IEEE Ultrasonics Symposium Proceedings, Puerto Rico, 2000.

Transurethral High Intensity Focused Ultrasound: Catheter Based Prototypes and Experimental Results

Ralf Seip, Mihir Biswas, Maksim Kuznetsov, Narendra T. Sanghvi
Focus Surgery, Inc. Indianapolis, IN 46226
Thomas A. Gardner
Indiana University School of Medicine, Indianapolis, IN 46202
Noshir F. Dabhoiwala
Department of Urology, Academisch Medisch Centrum, Amsterdam, The Netherlands

Abstract - Transurethral catheters containing multiple high-intensity focused ultrasound (HIFU) transducers at their tip have been designed, built and tested for the treatment of prostate tissue. These catheters address a need in the medical community for simple, fast, and effective treatments using low-cost, disposable, and application-specific devices for disease control through tissue ablation. The HIFU transducers used in the transurethral catheter prototypes have a focal length of 10 mm, operate at 5 MHz, and are able to generate total acoustic power levels exceeding 8 Watts. Experimental *in vitro* and *in vivo* results show that the catheters can ablate cylindrical tissue volumes > 5 cm^3 around the urethra in less than 15 minutes through simple catheter rotation. These results indicate that catheter-based HIFU transducers can be used to provide a viable alternative to current minimally-invasive therapies for prostate diseases, such as BPH. The technologies also show promise for the treatment of other diseases that would benefit from using small, minimally invasive HIFU transducers (such as esophageal, thoracic, and ear/nose/throat and OB/Gyn applications). Catheter prototypes are described, and *in vitro*, *in vivo*, and histology data are presented.

I. INTRODUCTION

In the last decade, transrectal HIFU devices have been successfully used in the clinic for the treatment of both benign and malignant prostate tissue [1,2]. There are many cases, however, because of anatomical structures and the morphology of the prostate, or protrusions within the bladder lumen that require a direct treatment approach. Catheter-based transurethral ultrasound therapy devices are ideally suited for these applications. Benefits of these devices include: 1) lower power and instrumentation requirements due to being in direct contact with the treatment site; 2) shorter treatment time (treatment limited around the urethra only); and 3) lower cost, utilizing available imaging systems for guidance and positioning. In contrast to non-focused approaches [3,4], catheters utilizing high-intensity focused ultrasound (HIFU) transducers as described herein allow for the precise placement of energy required for tissue ablation at high temperatures (>90°C) in a short time. Furthermore, HIFU catheters provide an additional advantage: they are inherently safe, since all intervening tissue (between the focal zone and the transducer) is treated – lesion formation starts in the focal zone and builds up to the transducer face. Post-focal tissue is left intact, thus "self-regulating" HIFU power deposition, eliminating the need for cooling devices.

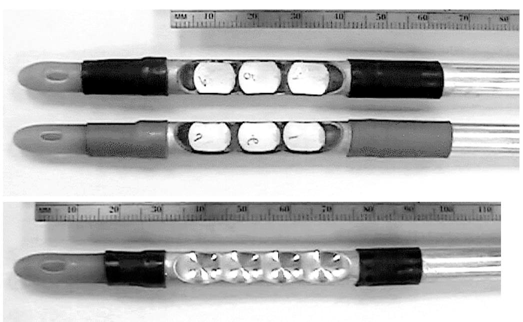
II. MATERIALS AND METHODS

Catheter Prototypes

A total of 8 different transurethral catheters with HIFU transducers were designed, fabricated, and tested. Two different configurations were examined: (i) catheters containing individual spherically-focused crystals mounted on a transducer carrier and (ii) catheters containing flat crystals mounted behind focusing aluminum (AL) lenses. The latter was developed because such configurations offer significant cost/ease of manufacturing benefits compared to catheters containing spherically-focused transducer crystals. The designed catheters follow the specifications listed in Table 1, and generally contain several focused transducer elements or acoustic lenses along the length of the catheter at its distal end, as shown in Figure 1. The short focal length of 10 mm of the individual catheter HIFU transducers limits the ultrasound energy penetration depth so that it is confined within the prostate tissue.

Table 1. HIFU transurethral catheter prototype and transducer element(s) specifications.

