

Review

Modified gleason grading. An updated review

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Summary. At an ISUP (International Society of Urological Pathology) consensus conference in 2005 in San Antonio, Texas, the old Gleason grading system for prostatic carcinoma from 1966 underwent its first major revision. With this modified Grading system a shift of the most frequent Gleason scores from 6 to 7a (3+4) in biopsy specimens and an increased degree of agreement between specimens of biopsies and radical prostatectomies with carcinoma of the prostate could be demonstrated. After modified grading of GS 3+4=7a tumours 95% were stage pT2, while 79% of GS 4+3=7b tumours were stage pT3-4. In cases with PSA <10ng/ml and tumour extent <20% the most frequent Gleason scores were 6 and 7a. Cases with serum PSA >10ng/ml or tumour extent >20% had higher scores (7b or higher). Cancers with tumour infiltration of <1mm in one of 12 cores and PSA <10ng/ml were mainly low grade (Gleason scores 6 and 7a) and may correspond to so called insignificant carcinoma of the prostate.

Conclusion: With the modified Gleason system, grade, stage, tumour extent and serum PSA show good correlations and characterize the difference between low and high grade malignancy of prostate carcinoma.

Key words: Adenocarcinoma of the prostate, Modified Gleason Grading, Core needle biopsy, Radical prostatectomy

Introduction

The Gleason grading system of prostate carcinoma is the predominant grading system around the world. The Gleason grading system is based on glandular architecture and may be divided into five patterns of glandular growth or differentiation. The Gleason score is the addition of the most prevalent i.e. primary and the

second most prevalent pattern (Gleason, 1966). In contrast to other grading systems such as the WHO grading system, nuclear or nucleolar atypia or cytoplasmic features are not evaluated (Helpap et al., 1985; Mostofi et al., 2002). However, during the last years the frequency of core needle biopsy and radical prostatectomy specimens have increased dramatically. This situation differs from when Gleason proposed his grading system and therefore it seemed to be necessary to adapt the grading system. A modified Gleason grading system was introduced 2005 (Egevad et al., 2005; Epstein et al., 2005) and in the following we discuss its significance in biopsy and radical prostatectomy specimens and its relationship to other prognostic factors, such as tumor extent and serum PSA (Helpap and Egevad 2006, 2007, 2008a-c).

The conventional (c) and modified (m) Gleason Grading

In 1966 DF Gleason developed his grading system of prostatic carcinomas based on hematoxylin and eosin stained histological slides and low magnification using a 4 or 10x lens (Gleason, 1966). Gleason grading is now the world wide grading system for prostatic carcinomas, and also the grading system of the WHO tumour classification of prostatic carcinomas (Epstein et al., 2004). Previously, other grading systems had been considered, such as the modified histo-cytological WHO grading of 2002 from Mostofi and the Helpap subgrading system (Helpap, 1993; Helpap et al., 1985; Mostofi et al., 2002). More than 40 years have elapsed since the introduction of the Gleason grading. During this time the clinical and diagnostic steps to find a carcinoma of the prostate and the therapeutical consequences have distinctly changed. Today PSA screening and core needle biopsies are the most frequent steps in the diagnosis of a prostatic carcinoma, and the therapeutic consequences are radical prostatectomy or radiation therapy, especially brachytherapy for a organ

confined carcinoma (Raagde et al., 2000; Helpap and Sinicina, 2002; Epstein et al., 2005).

The basis of the Gleason grading system 40 years ago was the morphological knowledge of simple prostatectomy specimens. Core needle biopsies which are today the most frequent diagnostic method, were very rare at that time and classical radical prostatectomy like today was unknown. The Gleason grading was slightly modified in 1966/1967 and in 1974/1977 and then officially unchanged until recently (Gleason 1966, 1977, 1992; Gleason and Mellinger, 1974). But the degree of agreement of the Gleason score of the old conventional grading system between specimens of biopsies and radical prostatectomy ranged only between 35 and 45% (Kramer et al., 1980; Lang and Narayan, 1983; Garnett et al., 1984; Mills and Fowler, 1986; Bostwick, 1994; Steinberg et al., 1997; Lopez-Beltran et al., 2006). Although other grading systems have better results in agreement between specimens of biopsies and radical prostatectomies such as the old and new WHO grading or the nucleolar subgrading of Helpap, the remaining grading system was that of Gleason (Helpap et al., 1985; Gallee et al., 1990; Helpap, 1993; Mostofi et al., 2002; Epstein et al., 2005) After the publication of the new WHO tumour classification of urogenital system in 2004, an intensive discussion was started about the valence of the Gleason grading of carcinomas in core needle biopsies (Epstein et al., 2005).

