Photoacoustic imaging of prostate brachytherapy seeds with transurethral light delivery

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ABSTRACT

We present a novel approach to photoacoustic imaging of prostate brachytherapy seeds utilizing an existing urinary catheter for transurethral light delivery. Two canine prostates were surgically implanted with brachytherapy seeds under transrectal ultrasound guidance. One prostate was excised shortly after euthanasia and fixed in gelatin. The second prostate was imaged in the native tissue environment shortly after euthanasia. A urinary catheter was inserted in the urethra of each prostate. A 1-mm core diameter optical fiber coupled to a 1064 nm Nd:YAG laser was inserted into the urinary catheter. Light from the fiber was either directed mostly parallel to the fiber axis (i.e. end-fire fire) or mostly 90° to the fiber axis (i.e. side-fire fiber). An Ultrasonix SonixTouch scanner, transrectal ultrasound probe with curvilinear (BPC8-4) and linear (BPL9-5) arrays, and DAQ unit were utilized for synchronized laser light emission and photoacoustic signal acquisition. The implanted brachytherapy seeds were visualized at radial distances of 6-16 mm from the catheter. Multiple brachytherapy seeds were simultaneously visualized with each array of the transrectal probe using both delay-and-sum (DAS) and short-lag spatial coherence (SLSC) beamforming. This work is the first to demonstrate the feasibility of photoacoustic imaging of prostate brachytherapy seeds using a transurethral light delivery method.

Keywords: optoacoustic imaging, side-fire probe, side-looking probe, beamforming, prostate cancer

1. INTRODUCTION

Prostate cancer is the second most common cancer among males with 238,590 new cases estimated in the year 2013.[1] Brachytherapy is emerging as a common form of localized treatment for prostate cancer, due to its convenience.[2,3] Treatment is administered by permanently implanting tiny, radioactive, metallic capsules, or "seeds", in the prostate. Once the seeds are implanted, radiation is slowly released from the seeds to treat the tumor.

Brachytherapy seed insertion is guided with real-time transrectal ultrasound imaging, yet seeds often migrate after they are placed. Seed migration alters the calculated radiation distribution, resulting in portions of the prostate that are over- or under-dosed. Ideally, transrectal ultrasound imaging would be employed to localize seeds after placement, because it is safe and cost effective, it does not require transporting the patient to a different room after the brachytherapy operation, and it is currently utilized to guide seed implantation.[4] However, brachytherapy seeds are difficult to visualize with ultrasound, due to their small size, the presence of microcalcifications that are often mistaken for seeds, and acoustic noise artifacts (e.g. multiple reflections due to sound reverberations and shadowing due to poor ultrasound penetration through the seeds). Acoustic noise artifacts are particularly disadvantageous as the implanted brachytherapy seed count increases.[5]

Photoacoustic imaging is an excellent complement to ultrasound imaging when localizing brachytherapy seeds.[6–8] In PA imaging, tissue is illuminated with nanosecond pulses of low-energy laser light. The light is

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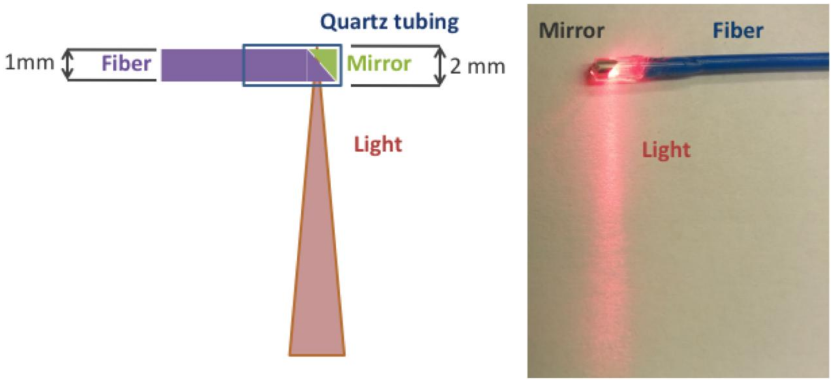


(a) (b)

Figure 1. (a) Cross section of side-fire fiber tip design. (b) Custom-built, side-fire fiber prototype.

