
Urethral erosion	2	(1.6)	1	(0.8)
Other, including headache + nausea	22	(18.0)	16	(12.8)
Totals	72/122	(59.0)	68/125	(54.4)

Ghoniem et al. J Urol 2009; 181:204-210

Carbon Beads - Durasphere



- Biocompatible, non-migratory, non-reactive, nonabsorbable pyrolytic carbon-coated zirconium beads in a carrier gel (Particle size 251-300 µm)

Durasphere AEs

	Durasphere	Collagen	P value
Urgency	24.7%	11.9%	<0.001
Retention	16.9%	3.4%	<0.001
Resolved urgency	90%	65%	0.021

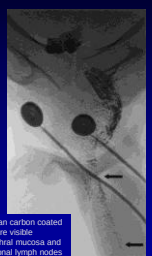
- No immunologic response to Durasphere
- No evidence of migration
  - Pelvic X-rays at 1 and 2 years showed stability of agent at injection site

Lightner et al. Urology 2001; 58:12-15

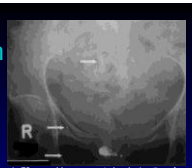
Durasphere AEs

- Pannek et al. J. Urol 2001; 166:1350-1353
  - 1 y after injection – 33% of 12 women improved
  - Particles demonstrated in distant sites on X-ray

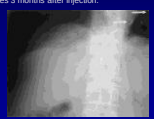
Durasphere migration



In 42-year-old man carbon coated beads (arrows) are visible spreading in urethral mucosa and migrating to regional lymph nodes 3 months after injection.



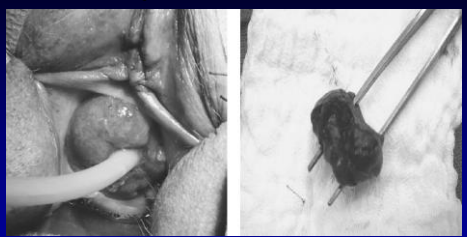
In 79-year-old woman note local migration of carbon coated beads (arrows) to pelvic lymph nodes 3 months after injection.



In 79-year-old woman distant migration of carbon coated beads (arrows) are visible 3 months after injection.

Pannek et al. J Urol 2001; 166:1350-1353

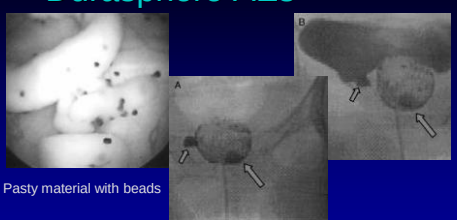
Durasphere AEs



- Mucosal prolapse excised in 83 y.o.

Ghoniem. Int Urogyn J 2006; 17:297

Durasphere AEs



Pasty material with beads

- 4 periurethral masses (2.9%)
- All drained transvaginally +/- transurethrally

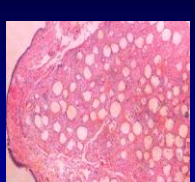
Madgar et al. J Urol 2006; 175:1408-10

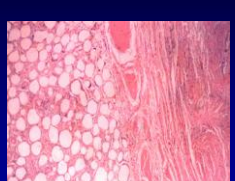
Calcium Hydroxylapatite

- Hydoxylapatite spheres in carboxylmethylcellulose carrier
- Indicated in dental restoration / orthopedics
- Biocompatible / non-encapsulated / adheres to tissue
- Ease of injection / radiographic correlation
- Maintains volume

Calcium hydroxylapatite Particulate Composition

Calcium hydroxylapatite Histologic Interactions



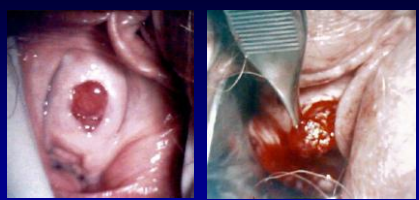


Coaptite AEs

	Coaptite	Collagen	P value
UUI	5.7%	12%	<0.05
Retention	41%	33%	>0.05
Vaginal erosion	1	-	-
Subtrigonal dissection	1	-	-
AEs (n=33)	11	12	-

Mayer et al. Urology 2007; 69:876-880

Coaptite AEs

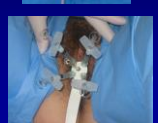


- Urethral mucosal prolapse excised

Lai et al. Int Urogyn J 2008; 19:1315-17

Dextranomer/hyaluronic acid copolymer microspheres (Deflux/Zuidex)

- Dextranomer microspheres (80-250µm) in a carrier gel of non-animal stabilized hyaluronic acid
- Approved for use in reflux



Zuidex AEs

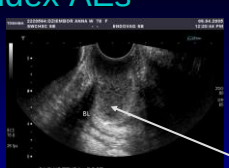
Adverse event	No. of occurrences
Urinary retention	29 (of which 14 were classified as serious)
Urinary tract infection	17
Micturition urgency	17
Dysuria	11
Injection site reaction	11
Vaginal discomfort	10
Cystitis	8
Injection site pseudocyst	6 (of which 1 was classified as serious)
Injection site pain	6
Injection site infection	3 (all of which were classified as serious)
Fever	6
Micturition frequency	5

All were classified as non-serious, except where indicated.

- 142 pts; 157 AEs affecting 81 pts. (57%)
- 83% mild and transient lasting a median of 7 days
- 2/6 pseudocysts drained and one incised and drained

Chapple et al. Eur Urol 2005; 48:488-94

Zuidex AEs



Transvaginal ultrasound

- 6/25 patients
- 4 drained transvaginally, 1 transurethrally
- 1 positive culture for *streptoccocus angiosus*

Herschorn EAU 2008

Autologous myoblasts

- 63 women with SUI
  - 42 randomly assigned to receive transurethral ultrasound-guided autologous myoblasts and fibrobalsts
  - 21 conventional collagen
- At 12 months 38/42 were completely continent versus 2/21 with collagen
- No adverse effects

Strasser H. et al. Lancet 2007;369:2179

Autologous myoblasts

- Strasser et al. article retracted
- Editors concluded that the study was conducted neither according to Austrian law nor GCP
- Critical deficiencies
  - Patient consent
  - Source data documentation
  - Ethics approval

Kleinert, Lancet 2008;372:789

Injectable Complications

- Occurs with all substances
- Most are mild and transient
- Occasionally severe
- Some have been severe enough to prevent the use of the injectable (Teflon, fat, EVOH)
- Necessary to follow patients for long term problems