reported that radiation can induce changes in CT texture features in tumor during RT delivery for lung cancer and such changes can be potentially used to assess RT response. In this work, we investigate if radiation-induced changes in CT Hounsfield unit (HU) histogram feature in the periphery of lung tumor can be correlated to tumor response.

Materials/Methods: Diagnostic-quality CTs acquired with an in-room CT (CT-on-Rails) during daily CT-guided RT for 10 lung cancer patients, including 2 cases from an external source, were analyzed. For each case, all CT sets were acquired with the same protocol. Lesion for each case was contoured using a thresholding algorithm set at a minimum of −100 HUs to exclude lung tissue. This contour was expanded by 1 cm to form the periphery, then cloned and translated to the contralateral lung as control. To obtain the peripheral and contralateral contours, a second threshold region was set to only obtain regions between −1024 and −100 HU within the expanded (peripheral) and translated (contralateral) contours. Various HU histogram characteristics were extracted from both regions and were correlated with tumor response as characterized by good response (e.g., local recurrence-free survival above 3 years) and poor response (e.g., local recurrence within 1 year or high SUV uptake in follow-up PET).

Results: After normalization to account for changes in the volume of the tumor lesion, the HU histograms of different RT fractions in the tumor periphery in patients with good RT response showed a shift toward normal lung histograms as determined using the contralateral lung. These changes could be characterized with 2 general trends: (*1*) positive shift in peripheral histogram values by at least 20 HU, resulting in overlap with the normal lung; and (*2*) decrease in the percentage of volume within the shoulder region above the peak. Poorly responding patients showed minimal change in the peripheral HU histograms during RT. Despite decrease in lesion sizes for most patients, overall shape and characteristics of normalized tumor HU histograms remained consistent throughout the course of treatment. No/minimal change was seen in the contralateral lung.

Conclusion: Radiation can induce changes in CT HU histogram features in the tumor periphery during RT delivery for lung cancer patients who have good responses to RT. During RT delivery, HU histograms in the periphery of lung tumors appear to exhibit a treatment-related shift toward histograms more characteristic of normal lungs. Such a shift was observed even for a case with no shift in the HU histograms in the tumor. This shift does not occur in patients who are responding poorly to RT. These radiation-induced changes in HU histogram features in tumor periphery may be used to assess radiation response during RT delivery.

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In Vivo Measurements of CEST Magnetic Resonance Imaging Signal in Breast Cancer Xenografts at 7T

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Purpose/Objective(s): Chemical exchange saturation transfer magnetic resonance imaging (CEST MRI) represents a new technique for detecting cell death in vivo, without the need for injected exogenous contrast media or lengthy wait times (as with standard anatomical assessment of tumor response). Changes in CEST signal parameters corresponding to amide, amine, and aliphatic tissues have been suggested to correlate with apoptosis. In this study, we sought to characterize the changes in CEST parameters over time to help determine the optimal time point to detect cell death.

Materials/Methods: CEST MRI data were acquired from xenografted MDA-231 breast cancer tumors (n = 12) before and after injection with doxorubicin (100 mg/m^2) and paclitaxel (50 mg/m^2) chemotherapy. Tumors were scanned at baseline and 3 different treatment times—4, 8, and 12 hours after injection. Acquired data was fitted to Lorentzian shapes using a previously described method. The peak amplitude was measured as a unitless ratio of the measured signal to the CEST signal of bulk water; area under the curve was in units of parts per million (ppm), related to the resonant frequency of measured protons. Baseline CEST parameters were compared to parameters at each treatment time using 2-tailed t tests with a P value for significance of ≤ 0.05.

Results: For the aliphatic peak, amplitude measured 0.063±0.009 at baseline, 0.066±0.009 at 4 hours, 0.095±0.013 at 8 hours, and 0.065±0.019 at 12 hours postinjection; only the change from baseline to 8 hours was statistically significant ($P = 0.02$). Significant change in area under the curve (0.051±0.014 to 0.115±0.015 ppm; $P = 0.006$) was also observed at 8 hours postinjection but not at 4 or 12 hours. For the amine peak, significant changes in amplitude were observed at 8 hours ($P < 0.001$) and 12 hours ($P < 0.001$) postinjection; amplitude change was not significant at 4 hours nor was any change in peak area at any time point. For the amide peak, no significant differences were seen from baseline at any time point for peak amplitude or area.

Conclusion: Our results suggest that 8 hours after injection of chemotherapy may represent the optimal time to measure cell death using CEST MRI, as significant changes were observed in aliphatic and amine peak amplitudes at this time point.

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Impact of Breathing Periods on Dose Uncertainties for Lung Volumetric Modulated Arc Therapy—Stereotactic Body Radiation Therapy: A Novel FFT Approach

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Purpose/Objective(s): VMAT-SBRT becomes popular in treating inoperable early-stage lung cancers. However, dynamic delivery of VMAT coupled with respiratory motion causes dose uncertainties, which increase with fewer treatment fractions and faster delivery. Monte Carlo (MC) can compute dose uncertainties, but with statistical errors. This is the first known study to utilize the novel fast Fourier transform (FFT) approach in efforts to reduce these statistical errors. By taking advantage of the periodic breathing motion, dose uncertainties were computed using FFT, as an analytic and natural approach since FFT uses periodic trigonometric functions. Dose uncertainties due to different breathing periods were studied.

Materials/Methods: Dose uncertainties were computed using a sinusoidal moving phantom treated with a half beam block, and a lung patient case. The half beam block case was chosen to benchmark FFT with MC. The workflow for the lung case includes the following steps: (*1*) A VMAT-SBRT plan was created using a single arc with 84.3 sec delivery time and 90 control points. (*2*) The VMAT plan was applied to 8 CT image sets, corresponding to 8 breathing phases acquired from the 4DCT. (*3*) For each of the 90 control points, 8 dose distributions were exported for 8 breathing phases. (*4*) All breathing phases were registered to the 0% inhale phase using deformable image registration. (*5*) With breathing periods of 2 to 6 sec, dose uncertainties were computed using both MC and FFT. (*6*) Contours of dose uncertainties were overlaid in the planning CT, to anatomically visualize where greater dose uncertainty occurred.

Results: For the moving phantom treated with a half beam block, relative dose uncertainty using FFT was 0.9%, agreeing with MC computations. Statistical errors in MC were 0.9±1.0%, 0.9±0.7%, 0.9±0.5%, and 0.9±0.2%, corresponding to 10, 50, 100, and 1000 iterations, respectively. For a lung PTV treated with 50 Gy in 5 fractions, results from MC also agreed with FFT, and the FFT computations are presented. Corresponding