Treatment planning for prostate focal laser ablation in the face of needle placement uncertainty

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Purpose: To study the effect of needle placement uncertainty on the expected probability of achieving complete focal target destruction in focal laser ablation (FLA) of prostate cancer.

Methods: Using a simplified model of prostate cancer focal target, and focal laser ablation region shapes, Monte Carlo simulations of needle placement error were performed to estimate the probability of completely ablating a region of target tissue.

Results: Graphs of the probability of complete focal target ablation are presented over clinically relevant ranges of focal target sizes and shapes, ablation region sizes, and levels of needle placement uncertainty. In addition, a table is provided for estimating the maximum target size that is treatable. The results predict that targets whose length is at least 5 mm smaller than the diameter of each ablation region can be confidently ablated using, at most, four laser fibers if the standard deviation in each component of needle placement error is less than 3 mm. However, targets larger than this (i.e., near to or exceeding the diameter of each ablation region) require more careful planning. This process is facilitated by using the table provided.

Conclusions: The probability of completely ablating a focal target using FLA is sensitive to the level of needle placement uncertainty, especially as the target length approaches and becomes greater than the diameter of ablated tissue that each individual laser fiber can achieve. The results of this work can be used to help determine individual patient eligibility for prostate FLA, to guide the planning of prostate FLA, and to quantify the clinical benefit of using advanced systems for accurate needle delivery for this treatment modality. © 2014 Author(s). All article content, except where otherwise noted, is licensed under a Creative Commons Attribution 3.0 Unported License. [http://dx.doi.org/10.1118/1.4842535]

Key words: prostate cancer, focal therapy, treatment planning, needle guidance

1. INTRODUCTION

The concept of focal therapy for the treatment of patients with clinically localized, low- to intermediate-risk prostate cancer is receiving increased attention, and the safety and efficacy of a variety of focal therapy delivery modalities is being evaluated in a number of trials.¹ One particularly attractive modality is focal laser ablation (FLA). Prostate FLA involves interstitial placement of one or multiple diffusing laser fibers into the “dominant lesion” or “index” tumor.² With recent advances in multiparametric magnetic resonance (MR) imaging and its reported high sensitivity in detecting clinically significant tumors, localization of the tumor selected for FLA is commonly based on an assessment of T2-weighted,
diffusion-weighted, and dynamic contrast-enhanced (DCE) MR images. This process provides the interventionalist with a well-delineated 3D target for FLA (hereafter referred to as the target or focal target). Most commonly, diode lasers at 980 nm (infrared) are used for ablation, as this technology is cheaper and more compact than alternatives such as Nd-YAG lasers, and water has good absorption at this wavelength. In addition, systems with FDA approval for use in prostate are now available. Once a fiber has been placed within the target region, usually through the perineum via a coaxial cannula system, ablation is performed for a period of 2–10 min at a laser power of 5–15 W. By performing multiple laser fiber insertions, regions of ablated tissue up to several cm³ can be produced. FLA is MR-compatible, allowing for intraoperative visualization of prostate cancer, clear visualization of optical fiber placement in the prostate, and tissue temperature monitoring using MR thermometry. In addition, FLA allows the possibility of retreatment or secondary radical surgery, if necessary; has been shown to cause limited treatment-related morbidity in several Phase I clinical trials; and the ability to create confluent regions lacking any remaining viable cells using FLA has been demonstrated. As many of the academic centers studying FLA move towards Phase II studies, the level of oncologic control achievable using this technique will need to be proven. It is important at this transition stage to address any flaws identified during the Phase I trials of FLA, and correct them before moving forward. Such a strategy will ensure an accurate evaluation of the true potential that FLA offers for the treatment of prostate cancer.

While the accurate specification of surrogate endpoints for prostate focal therapy is not yet established, one fact regarding the planning of focal therapy remains true: any method of focal therapy should aim to destroy 100% of the tissue in the index tumor. While FLA has shown more promise in terms of preserving urinary, bowel, and erectile function than alternatives such as high intensity focused ultrasound and cryoablation, evidence from the Phase I clinical trials and case studies on prostate FLA completed to date suggest that complete focal target destruction is not consistently being achieved. In their Phase I trial studying US-guided FLA in 12 patients, Lindner et al. reported a median fraction of pretreatment target volume treated of 53% overall and 81% in the last four patients treated. In another trial, in which nine men were treated with MR-guided FLA, Oto et al. found that the target was not completely overlapped by the ablation zone seen on immediate postprocedure DCE MR images in two cases. Furthermore, in most of these cases, one of the reasons for finding positive biopsy cores in the region previously treated (defined as treatment failure in these studies) was suspected to be poor overlap between the ablated and targeted regions. It has been hypothesized by several clinicians working in this field that a primary reason for insufficient overlap is error in needle placement, and several authors have identified the need for methods of planning prostate focal therapy. These hypotheses are consistent with the findings of several previous studies in which the effects of needle placement errors on the dose delivered in prostate brachytherapy were shown to cause clinically significant deviations from the prescribed dose, and modifications to treatment planning methods were required to compensate for this effect. At the time of writing, no systematic methods of planning laser fiber placement for FLA have been published.