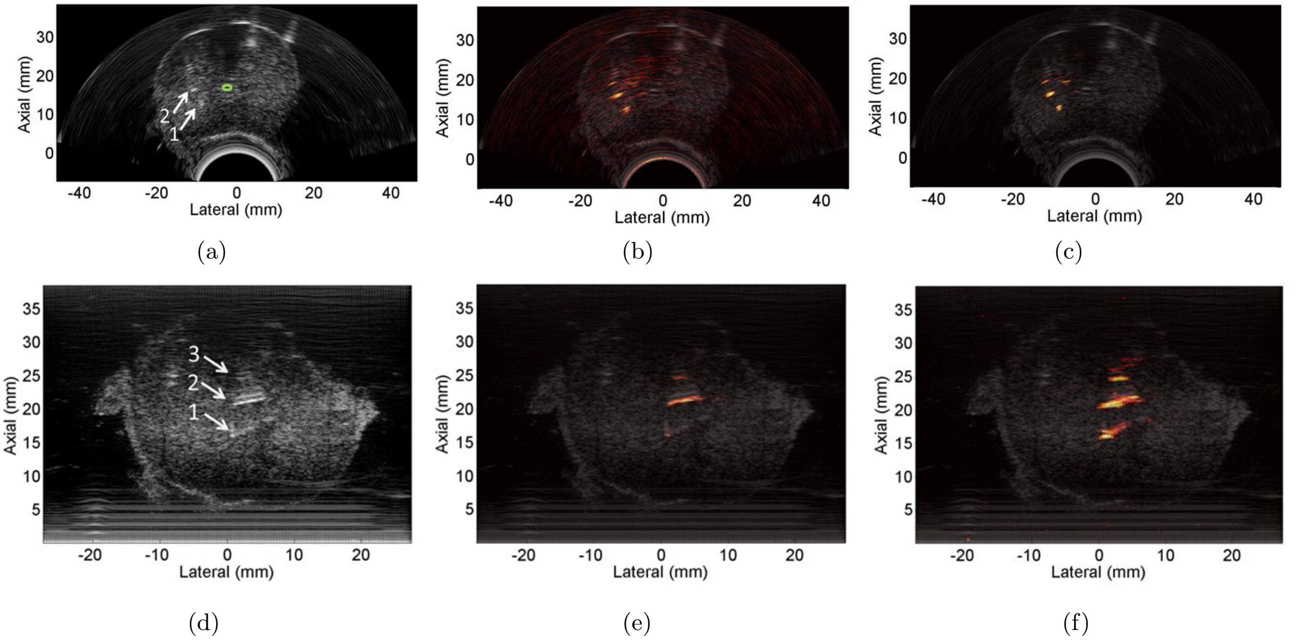
absorbed by the tissue and ambient structures, and the associated heating due to optical absorption causes thermoelastic expansion. This expansion generates broadband sound waves within the illuminated volume, and the emitted sound waves are detected by an ultrasound transducer. The detected signals are used to form an image that is related to the local optical absorption of tissue and surrounding structures. PA imaging provides optimal contrast between metals and the surrounding tissue, because the optical absorption of metals is orders of magnitude larger than that of the surrounding tissue. Several groups have successfully demonstrated the feasibility of using photoacoustic imaging combined with ultrasound for localization of brachytherapy seeds.[6–9] These previous explorations suggest transperineal or transrectal light delivery to illuminate the brachytherapy seeds.

