

Intelligent Planning for Cryoprobe Placement during Cryosurgery

Seyed Hadi Deljou¹, Siamak Haghypour², Amrollah Bayat³

¹ Department of Mechatronics Engineering, Tabriz Branch, Islamic Azad University, Tabriz, Iran

² Department of Biomedical Engineering, Tabriz Branch, Islamic Azad University, Tabriz, Iran

³ Faculty of surgery, Tabriz University of Medical Science, Tabriz, Iran

Abstract: Cryosurgery is a surgical technique with minimal invasion which employs extreme cold to destroy diseased or abnormal tissues. As a part of ongoing efforts to develop computerized planning tools for cryosurgery, this study focuses on 2D modeling tissue, modeling heat transfer in tissue, modeling cryosurgery based on partial differential equations. The goal of this research is maximizing the destruction of diseased tissue and also minimizing the injury to surrounding healthy tissue. For optimizing the result of surgery, we have used an array of cryoprobes in accordance with the geometrical shape of tumor and have designed the best cryoprobe layout planning by using Genetic Algorithm. In this condition we have optimized the destruction of diseased tissue and the destruction of surrounding healthy tissue; finally by having enough knowledge about result of surgery and in fact predicting the result of surgery, we are ready to have a robotic surgery with high accuracy.

[Hadi Deljou S, Haghypour S, Bayat A. **Intelligent Planning for Cryoprobe Placement during Cryosurgery.** *Life Sci J* 2013;10(3s):552-557] (ISSN:1097-8135). <http://www.lifesciencesite.com>. 87

Keywords: Cryosurgery, Cryoprobe, Genetic Algorithm, Heat transfer simulation, Tumor

1. Introduction

Cancer is defined as a disease which can be triggered and influenced by a wide range of factors such as viruses, genes, and chemical and physical agents. The factors concerned in a particular tumor may be single or multiple [1]. In 1996 there were 10 million new cancer cases worldwide and six million deaths attributed to cancer. Deaths from cancer worldwide are projected to continue increasing, in 2020 there are predicted to be 20 million new cases and 12 million deaths [2]. Cancer mortality can be reduced if cases were detected and treated early. If cancer not cured early cancerous tissue may become larger or it may cause metastasis.

Cryosurgery is a surgical technique with minimal invasion which employs extreme cold to destroy diseased or abnormal tissues [3]. Modern cryosurgery is frequently performed by means of a number of cryoprobes which are inserted into the target region to be treated [4]. The ancient Egyptians, and later Hippocrates, were aware of the analgesic and anti-inflammatory properties of cold. Over the past 200 years cold treatment has evolved from generalized application such as hydrotherapy to definite local destruction of tissue. James Arnott (1797-1883) was the first scientist who used extreme cold for destruction of breast cancer, uterine cancer, and some skin cancers [5]. Cryosurgery is widely applied in the treatment of various undesired cancerous and non-cancerous tissues in liver, lung, kidney, prostate, brain, skin, breast, bone, etc [6].

Suboptimal cryoprobe localization may leave areas in the target region untreated, may lead to cryoinjury of healthy surrounding tissues, require an

unnecessarily large number of cryoprobes, and increase the duration of the surgical procedure due to suboptimal localization of cryoprobes, all of which affect the quality and cost of the medical treatment. Computerized planning tools would help to alleviate these difficulties [7-11]. Cryosurgeons use image guiding techniques like ultrasound, magnetic resonance imaging (MRI) and electrical impedance tomography (EIT) to guide the cryoprobes to locations in the body that must be treated [12-15].

For having successful cryosurgery, before the surgery it is important to carefully design the optimized freezing parameters like: number of cryoprobes, location for cryoprobe placement, and insertion depth of cryoprobes. Ignoring the above mentioned parameters causes insufficient or additional freezing. As in clinics usually we are encountering with tumors with disordered geometrical shapes, often it is necessary to use multicryoprobes, this causes the difficulty of parameter optimization.