In this work, a systematic method of planning target points for the placement of laser fibers for prostate FLA is developed. The method assumes that the shape of the ablated tissue region created by each laser fiber is known to the interventionalist for a given laser power and application time, and assumes that ablated regions created by each fiber are independent. Each target is modeled as an ellipse of minimum area that encloses a projection of the true focal target along the needle insertion direction and assumes that FLA can create a cylindrical volume of ablated tissue that is elongated along the direction of needle insertion. This type of geometric planning has been employed for planning various types of ablative therapy including rf ablation of liver tumors and rf ablation of lung tumors. In these works, each ablation volume was modeled as either a sphere or cylinder, and planning consisted of finding an optimal geometric arrangement of the ablation volumes to completely ablate the tumor. Other authors have identified a combined effect of performing multiple ablations in close proximity, resulting in a larger volume of ablated tissue than would be achieved by performing each of the ablations separately. However, the response of tissue to thermal therapy has been shown to vary greatly depending on the organ, and a method of accurately specifying thermal properties and levels of perfusion in human prostate tissue has yet to be developed, an initial conservative approach of assuming independent ablations is taken in this work.

Following the planning method, a method of estimating the probability of achieving complete target ablation for a given plan is presented, and results are shown for a range of realistic focal target sizes and shapes, and levels of needle placement uncertainty. Finally, a table is provided for estimating the maximum target size that can be confidently ablated over a range of target and FLA geometrical parameters, and the level of needle placement uncertainty expected. This table can be used to estimate patient eligibility for FLA based on a minimum required probability of achieving complete target ablation.

2. METHODS

2.A. Treatment planning

In this section, a systematic method for specifying the desired placement of laser fibers is developed. The method begins with a simplification of the geometry of the problem, thereby reducing the degrees-of-freedom in treatment planning. Next, the minimum plan required to completely cover a focal target of given shape and size with a fixed size of ablation region is defined, followed by a systematic method of augmenting the minimum plan by increasing the number of laser fibers.
2.A.1. 3D ablation volume model

In FLA, laser light is directed into tissue using a diffuser at the end of an optical fiber. Absorption of light energy causes an increase in tissue temperature over time, eventually resulting in irreversible tissue damage. In thermal therapy for cancer treatment, the ablated region is defined as the boundary within which the tissue is definitely irreversibly injured. Estimation of the boundary of irreversible thermal injury is generally performed by monitoring tissue temperature over time, and is defined by thresholding either temperature or an integral parameter (e.g., Arrhenius integral or cumulative equivalent minutes at 43 °C). For pretreatment planning, estimation of the boundary of the ablated region can be performed by numerical simulation of the 3D distribution of tissue temperature over time. Most commonly, such a simulation amounts to solving the Pennes bioheat equation using finite element or similar methods.

The most common type of laser diffuser used for FLA is cylindrical. Evidence from numerical simulations and DCE MRI indicate that the resulting volumes of ablated tissue are approximately ellipsoidal, and elongated in the needle insertion direction. Images of ablation regions, as visualized on immediate post-treatment dynamic contrast enhanced MR imaging, are shown in Fig. 1. If each region of ablated tissue can be assumed to be independent and tissue properties are uniform, pretreatment planning can be simplified as a geometric problem, i.e., the ablated region resulting from multiple confluent laser applications is equivalent to the superimposition of each individual ablation region. Ablated regions are expected to be independent if

i. laser fibers in close proximity are not fired simultaneously, and
ii. for fibers that are fired in succession in close proximity, the amount of thermal tissue damage beyond the boundary of definite irreversible damage does not substantially contribute to the thermal damage caused by the next laser application.

2.A.2. 2D approximation

After a single catheter insertion, multiple confluent ablation regions can be created along the catheter’s axis by retracting the laser fiber in between or during laser application. In accordance with this technique, and assuming that the extent of all positions of laser application covers the farthest and nearest volume of the target along the catheter axis, an ablation region can be idealized as a cylinder of diameter $D_{\text{treat}}$. This idealized ablation region shape is conservative with respect to ensuring target ablation, since the actual ablation region will always be slightly larger. The idealized cylindrical ablation region concept is shown