This work is the first to introduce a transurethral light delivery method, which may serve as a complement or alternative to transperineal or transrectal light delivery. This approach can be implemented with insertion of a transparent urinary catheter, an existing step in brachytherapy procedures. An optical fiber would then be passed through the catheter to illuminate the brachytherapy seeds in the prostate. We explore two types of illumination methods, one with light emitted parallel to the fiber axis (i.e. end-fire fiber). The second method requires light to be emitted in one primary direction that is orthogonal to the fiber axis (i.e. side-fire fiber), as in intravascular photoacoustic imaging,[10] optical spectroscopy,[11] or prostate laser vaporization[12,13] applications.

2. MATERIALS AND METHODS

A photoacoustic imaging system consisting of an ultrasound scanner (SonixTouch, Ultrasonix, Richmond, BC, Canada), transrectal ultrasound probe (BPC8-4 and BPL9-5, Ultrasonix), data acquisition unit (SonixDAQ, Ultrasonix), and 1064 nm Nd:YAG laser (Phocus InLine, Opotek, Carlsbad, CA) was utilized to acquire photoacoustic data from two canine prostates that were surgically implanted with decayed brachytherapy seeds (TheraSeed, Theragenics Corporation, Buford, GA, USA). The seeds were coated with black ink to increase optical absorption. The locations of seeds implanted in the prostate were confirmed with intraoperative ultrasound images and post-operative CT images. Photoacoustic images were beamformed using a conventional delay-and-sum (DAS) beamformer with 33-element sub-apertures and an advanced short-lag spatial coherence (SLSC) beamformer with short-lag values of 4 and 10 for linear and curvilinear images, respectively, as described in a previous publication.[14]

The laser was coupled to an optical fiber that either emitted light along the axis of the fiber (i.e. end-fire fiber) or 90° to the fiber axis (i.e. side-fire fiber). The end-fire fiber was a conventional 1-mm core diameter fiber with a numerical aperture of 0.37. The side-fire fiber was custom designed as shown in Fig. 1 (a), where a conventional 1-mm core diameter fiber with a numerical aperture of 0.39 was polished at a 45° angle. This angle directed a fraction of the light 90° to the fiber axis using principles of total internal reflection. The remainder of the light was redirected at an angle less than 90° to the fiber axis. The fiber tip was capped with a mirror constructed from a metal rod polished to a 45° angle to redirect the remaining light and create the side-fire fiber



(a) (b) (c) (d) (e) (f)

Figure 2. (a,d) Ultrasound images of brachytherapy seeds acquired with the curvilinear and linear ultrasound arrays, respectively. (b,e) DAS beamformed photoacoustic images acquired with the end-fire fiber and overlaid on the corresponding ultrasound images. (c,f) SLSC beamformed photoacoustic images acquired with the end-fire fiber and overlaid on the corresponding ultrasound images.

