Published in final edited form as:

Proc SPIE Int Soc Opt Eng. 2017 January 28; 10066: . doi:10.1117/12.2257151.

A Computerized Tutor Prototype for Prostate Cryotherapy: Key Building Blocks and System Evaluation

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Abstract

This paper focuses on the evaluation of a prototype for a computer-based tutoring system for prostate cryosurgery, while reviewing its key building blocks and their benchmark performance. The tutoring system lists geometrical constraints of cryoprobe placement, displays a rendered shape of the prostate, simulates cryoprobe insertion, enables distance measurements, simulates the corresponding thermal history, and evaluates the mismatch between the target region shape and a pre-selected planning isotherm. The quality of trainee planning is measured in comparison with a computer-generated plan, created for each case study by a previously developed planning algorithm, known as bubble-packing. While the tutoring level in this study aims only at geometrical constraints on cryoprobe placement and the resulting thermal history, it creates a unique opportunity to gain insight into the process outside of the operation room. System validation of the tutor has been performed by collecting training data from surgical residents, having no prior experience or advanced knowledge of cryotherapy. Furthermore, the system has been evaluated by graduate engineering students having no formal education in medicine. In terms of match between a planning isotherm and the target region shape, results demonstrate medical residents' performance improved from 4.4% in a pretest to 37.8% in a posttest over a course of 50 minutes of training (within 10% margins from a computer-optimized plan). Comparing those results with the performance of engineering students indicates similar results, suggesting that planning of the cryoprobe layout essentially revolves around geometric considerations.

Keywords

Cryosurgery; Prostate; Simulation; Optimization; Planning; Training; Evaluation

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1. INTRODUCTION

Prostate cancer is the second leading cause of cancer death in men according to the American Cancer Society ¹. In 2016, it is estimated that over 180,000 new prostate cancer cases will be diagnosed and over 26,000 men will die of this disease. About 1 in 7 men will be diagnosed with prostate cancer during his lifetime and about 1 in 39 men will die as a result of it. More than 2.9 million men in the United States who have been diagnosed with prostate cancer at some point are still alive today. Prostate cancer can be a serious disease with broad implications on the quality and cost of healthcare.

Prostate cryosurgery is a minimally invasive procedure that is designed to destroy the prostate tissue by freezing. In broad terms, ice crystallization triggers a sequence of events, causing injury to the tissue and eventually leading to cell death ². Minimally invasive cryosurgery is performed by strategically placing an array of cooling probes (also known as *cryoprobes*) within a target region. Each cryoprobe is similar to a long hypodermic needle, with a cylindrical active cooling surface extending from its sharp-pointed tip. The target region in prostate cryosurgery may be the entire gland or a portion of it ³. Prostate cryosurgery is performed under image guidance, most frequently with the use of a transrectal ultrasound transducer (TRUST). Once placed in the tissue to be treated, the thermal history of the cryoprobes is controlled to match the cryo-injured volume with the shape of the target region. Up to 14 cryoprobes are frequently operated in concert in order to achieve the required frozen region shape in the case of prostate treatment.

In order to maximize freezing damage to the target region while minimizing freezing injury to its surrounding tissues, the cryoprocure must be carefully planned ³, where the key parameters are the number of cryoprobes, their layout, and the thermal history at the active surface of each cryoprobe. An ideal cryoprobe plan involves the creation of a three-dimensional (3D) thermal field such that a pre-selected isotherm (i.e., the planning isotherm) matches perfectly to the contour of the target region. The planning isotherm may be: (a) the temperature at the onset of freezing, which is closely related to the visualized frozen region by means of medical imaging; (b) the lethal temperature—a temperature threshold below which maximum destruction is assumed; or, (c) a clinically relevant temperature, selected based on the surgeon's own preference ^{4,5}.

