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MRI for Cervical Cancer: Not only Correlates with Tumor Hypoxia, but also Predicts Ultimate Outcome – In Regard to Lim *et al.*

Jian Z. Wang, PhD[†], Nina A. Mayr, MD[†], Dongqing Zhang, PhD[†], and William T. C. Yuh, MD, MSEE[§]

[†]Department of Radiation Medicine, The Ohio State University, Columbus, OH 43210, USA

[§]Department of Radiology, The Ohio State University, Columbus, OH 43210, USA

To the editor: We congratulate Lim *et al.* (1) for the publication of an important study using Magnetic Resonance Imaging (MRI) to monitor cervical cancer regression during fractionated external-beam radiotherapy. In their study, weekly MRI was used to measure tumor volume during treatment, and oxymetry with the Eppendorf electrode was used to measure the partial pressure of oxygen to assess tumor hypoxia fractions. Based on a study of 27 patients, Lim *et al.* (1) found that the survival fraction after 2 Gy (SP_2) correlated significantly with tumor hypoxia at diagnosis. These results are intriguing and unique, as most centers are not able to obtain weekly MRI scans with clinical patients. This study sheds more light on the complex radiobiological modeling of tumor response to ongoing radiation therapy. If correlations of these parameters with outcome (tumor control, overall survival) can be validated, this technique may have a great impact on clinical care of cervical cancer patients.

In a similar radiobiological modeling study in 2006, we found that a correlation of such radiobiological parameters with clinical outcome indeed exists (2). In our study, 3D volumetric MRI was performed before treatment, approximately every 2 weeks during external-beam radiotherapy, and after low-dose-rate brachytherapy. We developed a kinetic model incorporating three major effects and model parameters similar to Lim *et al.*'s study: radiation cell-killing, tumor repopulation, and resolution of dead/inactivated cells. This kinetic model was used to fit the volume regression data of 79 patients and was correlated with long-term local tumor control with a mean follow-up time of 6.2 years. Our results demonstrated that the tumor regression rate and the model parameters strongly correlated with treatment outcome ($p < 0.001$): 2 Gy surviving fraction $S_2 = 0.61$ for locally controlled tumors and $S_2 = 0.66$ for locally recurrent tumors. Our data for S_2 correlation with tumor control is remarkably similar to their data of SP_2 correlation with tumor hypoxia. These joint findings underscore the powerful role that hypoxia plays in radio-responsiveness of cervical cancer. In addition, our data showed a significant correlation between local tumor control and $T_{1/2}$ (half-time of the resolution of dead-cells, a parameter similar to Lin *et al.*'s cell clearance T_c): In our study, $T_{1/2}$ was 10 days and 20 days for locally controlled and recurrent tumors, respectively. It would be interesting to see if such a correlation exists between Lim *et al.*'s T_c and hypoxia.

Corresponding author: Jian Z. Wang, Ph.D., Dept of Radiation Medicine, James Cancer Hospital and Solove Research Institute, The Ohio State University, 300 West 10th Ave, Rm 094, Columbus, OH 43210, Tel: 614-293-6502, Fax: 614-293-4044, Email: wang.993@osu.edu.

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Finally, it would be most revealing and important to see the correlation of Lim *et al.*'s model parameters with outcome in their patients. Although they do not have long-term outcome data, surrogate outcome endpoints could be used to estimate the prediction power of these parameters for tumor control. Based on our earlier study, the residual tumor volume 1–2 months after radiotherapy is a strong predictor of ultimate tumor control and disease-free survival (3). Correlation of Lim *et al.*'s data with such a surrogate endpoint would be another step in determining the significance of the radiobiological modeling on outcome prediction. Furthermore, based on the imaging-based modeling and clinical information, we may be able to develop a multivariate strategy to more precisely identify patients at greater risk of treatment failure (4–6). In combination with clinical data, non-invasive assessment of MRI parameters during radiation therapy may help to guide individualized therapy strategies for better outcome.

References

1. Lim K, Chan P, Dinniwell R, et al. Cervical cancer regression measured using weekly magnetic resonance imaging during fractionated radiotherapy: radiobiologic modeling and correlation with tumor hypoxia. *Int J Radiat Oncol Biol Phys* 2008;70:126–133. [PubMed: 17768016]
2. Wang JZ, Mayr NA, Yuh WTC, et al. Kinetic Model of Tumor Regression During Radiation Therapy of Cervical Cancer. *Int J Radiat Oncol Biol Phys* 2006;66:S603.
3. Wang JZ, Mayr NA, Yuh WT, et al. Dynamic tumor regression during radiation therapy predicts treatment outcome in cervical cancer. *Proc Intl Soc Mag Reson Med* 2006;14:759.
4. Mayr NA, Wang JZ, Zhang D, et al. Synergistic Effects of Hemoglobin and Tumor Perfusion in Tumor Control for Cervical Cancer. *Int J Radiat Oncol Biol Phys* 2007;69:S116.
5. Wang, J.; Zhang, D.; Mayr, NA., et al. Tumor Volume and Perfusion Parameters of Cervical Cancer During Therapy - Optimal Timing of Outcome Prediction; Proceeding of 93rd RSNA Annual Meeting; 2007.
6. Zhang D, Mayr NA, Wang JZ, et al. Tumor Perfusion and Metastatic Failure in Cervical Cancer. *Int J Radiat Oncol Biol Phys* 2007;69:S117.