![Fig. 1. Estimated regions of ablated tissue in four patient’s prostates, as seen on immediate post-treatment dynamic contrast-enhanced MR images (coronal slices): (a) and (b) single fiber insertion with laser application at only one axial position; (c) and (d) single fiber insertion with multiple laser applications at multiple axial positions, which created a region of ablated tissue that is elongated in the direction of the laser fiber (needle) axis. In all cases the insertion direction was approximately superior-inferior, with case (d) showing a slight lateral angulation.](image)
FIG. 2. Idealized ablation volume. A set of confluent regions of ablated tissue in the direction of the needle insertion is modeled as a cylinder of maximum diameter that can be enclosed by the actual ablated region. As the axial spacing between laser applications is reduced, the amount of under-prediction of ablated tissue around the periphery of the ablation region decreases, and it increases at each end.

in Fig. 2. The amount of healthy tissue damaged beyond the idealized cylindrical model of the ablated region depends on the separation between individual ablations along the axis of the laser fiber. If the laser fiber is retracted at a constant rate, the resulting ablation region is expected to be cylindrical (in the absence of any heat sink effects).

Using this model of ablation volume shape, planning for FLA only requires consideration of the target shape as projected onto a plane perpendicular to the needle insertion direction (i.e., as seen from the “needle’s eye view”). The targets are then idealized as an ellipse of minimum area that completely encloses the projection of the target onto this plane. Moreover, use of this model assumes that all needle trajectories are approximately parallel to each other and that the depth of laser fibers can be accurately measured and controlled (e.g., using imaging).

These simplified models of ablation and target shapes result in a reduction in the dimensionality and computational requirement of the problem (from 3D to 2D), and a reduction in the number of degrees-of-freedom in treatment planning. The resulting idealized problem can be systematically studied with much greater simplicity.

Consideration of the planned axial positioning of the laser fibers must also be made in order to avoid strongly violating the cylindrical model of confluent ablation regions. The cylindrical model will be valid if the planned margin \( m_p \), as seen from the needle’s eye view, is equal to the minimum distance from the target to the planned ablation volume in the direction perpendicular to the laser fiber’s axis \( m_{\text{min}} \), as illustrated in Fig. 3. As the primary aim of this work is to study the effect of needle placement error on treatment coverage in FLA therapy, it is assumed that this condition will be met. This assumption is deemed reasonable since it is much easier to accurately control the depth of a needle than its position perpendicular to the insertion direction (the former can be adjusted after insertion, while the latter requires retraction and reinsertion).

FIG. 3. Effect of laser fiber axial positioning on the validity of the cylindrical ablation region model. (a) and (c) View from “needle’s eye view;” (b) and (d) view perpendicular to needle axis. The cylindrical ablation region model is valid if the axial extent of the planned ablation region is chosen such that \( m_p = m_{\text{min}} \). In (a) and (b), the planned ablation region is not long enough (\( m_p > m_{\text{min}} \)); in (c) and (d), \( m_p = m_{\text{min}} \) and therefore the 2D model would reliably predict when needle placement error results in untreated target tissue.

2.A.3. Specification of planned laser fiber locations

A systematic method of planning the placement of laser fibers was designed based on the following constraints and guidelines:

- For a given plan, an increase in the ablation diameter should result in a nearly uniform increase in margin of the treatment plan around the periphery of the target;
- A maximum of eight target points (number of laser fibers) is permitted; and
- All individual ablation regions are of equal diameter.

Following these guidelines, two possible patterns of fiber placement were defined: Pattern A: the placement of laser fibers is equally distributed along the major axis of the ellipse-shaped target (linear pattern) and Pattern B: laser fibers are placed around an ellipse that is concentric to the idealized target ellipse boundary (concentric ellipse pattern). These two patterns are shown in Fig. 4.

For each combination of target length, target aspect ratio AR (length divided by width), and number of laser fibers, the

FIG. 4. The two patterns considered for the ideal placement of laser fibers: (a) Pattern A (linear pattern) and (b) Pattern B (concentric ellipse pattern). (Solid black contour) Idealized target boundary, (red contours) idealized ablation region boundaries, and (dashed contour) concentric planning ellipse. For a given target width, target aspect ratio, and number of laser fibers, the ideal pattern of the two is that which requires the smallest ablation diameter.
FIG. 5. Minimum treatment plan required to achieve complete target coverage for varying target aspect ratio and number of laser fibers used. Either Pattern A (fibers equally distributed along the major axis of the target) or Pattern B (fibers distributed around an ellipse concentric to the target boundary) is employed, based on whichever pattern gives the minimum required size of ablation region. (Black contour) Idealized target boundary and (red circle) idealized ablation region boundary.

minimum required ablation radius and corresponding pattern can be defined as that for which the total ablation region completely covers the target with zero margins (i.e., the minimum distance from the target boundary to any exterior ablation region boundary.

