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13. Abstract ***(Maximum 200 Words)*** *(abstract should contain no proprietary or confidential information)*

We have analyzed the delivery of a novel form of radiation therapy for the treatment of breast cancer: modulated electron beam radiation therapy (MERT). The perturbations introduced by a realistic collimator system have been assessed using Monte Carlo radiation transport simulations. The changes in the electron and photon fluence have been quantified and found to be non-trivial. In particular the electron beam penumbras may be changed by interaction with the electron multileaf collimator, and photon contamination contributes significantly to the total energy fluence. An optimization system for correcting for these perturbations has been developed and reported. We propose a two stage optimization, in which the first stage selects leaf positions, while the second stage sets segment weights. This system satisfies two key requirements: the treatment plan is optimized with the inclusion of knowledge of realistic delivery effects, and the computed fluence is an accurate representation of the delivered fluence. The accuracy of the computed fluence model is necessary for any beam verification system for MERT.

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Beam Delivery Verification for Modulated Electron Radiation Therapy Treatment of Breast Cancer

Michael C. Lee, Ph.D.

Annual Report for DAMD17-01-1-0402

1. Introduction

The primary of this predoctoral fellowship was on beam delivery verification for a new treatment modality: modulated electron beam radiation therapy (MERT). This technique is the extension of the current state of the art, photon intensity modulated radiation therapy (IMRT) to include the use of high energy (6-20 MeV) electron beams. Because electrons dose deposition is limited to shallow depths, it is hoped that MERT will allow treatment of shallow targets while sparing underlying structures. In the context of breast cancer therapy, it is hoped that electron beams can be used to treat the breast, conforming the border of the high dose region to the chest wall while sparing the underlying heart and lung. Both photon IMRT and MERT require the delivery of multiple overlapping fields to create the intensity modulation. In particular, MERT will employ the use of an electron multileaf collimator (EMLC), which will use retractable tungsten bars to shape the electron field. By using this EMLC to create and sequentially delivery fields of multiple shapes, a two-dimensional intensity pattern, or map, can be delivered. The overall goal of this research grant was to develop a system by which the delivered radiation field could be measured and compared with the expected field. This is a critical quality assurance step that would be essential for patient safety during the clinical deployment of MERT. Two key elements are required: the expected beam intensity map, and the delivered intensity map. In this initial phase of the project, we sought to examine the first aspect: the expected beam intensity map.

2. Summary of Research Accomplishments

Treatment planning system

Treatment planning software for MERT was written to generate theoretical intensity maps that would be used in the subsequent analyses. A conjugate gradient optimization process was used to minimize an objective function consisting of dose-volume histogram constraints. This treatment planning system can use Monte Carlo computed doses as input data, and in addition to the electron beam therapy described here, has also been used for research in photon and proton beam therapies. For this research, treatment plans were generated for hypothetical two-dimensional and three-dimensional targets.

Analysis of Fluence Perturbations

The next phase of this project was to assess the perturbations to the desired intensity maps caused by the EMLC. This could not yet be performed experimentally,

since the proposed EMLC had not yet been constructed. Instead, Monte Carlo simulations were performed, explicitly including the proposed EMLC design in the particle transport simulation geometry. It was found that the delivered radiation fluence distribution would differ substantially from the planned distribution. Fully quantifying and understanding this perturbation is essential in order to have meaningful fluence comparisons during beam delivery verification.

By tracking particle interaction sites during Monte Carlo simulations, it was determined that the fluence perturbations consisted of several components. Electrons could be absorbed in the edges and ends of the EMLC leaves. This would reduce the number of particles that actually pass through the collimator, and thus reduce the delivered intensity. Electrons could also scatter off the ends and edges of the leaves. This would result in a blurring of the electron field edges. The photon component was absent during planning, and should also be considered. Electrons incident upon the EMLC leaves could generate bremsstrahlung photons. These photons would increase the particle fluence in the regions that should be blocked, thus causing a non-uniform increase in the background intensity. Additionally photons produced in the treatment head (so-called 'contaminant photons') may pass through the EMLC with only modest attenuation, thus again contributing to the non-uniform increase in the background intensity. This separation into photon and electron components is very important, as the two forms of radiation have different response functions on the film and beam imaging systems that would be used during verification.