In 2004/2005 the WHO and ISUP organized consensus conferences in Stockholm and San Antonio, TX, respectively, about a modification of the Gleason grading and an adaptation to the core needle biopsies. Before the ISUP meeting pathologists round the world answer a survey study on Gleason grading which then became the basis of the modification of the Gleason grading system (Egevad et al., 2005; Epstein et al., 2005).

Gleason patterns

In the old Gleason grading system pattern 3 was characterized by numerous large and small well-formed

glands and also of cribriform patterns. In the modified grading some cases of this pattern have shifted to pattern 4. Pattern 3 of the Gleason grading now shows only rare cribriform glands (Figs. 1, 2).

In contrast to TUR material with incidental carcinoma or atypical adenomatous hyperplasia in anterocentral regions of the prostate, carcinomas with pattern 1 and 2 or score 2, 3 and 4 are not localized in the peripheral zone of the prostate (Epstein, 2000; Epstein et al., 2004, 2005; Egevad et al., 2005). A recommendation was therefore issued by the ISUP that with extremely rare exceptions Gleason score of 1 + 1 = 2 should not be diagnosed in any type of specimen, and that Gleason score 4 should rarely, if ever, be diagnosed on needle biopsies (Fig. 2). The results after modified Gleason grading system of biopsy and radical prostatectomy specimens agree with this concept (Epstein, 2000; Epstein et al., 2004, 2005; Egevad et al., 2005). A series of biopsy specimens from different periods were graded according to conventional and modified grading (1995, 2000 and 2006). During these periods no scores of 2 and 4 were observed when using modified Gleason grading (Helpap and Egevad, 2008 b).

Pattern 4 is characterized by the fusion of small tumour glands or abundant cribriform structures. This pattern is one of the most frequent in radical prostatectomy specimens (Figs. 1, 2). Now pattern 4 also includes poorly formed glands, which fits well into the general concept of this pattern.

Gleason score

It is decisive how the modified Gleason grading system will perform in the pathological routine diagnostics and how well the agreement of Gleason scores between core needle biopsies and radical prostatectomy specimens will be. The estimation of a score depends on all histological patterns present, e.g. primary, secondary and tertiary patterns (Steinberg et al., 1997; Pan et al., 2000; Mosse et al., 2004). The score of biopsy specimens now includes the most prevalent and the worst pattern. In radical prostatectomy specimen all

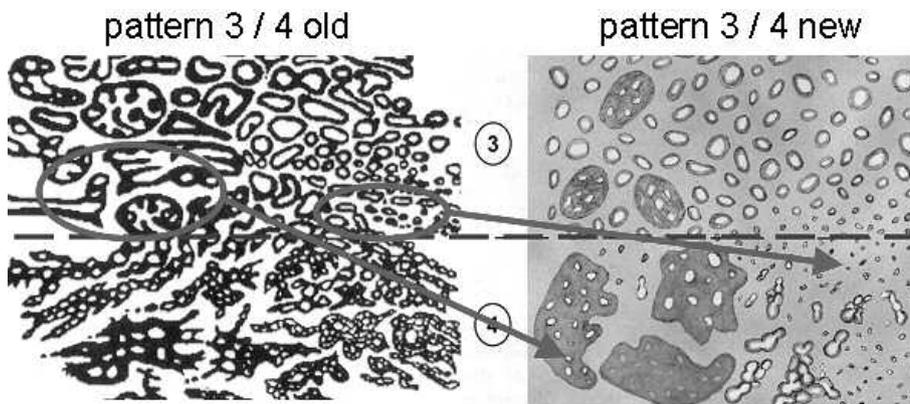


Fig 1. Gleason pattern 3 and 4 of the conventional (left) and modified (right) Gleason grading (reproduced from Fig. 12 of Am. J. Surg. Pathol 29, 1228-1242 modified by J. Köllermann, Congress of German Urological Society Berlin 2007) with permission of Lippincott Williams and Wilkins, Baltimore, MD, USA.