2.B. Estimation of treatment overlap

Errors in the final placement of needles relative to their planned locations will be present in all cases and may result in the fraction of target treated being less than 100%. The actual result will be a function of the planned locations of laser fibers, the size of the ablation regions, and the probability density function (PDF) of needle placement error. In this section, a mathematical description of treatment overlap in the presence of needle placement uncertainty is presented. Next, the PDF used to model needle placement error is specified.

2.B.1. Mathematical description of treatment overlap

For a given target and corresponding treatment plan, the probability of ablating a specified fraction (or greater) of the target volume is desired to be known. This probability is given by the complementary cumulative distribution function (CCDF) $\bar{F}$ of the fraction of target treated:

$$\bar{F}(y) = P(f_t \geq y), \quad 0 \leq y \leq 1,$$

where $f_t$ is the fraction of the target volume treated and $\bar{F}(y)$ is the probability that $f_t$ is greater than or equal to a given value $y$. Given $\bar{F}(y)$ for a specific target and treatment plan, one could answer questions such as: “what is the probability that at least 90% of the target volume will be ablated?” or “what is the probability that the entire volume of the target will be ablated?”

FIG. 6. Examples showing how the planned number of laser fibers can be increased. Pattern A (the linear pattern) is used when the diameter of the ablation is large relative to the target width. Pattern B (concentric ellipse pattern) is used when the ablation diameter is small relative to the target width, in which case it becomes necessary to distribute laser fibers around the periphery of the target. As the number of laser fibers increases, Pattern B can be employed to increase the treatment margin around the periphery of the target.

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TABLE I. Minimum required ratio of ablation diameter to target length RA for varying target aspect ratio and number of planned laser fibers.

| Target aspect ratio (AR) | 1     | 1.5   | 2     | 2.5   |
|-------------------------|-------|-------|-------|-------|
| 1                       | 1.00a | 1.00a | 0.87b | 0.58b |
| 1.5                     | 1.00a | 0.72a | 0.68b | 0.45b |
| 2                       | 1.00a | 0.63a | 0.54a | 0.36b |
| 2.5                     | 1.00a | 0.58a | 0.47a | 0.33b |

| Number of laser fibers (n) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|----------------------------|---|---|---|---|---|---|---|---|
| 1                          | 0.54b| 0.56b| 0.58b| 0.62b| 0.71b| 0.87b| 1.00a| 1.00a|
| 2                          | 0.40b| 0.42b| 0.45b| 0.50b| 0.60b| 0.68b| 0.72a| 1.00a|
| 3                          | 0.33b| 0.36b| 0.39b| 0.45b| 0.52b| 0.54b| 0.58a| 1.00a|
| 4                          | 0.29b| 0.32b| 0.36b| 0.42b| 0.47b| 0.54b| 0.58a| 1.00a|

*Fibers placed according to Pattern A.

*bFibers placed according to Pattern B.

\[ f_i = \frac{V_{T_i}}{V_{T}} \] (2)

For a target region \( T \) and \( n \) planned ablation regions \( A_1, \ldots, A_n \) with planned target points \( p_{i1}, \ldots, p_{in} \), the expression for \( V_{T_i} \) becomes

\[
V_{T_i}(e_i', \ldots, e_n', p_{i1}, \ldots, p_{in}) = \int_{T} T(x) \cap [A_1(p_{i1} + e'_1) \cup \ldots \cup A_n(p_{in} + e'_n)] dx.
\] (3)

where \( e_1, \ldots, e_n \) are the needle placement errors for each of the \( n \) ablation regions, and \( T \) and \( A_i \) are defined as

\[
T(x) = \begin{cases} 1, & x \text{ is within projected target boundary} \\ 0, & \text{elsewhere} \end{cases}
\] (4)

and

\[
A_i(x) = \begin{cases} 1, & x \text{ is within region of ablated tissue} \\ 0, & \text{elsewhere} \end{cases}
\] (5)

\( F \) can be found by solving the integral

\[
\hat{F}(y) = \int \cdots \int \prod_{i=1}^{n} g_i(e_i') d^2 e_1', \ldots, d^2 e_n'.
\] (6)

where \( g_i(e_i') \) is the PDF of needle placement error of the \( i \)th needle \( e_i' \), and \( J(y) \) is the set of \( e_1, \ldots, e_n \) for which \( f_i \) is greater than or equal to \( y \)

\[
J(y) = \{ e_1, \ldots, e_n | f_i \geq y \}.
\] (7)

If the integration of Eq. (6) is performed numerically, the computation time required is proportional to \( N_p^n \), where \( N_p \) is the number of grid points in each direction of a 2D numerical grid. In focal laser ablation of prostate cancer, most targets require multiple laser fibers (target points), making the direct numerical integration of Eq. (6) impractical in terms of computation time.\(^5\)\(^6\) For example, if four ablation regions are planned, the integration becomes eight-dimensional. Using 100 grid points in each direction, the total time to numerically compute an eight-dimensional integral that takes 1 \( \mu \)s for each 2D component is 278 h. This is impractical.

