# Optimization of Cervical Cancer Radiation Therapy through Functional Bone Marrow Sparing


**Philip J. Loury, Jakub Pritz, Yun Liang, Loren K. Mell**

*Department of Radiation Oncology, Moores Cancer Center*
University of California, San Diego, La Jolla, CA


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## Abstract

The objective of this study is to improve cervical cancer treatment outcomes by minimizing the adverse effects of chemo-radiation 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 chemo-radiation 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 estimate of 530,000 cases worldwide in 2008.[1] 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.[2] 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.[3] 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 cisplastin (chemotherapy) regimen.

| | *Conventional RT* | *CT-based IMRT* | *IG-BMS-IMRT* | *p (Wilcoxon)* |
|---|---|---|---|---|
| **Active BM V20** | **95%** | **82%** | **69%** | **0.03** |
| Total BM V20 | 93% | 65% | 69% | 0.19 |
| Tissue Max | 112% | 112% | 114% | 0.13 |
| PTV V100% | 95% | 95% | 95% | 1.00 |
| Bladder V100% | 86% | 49% | 46% | 0.09 |
| Rectum V100% | 87% | 68% | 65% | 0.31 |
| Bowel V45 | 212 cc | 134 cc | 144 cc | 0.06 |

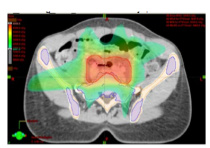
IMRT, intensity modulated radiation therapy; CT, computed tomography; PTV, planning target volume; Vx, volume receiving ≥ x Gy; Vx%, volume receiving ≥ x% of the prescription dose

Table 1: Demonstration of the efficacy of CT-guided IMRT in reducing radiation to benign tissue

IDEAL MRI scans were acquired and used to compute individual voxel-wise fat fractions. IDEAL technology uses differing MR relaxation rates to quantify the fat/water composition of human tissue.[4] IDEAL fat fraction metrics were selected as a potential method for identifying critical bone marrow regions due to the underlying nature of hematopoietically active bone marrow. Bone marrow that actively generates leukocytes is more vascularized and histologically characterized as "red marrow" with lower fat percentages than inactive "yellow marrow", making fat fraction analysis a potentially useful tool in radiation therapy treatment planning.

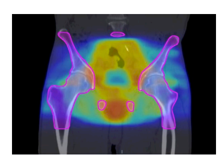
Next, PET-and CT image scans were acquired to overlay the patient's physiological tracer information on top of their skeletal structures. The hematopoietic activity of pelvic bone marrow was quantified using gold standard FDG PET image analysis. Fluorodeoxyglucose is a radiopharmaceutical tracer linked to cellular glucose uptake and is often used in medical imaging to detect cellular activity.

A statistical analysis was performed to find the correlation between regions of high hematopoietic activity and regions low in fat fraction, in order to assess the viability of using fat fraction analysis in as a non invasive method for guiding IMRT treatment planning. The dose-dependent changes in both fat fraction and SUV for FDG tracer were then mapped in response to IMRT treatment.



Transverse Plane Intersection of bone marrow sub-regions (blue) with radiation dosage heat map

*Courtesy of Yun Liang*

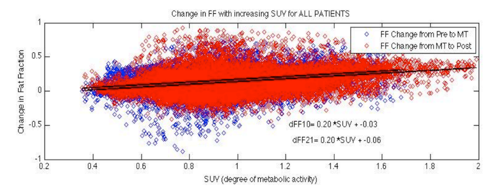


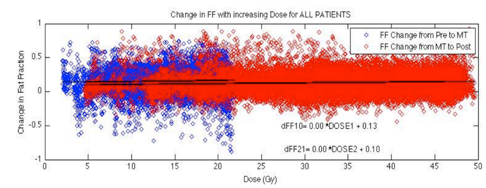
Coronal Plane Intersection of bone marrow region of interest (pink) with radiation dosage heat map

*Courtesy of Jakub Pritz*

## 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.




**(Top)-** this scatter plot demonstrates the that fat fraction tended to increase in bone marrow subregions with higher SUV values.
**(Bottom)-** the scatter of dosage versus change in fat fraction indicated no increased change in fat fraction with increased dosage.

## 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 hematological toxicities.

## References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