Modified Gleason grading

different pattern are be documented (Epstein et al., 2004, 2005; Lopez-Beltran et al., 2006). In the past, Gleason score 6 was the most frequent score in biopsy, while in radical prostatectomy specimens score 7 was the most common (Young et al., 2000). The agreement between biopsy and radical prostatectomy specimens ranged

between 35 and 45%. This relatively poor agreement was caused by undergrading of low grade carcinomas in needle biopsies, while the agreement was more exact in high grade carcinomas of the prostate (Lang and Narayan, 1983; Garnett et al., 1984; Mills and Fowler, 1986; Young et al., 2000). Biopsies have been found to undergrade in 24–60 % (pooled data 45%) and overgrade in 5–32% (pooled data 10.4%) (Egevad et al., 2001).

The distribution of Gleason scores 6, 3+4=7a, 4+3=7b, 8, 9 and 10 after modified Gleason grading in core needle biopsy specimens changed significantly and the most frequent score changed from 6 to 7, particularly 7a. The prevalence of score 7b is similar or a little lower (Helpap and Egevad, 2006, 2007, 2008c) (Fig. 3).

The distribution of Gleason scores of radical prostatectomy specimens depends on the tumor extent and is therefore different in stage pT2 and pT3. Carcinomas of stage pT2a are predominantly of Gleason scores 6 and 7a, while pT2 b or pT2c carcinomas are usually Gleason scores 7a or 7b. In pT3 prostate cancer the grade is generally higher with scores of 7b, 8 or higher (Helpap and Egevad, 2008a).

The identification of a biopsy Gleason score 3+4=7a and its high degree of agreement with radical prostatectomy specimens is clinically important because this grade may call for a different treatment than Gleason score 4+3=7b. Several studies have shown that there is a prognostic difference between Gleason scores 7a and 7b (Chan et al., 2000; Sakr et al., 2000; Lau et al., 2001). Prostatic carcinoma of Gleason score 7a should possibly not be considered high grade prostate cancer and needs to be distinguished from Gleason score 4+3=7b if treatment with curative intention is considered (Helpap and Egevad, 2008b).

Numerous morphological and clinical studies have shown that the most important prognostic factor of prostate carcinomas is the Gleason score (Partin et al., 1997; Bostwick et al., 2000; Chan et al., 2000; Egevad et al., 2002; Humphrey, 2004; Amin et al., 2005; Epstein et al., 2005; Lopez-Beltran et al., 2006). Until now a favourable prognosis is characterized by a Gleason score

