Optimization of Cervical Cancer Radiation Therapy through Functional Bone Marrow Sparing

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Abstract
The objective of this study is to improve cervical cancer treatment outcomes by minimizing the adverse effects of chemoradiation therapy (CRT) on the immune system. Known as hematologic toxicities (HT), these effects weaken the body’s ability to fight off infections and often force a delay in life-prolonging treatment. Hematologic toxicities originate in pelvic bone marrow, where chemoradiation suppresses the growth of bone marrow stem cells that produce the body’s white blood cells. MRI technology was used to pinpoint bone marrow regions low in fat fraction, and a cohort of patients were treated with intensity modulated radiation therapy (IMRT) to reduce radiation dosage to these sub-regions. The resulting analysis demonstrated that bone marrow fat fraction increased as radiation dosage increased, indicating that bone marrow fat fraction analysis may prove to be crucial to optimizing radiation treatment planning.

Introduction
Cervical cancer is the third most common cancer in women, with an estimated 530,000 cases worldwide in 2008. Standard methods of radiation treatment are often constrained by the suppression of the patient’s immune system, known as hematologic toxicities. Bone marrow is known to be rich with stem cells that are responsible for the production of new white blood cells. Concurrent chemotherapy and radiation treatment has been shown to inhibit the bone marrow’s ability to produce new white blood cells, and as a result, patients are at risk of developing infections or requiring hospitalization. Hematologic toxicities often prevent doctors from intensifying chemotherapy regimens necessary to prevent metastases. Pelvic bone marrow accounts for nearly 50 percent of the body’s total bone marrow, making pelvic cancers particularly problematic in confronting hematologic toxicities. Although current radiation techniques do their best to minimize radiation dosage to healthy tissues, basic CT imaging is unable to properly identify the critical non-cancerous tissues that are integral to a patient’s ability to withstand chemotherapy. Being able to significantly limit radiation exposure to critical areas of the bone marrow may limit the occurrence of hematologic toxicity and provide a breakthrough in a doctor’s ability to effectively use chemotherapy.

Materials and Methods
The Center for Advanced Radiotherapy Technologies research group at the UCSD Moores Cancer Center has developed a form of intensity modulated radiation therapy (IMRT). A treatment method that has been shown to help spare pelvic bone marrow from radiation and provide less toxic treatments in cervical cancer patients. IMRT gives a radiation oncologist the ability to modulate radiation intensities in order to maximize the radiation to the tumor while minimizing dosage to healthy tissues.

This retrospective study focused on identifying the pelvic bone marrow sub-regions that are critical to leukogenesis. A sample of medical imaging data was collected from 14 cervical cancer patients as they underwent IMRT with concurrent cisplatin (chemotherapy) regimen.

Results
The data was sub-divided into two sets, tracking the change in fat fraction from pre treatment to mid-treatment, and from mid-treatment to post-treatment. A least squares regression was then used to linearly fit the data.

Conclusion
Higher FDG uptake (SUV) was shown to correlate to larger increases in fat fraction in response to IMRT, while the correlation between radiation dosage and change in fat fraction was deemed not significant. This indicates that regions lowest in fat fraction are most susceptible to radiation therapy and must therefore be spared in order to reduce hematologic toxicities.

References

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