SAFETY AND MECHANISMS OF ACTION SUPPORTING NONABLATIVE RADIOFREQUENCY THERMAL THERAPY 
FOR VAGINAL INTROITUS LAXITY OCCURRING IN WOMEN AFTER CHILDBIRTH: HISTOLOGICAL STUDY IN THE SHEEP VAGINAL MODEL

James E. Coad MD1, Jeffrey A. Vos MD1, Alan Curtis BS2 and Michael Krychman MD3

1Pathology Laboratory for Translational Medicine, West Virginia University School of Medicine, Robert C. Byrd Health Sciences Center, Morgantown, WV; 2Viveve, Inc., Sunnyvale, California; 3Southern California Center for Sexual Health and Survivorship Medicine, Newport Beach, California

INTRODUCTION

A non-surgical, office-based procedure using low-dose radiofrequency (RF) energy is under clinical evaluation to treat vaginal introital laxity following vaginal childbirth. This treatment utilizes non-ablative, deep, soft tissue RF heating with surface protective cryogen cooling to induce tissue remodeling. To evaluate the safety and mechanism of action of non-ablative RF-induced thermal heating on vaginal tissue using the in vivo ovine vaginal introitus model. The sheep were treated with a single RF procedure simulating its future use in the human clinical setting.

AIM OF STUDY

To evaluate the safety and mechanism of action of non-ablative RF-induced thermal heating on vaginal tissue RF heating with surface protective cryogen cooling to induce tissue remodeling. To assess the mucosa and submucosa of the vaginal introitus for histologic signs of thermal tissue injury, emulating its future use in the human clinical setting.

METHODS

- Ovine (Ovis aries) vagina model was used due to histological similarities between the sheep and human vaginas.
- Treatment Group: Vaginal introitus of 16 sheep were treated with a single topical treatment using a gradient of RF energies (4 sheep each at 60, 90, 120 or 160 J/cm²). Each Viveve® Vaginal Lady RF Therapy (Viveve, Inc., Sunnyvale, CA) treatment was delivered using 5 treatment passes as used in the current human clinical trials.
- Controls: 3 sheep each had a sham treatment or surface cryogen cooling only.
- Study conducted in accordance with FDA Good Laboratory Practice and West Virginia University Pathology Laboratory for Translational Medicine standard operating procedures.

PRIMARY HISTOLOGIC OBJECTIVES

- To assess the mucosa and submucosa of the vaginal introitus for histologic signs of thermal tissue injury, fibroblast activation and qualitative collagen increases.

RESULTS

- Series of 96 RF-treated and 15 control ovine vaginal introitus biopsies were evaluated over the 7 to 90 day post-treatment study period.
- Over the 90-day study period, the 90 J/cm² and 120 J/cm² energy level treated sheep showed significantly increased submucosal fibroblast activation without mucosal erosion-ulceration, tissue necrosis, granulation tissue or extensively increased collagen (hypertrophic scar-like).
- The Viveve® RF Therapy treated the introitus while maintaining an intact epithelial mucosa.
- The treatment stimulated tissue restoration without causing tissue necrosis or hypertrophic scarring.

DISCUSSION

- The Viveve® RF Therapy uses low-dose, non-ablative RF energy to treat vaginal introital laxity in women. This animal study histologically assessed a series of in vivo treated ovine vaginal introitus biopsies that were obtained on Day 7, Day 30 and Day 90 following treatment. In this study, the Viveve RF Therapy was used in a fashion that simulated its future clinical use.
- When compared to the controls, the 7, 30 and 90 day post-treatment biopsies showed 1x, 2x and 3x more fibroblast activation with the 3 treatment passes of RF at 90 J/cm². With this energy setting, the submucosal tissues demonstrated fibroblast activation while preserving the mucosal epithelium.

CONCLUSIONS

- Tissue ablative changes were not identified. There was no necrosis, granulation tissue and hypertrophic scarring.
- Following non-ablative RF thermal therapy at the doses studied, histological evaluation of the sheep vaginal introitus over the three month study period supports an acceptable safety profile for continued clinical study.
- The histologic changes are consistent with thermal fibroblast activation leading to collagen regeneration and subsequent tissue integrity enhancement as the mechanism of action.

REFERENCES


Technical writing provided by Elaine K. Orenberg, PhD

Research supported by Viveve, Inc., Sunnyvale, California