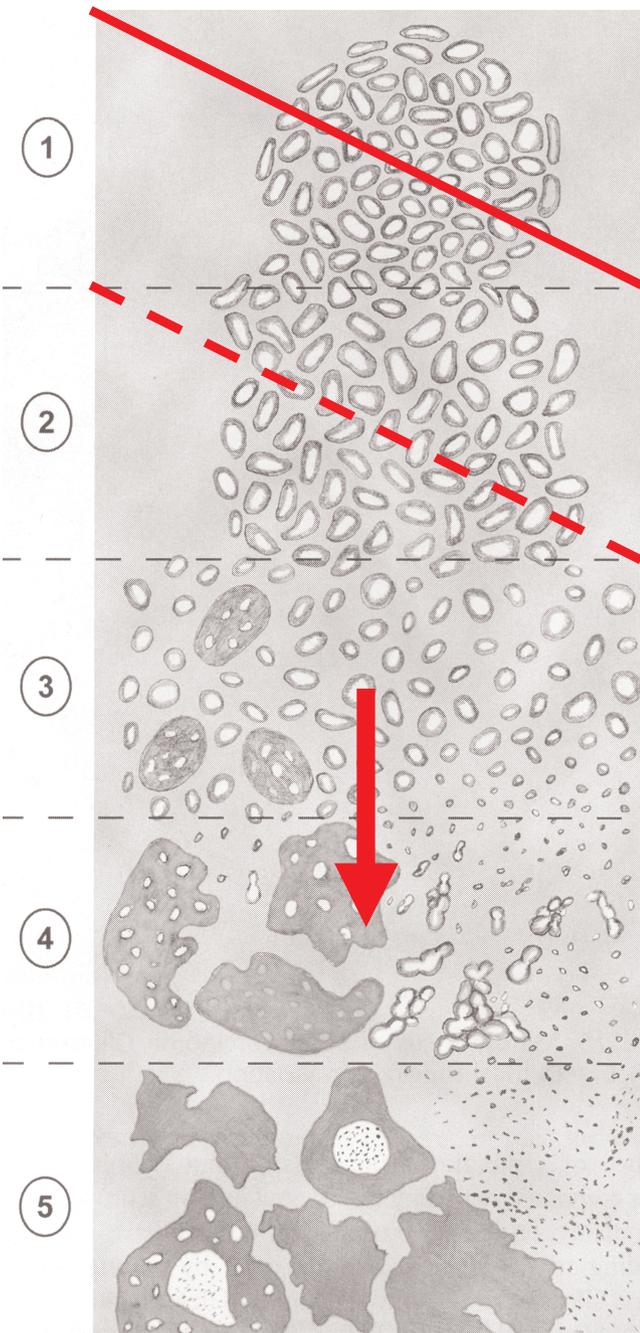


Fig. 2. Modified Gleason grading pattern (reproduced from Fig. 12 of Am. J. Surg. Pathol 29, 1228-1242 modified by J. Köllermann, Congress of German Urological Society Berlin 2007) with permission of Lippincott Williams and Wilkins, Baltimore, MD, USA. Pattern 1 and 2 are not diagnostic in carcinomas of the peripheral zone of the prostate.

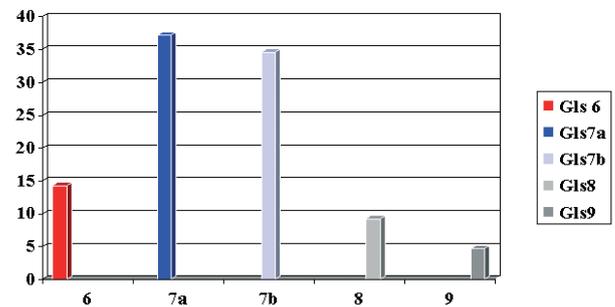


Fig. 3. Distribution of Gleason scores (%) after modified grading of prostatic carcinomas of consecutive core needle biopsies (Helpap and Egevad 2008c).

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≤ 6, small tumor extent (≤ 1mm) in biopsy specimens and a PSA value ≤ 10ng/ml. These data correlate with low grade of malignancy and with findings in radical prostatectomy specimens with Gleason score 6, tumor stage pT2, negative margins, negative lymph nodes (R0, pN0,PM0) and no postoperative recurrence (Partin et al, 1997). The shift from Gleason score 6 to 7a after modified Gleason grading correlate with pT2 stage too, whereas Gleason score 7b is more often associated with tumour stage pT3. Also, the grade distribution among cases with low serum PSA values (<10ng/ml) has shifted to Gleason score 6 and 7a (Helpap and Egevad 2006, 2008 a,b).

Core needle biopsy specimens with less than 10% tumor extent of prostatic carcinoma and PSA values < 10ng/ml often have carcinomas with Gleason score ≤ 7a. High grade carcinomas with Gleason score ≥ 7b have greater tumor extent and higher serum PSA values. (Helpap and Egevad 2008b,c).

Agreement and reproducibility

The agreement of Gleason score between core needle biopsy and radical prostatectomy specimens after modified Gleason grading is 88.5% for Gleason score 7a, which is significantly higher than with the old conventional Gleason grading system (45%) (Helpap

and Egevad 2006; Lopez-Beltran et al., 2006). The interobserver reproducibility with values above 80% is also good and better than that of the old conventional Gleason grading (Glaessgen et al., 2002; Melia et al., 2006).

