Apparent Diffusion Coefficient (ADC) Measured by Diffusion Weighted MRI Was Highly Correlated with Tumor Cell Survival in Non-Small Cell Lung Cancer (NSCLC) Cell Lines Under Stereotactic Body Radiotherapy (SBRT) Regimens

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Introduction

There is an increasing awareness that current metric for assessing cancer treatment response based solely on tumor volume change is inadequate. Diffusion-weighted (DW) MRI has shown the ability to depict the microstructural change and may be more suitable for evaluating therapy response. Stereotactic body radiation therapy (SBRT) has been shown safety and efficacy in treating non-small cell lung cancer (NSCLC). We aim to study the relationship between apparent diffusion coefficients (ADC) measured by DW-MRI and tumor survival fractions in NSCLC cell lines A549 and H1229 under different SBRT regimens.

Methods

Two NSCLC human cell lines A549 and H1229 were purchased and cultured. $1x10^5$ tumor cells were plated per well and were irradiated with RTOG 0813 protocols, i.e., 40-60Gy in 5 fractions at SSD=100 cm and depth=1.5cm using 6 MV on a clinically commissioned TrueBeam linac. Films were used to verify dose accuracy. Cell plates were then scanned using a phase array coil on a 1.5T Siemens Avanto scanner using single-shot echo planar imaging (SS-EPI) to obtain ADC. The number of survival colonies was normalized to the control (no radiation) condition.

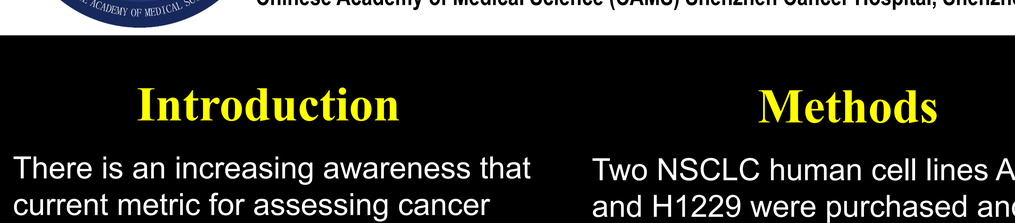

Fig 1. The crystal violet of non small cell lung cancer (NSCLC) human cell lines A549 and H1229 with and without SBRT.

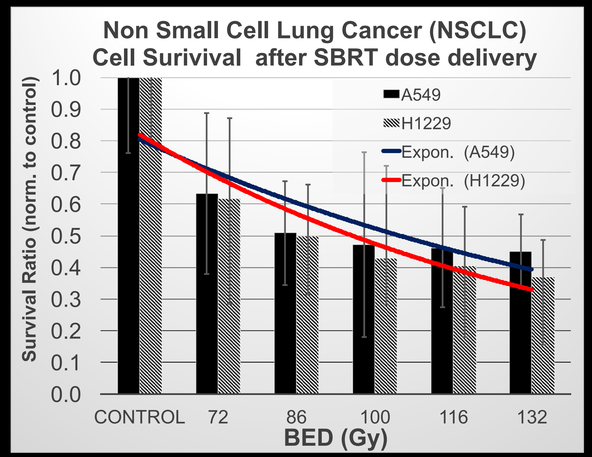

Fig 2. Survival ratio of NSCLC cell lines of A549 and H1229 after different radiation regimens shows the cell survival has been mono-directionally decreased with the increase BED.

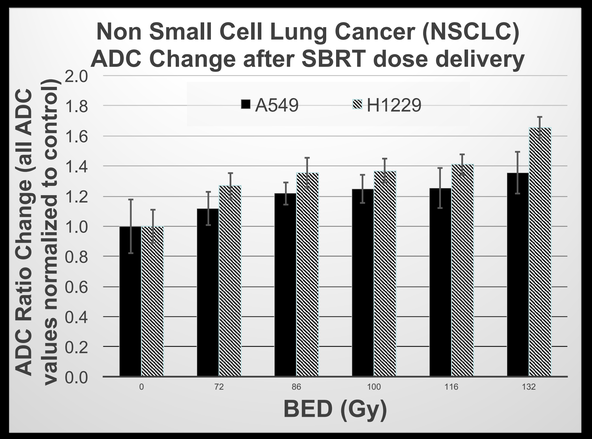

Fig 3. ADC values (in the unit of um2/sec) were normalized to the control show mono-directional increase with the increased biological equivalent dose (BED) delivery.

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Results

Reduced cell density and increased ECM space were observed in Figure 1. For both cell lines, survival was mono-directionally decreased with the increasing BED, with H1229 cells showing more radiosensitivity (Figure 2). The ADC values linearly increased with BED (Figure 3). The ADC ratio was highly correlated with survival ratio for both A549 and H1229 (R = 0.85 and 0.83, respectively; Figure 4).

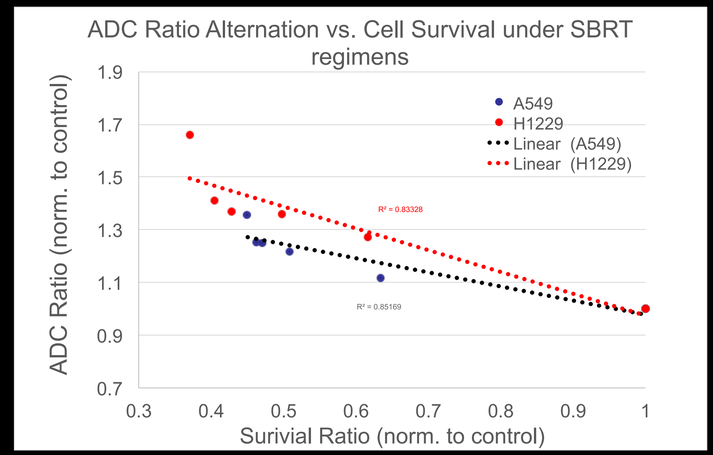

Fig 4. ADC increase is moderately correlated with the decreased survival ratio for NSCLC A549 and H1229.

Conclusion

ADC of NSCLC cell lines A549 and H1229 was measured noninvasively under SBRT regimens. Decreased survival and increased ADC values were observed with the increased SBRT dose. In addition, a highly correlated inverse linear relationship between ADC and survival endpoint was found. ADC has great potential as a non-invasive biomarker for treatment response evaluation.