

AbstractID: 13279 Title: Combining Model Parameters – Radiosensitivity and Dead-cell Resolving Time to Predict Outcome of Radiation Therapy for Cervical Cancer

Purpose: Individual kinetic modeling parameters can provide important information on predicting clinical outcome in tumors. The combination of model parameters might be very useful in enhancing outcome prediction. This study was to investigate combined effects of radiosensitivity and dead-cell resolving time on outcome prediction in cervical cancer during radiation therapy (RT).

Methods and Materials: Four sequential MRI scans were performed at pre-RT, every 2–2.5 weeks during RT and post-RT for 80 patients with Stage IB2–IVA cervical cancer. Data of 3D-volumetric tumor regression were analyzed. A kinetic model incorporating effects of radiation cell killing, tumor repopulation, and resolution of dead/inactivated cells, was used to fit the tumor regression data for individual patients, resulting in two model parameters: the radiation sensitivity after 2 Gy (S_2) and the half-time of dead-tumor-cell resolving ($T_{1/2}$). Patients were stratified into four subgroups according to optimal cut-points of S_2 and $T_{1/2}$: low S_2 /low $T_{1/2}$ (low-low), high S_2 /low $T_{1/2}$ (high-low), low S_2 /high $T_{1/2}$ (low-high), and high S_2 /high $T_{1/2}$ (high-high). These combined parameters were correlated with long-term clinical outcome (follow-up time: 6.2 years, range: 0.2–9.4 years).

Results: In multivariate analysis incorporating stage, tumor size, combined S_2 and $T_{1/2}$, the low-low and high-low parameters were independent prognostic factors for local recurrence and disease-specific survival (hazard ratio [HR]=0.026, 95% confidence interval [CI], 0.003-0.199, $p<0.001$; HR=0.102, 95% CI, 0.018-0.573, $p=0.01$, respectively). The 6-year local tumor control rate was 100%, 84.2%, 57.1%, and 9.1% for the low-low, high-low, low-high, and high-high subgroups ($p<0.001$), respectively. Similarly the 6-year disease-free survival was 79.1%, 73.7%, 42.9% and 18.2% for the low-low, high-low, low-high, and high-high subgroups ($p<0.001$), respectively.

Conclusion: The combination of kinetic model parameters significantly strengthened the predictive power for therapy outcome. This method has potential value to impact personalized risk-adapted treatment strategy in cervix cancer patient.