Quantifying radiation-induced changes to pulmonary anatomy through dose-binned Hounsfield Unit analysis pre and post-RT

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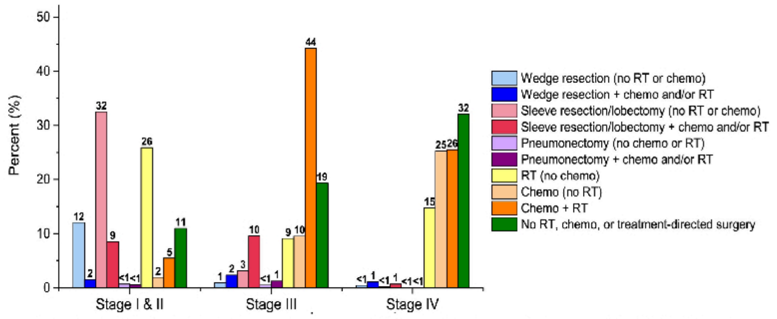
INTRODUCTION

- Lung cancer is the 2nd most common cancer and leading cause of cancer-related deaths[1]
- While the majority of lung cancer patients receive radiation therapy, post-therapy complications can arise that compromise a patient's quality of life
- In order to develop useful intervention methods, a thorough understanding of radiation-induced injury in pulmonary tissue is necessary



Kimberly D. Miller, Leticia Nogueira, Angela B. Mariotto, Julia H. Rowland, K. Robin Yabroff, Catherine M. Alfano, Ahmedin Jemal, Joan L. Kramer, Rebecca L. Siegel CA Cancer J Clin. 2019 Jun 11 Published online 2019 Jun 11. doi: 10.3322/caac.21565

METHOD

- Forty-one human subjects in an IRB-approved clinical trial underwent a standard course of RT consisting of 60 Gy delivered either 30 fractions of 2 Gy (standard fractionation) or 5 fractions of 12 Gy (SBRT).
- Five Wisconsin Miniature Swine (WMS)TM underwent an IACUC-approved research course of 12 Gy for 5 fractions delivered locally to a target in the lung using an MRI-LINAC system.
- Imaging on both subject groups was performed prior to and 3 months post-RT.
- Contours were created from the isodose lines to discretize analysis into 10 Gy dose bins
- B-spline deformable image registration[3] allowed for voxel-by-voxel comparative analysis of these contours between timepoints
- Dose-bin contours were mirrored onto the contralateral lung, which received <5Gy for comparison in the WMSTM subjects

3..H. J. Johnson and G. E. Christensen, "Consistent landmark and intensity-based image registration," in *IEEE Transactions on Medical Imaging*, vol. 21, no. 5, pp. 450-461, May 2002.

RESULTS

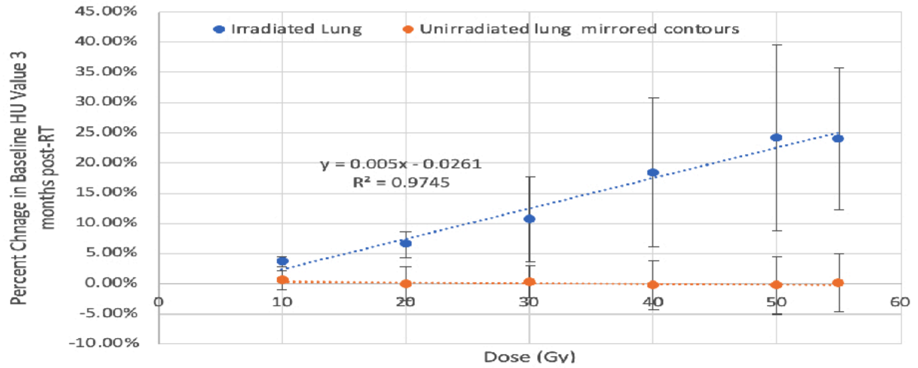


Figure 1: Percent change in HU vs. dose delivered for all WMS subjects 3 months post-RT (blue). Mirrored unirradiated contour changes are plotted in orange at the same dose coordinate for comparison however these regions did not receive radiation. HU change is shown to increase linearly with increasing dose while unirradiated regions showed no change.