In 2006, Jung developed a computerized treatment planning tool to aid surgeons to determine surgical parameters considering patient specific diagnostic information. In this study integration of these modules which is necessary to predict optimized surgical outcome has not done [16]. In 2007, Rossi et al focused on developing an efficient numerical technique for bioheat transfer simulations. The objective was to develop a finite difference numerical scheme for bioheat transfer simulations, which reduces the overall run time of computerized planning. The problem of this study is that they have not concentrated on maximizing the destruction of

diseased tissue and also they have not focused on making an intelligent system for destroying the diseased tissue although they have reduced the run time for computerized simulations [17]. In 2007, Tanaka focused on an automated computerized technique for cryosurgery planning. The quality of planning for each method was evaluated based on bioheat transfer simulations. Optimum planning leads to cooling of approximately 75% of the prostate volume below a specific temperature threshold. It is expected to fully destruct the tumor tissue which is not achieved in this study [18]. In 2008 Rossi et al focused on experimentally validating a planning scheme based on the so-called bubble-packing method. The main problem of this study is not arguing about the percent of destruction of diseased tissue [19]. In 2011, Giorgi et al presented an application of Ant Colony optimization (ACO) to cryosurgery planning, whereby the ACO cost function is computed by numerically solving several direct Stefan problems for biological tissues. This research has not discussed about the injury to the healthy tissue and also it has not discussed about the percent of tumor tissue destruction [20]. In 2012, Sehrawat et al focused on compiling literature data on the likelihood of cancer tumor growth and its effect on the prostate shape. They have not given us information about the ratio of healthy and tumor tissues destruction [21].

It is obvious that cryosurgery which is done by surgeon's own experience will injure the healthy tissue surrounding the tumor tissue. Mathematical modeling helps to reduce the injury to healthy tissue and also destruct the tumor tissue completely. As prior works show clinical surgery by surgeon's own experience injures the healthy tissues around the tumor so we want to minimize the injury. Mathematical modeling proved that it can be helpful to reduce the destruction of healthy tissue. We have concluded that for optimizing the destruction of healthy tissue and tumor, bioheat transfer equation can be a good selection.

In this research first the 2D simulation of tumor and healthy tissue has done in Matlab software PDE Toolbox. As the goal of this research is to fully destruct the tumor and also minimize the injury of healthy tissue around the tumor, then genetic algorithm is used to make the cryoprobe placement intelligent. Two conditions are considered for not overlapping cryoprobes and also not to have a touch with surrounding healthy tissue.

2. Materials and methods

The goal of this research is to determine the best points to localize the cryoprobes in those points by using bioheat transfer equations. Determining these points will lead to minimized injury to healthy tissue

surrounding the tumor and also maximize the destruction of tumor. In this section bioheat simulation has done by using Pennes classical bioheat equation. With involving physical parameters, heat transfer in tumor and healthy tissues has modeled. Then by the application of genetic algorithm cryoprobe placement has done.

2.1 Bioheat Simulation

The quality of the cryosurgical plan is evaluated from numerical simulations of bioheat transfer. The classical bioheat equation is used to model bioheat transfer in tumor and healthy tissue [22].

$$\rho C \frac{\partial T}{\partial t} = \nabla \cdot (k \nabla T) + \rho_b \dot{w}_b C_b (T_b - T) + \dot{q}_{met} \quad (1)$$

Where ρ is the density of tissue, 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, ρ_b is the density of blood, \dot{w}_b is the blood perfusion rate, C_b is the volumetric specific heat of the blood, and T_b is the blood temperature entering the thermally-treated area (core body temperature) and \dot{q}_{met} is the metabolic heat generation. The metabolic heat generation can be neglected during cryosurgery.

Numerous scientific reports have proved the mathematical consistency and validity of the above classic equation. It is assumed in the current study that a more advanced model of bioheat transfer with greater mathematical complications, does not warrant higher accuracy and also seems to be unnecessary in the current study [23].

2.2 Modeling heat transfer in tumor and healthy tissue

We have supposed a rectangle area for modeling healthy and tumor tissues in Matlab PDE toolbox. For simplicity, rectangle area has chosen. Lethal temperature threshold for destruction of tumor cells is supposed -45°C . Tumor tissue is exposed to -145°C by using cryoprobes. With having these parameters and also solving bioheat transfer equation we can model the heat transfer distribution in healthy and tumor tissue. Also we have modeled the destruction of tumor and the injury to healthy surrounding tissue by using these parameters.

Physical parameters that are used in modeling tumor and healthy tissue are showed in table 1.

2.3 Cryoprobe placement planning

The goal of planning tool is detecting the best location for cryoprobe placement based on bioheat transfer simulation. The optimal arrangement of the cryoprobes, which is known to have a dramatic effect on the quality of the cryo-procedure, is based on the cryosurgeon's experience. This procedure in most of conditions causes the injury to surrounding healthy

tissue. As the objective of this research is to maximize the freezing damage to the target region along with minimizing freezing damage external to the target region, or healthy surrounding tissue, it is necessary to design a preplanning tool for arranging cryoprobes in desired locations.