Alternatively, Eq. (6) can be rewritten as

\[ \hat{F}(y) = E[1_y], \] (8)

where \( 1_y \) is an indicator function, defined as

\[
1_y = \begin{cases} 1, & (e_1, \ldots, e_n) \in J(y) \\ 0, & \text{elsewhere} \end{cases}
\] (9)

and \( E[1_y] \) is its expected value. The function \( 1_y \) is equal to one when the final placement of needles, including needle placement error, results in a fraction of target treated that is greater than or equal to \( y \). Using this formulation, estimation of \( \hat{F}(y) \) can be obtained using a stochastic Monte Carlo simulation that computes the empirical CCDF

\[ \hat{F}(y) = \frac{1}{N} \sum_{j=1}^{N} (1_y)_j, \] (10)

which, by the strong law of large numbers, converges to the true CCDF of \( f_i \) as \( N \) approaches infinity.\(^3\)\(^1\) Using this approach, \( N \) random samples of \( 1_y \) are obtained to estimate the CCDF. The probability of achieving complete target ablation is of particular importance, and is defined as \( P_{00} = \hat{F}(1) \). This approach requires a model of the PDF of needle placement error \( E \), which is described in Sec. 2.B.2.

2.B.2. Statistical model of needle placement error

In this paper, needle placement error is defined as the shortest Euclidean distance between a needle’s final location in the tissue after insertion and its planned location (target point). Using this definition, errors in the needle depth are ignored; a simplification based on the observation that FLA can create elongated regions of ablated tissue along the direction of needle insertion. Needle placement error includes three major contributions: (1) error in registration between pre- and intraoperative images, which results in an error in specification of the planned target point in intraoperative image space, (2) errors in needle guidance caused predominantly by deflection of the needle during insertion, and (3) tissue motion and deformation during needle insertion. Prediction of a needle’s final position in human tissue is a difficult task, and requires a priori knowledge of the 3D distribution of tissue properties and structures. Even if real-time imaging is employed during needle insertion, measurement of the current needle position will contain error, and knowledge of the current position...
cannot be used to predict the future deviations of the needle. For these reasons, needle insertion is considered to be a stochastic process, and the error in final needle placement is modeled with a continuous PDF.\textsuperscript{32–34} This approach has been applied in several previous works studying the effects of needle placement error on: the dose distribution in transperineal prostate brachytherapy,\textsuperscript{16–18} the ability to detect prostate cancer using biopsy,\textsuperscript{36} and trajectory planning for steerable needles.\textsuperscript{32,33} In most of the aforementioned works, either the final placement error or the error in angulation of the needle is modeled with a 2D normal distribution with mean zero and equal variance $\sigma^2$ in all directions. This is the approach used in this work for modeling the needle placement error vector,

$$\mathbf{E} \sim N_2(0, \sigma^2 \mathbf{I}),$$  \hspace{1cm} (11)

where $\mathbf{I}$ is a 2D identity matrix. Modeling needle placement error in this way assumes that the needle is most likely to reach the point at which it was aimed and that each orthogonal component of needle placement error is independent. Thus, systematic errors, which may include biases in the system used to guide the needles, asymmetry of the needle tips, and prostate rotation during needle insertion, are assumed to be insubstantial. Systematic errors of this sort can reasonably be ruled out if: system biases have been detected and corrected (by device calibration), either symmetrically tipped needles are used or beveled needles are used and the steering effect of the bevel is compensated, and that the physician is anticipating prostate motion and compensating for it.\textsuperscript{37} In prostate FLA, symmetrically tipped needles are most commonly used, so the steering effect of a beveled needle is not likely to be an issue in the context of this work.

If the needle placement error is distributed as in Eq. (11), then the magnitude of needle placement error follows a Rayleigh distribution with parameter $\sigma$ (Ref. 31)

$$\|\mathbf{E}\| \sim \text{Rayleigh}(\sigma).$$ \hspace{1cm} (12)

The value of $\sigma$, which is equal to the standard deviation of each orthogonal component of needle placement error, depends on several factors, including: the diameter and material stiffness of the needles used, the imaging modality used for needle guidance, the depth to which needles are inserted, and technique and level of skill.\textsuperscript{37,38} Accordingly, a realistic range of $\sigma$ for transperineal insertion of needles into the prostate was estimated to be 1–4 mm, based on evidence from studies quantifying error in transperineal prostate needle placement.\textsuperscript{16,18,35,38–40}