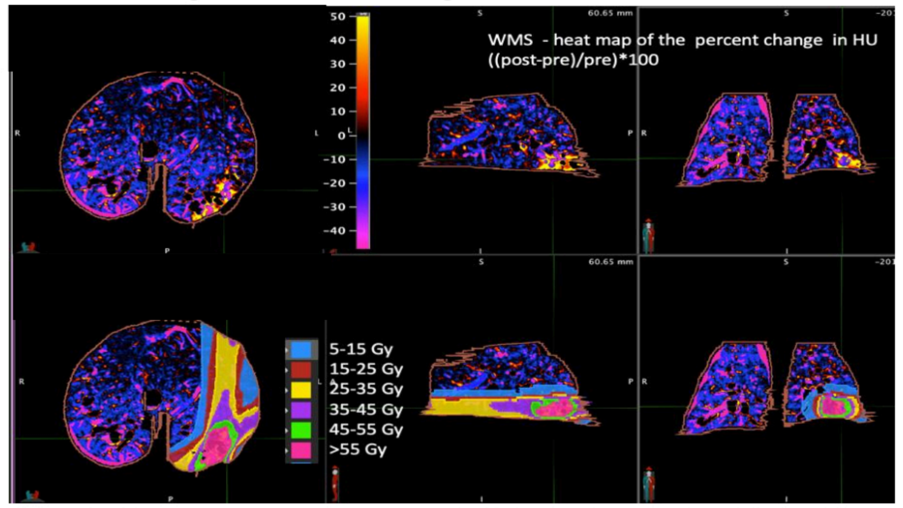


Figure 2: Heat map of percent changes in HU value for a typical WMS subject (top) and the same heat map with the dose distribution shown (bottom). Regions of significant HU increase correspond to the regions irradiated

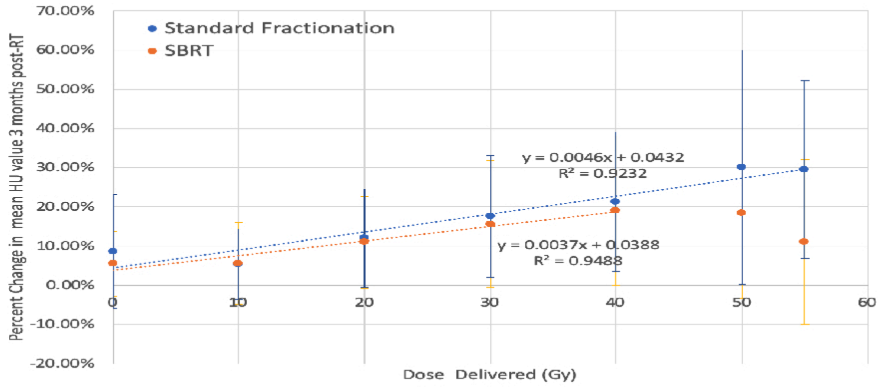


Figure 3: Percent change in HU vs. dose delivered for all Human subjects 3 months post-RT receiving standard fractionation (blue) and SBRT (orange). HU change is shown to increase linearly with increasing dose for all dose levels in standard fractionation patients and from 0-40 Gy for SBRT patients.

