Grading Of Differentiation In Cutaneous Squamous Cell Carcinoma: Evaluation Of Inter-rater And Intra-rater Reliability

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Poor differentiation is associated with aggressive forms of cutaneous squamous cell carcinoma (CSCC). Differentiation grading must be a reliable assessment across trained graders prior to implementation in CSCC staging systems. Our aim was to determine the inter-rater and intra-rater reliability of CSCC differentiation grading among dermatopathologists. This survey study was conducted from May 2020 to February 2021 and features a complete block design, where all raters graded the full set of 45 CSCC slides before and after a 6-week washout period. 22 fellowship-trained dermatopathologists from across the United States with at least 5 years of experience reviewing ≥ 1,000 slides per year were recruited. There was 1 dropout prior to data collection at the first time point (final N=21). 45 de-identified CSCC case slides were retrospectively selected from a pathology archive by an experienced dermatopathologist, with care to include approximately equal proportions of well, moderately, and poorly differentiated slides. Subjects rated the 45 CSCC case slides (presented in random order) at two time points separated by 6 weeks. Inter-rater (Light’s kappa) and intra-rater (Cohen’s kappa) reliability of dermatopathologists grading CSCC as either poorly differentiated or well to moderately differentiated. The survey study had a 95% response rate across the both surveys. Raters reported cellular atypia (95%), keratinization (90%), and architecture (81%) as the most important features when assessing grade. Moderate inter-rater ($T_0 \kappa = 0.5306$, 95% CI- 0.5110 to 0.5502; $T_1 \kappa = 0.5545$, 95% CI- 0.5345 to 0.5746) and intra-rater ($\kappa = 0.5577$, 95% CI- 0.4971 to 0.6183) agreement was found among the dermatopathologists, with significant variation in test-retest intra-rater reliability for individual raters. Reliable identification of CSCC tumors with poor differentiation is important for predicting outcomes and treatment course. Histological differentiation may enhance the prognostic capability of CSCC tumor staging systems with further standardization and development of grading protocols.