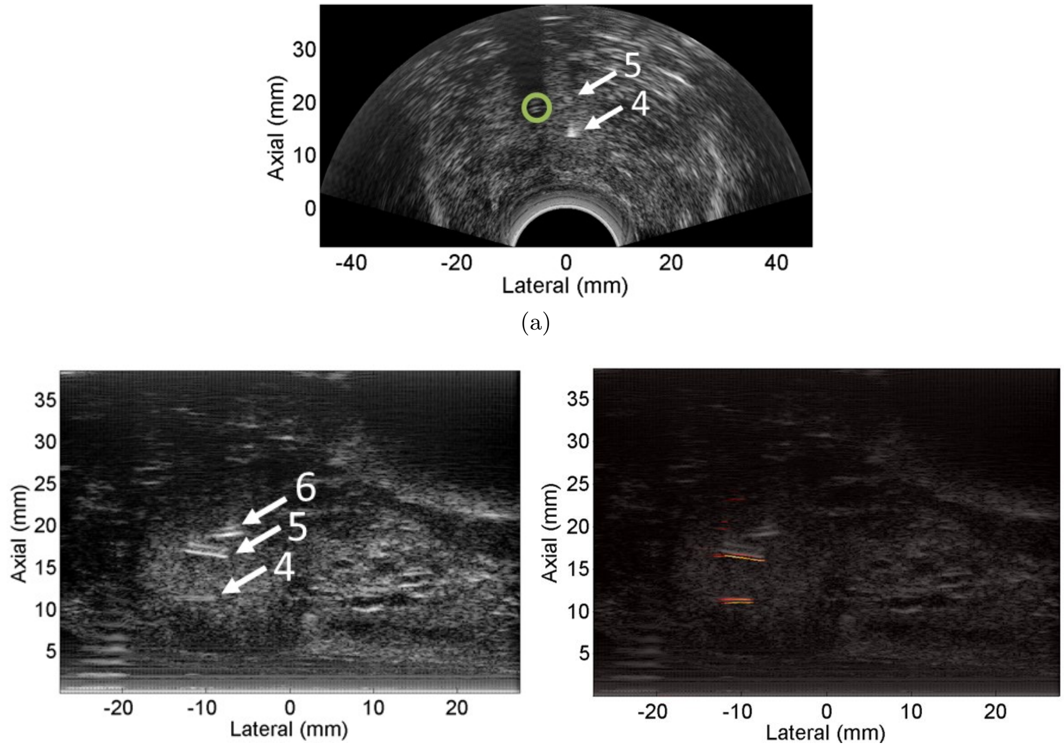
shown in Fig. 1 (b). The fiber and mirror were inserted into opposite ends of a quartz tube and oriented with their polished faces coincident to each other. Epoxy was used to permanently fix the fiber and mirror in this orientation inside the quartz tube. The tube had an outer diameter of 2 mm.

One prostate was excised and embedded in gelatin with a 14 French (4.7 mm outer diameter) urinary catheter passed through the urethra. The end-fire optical fiber was inserted in the catheter. A channel was drilled in the layer of gelatin located below the prostate to correspond with the anatomical relationship between the prostate and rectum. The transrectal probe, held and locked in place with a standard brachytherapy stepper (Nucletron, Veenendaal, The Netherlands), was inserted into the channel representing the rectum. Photoacoustic and ultrasound images of the prostate and implanted brachytherapy seeds were acquired with this setup. The average energy per pulse measured at the tip of the fiber was 16.7 mJ.

The second prostate was imaged post-mortem in the native tissue environment, approximately 1-2 hours after euthanasia. The abdomen of the dog was opened to access the prostate. A 16 French (5.3 mm outer diameter) urinary catheter was inserted through an incision in the bladder to avoid the curvature of the urethra near the canine's pubic bone. This curvature is not present in humans. The side-fire fiber was inserted into the open end of the catheter to image the implanted brachytherapy seeds. The transrectal ultrasound probe was locked in place with the brachytherapy stepper and inserted into the rectum. The average energy per pulse was 6.7 mJ.

3. RESULTS

After embedding the excised canine prostate in gelatin, the transrectal ultrasound probe was oriented to visualize three of the implanted seeds. B-mode images acquired with the curvilinear and linear arrays of the transrectal probe are shown in Fig. 2(a) and (d), respectively. The arrows in the B-mode image point to the implanted seeds. The urethra containing the 14 Fr urinary catheter is outlined with a circle. To acquire photoacoustic images, the bare fiber was placed in the urinary catheter at distance of 6 mm from tip of seed #2 in the lateral dimension of Fig. 2 (d). The three seeds are located at a radial distance of 13-16 mm from the center of the urethra.



(a)

(b) (c)

Figure 3. Ultrasound images of brachytherapy seeds in the second prostate, acquired with the (a) curvilinear and (b) linear arrays. (c) Photoacoustic image acquired with light directed toward seed #5 and shown with 8 dB dynamic range.

Photoacoustic images of the seeds were overlaid on the co-registered B-mode images. DAS beamformed images acquired with the curvilinear and linear arrays are shown in Fig. 2(b) and (e), respectively. The curvilinear image (Fig. 2(b)) shows the three implanted seeds, while the linear image (Fig. 2(e)) shows one of the three seeds most clearly (seed #2). This seed is primarily located within the ultrasound image plane, unlike seeds #1 and 3.