Description	Value	Units
Operating Frequency	5.0 (nominal)	[MHz]
Transducer Geometry	Truncated spherical shell or flat (AL lens)	
Focal Length	10.0 (curved) 8.0 (AL lens)	[mm]
Transducer Size	7x10, 5.5x10	[mm]
Crystal material	Nova 3B (Piezoceramic)	
Transducers	1-4 per catheter	
Catheter Size	18-24	French
Catheter configuration	Soft tip with stiff shaft, 1:1 torqueability	



(a)

(b)

Figure 1. HIFU transurethral catheter prototypes: with individual, spherically-focused HIFU transducers (a), and flat transducers and aluminum focusing lens (b).

The HIFU transducer elements in the catheter are individually driven by dedicated, wideband power RF amplifiers (50W each, 4 total), and can be driven together if desired under computer control. All catheters have a stiff shaft, allowing for accurate manual positioning and alignment of the catheter transducer section in the prostate. All HIFU catheters were electrically and acoustically characterized by measuring their electrical transducer impedance, resonance frequency, total acoustic output power (TAP), transducer efficiency, and focus quality.

In Vitro Experiments

The performance and efficacy of the transurethral catheters was evaluated in a series of *in vitro* experiments using fresh turkey breast tissue maintained at 37°C. Catheter operating parameters for reliable and consistent lesion creation were also determined during the *in vitro* experiments. Conically-shaped lesions are desired: these lesions start to form at the focal spot of the transducer, and grow towards the transducer as more ultrasound energy is deposited into the tissue. Operating parameters include: HIFU exposure “ON” time, tissue cooling “OFF” time, sonications/site, and RF power level. Once determined, these parameters were the starting point for the *in vivo* experiments. To ablate the large cylindrical tissue volumes around the urethra to alleviate the BPH condition, it is necessary to rotate the catheter to create ablated zones via the superposition of individual transducer lesions. The rotation increment (in degrees) was determined experimentally during the *in vitro* experiments. To reduce treatment time, all transducers were driven simultaneously during these experiments, coupled to the tissue with ultrasonic gel.

In Vivo Experiments

The HIFU catheters were also evaluated *in vivo* in the dog prostate. Male dogs under anesthesia (25Kg or more, 5 years and older, prostate size ≥ 18cm^3) were used in this acute procedure. Due to the local anatomy of the dog’s urethra and the stiff shaft of the catheters, is was necessary to introduce the catheter into the urethra through a small incision in the urethra at the base of the penis (urethrostomy). The transducer section of the catheter was positioned in the prostate of the animal using transrectal ultrasound guidance, and coupled to surrounding tissue using ultrasonic gel. The operating parameters determined during the *in vitro* studies were used to ablate a cylindrical tissue volume around the urethra through manual catheter rotation. After the procedure, the animal was euthanized, and its prostate and rectum was removed for visual and histological inspection.

III. RESULTS

Catheter Prototypes

Table 2 shows typical electrical and acoustic characterization results for various developed catheter prototypes. Notice that each individual element can easily generate more than 8 W of acoustic power at efficiencies of 55% for the spherically shaped transducers, and 25% for the flat/aluminum lens transducers. Such power levels correspond to focal peak intensities (I_{SPTA}) greater than 2000 W/cm^2 in tissue, and are capable of producing coagulative necrosis in the tissue. Focal spot size computer simulation results were validated with pressure field Schlieren images, as shown in Figure 2.

Table 2. HIFU transurethral catheter prototype characterization results.

Description	Value	Units
Output Power	>8 per transducer	[W]
Focus Size (-6dB)	~ 0.3 x 0.5 (for 7x10 mm transducer)	[mm]
Intensity	1790, for P=6 W, z=10 mm, f=5 MHz, α=40.4 Np/m	[W/cm^2]
Efficiency	~55 (focused) ~25 (AL lens)	[%]
Element Electrical Impedance	100-150 typical (curved) 70-100 typical (AL lens)	[Ω]

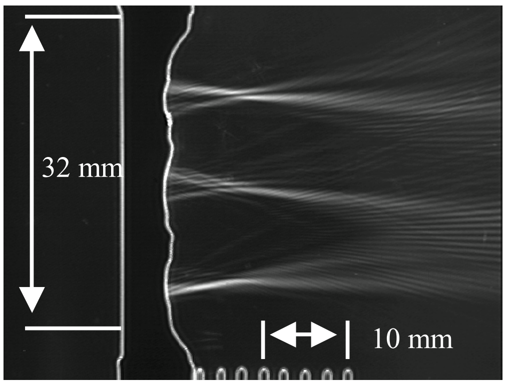


Figure 2. Schlieren image showing pressure field of individual HIFU transducers.

