Role of Cavitation during High Intensity Focused Ultrasound Treatment of Prostate Tissue

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Abstract: High intensity Focused Ultrasound (HIFU) has been known to produce coagulative necrosis of the deep-seated tissue. Therefore, HIFU is pursued as a noninvasive surgery tool in medicine. One of the HIFU applications has been practiced since 1992 is for the treatment of Benign Prostatic Hyperplasia (BPH) of prostate. The BPH condition is described as an abnormal enlargement of prostate gland. In our early experiments and studies to treat BPH with HIFU, we primarily adopted process of tissue necrosis by thermal mechanism that is due to absorption of ultrasound. However, thermally ablated tissue remained in the prostate gland to be removed by the natural phagocytosis process. This process took long time (in some cases weeks) and seemed not to relieve BPH symptoms immediately after the HIFU treatment. Thus, a new tissue destruction process using thermal plus localized transient cavitation mechanism was developed. This combined process offers advantages of noninvasive surgery in addition to faster removal of urethra and surrounding ablated tissue.

INTRODUCTION

Due to aging population of male in the world, there is prevalence of BPH cases. The common medical procedure for the treatment of BPH is known as Trans Urethral Resection of prostate (TURP). During TURP procedure, the excessive prostate tissue is removed by surgical means, which associates surgical process risks and requires hospital stay for the patients. While the transrectal HIFU procedure for the treatment of BPH is a noninvasive procedure and can be performed in an outpatient clinic (1). Thus HIFU procedure minimizes all surgery risks and offers cost reduction which makes an attractive alternative to TURP. However, in order for the HIFU procedure to be acceptable it must offer the similar results to BPH patients that are offered by TURP, namely quick relief of BPH symptoms and improved urinary flow rates. To achieve these goals, a HIFU procedure that utilizes both thermal and cavitation mechanisms has been developed.

MATERIAL AND METHODS

Equipment: The Sonoblate-200 (Focus Surgery, Inc., Indianapolis, IN) has been previously described in detail (2). Briefly, the system utilizes a focused transducer with dual segments on the same PZT ceramic crystal. The transrectal probe as shown schematically in Figure 1 operates at 4 MHz during imaging and therapy modes. The prostate is first imaged by mechanically scanning the transducer in both longitudinal and transverse planes. The prostate tissue and urethra are localized in the focal zone for the HIFU treatment. Thermal and cavitation lesions were produced in the canine model prior to adopting a safe method for human clinical studies. The development of these methods are briefly described below.

Figure 1. SB-200 transrectal HIFU probe. A rectangular box on the prostate prescribes the treatment zone

Thermal Ablative Treatment: In the previous studies, thermally coagulative necrosis of the tissue was achieved by setting the acoustic peak focal intensity at 1680 W / cm². Moving the transducer in a fixed format in
axial and transverse planes produced the volume lesions. These lesions were symmetrical in shape and did not disintegrate tissue and blood vessels immediately post treatment.

_Cavitation Induced Lesions at Higher Intensities:_ When the focal peak intensity was set at $2000 \text{ W/cm}^2$ and above, the lesions were produced with large holes of irregular shapes. These holes were filled with blood and disrupted tissue structures. Also, the size and shapes of the lesions were larger compared to thermal lesions. The images immediately following the treatment showed bright echo in the focal region. This bright echo was termed “Pop Corn”. The spectrum analysis of ultrasound signals received by a miniature hydrophone showed broadband noise below 4 MHz operating frequency with a distinct signal associated at 2 MHz (at 1/2 harmonic) (2).

_Lesions Induced by Ultrasound Contrast Agent:_ In an effort to reduce the total acoustic power requirements as well as higher intensities used during cavitation, experiments were carried out using Albunex, an US contrast agent (manufactured by MDI, San Diego) and HIFU. _In-vitro_ experiments proved that intensity threshold for cavitation in the degassed water with Albunex reduced by half. With this information, animal experiments were conducted to study the cavitation-induced lesions in the canine prostate. During the HIFU treatment at 1200 to 1680 W / cm$^2$, Albunex was introduced in the urethra and prostatic gland of canines. The lesions in the prostatic glands with Albunex were larger compared to thermally induced lesions in the same gland. These lesions were not as disruptive as cavitation lesions produced using very high intensities. The gross anatomy showed lesions with coagulative necrosis. However, there was no noticeable effect observed on the urethra. Although, there were bright echoes from the region of urethra when Albunex was injected, the enhanced HIFU effect was not present. Later, it was found that Albunex was rapidly dissolving in the presence of urine.

_Lesion Production with an Indwelling Catheter:_ Lesions in the canine were produced using an 18 or 24 French catheter (Dow Corning Corporation, MI) in the urethra during the HIFU treatment. During the treatment there was always a bright echo at the interface of urethra and catheter. This bright region continued to stay present for a long time even after the therapy. At very lower power level, high temperatures at the urethra and catheter were measured, indicating presence of localized cavitation. The catheter had small “drilled” holes in the region of treatment. The gross pathology of prostate showed very symmetrical lesions in the prostate gland with mechanical disruption and disintegration of urethra seen under a microscope. In many animals, within 72 hours post HIFU treatment a smooth cavity in the prostate surrounding the urethra was developed.

**RESULTS**

The method of lesion production with an indwelling catheter was utilized in a human clinical study under an approved protocol. The results showed faster relief of BPH symptoms and overall improved flow rates.

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