In order to make computerized planning clinically relevant, it must be done within minutes while the patient is on the operating table, otherwise, orientation of the target region may change, target region may deform, or even change size. Fast numerical techniques for bioheat transfer simulations will always be helpful for cryosurgery planning [25].

Table1. Physical parameters of tumor and healthy tissue [8,24].

Row	Parameters	Healthy Tissue Coeff	Tumor Tissue Coeff
1	$\rho(\text{kg/m}^3)$	1020	1050
2	$C(\text{J/m}^3\text{K})$	3770	3600
3	$k(\text{W/m K})$	0.5	0.5
4	$\dot{q}_{met} (\text{W/m}^3)$	1500	6000
5	$\rho_b \dot{W}_b C_b (\text{k W kg/ m}^6 \text{ K})$	1836000	1890000
6	$T(^{\circ}\text{C})$	37	37

2.4 Optimized search

This research presents a unique computerized planning tool for optimizing cryoprobe placement during cryosurgery. Presented methods in this research are specified to application of minimally invasive cryosurgery in tumor treatment. The most important challenge of this research is automatic planning of surgery while freezing the tumor efficiently, and minimizing the injury to surrounding healthy tissue.

In this section temperatures and coordinates of healthy and tumor tissues are separately extracted by writing program in Matlab software. Then by application of cryoprobes to tumor following relation can be extracted.

1. Number of not destructed points in tumor tissue divided to number of total points in the tumor equals to 't';
2. Number of destructed points in healthy tissue divided to number of total points in the healthy tissue equals to 'h'.

Expecting fully destruction of the tumor, the number of not destructed points divided to the number of total points in the tumor, must be minimum. On the other hand, healthy surrounding tissue must not be injured, so the number of destructed points in healthy tissue divided to number of total points in the healthy tissue must be minimum. In this research for finding extremum points, the

genetic algorithm is used. In this section the goal is minimizing t and h, so the cost function is defined as following:

$$CostFunction = \sqrt{t^2 + h^2} \quad (2)$$

By minimization of h and t, cost function becomes minimum.

At the next step, the study has focused on cryoprobe placement with satisfaction of minimization condition. Cryoprobes must be placed in a way that not only prevent overlapping, but also prevent touching the tumor boundary and entering from tumor boundary towards the healthy tissue, because doubtlessly this will cause injury to surrounding healthy tissue. To consider not overlapping condition in accordance with the following formula, the distance between the centers of two circles must be equal to or bigger than sum of radiuses.

$$d_{i,j} = \sqrt{(x_i - x_j)^2 + (y_i - y_j)^2} - r_i - r_j \geq 0, i \neq j \quad (3)$$

Where (x_i, y_i) are coordinates of ith circle centre, (x_j, y_j) are coordinates of jth circle centre, r_i is the radius of ith circle and r_j is the radius of jth circle.

Circles (cryoprobes) for the reason of not touching with the up, down, left and right boundaries must satisfy following conditions in order to not injure surrounding healthy tissue:

$$d_{i,s1} = x_i - r_i > 0 \quad (4)$$

$$d_{i,s2} = w - y_i - r_i > 0 \quad (5)$$

$$d_{i,s3} = y_i - r_i > 0 \quad (6)$$

$$d_{i,s4} = l - x_i - r_i > 0 \quad (7)$$

$d_{i,s1}$ is distance from left boundary, $d_{i,s2}$ is distance from upper boundary, $d_{i,s3}$ is distance from down boundary, $d_{i,s4}$ is distance from left boundary, w is width of rectangle and l is length of rectangle.

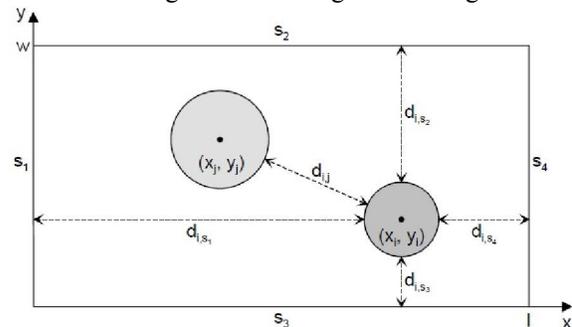


Figure 1. Having distance from surrounding healthy tissue

2.4 Cryoprobe placement in accordance with optimized search

Cryoprobe placement in accordance with optimized search is done with genetic algorithm in five sections. The First section which relates to main program of genetic algorithm, generates random values for x and y in a way that satisfies not overlapping and not touching with tumor boundaries conditions. It must be mentioned that for additional confidence in satisfaction of above conditions in three sections, in selecting random variables, mating, and mutation, these conditions must be checked. Genetic algorithm parameters have chosen as following table.