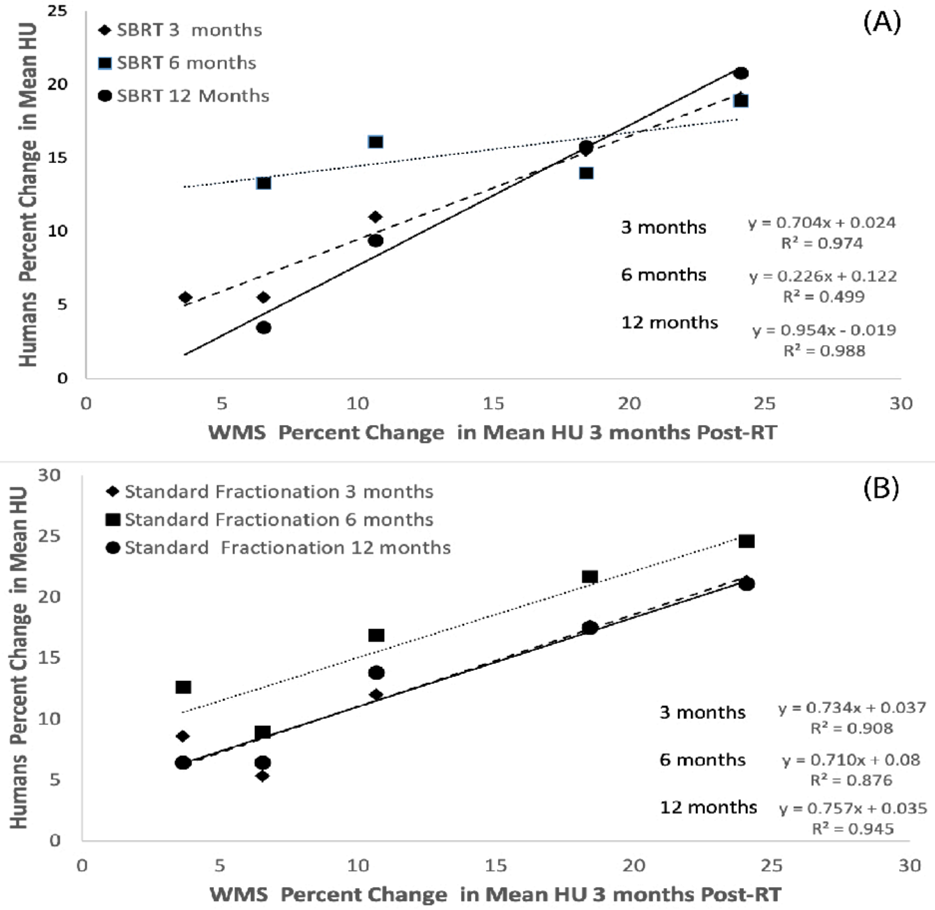


Figure 4: Correlation of the HU changes seen in the human subject pools with the WMS subject groups. Strong linear correlations were seen at all timepoints for both SBRT (A) and Standard Fractionation (B). The WMS group most closely predicted the standard fractionation human group at 3 months post-RT (slope = 0.95) and the SBRT human group at 12 months post RT (slope = 0.84). This delayed response seen in the 12 month post-RT human population is consistent with reports in literature of the WMS experiencing an expedited biological response. This supports the idea that the WMS is a good surrogate for analyzing radiation-induced changes in humans.

Dose Bin Center	Percent Change in Hounsfield Unit	
	Irradiated Lung	Unirradiated Lung Mirrored Contour
10	3.6% +/- 0.88%	0.59% +/- 1.6%
20	6.5% +/- 2.1%	-0.04% +/- 2.8%
30	10.6% +/- 7.0%	0.28% +/- 2.7%
40	18.4% +/- 12.4%	-0.28% +/- 4.1 %
50	24.1% +/- 15.3	-0.28% +/- 4.8 %
55	24.0% +/- 11.8	0.15% +/- 4.9%

Table 1: Percent change in HU vs. dose delivered for WMS subjects 3 months post-RT and mirrored unirradiated contour changes

CLINICAL IMPACT/ SIGNIFICANCE

- This work quantifies an anatomical response to radiation dose.
- Increased HU value could indicate damage such as an inflammatory response or the onset of fibrotic tissue.
- If verified to be correlated with a functional metric, opportunities for early intervention of these responses would be possible to improve patient care and outcome.
- The delayed response seen in the 12-month post-RT SBRT human population is consistent with reports in literature of swine models experiencing an expedited biological response[2]. Thus, the WMS model may be able to predict radiation induced changes in humans on faster time scale.

2. Schomberg, D. T., Tellez, A., Meudt, J. J., Brady, D. A., Dillon, K. N., Arowolo, F. K, Shanmuganayagam, D. (2016). Miniature Swine for Preclinical Modeling of Complexities of Human Disease for Translational Scientific Discovery and Accelerated Development of Therapies and Medical Devices. *Toxicologic Pathology*, *44*(3), 299–314.

CONCLUSIONS

- Radiation induced changes in pulmonary anatomy were observed at 3 months post-RT in both the humans and WMS subjects
- These effects showed a strong positive linear correlation with dose
- Changes observed in humans corresponded to changes seen in the WMS indicating the WMS model is a good surrogate for analyzing radiation-induced changes in humans.

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