The summary of "DEVELOPMENT OF A COMPUTATIONAL PARADIGM FOR LASER TREATMENT OF CANCER"

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SUMMARY:

The primary objective of this paper is to deal with the shortcomings in laser treatment of Cancer and hence increasing treatment's success factors by finding the ways to fix them**.** Effective cancer treatment requires complete destruction of the cancerous cell while maintaining the functionality of the infected organ. Traditionally, if cancerous tumors were in well-defined and non-vital organ, treatment was to surgically remove the affected tissue, but the problem was when tumors were very small and spread out in larger area. But now we have laser surgery, which have many advantages over traditional one, i.e., its less invasive, simpler to perform and needs less hospitalization after the treatment. It works by providing lethal dose of heat to small, poorly defined affected area, though taking care that minimum damage is done to the surrounding tissues, especially in case of vital organs, unlike traditional therapy. But avoiding damage to the surrounding areas has not been dealt till now.

The success factor of laser treatment increases with the ability to predict its outcome while the treatment is still in going on. This can be done through high fidelity computers. Though some success have been achieved in predicting the thermal necrosis of cell (death of cell as a result of high temperature) through the knowledge of temperature history versus time. But the problem is when temperature is not sufficient to coagulate the protein. In this case it is very difficult to predict the results. This difficulty is, in part, attributed to the expression of Heat Shock Protein (HSP). These are the family of gene products which are expressed in high concentration under extreme conditions like starvation, high temperature, injury etc. Though HSP's definition gives some negative idea about it but it is very important for cell survival and indicate the likelihood of cell proliferation.

So to tackle these problems we need some specific information like the measure of cell damage as a function of temperature and time for the specific patient. And also we should have the *knowledge of the temperature necessary to elicit the interaction in tumor resistance and cell damage to produce a desired tissue response and surgical outcome* [1]. All these requirements motivated to plan for a DDDAS system. The paper have *described an approach for guiding laser therapy of cancer, particularly prostate cancer, by accurate control and monitoring of the treatment process through computer simulation* [1]. This is possible through the use of data- driven, high fidelity computer simulation models correlated with the HSP expression, in vivo spacio-temporal temperature data, and cell damage data collection to adaptively control the thermo therapy of cancerous tissue. So, this paper mainly focuses on mathematical characterization of HSP expression, mesh generation and bio-heat transfer. As mentioned before HSP expresses more under stress conditions but is essential for cell survival. HSPs are defined according to their molecular weights. Thermal initiation of HSP 27 and 70 is shown to provide cellular resistance to radiation and

chemotherapy. So, its important for balancing out the relationship between tumor resistance and cell damage. For this purpose Rylander developed the model for HSP expression and cell damage based on Arrhenius model for a mouse. Main parameters used in this equation are - concentration of healthy cell before and after heating, activation energy of heating process, and the absolute temperature. The predictions for HSP expression and cell damage is assisted by temperature fields produced by library of bio-heat models. Here, Pennes model is used, which give good results for prostrate cancer. Pennes assumes that blood act as a volumetric heating source. Its space-time variational construct is used for developing the optimal control structure and for computational implementations. Main parameters used in this equation are - specific heat, arterial temperature, linear function of laser power. Now after all the calculations are done, first step for simulation is Mesh Generation. It is used to govern the equations within bio-heat transfer model. Mesh generation involves two steps. First is construction of finite element mesh with the help of MRI data. A hexadecimal mesh is created using semi-automatic segmentation method and then smooth boundaries are obtained by using cubic spline and lofting methods. *Then spatio-temporal temperature distribution is measured during laser treatment with update time less then 5 seconds per image and the thickness between the planes is 2.0 mm* [1]. In next step this measured temperature is accurately overlaid onto the geometry data and then by taking interpolant of the MRTI temperature data nodal temperature values are assigned to the mesh.

ANALYSIS:

This paper provides an intelligent view of how the DDDAS can be applied to control and monitor the laser treatment of cancer. The development process include three stages. First is development of general mathematical and computational model of bio-heat transfer, cell damage and tumor viability. Then is the dynamic calibration, validation and verification by comparing the laboratory and experimental data with the results from the simulations. Then finally based on all these predictions and outcomes, *design an effective thermo-therapeutic protocol. At the core of the proposed systems is the adaptive-feedback control of mathematical and computational models based on a posteriori estimates of errors in key quantities of interest, and modern Magnetic Resonance Temperature Imaging (MRTI) and diode laser devices to monitor treatment of tumors in laboratory animals* [1]. This system will operate over a computational grid connecting a Treatment/ Measurement Arena in Houston at the M.D. Anderson Cancer Center and a Computational/Simulation Arena in Austin at the University of Texas. This model is using few techniques like Grid-computing-enabled dynamic data driven planning and control systems which can give more conformal delivery of heat generated by laser. Supplementing it with the Image guided thermal ablation therapy surgery, that will provide a real time monitoring of the therapy i.e., the temperature and thermal dose feedback during treatment delivery. Also, by including Magnetic Resonance Temperature Imaging (MRTI), in addition to the conformal delivery, effect of heat to the surrounding tissues can be minimized. This innovative, data-driven DDDAS project is designed to select the model automatically on the basis of acceptance criteria provided beforehand.

Though its mentioned in the paper that the simulation model will be dynamic and patient specific but, its not made clear that which part of the model and how will it make patient specific. And also its stated that this project is better for prostate cancer, but its not mentioned that what makes it preferable for prostate cancer rather than other types of cancer.

Recently a new innovation have been done relating to the laser therapy of cancer. *The interaction of laser energy with different absorbing nanoparticles, such as carbon nanotubes, metal nanospheres, nanoshells or others. When nanoparticles are irradiated by short laser pulses they absorb the laser radiation and their temperatures rise very quickly and may reach the threshold of microbubble formation in the surrounding liquid medium. The potential advantage of this effect may include selective cancer-cell targeting by the conjugation of absorbing particles (e.g. Gold nanoparticles) with specific antibodies, localized tumor damage without harmful effects on surrounding healthy tissue, absorption at longer wavelengths in the window of transparency of most biotissues, no undesired side-effects (e.g. cytotoxicity or cutaneous photosensitivity as in photodynamic therapy) and relatively fast treatment involving potentially just one or several laser pulses* [2].

So, the proposed DDDAS should be designed to incorporate these type of latest advancements along with existing ones like Grid enabled computing and mesh generation, to make it more effective.

[1] **Development of a Computational Paradigm for Laser Treatment of Cancer** J.T. Oden, K.R. Diller, C. Bajaj, J.C. Browne, J. Hazle, I. Babuˇska1, J. Bass1, L. Demkowicz, Y. Feng, D. Fuentes, S. Prudhomme, M.N. Rylander, R.J. Stafford, and Y. Zhang

[2]. http://ej.iop.org/links/riCq55MR9/8itxOD1L2xGqHZVuav5vpA/d5_15_007.pdf "Microbubbles-overlapping mode for laser killing of cancer cells with absorbing nanoparticle clusters" V P Zharov, R R Letfullin, and E N Galitovskaya