

Feasibility Study of Non-Ablative Cryogen-Cooled Monopolar Radiofrequency Treatment for Stress Urinary Incontinence (SUI)

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**Presented at the 43rd Annual Meeting of International
Urogynecological Association**
June 27-30, 2018 Vienna, Austria

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Introduction:

Stress urinary incontinence (SUI) impacts millions of women. Current treatment options are limited. Pelvic floor exercises offer some benefit, but compliance and sustained benefit are common issues. More aggressive approaches to manage SUI involve pelvic surgery which presents more risk, complications and -recovery time. The gap in treatment options for SUI represents an opportunity to address an enormous unmet healthcare need for women. This study aims to investigate the efficacy & safety of a non-surgical cryogen-cooled monopolar radiofrequency treatment for SUI.

Treatment:

- **Monopolar RF energy with surface cooling**
 - Fibroblast activation-> new and restored collagen
 - Initiation of collagen remodeling (~ 30-90 days after tx)
- Procedure consists of 220 pulses (~8 seconds/pulse)
- Procedure lasts only 45-50 minutes, no anesthesia



Study Design:

Subjects: Diagnosed with mild-moderate SUI (1-50 g of leakage on 1-hour pad test)

Objective: Evaluate efficacy and safety of Viveve treatment for SUI

Randomization: Group A (1 treatment), Group B (2 treatments, 6 weeks apart)

Efficacy: Measured at 1, 3, 6 and 12 months post-treatment

Objective:

- 1-hour pad weight test
- 7-Day Bladder Voiding Diary

Subjective:

- Validated SUI-related patient reported outcomes (PROs)
 - Urinary Distress Index (UDI-6)¹
 - Incontinence Impact Questionnaire (IIQ-7)¹
 - International Consultation on Incontinence Questionnaire, Incontinence Module, Short Form (ICIQ-UI-SF)²
 - Female Sexual Function Index (FSFI)

Safety: Adverse event reporting

Subject Disposition:

	Group 1 (n)	Group 2 (n)	Total (n)
Randomized & Treated Subjects	21	14	36
6-Month Follow-Up: Randomized & Treated	16	13	29

Methods:

1-hour pad weight test

0-15 min: Drinking 500 mL of sodium-free liquid, resting

15-45 min: Walking including stair climbing up/down one flight

45-60 min: Standing up from sitting (10x), Coughing vigorously (10x), Running on the spot (1 min), Bending to pick up small object from the floor (5x), Washing hands in running water (1 min)

7-Day Bladder Voiding Diary – Example Entry

Urination Volume	Leakage Volume	Fluid Intake	Food Intake	Activity
Large	Medium	1 water bottle	Hot wings	Laughing
Small	None	1 cup of coffee	None	Sitting

VIVEVE Treatment for SUI Results in a Reduction in Incontinence Episodes/Day

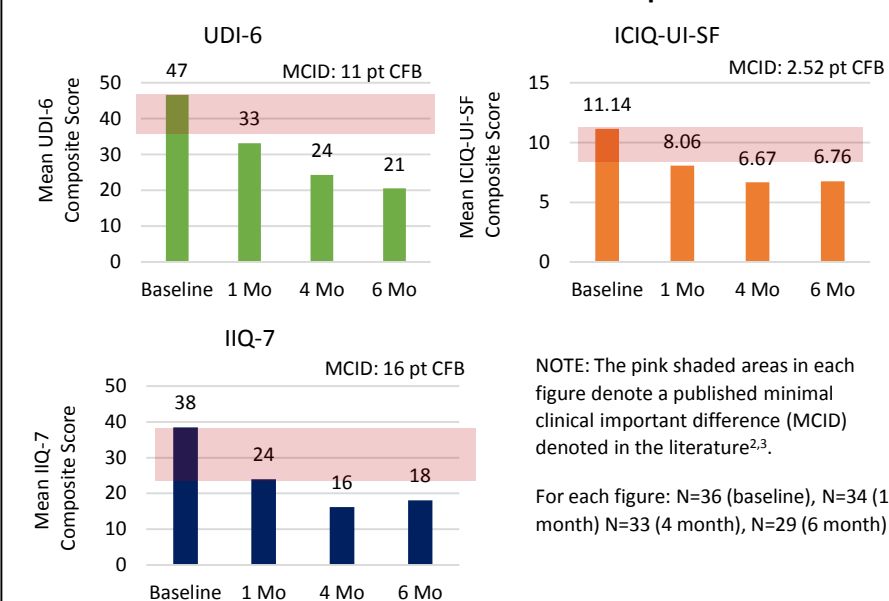
Group	AVG # Daily Incontinence Episodes	# of Incontinence Episodes/Day, % of subj w/ >50% reduction from baseline		
		1 mo	4 mos	6 mos
All Subjects	2.2 (N=35)	1.3, 44% (N=34)	1.3, 66% (N=32)	1.0, 61% (N=28)
Group A: 1 SUI Tx	1.9 (N=21)	1.1, 40% (N=20)	1.2, 72% (N=18)	0.7, 53% (N=15)
Group B: 2 SUI Tx	2.7 (N=14)	1.7, 50% (N=14)	1.3, 57% (N=14)	1.3, 69% (N=13)