The continuous trend of development in computer hardware and information technology has motivated researchers to develop computerized means in effort to improve, optimize, and guide the cryoprocure. The majority of those efforts have focused on computation methods to plan the cryoprobe layout ^{6,7,8–12}, while more sporadic efforts addressed simulation of TRUST guidance ¹³, prostate model reconstruction ^{14,15}, and acceleration of bioheat transfer simulations ^{16,17}. Unfortunately, since prostate cryosurgery is yet to be standardized, the computational means are yet to be reduced to practice. With the currently limited means to determine the optimal cryoprobe layout and the ideal scheme to orchestrate the operation of cryoprobes, undesired cryosurgery outcomes may occur. These may include untreated cancerous tissue within the target region, injury to healthy surrounding tissues, operating an inadequate number of cryoprobes, increased duration of the surgical procedure,

and increased likelihood of post-cryosurgery complications, all of which affecting the quality and cost of the medical treatment^{9,18,19}.

The concept of *defect region* has been developed by our research team in order to evaluate the quality of a given cryosurgery plan¹⁰. In broad terms, the defect region is an all-inclusive term including areas external to the target region that experiences cryoinjury and areas internal to the target region which are left with insufficient freezing damage. In practice, the defect region is quantified as a weighted distance between the target region shape and the curved surface defined by the planning isotherm. It is not just that the overall defect is of significance as a global quantity, but its distribution is equally important when trying to preserve critical tissues, such as the urethra and the nerve bundles.

While the overall defect in a procedure may be minimized by trial and error, possibly benefiting from clinical experience and common practices, computation tools appear to be the obvious choice to solve the defect-minimization problem. Furthermore, computational means can provide a virtual setup for computerized training, in efforts to shorten the learning curve and improve the outcome of the procedure. With this motivation in mind, the current presentation reviews a recently developed prototype for computerized training of cryosurgery^{5,20}, based on specialized computation tools for planning^{3,8–10,21,22}. This presentation reviews recent evaluation results of the computerized trainer by surgical residents^{5,20}, compares the results with a similar evaluation by engineering students with no medical background²³, and places the results in the context of geometric complexity for planning of the target region²⁴.

2. MATHEMATICAL MODEL

Computerized planning is based on two key building blocks: a bioheat transfer simulator and a cryoprobe layout planner. Both computation building blocks have been developed^{9,25,26}, verified experimentally in prior studies^{27,28}, tested for training purposes^{5,18}, and are described here in brief for the completeness of the presentation. In particular, the cryoprobe planner uses the bubble-packing method^{8,25}, which has been proven robust, characterized by a very short runtime and requires only a single bioheat transfer simulation at the final stage of planning¹⁷. The computation framework used in the current study is identical to the system developed for computerized training^{5,20,17,26}.

Bioheat Transfer Model

The bioheat transfer simulator is based on the classic bioheat equation²⁹:

$$C \frac{\partial T}{\partial t} = \nabla \cdot (k \nabla T) + w_b C_b (T_b - T) = q_{met} \quad (1)$$

where C is the volumetric specific heat of the tissue, T is the temperature, t is the time, k is the thermal conductivity of the tissue, w_b is the blood perfusion volumetric flow rate per unit volume of tissue, C_b is the volumetric specific heat of the blood, T_b is the blood temperature entering the thermally treated area, and q_{met} is the metabolic heat generation. Discussion

about the applicability of this equation to cryosurgery simulations of the prostate has been provided previously^{9,26}.

Cryosurgery Planning Objective Function

As highlighted in the introduction, the defect region concept is used in the current study as a measure of the mismatch between the shape of the target region and a planning isotherm¹⁰:

$$d = \frac{1}{V_t} \int_{V_s} u \, dV_s; \quad u = \begin{cases} 1 & T_p < T \\ 0 & T \leq T_p \end{cases} \quad \text{Interior to the target region}$$

$$u = \begin{cases} 1 & T \leq T_p \\ 0 & T_p < T \end{cases} \quad \text{Exterior to the target region} \quad (2)$$

where V_t is the volume of the target region, V_s is the volume of the simulated domain, u is a weight function, and T_p is the temperature of the planning isotherm. In the absence of specific requirements, a binary value is selected for the weight function in Eq. (2), while a higher weight may be assigned to critical areas to be treated, based on the cryosurgeon's decision.

