

Mechanism of Action of Transurethral Radiofrequency Energy Collagen Denaturation

TECHNOLOGY NOTE 1

The most common etiology resulting in female stress urinary incontinence (SUI) is hypermobility (referred to as bladder outlet or urethral hypermobility). Hypermobility refers to the rotational descent of the bladder neck and

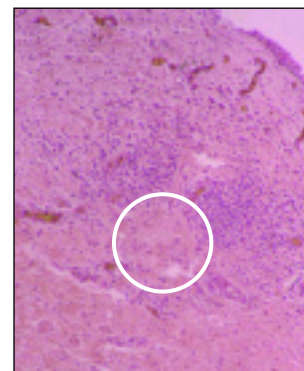
- **Microscopic RF collagen denaturation at sites circumferentially placed within the bladder neck and proximal urethral submucosa**
- **Reduces regional dynamic compliance without stricture or luminal narrowing**
- **Improves continence**

proximal urethra which occurs during periods of increased intra-abdominal pressure and which is a consequence of pelvic floor weakening.¹ As an isolated abnormality, hypermobility alone does not produce urinary incontinence. Radiologic studies “in both normal and stress-incontinent patients [have] demonstrated that opening (funneling) of the vesical neck was the common denominator underlying stress incontinence, not urethral hypermobility.”² The “urethral lumen is literally pulled open” during bladder neck and urethral descent as a result of the “unequal movement of the anterior and posterior walls of the vesical neck and proximal urethra.”² Thus, only when hypermobility is accompanied by inappropriate opening of the bladder neck and proximal urethra, allowing urine to enter the proximal urethral lumen, does urinary incontinence occur.^{1,2,3}

Understanding that SUI results from the combination of hypermobility and urethral opening, “the goal of stress incontinence surgery is to prevent opening of the urethra during increases in intra-abdominal pressure.”⁴ Thus while some procedures (such as bladder suspension) directly address hypermobility, others (such as mid-urethral slings) demonstrate that “the cure of stress incontinence does not require the correction of proximal urethral hypermobility.”⁵ In fact, studies have demonstrated that following some SUI treatments, “cured subjects demonstrating hypermobility preoperatively continued to do so post-operatively.”⁶ The success of these treatments results from the prevention of inappropriate proximal urethral opening during periods of rotational descent.

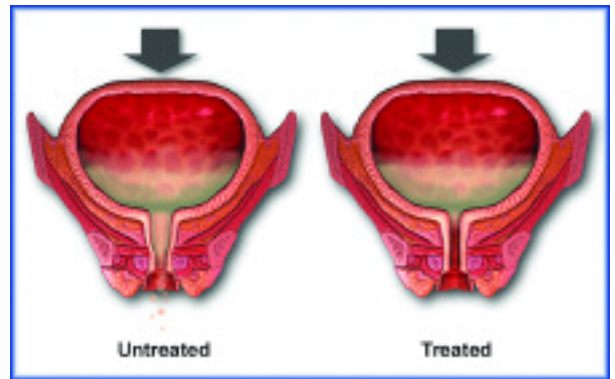
Transurethral radiofrequency energy (RF) collagen denaturation limits the inappropriate

opening of the bladder neck and proximal urethra during periods of descent in women with SUI secondary to hypermobility. The non-surgical treatment utilizes a transurethral device which allows for the denaturation of microscopic, submucosal collagen targets. Thirty-six discrete, microscopic sites distributed circumferentially within the bladder neck and proximal urethral submucosa undergo collagen denaturation in the 20 minute, outpatient procedure (which can be performed in the physician’s office using local plus oral anesthesia). Upon healing, the treatment sites are completely confined to the submucosa and measure approximately 200 μ in diameter (in the photograph of a porcine bladder neck, the white circle surrounds a submucosal treatment site 2 months following collagen denaturation). The treatment does not affect the mucosa, nor does it shrink or reduce luminal caliber. Rather, the functional effect of microscopic RF collagen denaturation is a reduction in the dynamic compliance of treated tissue.^{7,8,9,10,11} Thus while normal micturition is unaffected, inappropriate opening of the bladder neck and proximal urethra during periods of elevated intra-abdominal pressure is limited, resulting in a reduction in incontinence episodes and severity, and a subsequent improvement in patient quality of life.^{10,11} This mechanism of action (reduction in dynamic compliance of treated tissue) is supported by the results of a prospective, randomized, sham-controlled U.S. clinical trial in which Valsalva leak point pressure (VLPP) was measured prior to and 12 months following either microscopic RF collagen denaturation or “sham treatment” in blinded subjects. VLPP “serves as a measure of urethral function.”¹² While mean VLPP at 12 months dropped below pre-treatment level in women with SUI who had undergone “sham treatment,” mean VLPP increased in women who had undergone the RF treatment (p=0.02).¹³