References: 1. Uebersax JS et al. Short forms to assess life quality and symptom distress for urinary incontinence in women: the IIQ and the UDI. *NeuroUrol Urodyn.* 1995;14:131-9. 2. Sirls, Larry T., et al. "The minimum important difference for the ICIQ-UI-SF in women with stress urinary incontinence." *Neurourology and urodynamics* 34.2 (2015): 183-187. 3. Huber SA et al. Laparoscopic Burch urethropexy at time of mesh sling removal: A cohort study evaluating functional outcomes and quality of life. *World J Obstet Gynecol* 2016; 5(3): 210-217

VIVEVE Treatment for SUI Results in a Reduction in 1-hour Pad Weight

Group	Baseline Pad Weight	Pad Weight, % of subj w/ >50% Reduction in Pad Weight from Baseline		
		1 mo	4 mos	6 mos
All Subjects	7.11 g (N=36)	2.15 g, 56% (N=34)	1.27 g, 73% (N=33)	1.69 g, 69% (N=29)
Group A: 1 SUI Tx	6.95 g (N=22)	2.25 g, 60% (N=20)	1.11 g, 68% (N=19)	1.81 g, 69% (N=16)
Group B: 2 SUI Tx	7.36 g (N=14)	2.00 g, 50% (N=14)	1.50 g, 79% (N=14)	1.54 g, 69% (N=13)

VIVEVE Treatment for SUI Results in PRO Improvements



Conclusions: The outcome measures indicate a significant improvement in SUI symptoms as evaluated by the 1-hour pad weight test, incontinence episodes and several SUI-related PROs. The Viveve treatment was well tolerated and no treatment-related AEs were reported. The sustained benefit of the Viveve RF treatment may offer a novel approach to treat SUI, offering a much-needed option for women.

Peer-reviewed materials on the Viveve device are included here.

Please note the following:

- In the United States, the Viveve System is indicated for use in general surgical procedures for electrocoagulation and hemostasis.
- FDA has not cleared the Viveve System as safe and effective for the uses described in the attached information.
- Some of the author(s) of these articles are employees of Viveve, or have a financial interest in the manufacturer or its products.
- There are no significant risks or safety concerns associated with the unapproved use(s) of the Viveve system that are known to Viveve, but not discussed in the attached documents.

Viveve Label: Viveve treatment tips: Instructions for Use

Symbols/Abbreviations

	Single Use only		Do not Re-sterilize
	Follow Instructions for Use		Do not use if packaging is damaged
	Reference Number		Lot number
	Sterilization by Ethylene Oxide		Legal Manufacturer
	Use by		Date of Manufacture
	Latex-Free		Prescription Only
	Separate Collection		DEHP Free
			

- Do not re-use the treatment tip. It is a single-patient-use item and is not intended for multiple patients. Reuse of the treatment tip can lead to failure and patient injury.