The entire target region is unfrozen at the beginning of a cryosurgery simulation and the defect is internal in its entirety, which defines its initial value (i.e., $d(t=0)=1$). As the freezing process progresses, the frozen region grows and the defect value decreases accordingly. Freezing may exceed the boundaries of the prostate at an advanced stage of the process, giving rise to the development of external defect regions. With a sufficient number of cryoprobes and time, the defect will continue to grow externally, up to limits dictated by the cooling power of the cryoprobes. There is a point of minimum defect in each simulated cryoprocure, where the rate of decrease of internal defect is equal to the rate of increase of external defect. It is the instant of minimum defect rate that defines the termination point for the bioheat transfer simulation, and the defect value at this instant is taken as a quality measure of the specific cryoprobe layout for the specific prostate geometry. Comparing minimum defect values from different cryoprobe layouts on the same geometry and under identical conditions are ranked-ordered for comparative evaluation. The defect with the smallest value from all simulations on the same prostate model is considered the global minimum and the corresponding layout is considered the computer-recommended layout out of those tested.

Cryoprobe Layout Optimization

The minimization of the planning objective function is achieved with the application of the bubble-packing method^{8,22}. This is a physically based method that efficiently finds an even distribution of an arbitrary number of objects inside a domain—the active surface of the cryoprobes within the prostate in this study. First, bubbles are seeded in the domain, at a number equal to the cryoprobes of interest. Next, van der Waals-like forces virtually attract and repel bubbles, until force equilibrium configuration is reached. At this point, the active surface of the cryoprobes are placed at the center of each bubble, and the resulted cryoprobe layout is considered the computer-recommended layout for computerized training. The

bubble-packing method has been shown robust and faster by orders of magnitude than the following bioheat transfer simulation. Hence, computer runtime benchmarking focuses on bioheat transfer considerations.

3. COMPUTER RUN TIME BENCHMARKING

Significant efforts have been devoted to develop an efficient numerical scheme for bioheat transfer¹², specialized for parallel computation¹⁶, in order to minimize the cryosurgery simulation runtime. It has been demonstrated that a tailored software must be developed in order to achieve a clinically relevant runtime of under 2 sec¹⁷.

Table 1 displays benchmarking results for bioheat transfer simulations of prostate cryosurgery, using 14 cryoprobes at an optimized layout with the application of single insertion depth, on four typical machines. These results were obtained on a 35 *ml*/prostate model, typical to cryosurgery candidates, which was reconstructed from 3D ultrasound data³⁰. Beyond the clinical advantages of an optimized cryoprobe layout, its implication on computer simulations is a shorter simulated time. For example, a simulated procedure of only 201 s was found using an optimal cryoprobe layout for the case studied above, when all cryoprobes are operated simultaneously¹⁷.

Benchmark results from four computers of a similar age are listed in Table 1, representative of a laptop computer, a home PC, a gaming PC, and a personal workstation. The superiority of the graphical processing unit (GPU) over the central processing unit (CPU) is evident from Table 1, regardless of the platform used. The strongest GPU tested, resulted in computation runtime faster by two orders of magnitude than the simulated cryosurgery, for a numerical grid of 80,000 nodes¹⁷. This means that, within a couple of seconds the clinician may get a prediction of the shape of the frozen region for a particular cryoprobe layout and geometry. This also means that a sequence of what-if scenarios can be executed during an educational session, at a fast enough pace such that the trainee will not lose focus on the progression of training.

Comparing up-to-date computation platforms with the hardware referenced in Table 1 reveals that the CPU computation power has doubled, the GPU computation power has increased five-fold, and the number of GPU computation cores has increased seven-fold. While the runtime of CPU-based bioheat simulations is by and large linear with the number of CPU cores, the runtime of GPU-based simulation may show a more complex relationship. In broad terms, the increased GPU computation cores facilitates not only parallel computation for a single bioheat simulation, but also the simultaneous simulation of a batch of cases, which can be a powerful feature for training applications. While specific runtime for specific cases and hardware may vary, a general conclusion emerges, that future computation efforts should now focus on training means and methodologies rather than on new numerical schemes of possibly over-simplified bioheat models.

