

Radiofrequency Energy in Medicine

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Radiofrequency energy (RF) allows for the controlled heating of gross or microscopic tissue targets. Used clinically for decades in the non-surgical treatment of cardiac arrhythmias, RF now serves as the basis of numerous medical device systems used to treat a variety of medical disorders.

Radiofrequency Energy Tissue Ablation For Obstructive, Hemorrhagic, and Metastatic Disorders

RF tissue ablation is a process in which obstructive, hemorrhagic, or metastatic tissue is heated on a gross scale to temperatures at which tissue necrosis occurs. RF tissue ablation has proven to be a safe and successful non-surgical modality for the treatment of benign prostatic hyperplasia^{1,2} (transurethral gross shrinkage of obstructive prostatic tissue), sleep apnea³ (gross shrinkage of obstructive oropharyngeal), menorrhagia⁴ (destruction of hemorrhagic endometrial), and hepatic metastatic disease.⁵

Microscopic Radiofrequency Energy Collagen Denaturation For Luminal Disorders

Unlike obstructive, hemorrhagic, or metastatic disorders, conditions such as gastroesophageal reflux disease (GERD), fecal incontinence (FI), and stress urinary incontinence (SUI) are characterized by grossly normal luminal tissues which no longer prevent the inappropriate passage of intraluminal contents. Such conditions are referred to as *luminal barrier function disorders*. Applying RF tissue ablation techniques to normal luminal walls would likely result in either acute perforation or luminal narrowing, stricture, and obstruction.

RF is, however, successfully used to treat luminal barrier function disorders through the technique of *microscopic RF collagen denaturation*.^{6,7,8} Microscopic RF collagen denaturation targets microscopic tissue sites within the luminal wall at which the temperature is raised to produce focal areas of microscopic collagen denaturation while avoiding tissue necrosis. Thus microscopic RF collagen denaturation avoids gross tissue shrinkage and luminal narrowing. Functionally, microscopic RF collagen denaturation

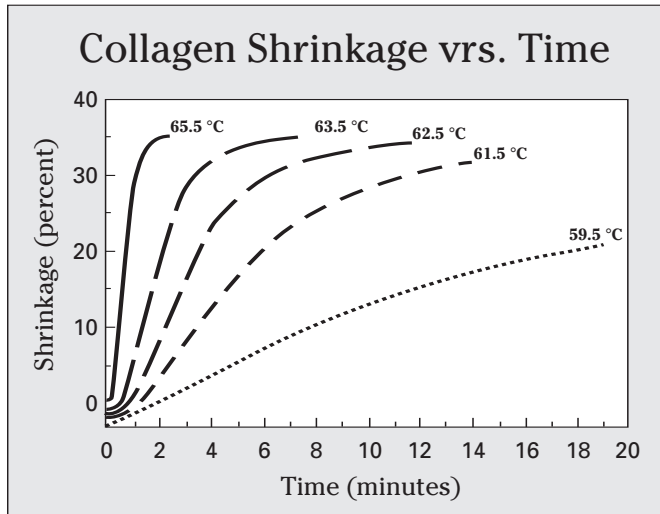
results in a reduction in the dynamic compliance of luminal wall tissue which results in barrier function and symptomatic improvement.

Recently, the reduction in dynamic tissue compliance was demonstrated in a prospective, randomized, sham-controlled clinical trial for women suffering from SUI. At 12 months, women who had undergone non-surgical, transurethral microscopic RF collagen denaturation demonstrated an elevation in mean leak point pressure above pre-treatment level, while women who had undergone a virtually identical “sham treatment” (without RF delivery) demonstrated a reduction in mean leak point pressure below baseline level ($p=0.02$).⁹ The treated women demonstrated no evidence of urethral narrowing or obstruction.