Viveve[®] System and Accessories

Model 88003

- Viveve Console, Catalog Number VIVGE01
- Viveve Handpiece, Catalog Number VIVHP01
- Viveve Footswitch, Catalog Number VIVFS01
- Viveve Return Cable, Catalog Number VIVRC01
- Viveve 5 cm Treatment Tip, Catalog Number VIVTT01

Model 88003S

- Viveve Console, S, Catalog Number VIVGE01S
- Viveve Handpiece, S, Catalog Number VIVHP01S
- Viveve Footswitch, Catalog Number VIVFS01
- Viveve Return Cable, Catalog Number VIVRC01
- Viveve 5 cm Treatment Tip, S, Catalog Number VIVTT01S

Accessories

- Viveve 8 cm Treatment Tip, Catalog Number VIVTT02
- Viveve Return Pad, Catalog Number VIVRP01
- Viveve Cryogen Canister, Catalog Number VIVCC01
- Viveve Coupling Fluid, Catalog Number VIVCF01
- Viveve Power Cords: United States, Canada, Mexico, Latin America, Thailand, Catalog Number VIVPC01

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CAREFULLY READ ALL INSTRUCTIONS PRIOR TO USE. OBSERVE ALL WARNINGS AND PRECAUTIONS NOTED THROUGHOUT THESE INSTRUCTIONS. FAILURE TO DO SO MAY RESULT IN COMPLICATIONS.

The Viveve[®] System Technical User's Manual (TUM) is supplied as a separate document. The (TUM) contains detailed information describing the Viveve[®] System components, console set up, and guide to operation, maintenance, trouble shooting, and specifications. Please read the TUM prior to operation of the Viveve[®] System.

Description

The Viveve treatment tips contained in this package are a sterile single use component of the Viveve[®] System and designed to deliver radiofrequency (RF) energy from the Viveve console. The Viveve treatment tips can only be used in conjunction with the dedicated Viveve[®] System.

The following Instructions for Use (IFU) describe the use of the Viveve[®] System. Review instructions in the Viveve TUM carefully on how to set up the system, including the warnings and precautions. Read all manuals and instructions completely before using the Viveve[®] System or performing any procedures.

Indications for Use

The Viveve[®] System is indicated for use in General Surgical procedures for electrocoagulation and hemostasis.

Contraindications

The Viveve[®] System is contraindicated for use in patients with either an Implantable Pacemaker or an Automatic Implantable Cardioverter/Defibrillator (AICD), or any other implantable electrical device, as they may be adversely affected by radio-frequency (RF) fields or current.

Storage Conditions

Store in a cool, dry place.

Warnings

- Never touch the treatment tip's electrode surface or allow the electrode surface to contact unintended tissue when RF power is being applied. Heating could occur to tissue below the surface resulting in protein denaturation of the subsurface tissue.

Procedural Instructions

1. Clean and prepare the treatment area and the surrounding surface with a non-alcohol based cleaner.
2. Confirm that the Viveve[™] System, console with cooling Module, hand piece and footswitch (if used), is set up properly as described in the User Technical Manual.
3. The use and proper placement of the return pad is a key element in the safe and effective use of this device, particularly in the prevention of burns.
4. Apply the return pad onto a clean dry area of the skin of the patient near the designated area to be treated. Ensure the entire area of the return pad is in contact with the tissue.
5. Ensure that the treatment tip is fully connected with the handpiece before using.
6. Coupling fluid is applied to the treatment area and on the treatment tip regularly throughout the treatment to ensure good electrical contact with the treatment surface. Failure to have good electrical contact could affect the treatment outcome.
7. While ensuring that the treatment tip is in good contact with the treatment surface and confirming that the flashing blue light on the handpiece is illuminated, apply the RF energy to the target area by depressing the footswitch.
 - a. The energy setting is 180 Joules.
 - b. The energy density is 90 Joules/cm².
 - c. Each energy application will treat a 1 cm x 2 cm area.
8. Repeat until treatment is complete.
 - a. A total of five (5) passes are made in the treatment area.
 - b. To ensure complete coverage, overlap the energy application by 50% or 0.5 cm².
 - c. Apply additional Viveve coupling fluid during the treatment procedure.
9. After treatment is complete:
 - a. The patient and her healthcare professional should have a conversation about when to resume certain activities based on the patient's medical history and tolerability during the procedure.
 - b. The Viveve treatment tip must be disposed of properly in accordance with the applicable national/local/state environmental laws. Check local regulations for proper disposal of the treatment tip.