In addition to complicating beam verification, this fluence perturbation can lead to significant changes in the delivered doses, with potentially adverse effects on the patient. After investigation of the patterns of these dose perturbations, it was concluded that a second stage optimization would significantly reduce the dose perturbation effect. In particular, the first optimization would generate the appropriate leaf positions, while the second optimization would leave the leaves at these positions but optimize the number of monitor units delivered through each leaf setting. Thus, the leaf effects could be explicitly included in the second optimization. The final calculated dose would then match the delivered dose, and the calculated fluence distribution would match the delivered fluence distribution.

Analytical modeling

An analytical model for the fluence perturbation was also examined. A sigmoidal function was found to adequately describe the penumbra of the electron beams after collimation by the EMLC and transport through air. Appropriate parameters were derived for beams of varying energies and fields of varying sizes (Deng *et al* 2002).

3. Training

In September 2001, the original mentor for this predoctoral fellowship and principal advisor for the principal investigator's thesis, Dr. Chang-Ming Ma, left Stanford University for Fox Chase Cancer Center. This necessitated a change in mentor and advisor. Professor Arthur L. Boyer replaced Dr. Ma in these capacities. Under Professor Boyer's guidance, the principal investigator completed his doctoral thesis project on

Monte Carlo simulations for the development of MERT, and graduated from Stanford University. As of July 2002, the principal investigator concluded his affiliation with Stanford University and this research grant.

4. Key accomplishments

1. Development of a comprehensive treatment planning system for MERT.
2. Quantification of the degree of electron and photon fluence perturbation caused by transport through the EMLC and the collimator to patient air gap.
3. Development of analytical functions to describe the fluence at the position of an imaging screen.

5. Conclusions

As a result of this research, we conclude that intensity perturbations caused by the electron field delivery mechanism are very significant. Any treatment planning system for electron intensity modulated radiation therapy must account for these effects. Additionally, any beam verification system, such as that under investigation in this award, must include these fluence perturbations. We have found that Monte Carlo simulations can properly quantify these effects, and that a two-stage optimization procedure can properly account for these effects in treatment planning.

6. Reportable results

Lee MC (2002). Application of Monte Carlo Simulations to the Development of Energy- and Intensity-Modulated Electron Beam Radiation Therapy. *PhD thesis.* Stanford University.

Deng J, Lee MC, and Ma C-M. Leaf scattering effect on beam delivery for modulated electron radiation therapy. *Med. Phys.* (submitted 2002).

Song Y, Lee MC, and Boyer AL. Energy and Intensity Modulated Electron Radiotherapy: A Comparative Dosimetric Study of MERT and IMRT for Head and Neck Cancer. Annual Meeting of the American Association of Physicists in Medicine (Montreal, Quebec, 14 – 18 July 2002).

Lee MC, Ma C-M, and Boyer AL. Energy- and Intensity-Modulated Electron Beams for Chest Wall Irradiation. Annual Meeting of the American Association of Physicists in Medicine (Montreal, Quebec, 14 – 18 July 2002).

Ma C-M, Pawlicki T, Lee MC, Li JS, Deng J, Ding M, Jolly J, Boyer AL, and Goffinet D. MERT vs Tangential Photon Beams vs IMRT for Breast Cancer: A Comparative Dosimetry Study. Annual Meeting of the American Society for Therapeutic Radiology and Oncology (San Francisco, CA, 4 – 8 Nov 2001).

The principal investigator of this fellowship was awarded the degree of Doctor of Philosophy in Biophysics from Stanford University, based in part on work done by this award. Also in part based on the experience and training supported by this award, the principal investigator was offered and has accepted a position as a Visiting Postdoctoral Scholar at the Magnetic Resonance Research Center of the University of California at San Francisco. Other possible employment opportunities applied for on the basis of experience and training supported by this award included postdoctoral positions at the Massachusetts General Hospital, the UCSF VA hospital, the Fox Chase Cancer Center, and Stanford University.