Tumour extent

The highest frequency of tumour extents between 5 and 20% per core needle biopsy specimens has been found in carcinomas of Gleason scores 5 and 6 after conventional Gleason grading and of score 7a after modified grading. Tumour extents of more than 50% are distributed to scores 6-8 without significant differences. In 2-8.8% (mean value 5.2%) tumour infiltration of < 1 mm in 1 core needle biopsy specimen with PSA values ≤ 10ng/ml and Gleason score < 7a occurs (Helpap and Egevad, 2008b) (Fig. 4).

Insignificant carcinoma

Modified Gleason grading system may also be helpful in the discussion about insignificant carcinoma within the peripheral zone of the prostate. Today the definition of an insignificant prostate cancer in a needle biopsy is not more than 1 mm cancer infiltration (Allan et al., 2003; Bastian et al., 2004) in only one of six or more core needle biopsy specimens, serum PSA value < 10 ng/ml and a Gleason score ≤ 7a. However, only 5% of carcinomas in a consecutive series of needle biopsy specimens fulfill these criteria and only 25% of such patients have a pT2a tumour after radical prostatectomy. With this definition a clinically insignificant carcinoma in the periphery of the prostate that is managed by active surveillance by the urologist may be very rare (Helpap and Egevad, 2008c) (Fig. 5).

Age

The highest frequency of detected carcinomas is between 60 and 80 years (Helpap and Egevad, 2008c). With conventional Gleason grading score 6 and with modified grading score 7a are most common. There is no

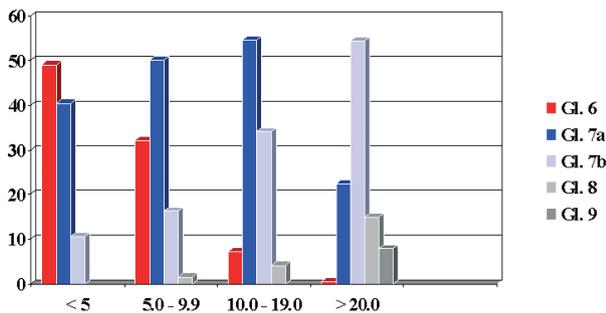


Fig. 4. Correlation of tumour extent (%) and Gleason score (%) (Helpap and Egevad, 2008c).

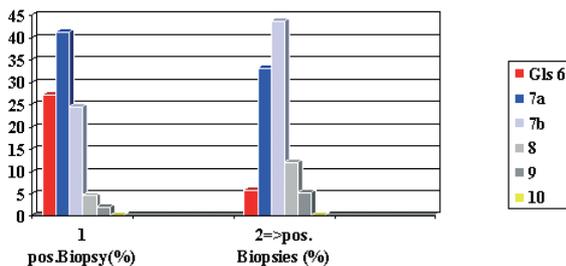


Fig. 5. Correlation of Gleason score (%) and one or two and more positive core needle biopsies (Helpap and Egevad, 2008c).

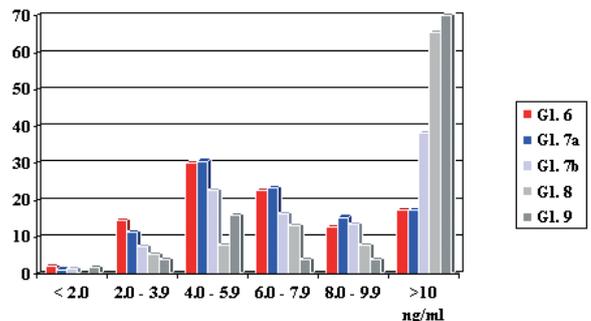


Fig. 6. Gleason score (%) and PSA ng/ml (Helpap and Egevad, 2008c).

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significant shift to younger men. However, mainly high grade carcinomas with Gleason score > 7a and with tumour extent > 20% in more than one core needle biopsy specimen are found in patients younger than 50 years (range of 25-50 yrs) (Helpap and Egevad, 2008c).

Serum PSA

The border between low and high grade carcinoma of the prostate (Gleason scores 6/7a and 7b, respectively) in terms of serum PSA values is 10ng/ml. In combination with tumour extent core needle biopsy specimens with less than 10% tumour extent of prostatic carcinoma and PSA values < 10 ng/ml have carcinomas with Gleason score ≤ 7a. High grade carcinomas with Gleason score ≥ 7b have more extensive cancer and PSA values > 10 ng/ml (Helpap and Egevad, 2008b,c) (Fig. 6).