Table 2. Genetic algorithm parameters

Selection Method	Number of Iterations	Mutation Rate
Rank	100	0.2

In the second section the state of not overlapping is checked. The third section relates to checking the condition of cryoprobes not touching with boundaries. In the section four, separating healthy tissue from tumor tissue is done. The ability of this section is extracting the below factors:

1. Number of points in healthy tissue;
2. Number of points in tumor tissue;
3. Temperature related to the internal section of each tissue and number of not destructed points in tumor divided to total number of points in the tumor;
4. Number of destructed points in healthy tissue divided to total number of points in the healthy tissue with the goal of minimizing cost function.

In the section five, optimal coordinates extracted from main program of genetic algorithm are presented and points in which cryoprobes must be placed are automatically detected.

3. Results

In figure 2, Rectangle 2D area, which represents tumor and healthy tissues have shown. The inner rectangle with red boundaries represents tumor. The outer areas represent healthy tissue. Number of mesh points that has shown in following figure, are used as total numbers in tumor and healthy tissues. These numbers have used in our programs to specify the limitations of tumor and healthy tissues.

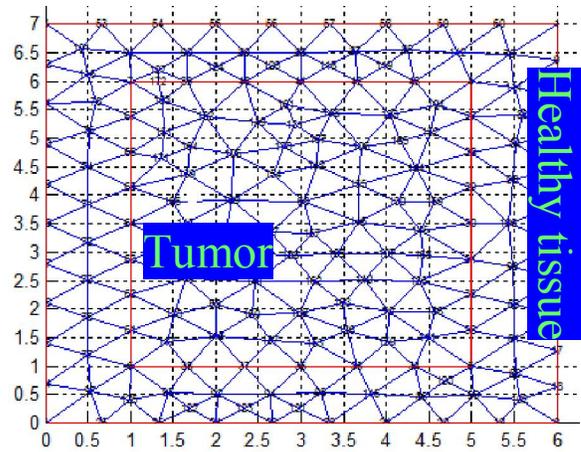


Figure 2. Rectangle 2D area which represents tumor and healthy tissue

By using physical characteristics of tumor and healthy tissue (Table.1) and solving Pennes bioheat equation in Matlab software PDE Toolbox, the simulation of heat transfer in tumor and healthy tissue is done as shown in following figure.

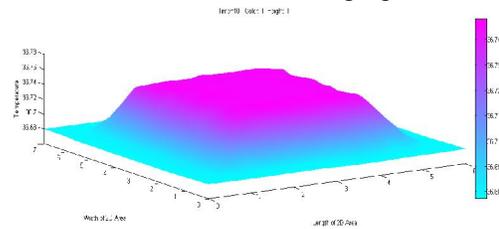


Figure 3. simulation of heat transfer in tumor and healthy tissue

In figure 4 simulation of tumor destruction which has done by using manual placement of cryoprobes is demonstrated. Manual destruction of tumor has done by using 20 cryoprobes.

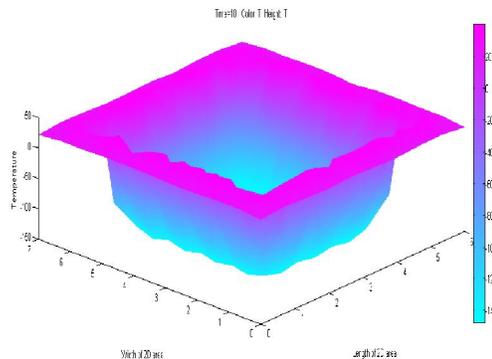


Figure 4. simulation of tumor destruction which has done by using manual placement of cryoprobes

Obviously here, the surrounding healthy tissue was injured. Simulations used in above figure persist

on the necessity of using a mechanism which causes the intelligently selecting cryoprobes due to maximizing the destruction of tumor, while minimizing the injury to surrounding healthy tissue.