4. A COMPUTERIZED TRAINING PROTOTYPE

The Trainer is designed to create a cryosurgery education environment by means of virtual case practices. With reference to Fig. 1, the Trainer architecture integrates four key

modules ⁵: (i) a Layout Planner, to generate a computer-optimized, target cryoprobe layout for training; (ii) a Cryosurgery Simulator, to simulate the bioheat transfer process in the prostate during cryosurgery; (iii) a Tutor, to guide the trainee through the process of cryosurgery planning, monitoring, and to provide real-time training performance evaluation; and (iv) a Database, containing geometric models of organs to be treated, computer-generated optimized plans, trainee performance, and all trainee keystrokes from the session for further evaluation of training patterns.

This study focuses on the design of a 3D cryoprobe layout based on two key features: (i) commonly practiced geometric constraints for cryoprobe placement, and (ii) the defect size ^{5,20}. These constraints include a minimum distance of 3 mm between a cryoprobe and the prostate capsule and/or the urethra, and a variable insertion depth strategy for the cryoprobes ²⁰. Here, a computer-generated, defect-minimized cryoprobe layout is taken as the training target. Ultimate training success is considered when the trainee can place a pre-selected number of cryoprobes in the target region without violating geometric constraints, while meeting or outperforming the defect value suggested by the planner.

Tutor feedback is provided in the form of violations on cryoprobe placement, by displaying the simulated cryosurgery outcome for the trainee-planned cryoprobe layout, along with the computer generated optimum cryoprobe layout. While the Trainer can simulate any cryosurgery hardware and target-region shape, the current system development focuses on Joule-Thomson cooling, prostate shape, and common limitations in cryoprobe placement during prostate cryosurgery. The tutor encompasses graphical means and numerical data to present the trainee with a planning case and the corresponding trainee layout evaluation ^{5,20}. A tutor screenshot is displayed for example in Fig. 2.

5. TRAINING EVALUATION

Two evaluation studies have been performed for the tutor prototype; the first testing an intelligent approach to computer tutoring ⁵, while the second is primarily based on student exposure time ²⁰. Statistical comparison of differences between those two studies suggested that the training time is a key factor, while attempts to accelerate tutoring by intelligent means yielded little to no differences. Another design difference between the two studies was in the cryoprobes placement strategy, in either a single insertion depth ⁵ or a variable insertion depth ²⁰. It was found that a variable insertion depth is easier to plan. Defect results from the latter study ²⁰ are displayed in Fig. 3, comparing the ability to plan a cryoprobe layout before and after a 50 minutes session of an unstructured training.

A third study is currently underway, which replicates the training strategy presented in the second study ²⁰ using graduate mechanical engineering students with no formal education in medicine as trainees, instead of surgical residents. Table 2 displays preliminary results of the mean trainee performance based on defect obtained in each group after following the exact same training scheme, using the same prostate models and surgical constraints. Using student t-test analysis, it appears that the results from both groups belong to the same population. This result supports the notion that cryoprobe layout planning may not benefit from medical background, but mostly from computer training exposure time. Of course, this

discussion does not suggest that medical background is not unnecessary for a comprehensive cryosurgery training and education.

A fourth ongoing study is currently underway ²⁴ to test the relationship between geometric complexity and the level of training difficulty. Preliminary results of this study suggest that cryosurgery planning is easier to perform on a symmetric prostate. Additionally, this study suggests that the planning difficulty further decreases the closer the prostate model resembles a sphere.

6. CONCLUSIONS

This paper reviews the key building blocks of a software prototype developed for the application of computerized training of prostate cryosurgery. Benchmark performance evaluation indicates that a heat transfer simulation of a prostate cryoprocure can be performed in a few seconds on over 6 years old machines. Using a proprietary algorithm called bubble packing, cryoprobe layout planning is performed in an insignificantly short period of time compared with the corresponding bioheat transfer simulation. This runtime scale suggests that computerized planning is a viable application for medical training and for clinical practice. It is suggested that the use of GPU as a computation platform can facilitate simultaneous solution of an array of closely related problems. This feature can enhance the training experience, while exploring “what-if” scenarios in effort to optimize cryosurgery planning.