Mechanism of Action of Transurethral Radiofrequency Energy Collagen Denaturation

Non-surgical, transurethral RF collagen denaturation improves or restores continence by limiting the inappropriate opening of the bladder neck and proximal urethra associated with hypermobility during periods of increased intra-abdominal pressure. The microscopic changes in submucosal collagen do not alter luminal caliber and are associated with a safety profile similar to that of a brief bladder catheterization.¹⁴ The mechanism of action of this treatment is a reduction in dynamic compliance, and this therapeutic approach has proven successful in the treatment of several luminal disorders, including gastroesophageal reflux disease,^{9,15} fecal incontinence,^{7,8,16} and stress urinary incontinence.^{10,11,13,17}



Inappropriate luminal opening during rotational descent

Reduced/no inappropriate luminal opening during rotational descent

References

- 1 Blaivas JG and Heritz DM: Classification, diagnostic evaluation, and treatment overview, in Blaivas JG (Ed): *Evaluation and Treatment of Urinary Incontinence*. New York, Igaku-Shoin, 1996, pp 22-45.
- 2 Blaivas JG, Romanzi LJ, and Heritz DM: Urinary incontinence: pathophysiology, evaluation, treatment overview, and nonsurgical management, in Walsh PC, Retik AB, Vaughan ED, and Wein AJ (Eds): *Campbell's Urology*. Philadelphia, W.B. Saunders Company, 1998, seventh edition, pp1007-1043.
- 3 Haderer JM, Pannu HG, Genadry R, et al. Controversies in female urethral anatomy and their significance for understanding urinary continence: observations and literature review. *Int Urogynecol J Pelvic Floor Dysfunct* 4:236-252, 2002.
- 4 Mostwin JL, Genadry R, Sanders R, et al. Anatomic goals in the correction of female stress urinary incontinence. *J Endourol* 3:207-212, 1996.
- 5 Klutke JJ, Carlin BI, and Klutke CG. The tension-free vaginal tape procedure: correction of stress incontinence with minimal alteration in proximal urethral mobility. *Urology* 4:512-4, 2000.
- 6 Mutone N, Mastropietro M, Brizendine E, et al. Effect of tension-free vaginal tape procedure on urodynamic continence indices. *Obstet Gynecol* 4:638-645, 2001.
- 7 Takahashi T, Garcia-Osogobio S, Valdovinos MA, et al. Radio-frequency energy delivery to the anal canal for the treatment of fecal incontinence. *Dis Colon Rectum* 45:915-922, 2002.
- 8 Takahashi T, Garcia-Osogobio S, Valdovinos MA, et al. Extended two-year results of radio-frequency energy delivery for the treatment of fecal incontinence (the Secca procedure). *Dis Colon Rectum* 46:711-715, 2003.
- 9 Lufti RE, Torquati A, Richards WO. The endoscopic radiofrequency approach to management of GERD. *Curr Opin Otolaryngol Head Neck Surg* 12:191-196, 2004.
- 10 Sotomayor M, Bernal GF. Transurethral delivery of radiofrequency energy for tissue micro-remodeling in the treatment of stress urinary incontinence. *Int Urogynecol J Pelvic Floor Dysfunct* 14:373-379, 2003.
- 11 Sotomayor M, Bernal GF. Twelve-month results of nonsurgical radiofrequency energy micro-remodeling for stress incontinence. *Int Urogynecol J Pelvic Floor Dysfunct* 2004 (in press).
- 12 Nygaard I. Physiologic outcome measures for urinary incontinence. *Gastroenterology* 126:S99-S105, 2004.
- 13 Wells WG, Kanellos A. Impact of menopausal status on leak point pressure following non-surgical radio-frequency energy tissue micro-remodeling in women suffering from stress urinary incontinence. *International Continence Society Annual Meeting* (abstract), 2004.
- 14 Appell RA, Lenihan JP, Singh G. The need for "sham treatment" arms in medical device clinical trials for adequate safety evaluation. *American Urogynecologic Society Annual Meeting* (presentation), 2004.
- 15 Go MR, Dundon JM, Karlowicz DJ, et al. Delivery of radiofrequency energy to the lower esophageal sphincter improves symptoms of gastroesophageal reflux. *Surgery* 136:786-794, 2004.
- 16 Efron JE, Corman ML, Fleshman J, et al. Safety and effectiveness of temperature-controlled radio-frequency energy delivery to the anal canal (Secca procedure) for the treatment of fecal incontinence. *Dis Colon Rectum*. 46:1606-1616, 2003.
- 17 Reilley SF, Sotomayor M, Bernal GF. Durable quality of life improvement for women with moderate to severe stress urinary incontinence following non-surgical radiofrequency energy tissue micro-remodeling. *International Continence Society Annual Meeting* (abstract), 2004.

Novasys Medical, Inc. • www.novasysmedical.com
39684 Eureka Drive • Newark, CA 94560
(510) 226-4060 • Fax (510) 353-0524
Toll Free: 866-784-4777

 Novasys Medical®

PM0017E 07-05
Page 2 of 2