\subsection*{2.B.3. Numerical implementation considerations}

\subsubsection*{2.B.3.a. Sample size.} A practical value of the number of samples $N$ that gives a reliable estimate of $P_{100}$ is desired. The minimum $N$ required to estimate a proportion within an error of $\varepsilon$ with $100(1 - \alpha)\%$ confidence is\textsuperscript{41}

$$N_0 = \left(\frac{Z_{1-\alpha/2}}{\varepsilon}\right)^2 P_{100}(1 - P_{100}),$$  \hspace{1cm} (13)

where $Z_{1-\alpha/2}$ is the $(1 - \alpha/2)$th percentile of the standard normal distribution and $\alpha$ is the error percentile. Alternatively, since the true value of $P_{100}$ is not known, a conservative estimate of $N$ can be obtained by substituting 0.25 for $P_{100}(1 - P_{100})$, since this is the maximum value this expression can achieve. For $\alpha = 0.05$ and $\varepsilon = 0.01$, the minimum required number of samples is $\sim$10000. This value was used for all computations.

\subsubsection*{2.B.3.b. Grid convergence.} The method of computing target overlap involves a binary image representation of target and ablation regions, and the accuracy of the solution depends on the pixel size of these images. To ensure that the grid convergence was achieved, the pixel size was successively refined until the estimate of $P_{100}$ (for cases with $P_{100} \geq 0.9$) did not change by more than 0.02 with a decrease in pixel size by a factor of 2. Following this criteria, a final pixel size of 0.125 mm was used for all simulations.

\subsubsection*{2.B.3.c. PDF truncation.} Modeling the magnitude of needle placement error $\|\mathbf{E}\|$ with a Rayleigh distribution implies that it can truly take on any value in the range $[0, \infty)$. However, due to the stiffness of the needle and, ultimately, its finite length, $\|\mathbf{E}\|$ will be limited to a finite range in practice. Therefore, to avoid overestimation of the effect of needle placement error, random samples of needle placement error must come from a truncated Rayleigh distribution. Evidence from studies quantifying needle placement error in human prostate suggest that the true truncation point is between $2\sigma$ and $3\sigma$, where $\sigma$ is the parameter of the Rayleigh distribution.\textsuperscript{39,40} The sensitivity of the results to the specification of the truncation point within this range was quantified. It was found that truncating random samples of needle placement error at $3\sigma$ compared to that at $2\sigma$ resulted in, at most, an increase in the estimated number of laser fibers required of one. For the results presented, $3\sigma$ was used, as this makes the results more conservative.

\section*{2.C. Treatment simulation parameters}

Monte Carlo stochastic simulations of treatment coverage were performed over a range of target lengths and aspect ratios, treatment region radii, and levels of needle placement standard deviation. Realistic ranges of each of these parameters were chosen based on evidence found in the clinical literature, and that from an ongoing Phase I/II trial studying FLA of prostate cancer (ClinicalTrials.gov ID: NCT01094665).\textsuperscript{9} The ranges of the parameters are summarized in Table II and the choice of each range is justified in Secs. 2.C.1 and 2.C.2.

\begin{table}[h]
\centering
\begin{tabular}{lll}
\hline
Parameter & Range & Units \\
\hline
Target aspect ratio (AR) & 1–2.5 &  \\
Target length (L) & 5–30 & mm \\
Ablation diameter (D\textsubscript{abl}) & 10–20 & mm \\
$\sigma$ & 1–4 & mm \\
\hline
\end{tabular}
\caption{Ranges of the parameters varied for simulations of the fraction of target treated.}
\end{table}
2.C.1. Treatment target shapes

A realistic range of focal target shapes was estimated using data from an ongoing phase I/II clinical trial investigating the use of FLA in men with localized prostate cancer. A total of 47 target contours were considered. Each contour was defined by an expert radiologist (either M.A.H. or S.G.) on preoperative multiparametric MR images using T2-weighted, dynamic contrast-enhanced, and diffusion-weighted MR sequences. Each 3D target volume was projected onto a plane along the needle insertion direction (approximated as the superior-inferior direction since needles are delivered transperineally) and an ellipse of minimum area was found for each. Histograms of the widths and aspect ratios of the fitted ellipses for the 47 targets considered are shown in Fig. 7. Six examples of projected target volumes (generated from the set of 47 expertly delineated targets described above) and their corresponding elliptical representations are shown in Fig. 8.

Based on the data shown in Fig. 7, a range of target aspect ratios of 1–2.5, and a range of target lengths of 5–30 mm were chosen for the simulations.