In terms of match between a planning isotherm and the target region shape to be cryotreated, results demonstrate improvement of medical residents’ performance from 4.4% in a pretest to 37.8% in a posttest over a course of 50 minutes of training when 10% margins in the defect is allowed from the computer-optimized plan. Comparing those results with the performance of engineering students indicates similar results, suggesting that planning of the cryoprobe layout essentially revolves around geometric considerations.

While this paper focuses on prostate cryosurgery, many of the presented computation tools and mathematical models are translational to other multifocal therapies such as brachytherapy, high frequency ultrasound (HIFU), interstitial photodynamic therapy (I-PDT), radio frequency (RF) ablation, irreversible electroporation (IRE), and thermal ablation using nanoparticles.

Acknowledgments

This study has been supported in parts by Award Number R01CA134261 from the National Cancer Institute. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Cancer Institute or the National Institutes of Health.

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Figure 1. Cryosurgery Trainer architecture, including the cryosurgery computational tools (CCT) developed

Figure 2.

A screenshot of the Trainer prototype taken during a training session, where the following labels have been added to point to the (a) reconstructed prostate model, including the cryoprobes and the urethra; (b.1)-(b.3) orthogonal side views of the prostate contour with the application of a distance-measuring tool, as could be performed during ultrasound imaging; and (c) a snapshot from a computer-generated movie of the resulted temperature field at the end of simulation. The goal defect results defined by the cryosurgery planner and the trainee's layout defect are displayed on the top-right.

Figure 3.

Comparison of pretest versus posttest results performed by 15 medical residents, based on defect ratio calculations. Green symbols represent an improvement in terms of constraint violations from pretest to posttest, while red symbols represent no improvement. Actual symbols correspond to improvement categories, while “n” indicate that any number of probe constraint violations have been recorded, ranging between 1 and 10 in this study. The area under the dashed horizontal line represent posttest goal, while any symbol below the diagonal line represent an improvement between the pretest to the posttest in terms of defect calculations²⁰. (Reproduced with permission from the Journal of Technology in Cancer Research and Treatment)

Computer run time benchmarking results for a cryosurgery simulation on a 35 ml prostate using 14 cryoprobes in a single insertion depth and optimized layout. Data compiled from 16 and 17.

Table 1

		Laptop	Home PC	Gaming PC	Workstation
CPU	Type	Intel Core i7 M620	Intel Core i7 950	Intel Core i7 960	Intel Core i7 870
	Memory	4 GB DDR2	9 GB DDR3	9 GB DDR3	8 GB DDR3
	Cores/Threads	2/4	4/8	4/8	4/8
	Model *	1/2010	6/2009	10/2009	9/2009
GPU	Type	AMD Mobility Radeon HD 5450	AMD HD Radeon 5570	Nvidia GeForce GTX 580	Nvidia Quadro 600
	Memory	512 MB Dedicated 2202 MB Total DDR3	1 GB DDR3	1.5 GB GDDR5	1GB DDR3
	Cores	80	400	512	96
	Model *	1/2010	2/2010	11/2010	12/2010
AccelerationRatio	CPU	× 3.6	× 6.1	× 6.5	× 6.8
	GPU	× 10.7	× 31.4	× 31.4	× 91.4
5 min Simulation Runtime	CPU	55.8 sec	33.0 sec	30.9 sec	29.6 sec
	GPU	18.8 sec	6.4 sec	6.4 sec	2.2 sec

* Refers to the release date of the particular model

Table 2

Training performance results (95% confidence interval) comparison between medical residents and engineering students (n=15 for surgical Residents, n=20 for engineering students).

Defect ratio of trainee planning to computer planning	Surgical Residents		Engineering Students	
	Mean Pretest Performance	Mean Posttest Performance	Mean Pretest Performance	Mean Posttest Performance
1.0	2.2% (4.4%)	15.6% (8.7%)	1.7% (2.9%)	6.7% (3.3%)
1.1	4.4% (8.7%)	37.8% (21.8%)	5.0% (3.26%)	35.5% (20.4%)
1.2	20.0% (24.3%)	64.4% (11.5%)	21.7% (11.8%)	60.0% (19.6%)