This distinction may also be of prognostic importance, as shown in the tables of Partin (Partin et al., 1997). Therefore, prostatic carcinoma of Gleason score 7a should possibly not be considered high grade prostate cancer and therefore needs to be distinguished from Gleason score 7b prior to treatment, for example in brachytherapy (Raagde et al., 2000).

Conclusion

By providing a more accurate prognostic information prior to treatment, the modified Gleason grading contributes to a safer treatment decision. So, low grade prostate carcinoma is characterized by a Gleason score up to 7a, PSA value < 10 ng/ml and small tumour volume of 1-5% of core needle biopsy specimen. Such carcinomas correlate with pT 2, pN0, pM0 and mostly negative margins after radical prostatectomy. This should be included in prognostic tables of urological oncology.

References

- Allan R.W., Sanderson H. and Epstein J.I. (2003). Correlations of minute (0.5 mm or less) focus of prostate adenocarcinoma on needle biopsy with radical prostatectomy specimen: role of prostate specific antigen density. *J. Urol.* 170, 370-372.
- Amin M., Boccon-Gibod L., Egevad L., Epstein J.I., Humphrey P.A., Mikuz G., Newling D., Nilsson S., Sakr W., Srigley J.R., Wheeler T.M. and Montironi R. (2005). Prognostic and predictive factors and reporting of prostate carcinoma in prostate needle biopsy specimens. *Scand. J. Urol. Nephrol.* 39,20-337.
- Bastian P.J., Mangold L.A., Epstein J.I. and Partin A.W. (2004). Characteristics of insignificant clinical T1c prostate tumors. A contemporary analysis. *Cancer* 101, 2001-2005.
- Bostwick D.G. (1994). Grading prostate cancer. *Am. J. Clin. Pathol.* 102, 38-59.
- Bostwick D.G., Grignon D.J., Hammond M.E., Amin M.B., Cohen M., Crawford D.E., Gospodarowicz M., Kaplan R.S., Miller D.S., Montironi R., Pajak T.F., Pollack A., Srigley J.R. and Yabro J.W. (2000). Prognostic factors in prostate cancer. College of american pathologists consensus statement 1999. *Arch. Med.* 124, 995-1000.
- Chan T.Y., Partin A.W., Walsh P.C. and Epstein J.I. (2000). Prognostic significance of Gleason score 3+4 versus Gleason score 4+3 tumor at radical prostatectomy. *Urology* 56, 823-827.
- Egevad L., Norberg M., Mattson S., Norlen B.J. and Busch C. (1998). Estimation of prostate cancer volume by multiple core biopsies before radical prostatectomy. *Urology* 52, 653-658.
- Egevad L., Norlen B.J. and Norberg M. (2001). The value of multiple core biopsies for predicting the Gleason score of prostate cancer. *B.J.U. Int.* 88, 716-721.
- Egevad L., Granfors T., Karlberg L., Bergh A. and Stattin P. (2002). Prognostic value of the Gleason score in prostate cancer. *B.J.U. Int.* 89, 538-542.
- Egevad L., Allsbrook W.C. and Epstein J.I. (2005). Current practice of Gleason grading among genitourinary pathologists. *Hum. Pathol.* 36, 5-9.
- Epstein J.I. (2000). Gleason score 2-4 adenocarcinoma of the prostate on needle biopsy: a diagnosis that should not be made. *Am. J. Surg. Pathol.* 24, 477-478.
- Epstein J.I., Algaba F. and Allbrooks J. (2004). Acinar adenocarcinoma. In: World health Organization Classification of Tumours. Pathology and Genetics: Tumours of the urinary system and male genital organs. Eble J.N., Sauter G., Epstein J.I. and Sesterhenn I.A. (eds). IARC press. Lyon, France. pp 179-184.
- Epstein J.I., Allsbrook W.C., Amin M.B., Egevad L. and the ISUP Grading Committee (2005). The 2005 international society of urological pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma. *Am. J. Surg. Pathol.* 29, 1228-1242.
- Gallee M.P., Ten Kate F.J., Mulder P.G., Blom J.H. and van der Heul R.O. (1990). Histological grading of prostatic carcinoma in prostatectomy specimens. Comparison of prognostic accuracy of five grading systems. *Br. J. Urol.* 65, 368-375.
- Garnett J.E., Oyasu R. and Grayhack J.T. (1984). The accuracy of diagnostic biopsy specimens in predicting tumor grades by Gleason's classification of radical prostatectomy specimens. *J. Urol.* 131, 690-693.
- Glaessgen A., Hamberg H., Pihl C.G., Sundelin B., Nilsson B. and Egevad L. (2002). Interobserver reproducibility of percent Gleason grade 4/5 in total prostatectomy specimens. *J. Urol.* 168, 2006-2010.
- Gleason D.F. (1966). Classification of prostatic carcinomas. *Cancer Chemotherapy (Rep Part)* 50, 125-128.
- Gleason D.F. (1977). Histologic grading and clinical staging of prostatic carcinoma. In: *Urologic pathology. The prostate.* Tannenbaum M. (ed). Lea and Febiger. Philadelphia. pp 171-198.
- Gleason D.F. (1992). Histological grading of prostate cancer: a perspective. *Hum. Pathol.* 23, 273-279.
- Gleason D.F. and Mellinger G.T. (1974). Prediction of prognosis for prostatic adenocarcinoma by combined histological grading and clinical staging. *J. Urol.* 111, 58-64.
- Helpap B. (1993). Review of the morphology of prostatic carcinoma with special emphasis on subgrading and prognosis. *J. Urol. Pathol.* 1, 3-20.
- Helpap B. and Egevad L. (2006). The significance of modified Gleason grading of prostatic carcinoma in biopsy and radical prostatectomy specimens. *Virch. Arch.* 449, 622-627.
- Helpap B. and Egevad L. (2007). The value of the modified Gleason grading system of prostate adenocarcinoma in routine urological diagnostics. *Urologe* 46, 59-62.
- Helpap B. and Egevad L. (2008a). Correlations of modified Gleason Grading with pT stage of prostatic ncarcinomas after radical prostatectomy. *Analyt. Quant. Cytol. Histol.* 30, 1-7.

