Monitoring Bone Marrow Changes During Chemoradiotherapy Using MRI Fat Quantification

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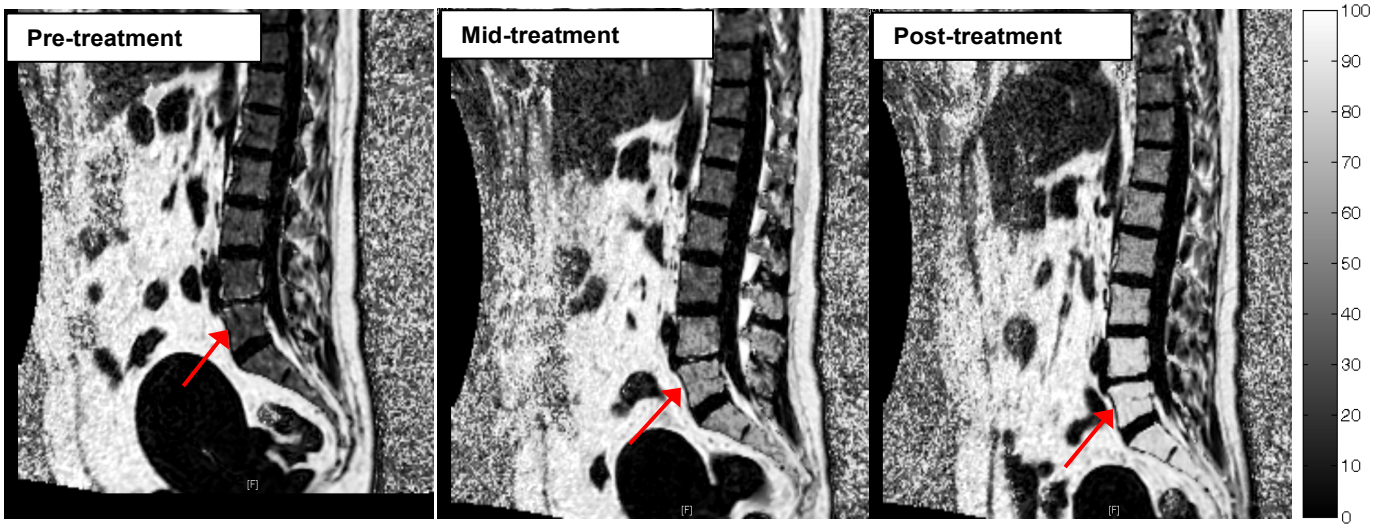
Introduction: Patients undergoing chemoradiotherapy for pelvic cancer are at high risk of acute hematologic toxicity due to damage to their red bone marrow. Radiotherapy of malignancies in the pelvis is a particular problem in this regard because about half of the body's red bone marrow is located in the bones around the pelvis and is therefore likely to be irradiated in treatment of pelvic tumors.

It is known from pathology that bone marrow is comprised of subregions of hematopoeitically active red bone marrow (with 20-40% fat) and inactive, fat-rich (80-95% fat), yellow bone marrow. Radiotherapy and chemotherapy cause red marrow cells to undergo apoptosis, which leads to an increase in fat content, and ultimately conversion to yellow marrow [Blankenberg 2008]. Reducing dose specifically to active subregions of pelvic bone marrow is likely to be beneficial in reducing hematologic toxicity, but the precise location of active subregions and the relationship between radiation dose to these regions and hematologic toxicity are not well known.

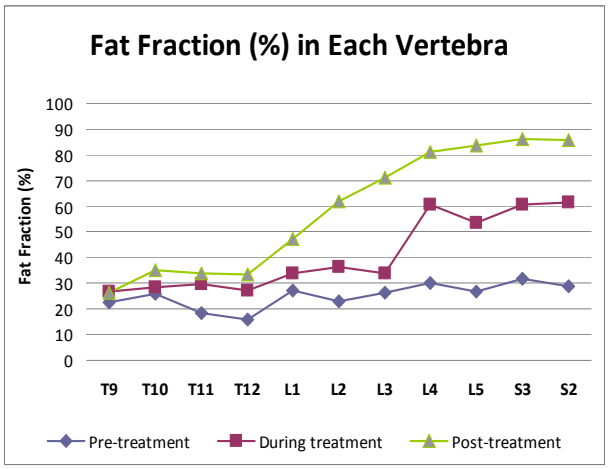
Magnetic resonance imaging can differentiate between red and yellow marrow due to the differences in fat composition [Otake 2002]. In particular, the characteristic short T1 of fat leads to an increase in signal intensity on T1-weighted sequences. While sufficient for distinguishing low fat from high fat, the signal intensity can depend on many factors in addition to T1, such as non-uniform RF excitation and reception. A more sensitive measure of fat is Iterative Decomposition of Water and Fat with Echo Asymmetric and Least Squares Estimation with T2* and fat spectrum correction (T2*-IDEAL) [Yu 2008], which exploits the frequency differences between water and fat protons. In this prospective study we evaluate the use of T2*-IDEAL to monitor changes in bone marrow during chemoradiotherapy.

Methods: Patients undergoing chemoradiotherapy for anal and pelvic cancers were imaged on a GE 3.0T scanner. 3D SPGR images were acquired with TR 11.5 ms, TE 1.1, 1.9, 2.8, 3.7, 4.5, 5.4 ms and flip angle 5° and processed with an investigational T2*-IDEAL method that corrects for B0 inhomogeneity, fat complexity, T1 and T2* relaxation. The percentage of fat was calculated in each pixel.

Results: The Figure below shows sagittal fat fraction images of the spine pre-, during and post- treatment. Note in L5 (arrow) the fat fraction changes from 27% to 84%, indicating almost complete transformation from red to yellow bone marrow. The Plot gives numerical values for the fat fraction throughout the vertebral body. In the pre-treatment data the fat fraction is around 20–30% in all vertebrae. After treatment this increases to around 90% in several vertebrae. The radiation dose falls off rapidly with distance from the radiation field (pelvis), however there are detectable changes in the marrow as far as L1, T12, T11 and T10, which is further than previously recognized. These changes may be due to a small amount of scattered radiation or the chemotherapy.



Conclusion: Quantitative fat imaging techniques can provide a sensitive measure of bone marrow composition. The spatial distribution and extent of damage to the red bone marrow due to chemoradiotherapy are readily measured, with high accuracy and spatial resolution. This is likely to be important in the planning and evaluation of intensity modulated radiation therapies designed to reduce hematologic toxicity [Mell 2008].



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