2.C.2. Ablation sizes

FLA, using a single 980 nm laser fiber, is capable of producing volumes of ablated tissue up to 50 mm in diameter (in a plane perpendicular to the laser fiber) using a bare fiber, and up to 80 mm in diameter when a cooling sheath is used. The cooling sheath consists of concentric tubes of recirculating fluid (saline) surrounding the laser fiber, and prevents the formation of carbonized tissue near the fiber, allowing the light to penetrate further into the tissue. However, due to the small size of the prostate gland, the range of ablation diameters practically used ranges from ~10 to 20 mm; thus this was the range considered in this paper.
3. RESULTS

3.A. Idealized treatment simulations

Figure 9 shows the estimated probability of achieving complete target coverage ($P_{100}$) over the range of parameters described in Sec. 2.C. Figure 9 illustrates the sensitivity of $P_{100}$ to the standard deviation of needle placement error under various conditions. When the target length is small relative to the ablation diameter, $P_{100}$ is largely insensitive to $\sigma$. Specifically, if the ablation diameter is at least 5 mm larger than the target length, nearly all cases achieve $P_{100} \geq 0.9$ using four laser fibers or less if $\sigma \leq 3$ mm. However, as the target length approaches the ablation diameter, $P_{100}$ decreases abruptly, and becomes considerably more sensitive to $\sigma$ and the number of laser fibers used. The effect of increasing aspect ratio (i.e., a narrower target) is to increase $P_{100}$, but this effect is only appreciable for targets that are larger in length than the ablation diameter. The sensitivity of $P_{100}$ to $\sigma$ is also noted to be higher when a small number of fibers are used (i.e., <4). This observation is intuitive, since an increase in the number of fibers increases treatment overlap between individual ablations, so that a portion of target tissue missed by one fiber is likely to be ablated by an adjacent one. As well, in the limits of treatability with eight fibers or less (targets with large length), the limiting factor is the uncertainty in needle placement error. It appears that $\sigma$ of 1 mm vs 2 mm would allow the size of targets that one could confidently ablate to substantially increase.
Fig. 9. (Continued.)
While Fig. 9 is useful for studying the trends in \( P_{100} \) as the various target and treatment parameters vary, it is difficult to interpolate between graphs for a particular case. A useful tool for determining eligibility for FLA is Table III, which shows the maximum target length allowable to maintain \( P_{100} \geq 0.9 \).

The maximum number of fibers used is assumed to be constrained by a limit on the total treatment time and allowable tissue damage due to needle insertions. Ablation diameter is based on the power of the laser used and laser application time, and other considerations such as proximity to critical structures. The level of needle placement uncertainty varies based on the system used to guide needles, the type of needles used, and the modality used for image guidance, among other factors.

In planning FLA for a particular clinical case, one would proceed as follows:

1. Estimate: the target’s length (major axis) and aspect ratio (length/width) as seen from the needle’s eye view, the diameter of ablation region achievable, and the level of uncertainty in needle placement.
2. Using Table III, find the minimum required number of laser fibers.
3. Using Table I, find the corresponding pattern of laser fibers.

4. DISCUSSION

We have developed a simplified method for estimating the fraction of focal target volume treated in prostate focal laser ablation when uncertainty in needle placement is expected. The method involves a 2D idealization of both focal target and ablation region shapes, and a Monte Carlo stochastic simulation of needle placement error to predict the probability of achieving complete target coverage. The result is a set of graphs and tables that can be easily referred to in the preoperative planning process for estimating the number of laser fibers required to completely ablate a given target. These results may also be used to determine a patient’s eligibility for prostate FLA, since it may not be possible to achieve a high probability of full coverage with a reasonable number of laser fibers. The results also quantify the potential clinical benefit of systems that can place needles in the prostate with high precision in the context of prostate focal laser ablation.

While these results provide a simple method of estimating the level of planning required for prostate FLA, there are several important clinical details that must be considered when interpreting them. The simulations do not consider the fact that the treatment outcome can potentially be predicted as treatment progresses (i.e., by measuring the locations of needles already inserted using imaging and/or monitoring tissue temperature using MR thermometry), and dynamically augmented by performing more ablations than planned. For this reason, the results are conservative, in that they attempt to predict the probability of treating the entire target in the absence of any dynamic plan augmentation (i.e., dynamic replanning). However, there are reasons why dynamic plan augmentation may not be reliably effective. Among them is the fact that image registration error may not be entirely detectable. In this case, while the needle placement error relative to the intra-treatment prostate image may be measurable, there will likely remain some uncertainty in the true location of the target volume that was delineated on pre-treatment imaging. Another reason is a desire to attain consistent and predictable treatment times, and levels of treatment-related side effects. A plan that is not optimized considering uncertainties in needle placement may result in several nonconfluent regions of target tissue left untreated. In this situation, the number of additional needles required to fully treat the target may result in a substantial (unplanned) increase in procedure time and an unnecessary increase in damage to healthy tissue from excessive needle insertions. Another potential deviation from the assumptions made in this work is variation in ablation diameter between laser applications, which may depend on: variations in performance of the equipment used, inhomogeneity of tissue optical and thermal properties, and the amount of local perfusion. To illustrate this effect, Fig. 10 shows two post-treatment DCE MRI scans acquired immediately after FLA treatments in two separate patients. It should also be noted that the non-perfused volume seen on post-treatment DCE MR imaging may not exactly represent the true volume of definite tissue necrosis.