Physiology of Microscopic Radiofrequency Energy Collagen Denaturation

Collagen is the most abundant structural protein in humans, where it primarily serves a supportive function within the extracellular matrix.¹⁰ Collagen exists in a triple helical form wherein the peptide chains are stabilized by hydrogen bonds. The thermal lability of these bonds has been well-established. “Thermal denaturation and shrinkage of type I collagen have been well documented. ...When heated above 60 [degrees] C, collagen fibers undergo a phase transition from a highly organized semicrystalline state to a melted gel.”¹¹ Temperature-time profiles at which the maximal gross physical effect of collagen denaturation (commonly measured as linear shrinkage) occurs have been developed (Figure 1).^{10,11,12,13,14} The potential to achieve maximal collagen denaturation (either gross or microscopic) is dependent on three variables: (1) the type of target tissue (based on collagen content, density, fiber orientation, etc.), (2) the target temperature, and (3) the target time (duration of treatment).

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Walt et al Thermal Modification of Collagen, 1999

Figure 1. "Plot of [gross tissue] shrinkage versus time for various constant temperatures..."¹³

As Figure 1 illustrates, once maximal collagen denaturation has been achieved at any given target temperature, increasing target time does not result in further collagen denaturation. Also as depicted in Figure 1, higher target temperatures do not promote additional collagen denaturation; rather, higher temperatures simply achieve maximal collagen denaturation more rapidly. On the other hand, lower target temperatures require greater target time in order to achieve maximal collagen denaturation.

The acute change in collagen structure resulting from microscopic RF collagen denaturation is illustrated in

Figure 2, which demonstrates the histological effect approximately 30 minutes following non-surgical, transurethral treatment of the porcine proximal urethral submucosa. Denatured, viable submucosal collagen stains bright blue (trichrome staining) at the site of microscopic RF collagen denaturation. The surrounding tissue, including the overlying mucosa, deeper submucosa, and deeper muscular layers, are unaffected. There is no significant tissue necrosis or vascular thrombosis.

Following thermal denaturation, treated tissues demonstrate "tightening effects... [including] collagen contraction, focal wound healing, remodeling, and tissue compliance reduction."^{7,15} The histological effect of microscopic RF collagen denaturation following healing is illustrated in Figure 3, demonstrating the porcine proximal urethra eight weeks following treatment. The treated site is identified as a 150-200 μ nodule of contracted, healed collagen within the submucosa (the tissue within the white circle in Figure 3), with unremarkable overlying mucosa, surrounding submucosa, and deeper muscular layers. While no gross anatomic luminal changes are produced, the creation of such focal, microscopic treatment sites circumferentially within the luminal wall results in reduced dynamic tissue compliance, the mechanism of action for microscopic RF collagen denaturation in the treatment of GERD,⁶ FI,^{7,15} and SUI⁸.

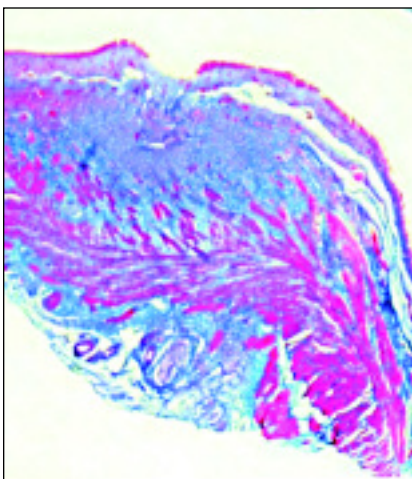


Figure 2

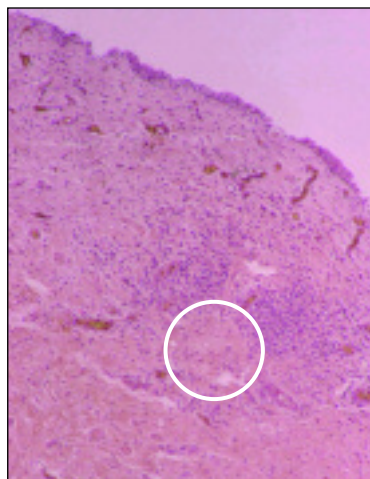


Figure 3

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Summary

RF is a useful modality for the heating of tissue. Target tissue, temperature achieved, and duration (time) of heating all impact the result of treatment. In addition, whether treatment is applied on a gross or microscopic scale has significant implications for the therapeutic role of RF. RF tissue ablation is useful when gross tissue destruction is the goal of treatment. Microscopic RF collagen denaturation is a useful technique as a non-surgical approach to luminal disorders such as stress urinary incontinence.

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