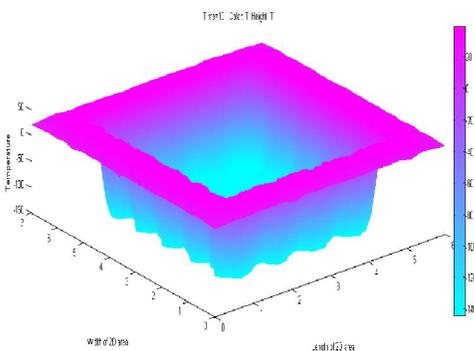


Figure 5. Tumor destruction optimization and reducing injury to surrounding healthy tissue

In output (Figure 5), by using optimized search method more than 95% of tumor has destructed and also the destruction of surrounding healthy tissue is not very significant.

4. Discussion

Cancer is defined as a disease which can be triggered and influenced by a wide range of factors such as viruses, genes, and chemical and physical agents. Cryosurgery is a surgical technique with minimal invasion which employs extreme cold to destroy diseased or abnormal tissues. Cryosurgery is conducted by means of a cryoprobe or multiprobes depending on shape and size of a tumor.

Surgeon's experience is most important factor in cryosurgery which is done clinics. In this condition some parts of diseased region may remain untreated or cryosurgery by the application of cryoprobes may injure healthy tissues around the tumor. It is necessary to find a method to predict the result of surgery when the patient is on the table.

The goal of this research is to maximize the destruction of tumor tissue and also minimizing the injury to surrounding healthy tissue. It is necessary to simulate the process of cryosurgery before doing the real surgery. For this reason we have simulated the tumor and healthy tissue in Matlab PDE toolbox. For simplicity we supposed a 2D rectangle area which represents the tumor in the center, and also represents healthy tissue that surrounds tumor. Then by applying physical parameters mentioned in table 1, the heat transfer in tumor and healthy tissue has modeled. In this study for destructing cancerous cells the tumor tissue has exposed to -145°C by using cryoprobes. Then the points in tumor tissue and healthy tissue have checked to know which points have temperatures below -45°C . The points which

have temperatures below -45°C are dead. This temperature is a criterion to recognize the destructed cells in tumor tissue. Then following factors are extracted with the goal of minimizing cost function:

1. Number of points in healthy tissue;
2. Number of points in tumor tissue;
3. Temperature related to the internal section of each tissue
4. Number of not destructed points in tumor divided to total number of points in the tumor;
5. Number of destructed points in healthy tissue divided to total number of points in the healthy tissue.

Optimal coordinates extracted from main program of genetic algorithm are presented and points in which cryoprobes must be placed are automatically detected. By using the mentioned techniques an array of heat transfer simulations were done. In this study due to geometrical shape of tumor, cryoprobes are located intelligently and automatically.

In figure 2, Rectangle 2D area, which represents tumor and healthy tissues have shown. The inner rectangle with red boundaries represents tumor. The outer areas represent healthy tissue. In figure 4 simulation of tumor destruction which has done by using manual placement of cryoprobes is demonstrated. Manual destruction of tumor has done by using 20 cryoprobes. It is obvious that surrounding healthy tissue has injured. This manual destruction is like the method which is done by surgeon's own experience. In figure 5, by using optimized search method more than 95% of tumor has destructed and also the destruction of surrounding healthy tissue is not very significant. Thus by optimized placement of cryoprobes on the desired places in the tumor location, success rate of surgery significantly increases. For future works we can implement these simulations in circular areas. Then it is possible for us to make 3D simulation of tumor and healthy tissue. Our last goal is making a robot which uses

real images of tumor and healthy tissue to do intelligent cryosurgery.

References

- [1] W. Sodeman and T. Sodeman, *Pathologic Physiology Mechanisms of Disease*, Philadelphia, London, Toronto: W. B. Saunders Company, 1985.
- [2] M. R. Alison, "Nature Publishing Group," 2001. [Online]. Available: <http://www.els.net>.
- [3] I. Lee and A. Cooper, "Cryostatic congelation: a system for producing a limited controlled region of cooling or freezing of biological tissues," *Journal of Nerve Mental Disability*, vol. 133, pp. 259-263, 1961.
- [4] A. Gage, "Cryosurgery in the treatment of cancer," *Surg. Gynecol. Obstet.*, vol. 174, pp. 73-92, 1992.