Corresponding SLSC beamformed images, created with short-lag values of 10 and 4 for the curvilinear and linear arrays, respectively, are shown in Fig. 2(c) and (f), respectively. The seeds in the curvilinear image (Fig. 2(c)) are shown with less background noise compared to the DAS beamformed image (Fig. 2(b)). The three seeds in the linear image (Fig. 2(f)) are more visible compared to the DAS beamformed image (Fig. 2(e)). These results demonstrate the ability to visualize brachytherapy seeds within approximately 1 cm of the urethra using an end-fire optical fiber.

In some cases, it may be more desirable to only visualize a few seeds at a time, rather than all seeds within the field surrounding the urethra. The side-fire fiber was tested to achieve this goal. A curvilinear B-mode image of two seeds implanted in the second prostate (#4 and 5) are shown in Fig. 3(a). The urethra containing the 16 Fr urinary catheter is outlined with a circle. The two seeds are located at a radial distance of 6-9 mm from the center of the urethra. A third seed (seed #6) is visualized in the linear image of the same prostate, as shown in Fig. 3(b). In this image, seeds #5 and 6 are in the ultrasound plane while seed #4 is partially out of plane. Light from the side-fire fiber was directed toward this out-of-plane seed, and the resulting photoacoustic image of this seed (seed #4) and the nearby in-plane seed (seed #5) is shown in Fig. 3 (c). This image was created with DAS beamforming.

4. DISCUSSION

The feasibility of transurethral light delivery was demonstrated for end-fire and side-fire fibers. The end-fire fiber enabled simultaneous illumination of seeds in multiple directions from the urethra, while the side-fire fiber enabled preferential illumination of selected seeds in a single direction. Each illumination method has unique advantages for seed localization in brachytherapy. For example, the end-fire fiber and coherence-based beamforming might be useful to identify all seeds within the region surrounding the urethra, particularly if the locations of multiple seeds in the region are unknown due to seed migration. On the other hand, the side-fire fiber would be more advantageous if *a priori* knowledge of a few seed locations require additional confirmation. This method may also be useful to target and identify reverberation artifacts that erroneously appear as duplicates of an implanted seed in an ultrasound image.

The coherence-based SLSC beamformer enabled better visualization of the implanted seeds, regardless of differences in signal amplitude, even if the seeds were slightly outside of the imaging plane. This is expected because the SLSC beamformer is more sensitive to differences in signal spatial coherence, rather than differences in signal amplitude.[14, 15] Quite contrary, the DAS beamformer is more sensitive to differences in signal amplitude, and the out-of-plane seeds have lower contrast in the B-mode and photoacoustic images (compared to in-plane seeds).

Transurethral light delivery is currently used in prostate photodynamic therapy, a treatment approach that requires preferential uptake of a photosensitive drug and delivery of laser light to activate the drug and initiate cell death.[16–18] The utilization of transurethral light delivery in photodynamic therapy suggests that this light delivery method is clinically viable. Although there are reports of side effects due to urethral necrosis,[17] the energies utilized in this preliminary investigation are several orders of magnitude lower than the energies required for photodynamic therapy. The lower permissible energies for photoacoustic imaging will likely translate to fewer complications with transurethral laser delivery.

5. CONCLUSION

Transurethral light delivery was implemented with end-fire and side-fire optical fibers. The custom-built side-fire fiber enabled preferential selection of seeds to be illuminated, while the end-fire fiber allowed illumination of seeds within approximately 1 cm of the prostate. Seeds that were slightly outside of the ultrasound image plane were better visualized with coherence-based beamforming, when compared to conventional amplitude-based beamforming. These seeds were also better visualized with the side-fire fiber pointed in their direction when relying on amplitude-based beamforming. The proposed light delivery method is a promising complement or alternative to transperineal or transrectal light delivery.

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