The 3-element curved transducer catheters were used in the *in vitro* and *in vivo* experiments due to their higher efficiency (as compared to the flat transducer/acoustic lens catheters) to avoid excessive, non-ultrasonic tissue heating around the catheter.

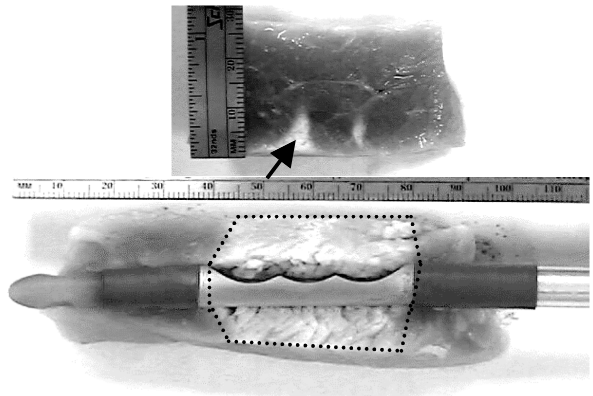
In Vitro Results

Table 3 shows the experimentally determined catheter operating parameters that yielded consistent single- and multiple lesions in the turkey breast tissue. The single lesions have the desired conical shape extending from the focal spot to the face of the transducer (thus limiting the lesion within the tissue), were created in less than 90 seconds, and were between 130 to 170 mm^3 in size, as shown in Figure 3(a).

Table 3. HIFU catheter operating parameters.

Parameter	Single lesion	Compound lesions
HIFU “ON” time [s]	4	4
HIFU “OFF” time [s]	10	9
Acoustic Power [W]	5.4 per Tx	6.0 per Tx
Sonications per site	7	8
Rotation Increment	N/A	45°

It was found that one complete catheter rotation with a 45° rotation increment was enough to create a complete, contiguous cylindrical lesion. Superposition of individual lesions generated ablated tissue volumes between 15 and 18 cm^3 in approximately 14 minutes, as shown in Figure 3(b).



(a)

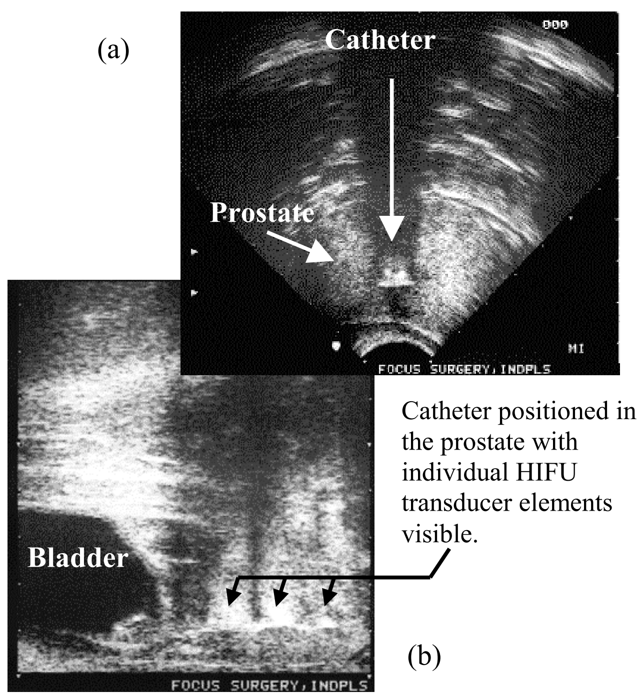
(b)

Figure 3. Cross-sections of *in vitro* conical single lesions (a) and *in vitro* multiple lesions (b) achieved through 360 degree catheter rotation (turkey breast tissue).

In Vivo Results

The transurethral catheters are easily identifiable with transrectal ultrasound imaging, making the positioning and alignment of the transducer section in the prostate a simple procedure, as shown in Figure 4.

