論　文　内　容　要　旨

Dosiomics for intensity-modulated radiotherapy in patients with prostate cancer: Survival analysis stratified by baseline PSA and Gleason grade group in a two-institutional retrospective study

（強度変調放射線治療が施行された局所前立腺癌患者における Dosiomics を用いた生化学的再発リスクの評価: Baseline PSA 及び Gleason grade group を用いた層別化解析）

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Prostate cancer is a prevalent malignancy, and external beam radiation therapy (EBRT) is one of the effective treatment options for patients with localized prostate cancer. However, approximately 15% of the patients develop biochemical recurrence (BCR) after EBRT, and the relationships between dosimetric factors related to treatment planning and BCR remained unclear. Thus, we focused on the quality of planned dose distribution in treatment planning using the dosiomics method. Dosiomics is a method inspired by radiomics, wherein numerous spatial features are extracted from dose-distribution images. Our previous study demonstrated that certain dosiomic features extracted from the clinical target volume (CTV) and planning target volume (PTV) significantly correlated with BCR after radiotherapy. However, it was still unclear which patients with specific clinical backgrounds are more significantly affected by planned dose distribution. This study aimed to evaluate the prognostic impact of the quality of dose distribution using dosiomics in patients with prostate cancer, stratified by pretreatment PSA levels and Gleason grade group (GG).

This is a retrospective, observational, multicenter study. In total, 721 patients (BCR; N=117, No-BCR; N=604) with localized prostate cancer treated by intensity-modulated radiation therapy were enrolled. Two predictive dosiomic features for BCR (*CTV_wavelet-HHH_glrlm_HGLRE* and *PTV_wavelet-HHH_firstorder_Entropy*) were selected, and patients were divided into specific groups stratified by pretreatment PSA levels (≤10 ng/ml vs. >10 ng/ml) and GG (1–5). Freedom from biochemical failure (FFBF) was estimated using the Kaplan-Meier method based on each dosiomic feature, and univariate discrimination was evaluated using the log-rank test.

The dosiomic feature extracted from PTV can significantly discriminate between the high- and low-risk BCR groups with PSA levels >10 ng/ml (7-year FFBF: 86.7% vs. 76.1%, $p < 0.01$), and GG 4 (92.2% vs. 76.9%, $p < 0.01$), and GG 5 (83.1% vs. 77.8%, $p = 0.04$). However, no significant differences were observed in the survival curves of patients with PSA levels ≤10 ng/ml and GGs of 1–3. This indicates that the quality of the planned dose distribution on the PTV may affect the prognosis of patients with poor prognostic factors. On the contrary, patients with favorable clinical backgrounds may be more tolerant of inferior dose distributions in treatment planning. To the best of our knowledge, this is the first study to demonstrate that the effects of dose distribution on prognosis differ depending on patient's background. This highlights the importance of stratified analysis in dosiomics research, even for specific cancer types. Our findings may aid decision-making in clinical practice, allowing clinicians to focus on more challenging cases.