
Epstein JI, Egevad L, Amin MB, Delahunt B, Srigley JR, Humphrey PA; and the Grading Committee.

Abstract
In November, 2014, 65 prostate cancer pathology experts, along with 17 clinicians including urologists, radiation oncologists, and medical oncologists from 19 different countries gathered in a consensus conference to update the grading of prostate cancer, last revised in 2005. The major conclusions were: (1) Cribriform glands should be assigned a Gleason pattern 4, regardless of morphology; (2) Glomeruloid glands should be assigned a Gleason pattern 4, regardless of morphology; (3) Grading of mucinous carcinoma of the prostate should be based on its underlying growth pattern rather than grading them all as pattern 4; and (4) Intraductal carcinoma of the prostate without invasive carcinoma should not be assigned a Gleason grade and a comment as to its invariable association with aggressive prostate cancer should be made. Regarding morphologies of Gleason patterns, there was clear consensus on: (1) Gleason pattern 4 includes cribriform, fused, and poorly formed glands; (2) The term hypernephromatoid cancer should not be used; (3) For a diagnosis of Gleason pattern 4, it needs to be seen at 10x lens magnification; (4) Occasional/seemingly poorly formed or fused glands between well-formed glands is insufficient for a diagnosis of pattern 4; (5) In cases with borderline morphology between Gleason pattern 3 and pattern 4 and crush artifacts, the lower grade should be favored; (6) Branched glands are allowed in Gleason pattern 3; (7) Small solid cylinders represent Gleason pattern 5; (8) Solid medium to large nests with rosette-like spaces should be considered to represent Gleason pattern 5; and (9) Presence of unequivocal comedonecrosis, even if focal is indicative of Gleason pattern 5. It was recognized by both pathologists and clinicians that despite the above changes, there were deficiencies with the Gleason system. The Gleason grading system ranges from 2 to 10, yet 6 is the lowest score currently assigned. When patients are told that they have a Gleason score 6 out of 10, it implies that their prognosis is intermediate and contributes to their fear of having a more aggressive cancer. Also, in the literature and for therapeutic purposes, various scores have been incorrectly grouped together with the assumption that they have a similar prognosis. For example, many classification systems consider Gleason score 7 as a single score without distinguishing 3+4 versus 4+3, despite studies showing significantly worse prognosis for the latter. The basis for a new grading system was proposed in 2013 by one of the authors (J.I.E.) based on data from Johns Hopkins Hospital resulting in 5 prognostically distinct Grade Groups. This new system was validated in a multi-institutional study of over 20,000 radical prostatectomy specimens, over 16,000 needle biopsy specimens, and over 5,000 biopsies followed by radiation therapy. There was broad (90%) consensus for the adoption of this new prostate cancer Grading system in the 2014 consensus conference based on: (1) the new classification provided more accurate stratification of tumors than the current system; (2) the classification simplified the number of grading categories from Gleason
scores 2 to 10, with even more permutations based on different pattern combinations, to Grade Groups 1 to 5; (3) the lowest grade is 1 not 6 as in Gleason, with the potential to reduce overtreatment of indolent cancer; and (4) the current modified Gleason grading, which forms the basis for the new grade groups, bears little resemblance to the original Gleason system. The new grades would, for the foreseeable future, be used in conjunction with the Gleason system [ie. Gleason score 3+3=6 (Grade Group 1)]. The new grading system and the terminology Grade Groups 1-5 have also been accepted by the World Health Organization for the 2016 edition of Pathology and Genetics: Tumours of the Urinary System and Male Genital Organs.