Ideally, a map of tissue properties and perfusion rate would be used as inputs to a numerical simulation that could predict the volume of ablated tissue at each planned laser fiber location. The planned placement of each laser fiber could then be adjusted, and the damage volume recomputed until the plan was deemed optimal. Such an approach has been taken for planning rf ablation. However, this approach requires knowledge of the level of perfusion and thermal properties of prostatic and surrounding tissue, and an accurate method of determining patient-specific maps of these properties is not currently available. In addition, uncertainty in the values of these properties between the pre- and intra-treatment times is expected, and their effect on the probability of achieving a complete ablation could only be accounted for if statistical models of their uncertainty were available. In the absence of this information, this work aims to develop approximate guidelines for planning the number of laser fibers required for confidently ablating prostate focal targets, and corresponding target size limits to improve selection criteria for ongoing clinical trials.

Another important consideration is the potential for damaging surrounding critical structures (i.e., rectal wall, urethra, neurovascular bundles, or urethral sphincters). Increasing the ablation diameter by increasing the laser power or ablation time will always improve the predicted fraction of target treated, but may increase the level of treatment-related morbidity. Such considerations must be made on a case-by-case basis, since the idealized target representation used in this work ignores the target location and orientation relative to the rest of the prostate gland. If the geometry of the critical structure in question was known relative to the target,
TABLE III. Maximum allowable target length (in mm) to maintain a minimum probability of complete target ablation (P100) of at least 90%.

| No. of laser fibers | Target aspect ratio = 1 | Target aspect ratio = 1.5 | Target aspect ratio = 2 | Target aspect ratio = 2.5 |
|---------------------|-------------------------|---------------------------|-------------------------|--------------------------|
|                     | D\(_{\text{treat}}\) = 10 mm | D\(_{\text{treat}}\) = 15 mm | D\(_{\text{treat}}\) = 20 mm | D\(_{\text{treat}}\) = 10 mm | D\(_{\text{treat}}\) = 15 mm | D\(_{\text{treat}}\) = 20 mm | D\(_{\text{treat}}\) = 10 mm | D\(_{\text{treat}}\) = 15 mm | D\(_{\text{treat}}\) = 20 mm |
| σ (mm)              | 2 <5                     | 2 <5                      | 2 <5                     | 2 <5                     | 2 <5                      | 2 <5                      | 2 <5                     | 2 <5                      | 2 <5                      |
|                     | 3 <5                     | 3 <5                      | 3 <5                     | 3 <5                     | 3 <5                      | 3 <5                      | 3 <5                     | 3 <5                      | 3 <5                      |
|                     | 4 <5                     | 4 <5                      | 4 <5                     | 4 <5                     | 4 <5                      | 4 <5                      | 4 <5                     | 4 <5                      | 4 <5                      |

the techniques used in this work could be applied to estimate the probability of damaging that structure (due to inaccurate needle placement). However, unless a biological heat transfer model was employed, this estimate is not expected to be accurate, since the thermal properties and rates of perfusion in the neurovascular bundles, and rectal and urethral mucosae are expected to differ from that of prostate tissue. In addition, the thermal dose required to damage such structures differs from that of prostate tissue. For these reasons, such results were not included.

FIG. 10. Immediate post-treatment axial dynamic contrast-enhanced MR images showing variation in ablation region symmetry: (a) more tissues were ablated medial to the laser fiber than lateral and (b) the region of ablated tissue was much more axisymmetric about the laser fiber axis.
Finally, the selection of the minimum desired value of $P_{100}$ is contentious and depends on the cost of performing a repeat treatment, among other factors. If retreatment can be performed safely and quickly, then a lower $P_{100}$ (higher rate of retreatment) may be acceptable.

5. CONCLUSIONS

Focal laser ablation of prostate cancer is receiving increased attention, as it has shown potential for ablating focal target regions within the prostate with a low rate of treatment-related morbidity. However, the effects of needle placement error on focal target treatment coverage have been suspected to be substantial, and the literature indicates a general consensus regarding the need for planning methods for prostate FLA. In this work, we used a simplified model of the focal target and ablation region shapes, and Monte Carlo stochastic simulations to quantify the effect of needle placement error on the probability of achieving complete target ablation. It was found that the predicted probability of completely ablating a focal target is sensitive to needle placement uncertainty, especially when the target width is large relative to the ablation size. The results of this work will be useful in planning prostate FLA, and quantify the potential clinical benefit of advanced systems for accurate needle delivery, several of which are currently under development.49–52

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