Feasibility Study of Non-Ablative Cryogen-Cooled Monopolar Radiofrequency Treatment for Stress Urinary Incontinence (SUI): Interim 12-Month Results

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FEASIBILITY STUDY OF CRYOGEN-COOLED MONOPOLAR RADIOFREQUENCY TREATMENT FOR STRESS URINARY INCONTINENCE (SUI): INTERIM 12-MONTH RESULTS

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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 represents an opportunity to address an unmet healthcare need for women.
- This study aims to investigate the efficacy & safety of a non-surgical cryogen-cooled monopolar radiofrequency (CMRF) treatment for SUI.

Study Design:

- **Subjects**: Women diagnosed with mild-moderate SUI (1-50 g of leakage on 1-hour pad weight test)
- **Objective**: Evaluate efficacy & safety of CMRF treatment for SUI
- **Unblinded study design**
- **Randomization**: Group A (1 tx), Group B (2 tx, 6 weeks apart)
- **Efficacy**: Measured at 1, 4, 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

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 of 90 J/cm^2
- Procedure lasts 45-50 minutes, no anesthesia

Subject Disposition:

	Group 1 (n)	Group 2 (n)	Total (n)
Randomized & Treated Subjects	**21**	**14**	**35**
12-Month Follow-Up (to date): Randomized & Treated	**7**	**13**	**20**

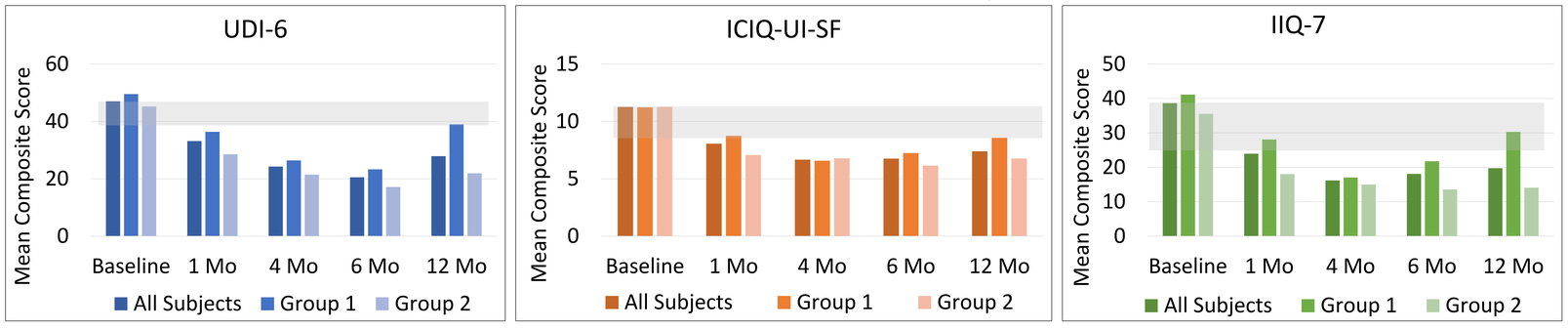
Methods:

- **1-hour pad weight test[3]**
  - 0-15 min: Drinking 500 mL of sodium-free liquid, resting
  - 15-45 min: Walking with stair climbing up/down 1 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)

CMRF Treatment for SUI Results in a Reduction in Leakage Volume on 1-Hour Pad Weight Test

Group	Baseline Pad Weight	Pad Weight Leakage Volume % of subj w/ >50% Reduction in Pad Weight from Baseline			
		Month 1	Month 4	Month 6	Month 12
All Subjects	7.29 g (n=35)	2.15 g 56% (n=34)	1.27 g 73% (n=33)	1.69 g 69% (n=29)	3.20 g 60% (n=20)
Group A: 1 SUI Tx	7.24 g (n=21)	2.25 g 60% (n=20)	1.11 g 68% (n=19)	1.81 g 69% (n=16)	2.57 g 71% (n=7)
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)	3.54 g 54% (n=13)

CMRF Treatment for SUI Results in PRO Improvements



NOTE: The shaded areas in each figure denote a published minimal clinical important difference (MCID) denoted in the literature[4,5]. For each figure: n=35 (baseline), n=34 (1 month) n=33 (4 month), n=29 (6 month), n=20 (12 month)

CMRF Treatment for SUI Results in a Reduction in Daily Incontinence Episodes (IE)

Group	AVG # Daily IE	Number of Daily IE % of subj w/ >50% reduction from baseline			
		Month 1	Month 4	Month 6	Month 12
All Subjects	2.2 (n=35)	1.3 44% (n=34)	1.3 66% (n=32)	1.0 61% (n=28)	0.8 50% (n=20)
Group A: 1 SUI Tx	1.9 (n=21)	1.1 40% (n=20)	1.2 72% (n=18)	0.7 53% (n=15)	1.2 43% (n=7)
Group B: 2 SUI Tx	2.7 (n=14)	1.7 50% (n=14)	1.3 57% (n=14)	1.3 69% (n=13)	0.6 54% (n=13)

Conclusions:

- The outcome measures indicate a significant improvement in SUI symptoms as evaluated by the 1-hour pad weight test, daily incontinence episodes and several SUI-related PROs.
- The CMRF treatment was well tolerated and no treatment-related AEs were reported.
- The sustained benefit of the CMRF treatment may offer a novel approach to treat SUI, offering another option for women.
- Of note, this study has since finished. The final data is consistent with what is presented here.

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. Avery K., et. al., ICIQ: a brief and robust measure for evaluating the symptoms and impact of urinary incontinence. Neurourol Urodyn. (2004); 23(4):322-30. 3. Krhut J. et. al., Pad Weight Testing in Evaluation of Urinary Incontinence. Neurourol Urodyn. 2014; 33:507-10. 4. 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. 5. Nystrom E., et.al., ICIQ symptom and quality of life instruments measure clinically relevant improvements in women with stress urinary incontinence. Neurourol Urodyn. 2015; 34(8):747-51.

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
REF	Reference Number	LOT	Lot number
STERILE EO	Sterilization by Ethylene Oxide		Legal Manufacturer
	Use by		Date of Manufacture
	Latex-Free	℞ ONLY	Prescription Only
	Separate Collection		DEHP Free
	Manufactured in U.S.A for: Viveve, Inc. Englewood, CO 80112 + 1 (720) 696-8100 www.viveve.com	EC REP	MedPass SAS 95 bis Boulevard Pereire 75017 Paris France

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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/Defribillator (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.
- 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

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/cm^2.
    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 cm^2.
    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.