- [5] S. M. Cooper and R. P. R. Dawber, "The history of cryosurgery," *Journal of the royal society of medicine*, vol. 94, 2001.
- [6] D. Lung, T. Stahovich and Y. Rabin, "Computerized planning for multiprobe cryosurgery using a force-field analogy," *Computer Methods in Biomechanics and Biomedical Engineering*, vol. 7(2), pp. 101-110, 2004.
- [7] Y. Rabin, D. Lung and T. Stahovich, "Computerized planning of cryosurgery using cryoprobes and cryoheaters," *Technology in Cancer Research and Treatment*, vol. 3(3), pp. 227-243, 2004.
- [8] D. Tanaka, K. Shimada and Y. Rabin, "Two-phase Computerized Planning of Cryosurgery Using Bubble packing and Force-field Analogy," *ASME Journal of Biomechanical Engineering*, vol. 128(1), pp. 49-58, 2006.
- [9] T. Stahovich and Y. Rabin, "Cryoheater as a means of cryosurgery control," *Physics in Medicine and Biology*, vol. 48, pp. 619-632, 2003.
- [10] M. Rossi, D. Tanaka, K. Shimada and Y. Rabin, "An efficient numerical technique for bioheat simulations and its application to computerized cryosurgery planning," *Computer Methods and Programs in Biomedicine*, vol. 85, no. 1, pp. 41-50, 2007.
- [11] D. Tanaka, M. Rossi, K. Shimada and Y. Rabin, "Towards intra-operative computerized planning of prostate cryosurgery," *The International Journal of Medical Robotics and Computer Assisted Surgery*, 2007.
- [12] G. Onik, J. Cohen, G. Reyes, B. Rubinsky, Z. Chang and J. Baust, "Transactional ultrasound-guided percutaneous radical cryosurgical ablation of the prostate," *Cancer*, vol. 72(4), pp. 1291-1299, 1993.
- [13] G. Onik, J. Gilbert, W. Hoddick, R. Filly, P. Callen, B. Rubinsky and L. Farrel, "Sonographic monitoring of hepatic cryosurgery in an experimental animal model," *Am. J. of Roentgenol*, vol. 144(5), pp. 1043-1047, 1985.
- [14] B. Rubinsky, J. Gilbert, G. Onik, M. Roos, S. Wong and K. Brennan, "Monitoring cryosurgery in the brain and the prostate with proton NMR," *Cryobiology*, vol. 30, pp. 191-199, 1993.
- [15] T. Schulz, S. Puccini, J. Schneider and T. Kahn, "Interventional and intraoperative MR: review and update of techniques and clinical experience," *Eur. Radiol*, vol. 14(12), pp. 2212-2227, 2004.
- [16] J. JUNG, "COMPUTER-AIDED PATIENT SPECIFIC TREATMENT PLANNING OF CRYOSURGERY FOR BREAST CANCER," in Thesis for getting master of science, 2006.
- [17] M. Rossi, D. Tanaka, K. Shimada and Y. Rabin, "An efficient numerical technique for bioheat simulations and its application to computerized cryosurgery planning," *computer methods and programs in biomedicine*, vol. 85, pp. 41-50, 2007.
- [18] D. Tanaka, "Computational Method for Cryoprobe-Layout Optimization via Finite Sphere Packing," in Thesis for getting degree of PH.D, 2007.
- [19] M. R. Rossi, D. Tanaka, K. Shimada and Y. Rabin, "Computerized planning of cryosurgery using bubble packing: An experimental validation on a phantom material," *International Journal of Heat and Mass Transfer*, vol. 51, pp. 5671-5678, 2008.
- [20] G. Giorgi, L. Avalle, M. Brignone, M. Piana and G. Caviglia, "An optimization approach to multiprobe cryosurgery planning," *Computer Methods in Biomechanics and Biomedical Engineering*, 2011.
- [21] A. Sehrawat, K. Shimada and Y. Rabin, "Generating prostate models by means of geometric deformation with application to computerized training of cryosurgery," *International Journal of Computer Assisted Radiology and Surgery*, 2012.
- [22] H. H. Pennes, "Analysis of tissue and arterial blood temperatures in the resting human forearm," *Journal of Applied Physiology*, vol. 1, pp. 93-122.
- [23] Y. Rabin and A. Shitzer, "A numerical solution of the multidimensional freezing problem during cryosurgery," *ASME Trans J Heat Transf*, vol. 120, pp. 32-37, 1998.
- [24] C. W. Chen, H. S. Kou, H. E. Liu, C. K. Chuang and L. Wang, "Computer Assisted Simulation Model of Renal Tumor Cryosurgery," in *International Conference on Modeling, Simulation & Visualization Methods*, 2008.
- [25] M. R. Rossi, D. Tanaka, K. Shimada and Y. Rabin, "Computerized Planning of Prostate Cryosurgery Using Variable Cryoprobe Insertion Depth," *Cryobiology*, vol. 60, no. 1, pp. 71-79, 2010.

1/8/2013