A new contemporary prostate cancer grading system: message to the Italian pathologists

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In 2005, the Gleason grading system underwent its first major revisions. Some of the changes were proposals that Gleason score 2-4 should not be assigned to cancer on needle biopsy. The consensus conference also came up with extremely stringent criteria for cribriform Gleason pattern 3 consisting of small glands with regular contour, regular distribution of lumina, and uniform round lumens. The 2005 ISUP consensus conference agreed with the original Gleason system that fused glands, irregular cribriform glands, and the hypernephromatoid pattern were designated as Gleason pattern 4. Whereas the original Gleason pattern 4 consisted of only irregular cribriform glands, the 2005 consensus conference concluded that ill-defined glands or acini with poorly formed glandular lumina also warrant the diagnosis of Gleason pattern 4. Whether glomeruloid glands and mucinous carcinoma were Gleason pattern 3 or 4 in the 2005 conference was not resolved. 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 further update the grading of prostate cancer. Changes from the 2005 conference were: 1) Gleason patterns 1-2 are virtually never made; 2) Gleason pattern 4 consists of cribriform (regardless of morphology) and glomeruloid glands along with fused, and poorly formed glands; 3) Hypernephromatoid pattern should no longer be used; and 4) Mucinous carcinoma should be graded based on its underlying morphology, whereby some contain Gleason pattern 3 and some pattern 4. The 2015 schematic Gleason diagram displays these updates. A contemporary prostate cancer grading photomicrograph montage was recently created by this author to more completely show the various patterns within each grade and to correlate with the new grading system described below. Despite modifications in 2005 and 2014, there are still problems with the Gleason system. It ranges from 2 to 10, yet in current practice it is rare for a score lower than 6 to be reported. Some men think that they have an intermediate prognosis tumor when they are told that they have a Gleason score 6 out of 10, which contributes to fear of undergoing active surveillance. Gleason scores have also been incorrectly grouped together for both treatment and prognosis purposes. For example, the widely used D’Amico prostate cancer risk classification system considers Gleason score 7 as a single score without distinguishing 3 + 4 versus 4 + 3. In 2013 based on data from Johns Hopkins Hospital, we proposed 5 prognostically distinct Grade Groups (Tab. I). The way that tertiary patterns are factored in with these grade groups are that on needle biopsy with 3 + 4 = 7 with a lesser amount of 5 it is called 3 + 5 = 8 (Grade Group 4), and 4 + 3 = 7 with lesser amount of 5 it is called 4 + 5 = 9 (Grade Group 5). On radical prostatectomy, 3 + 4 = 7 with <5% pattern 5 is graded as 3 + 4 = 7 with tertiary 5 (Grade Group 3 with minor high grade pattern), and 3 + 4 = 7 with > 5% pattern 5 is called 3 + 5 = 8 (Grade Group 4). On radical prostatectomy, 4 + 3 = 7 with <5% pattern 5 is called 4 + 3 = 7 with tertiary 5 (Grade Group 4 with minor high grade pattern), and 4 + 3 = 7 with > 5% pattern 5 is called 4 + 5 = 9 (Grade Group 5). This new system was subsequently validated in a multi-institutional study of > 20,000 radical prostatectomy specimens, > 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 and was accepted by the World Health Organization (WHO) for the 2016 edition of Pathology and Genetics: Tumours of the Urinary System and Male Genital Organs. 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)]. In summary, the new grading system has the following advantages: 1) reduces grades of prostate cancer down to the lowest number of grades, where each has a different prognosis; 2) is simple with only 5 grades, so that it
Fig. 1. From left to right:
1st row: Closely packed uniform sized and shaped large glands; Large variably sized and shaped glands, some with infolding; Uniform medium sized glands; Variably sized glands.
2nd row: Occasional tangentially sectioned glands amongst well-formed small glands; Occasional tangentially sectioned glands amongst well-formed glands with open lumina; Back-to-back discrete glands; Branching glands.
3rd row: Large irregular cribriform glands with well-formed lumina; Irregular cribriform glands with slit-like lumina, glomeruloid structures, and fused glands; Irregular cribriform glands with small round lumina; Small round cribriform glands.
4th row: Poorly-formed glands with peripherally arranged nuclei; Small poorly-formed glands; Small poorly-formed glands; Fused poorly-formed glands.
5th row: Sheets of cancer: Sheets of cancer with rosette formation; Small nests and cords of tumor with scattered clear vacuoles; Individual cells.
6th row: Nests and cords of cells with only vague attempt at lumina formation: Solid nests of cancer; Solid nests with comedonecrosis; Cribriform glands with central necrosis.

Discrete Well-formed Glands (Gleason Patterns 1-3)

Cribriform/Poorly-formed/Fused Glands (Gleason Pattern 4)

Sheets/Cords/Single Cells/Solid Nests/Necrosis (Gleason Pattern 5)
will be easier for patients and clinicians to understand; and 3) logically and in line with other grading systems starts with grade is 1 as the lowest grade, in contrast to Gleason scores which in current practice begins with 6.

References