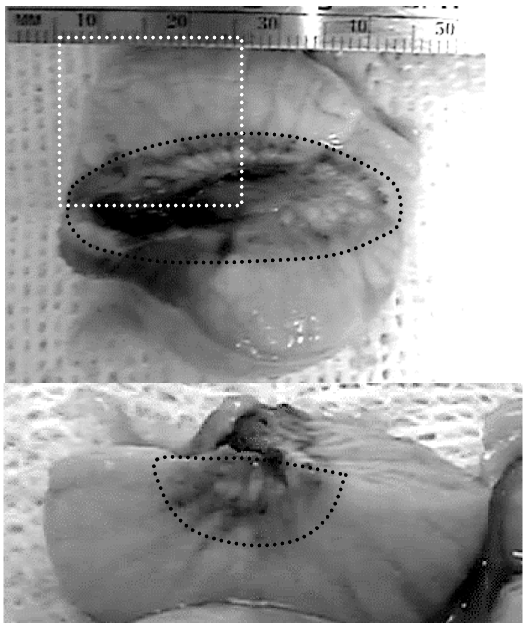
(a)



(b)

Figure 4. Transrectal ultrasound images: sector (a) and transverse (b) used for transurethral catheter positioning and alignment in the dog prostate.

Using the compound lesion creation parameters of Table 3 yielded a large cylindrical lesion in the dog prostate around the urethra, as shown in Figure 5 and 6. It was possible to ablate this tissue volume of 4.9 cm^3 in approximately 14 minutes.



(a)

(b)

Figure 5. Longitudinal (a) and transverse (half) (b) view of dog prostate 30 minutes after transurethral HIFU treatment showing cylindrical ablated volume (black dashed lines).

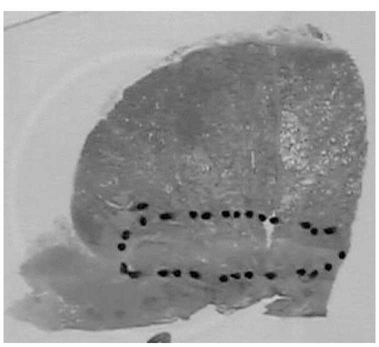


Figure 6. Histology slide of highlighted prostate section of Figure 5 (longitudinal section, one quarter of whole prostate) with ablated tissue zone marked in black.

No visible damage occurred to the rectal wall of the animals treated.

IV. DISCUSSION AND CONCLUSIONS

The results obtained clearly demonstrate that it is possible to apply high intensity focused ultrasound transurethrally for tissue ablation. The small, focused ultrasound transducers and developed catheters are able to easily generate the intensities required for this process leading to the ablation of large tissue volumes in a short amount of time. The catheters can be positioned using ultrasound guidance, and are easily operated. The transurethral application of HIFU is safe due to the short focal length (limited penetration depth) of the catheter transducers, and the fact that once the initial focal lesion has been created, additional deposited energy will only be absorbed by intervening tissue, just as desired.

It is conceivable that the small, focused transducers and catheters developed for prostatic tissue ablation could also be used in other applications requiring tissue ablation, such as esophageal, thoracic, ear/nose/throat and OB/Gyn applications. Future work will mainly be focused on implementing cost-effective catheters, treatment of additional animals to validate safety and refine catheter operating parameters (statistically valid dataset), and carrying out a feasibility study in humans.

ACKNOLEDGEMENTS

The authors want to thank Ms. Jayne Murphy and Dr. M. Mughadam for their assistance during the *in vivo* procedures, and Dr. Victor Rao for preparing the animal protocol.

REFERENCES

[1] N.T. Sanghvi, F.J. Fry, R. Bihrle, R.S. Foster, M.H. Phillips, J. Syrus, A.V. Zaitsev, and C.W. Hennige, "Noninvasive Surgery of Prostate Tissue by High-Intensity Focused Ultrasound," *IEEE Trans. On UFFC*, Vol. 43, No. 6, pp. 1099-1110, Nov. 1996.

[2] J. Y. Chapelon, M. Ribault, A. Birer, F. Vernier, R. Souchon, and A. Gelet, "Treatment of localized prostate cancer with transrectal high intensity focused ultrasound," *European Journal of Ultrasound*, Vol. 9, pp. 31-38, 1999.

[3] C.J. Diederich and E.C. Burdette, "Transurethral Ultrasound Array for Prostate Thermal Therapy: Initial Studies," *IEEE Trans. On UFFC,* Vol. 43, No. 6, pp. 1011-1022, Nov. 1996.

[4] C.L. Lafon, F. Prat, A. Arefiev, Y. Theillere, J.Y. Chapelon, and D. Cathignol, "Ultrasound Interstitial Applicator for Digestive Endoscopy: In Vivo Destruction of Bilary Tissues," 1999 *IEEE Ultrasonics Symposium Proceedings*, pp. 1447-1450.