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- Helpap B. and Egevad L. (2008b). Correlation of modified Gleason grading of prostate carcinoma with serum PSA, age and tumor extent in needle biopsy specimens. *Analyt. Quant. Cytol. Histol.* 30, 133-138.
- Helpap B. and Egevad L. (2008c). Clinical insignificance of prostate cancer, are there morphological findings. *Urologe* 47, (in press). (In German).
- Helpap B. and Sinicina I. (2002). Diagnostic measures for therapeutic steps of prostate adenocarcinoma. *Urologe (B)* 42, 121-127.
- Helpap B., Böcking A., Dhom G., Kastendiek R., Leistenschneider W. and Müller H.A. (1985). Klassifikation, histologisches und zytologisches Grading sowie Regressionsgrading des Prostatakarzinoms. Eine Empfehlung des pathologisch-urologischen Arbeitskreises "Prostatakarzinoms". *Pathologie* 6, 3-7.
- Humphrey P.A. (2004). Gleason grading and prognostic factors in carcinoma of the prostate. *Mod. Pathol.* 17, 292-306.
- Kramer S.A., Spahr J., Brendler C.B. Glenn J.F. and Paulson D.E.F. (1980). Experience with Gleason's histopathologic grading in prostatic cancer. *J. Urol.* 124, 223-225.
- Lang P.H. and Narayan P. (1983). Understaging and undergrading of prostate cancer. Argument for postoperative radiation of adjuvant therapy. *Urology* 21, 113-118.
- Lau W.K., Blute M.L., Bostwick D.G., Weaver A.L., Sebo T.J. and Zincke H. (2001). Prognostic factors for survival of patients with pathological Gleason score 7 prostate cancer: differences in outcome between primary Gleason grades 3 and 4. *J. Urol.* 166, 1692-1697.
- Lopez-Beltran A., Mikuz G., Luque R.J., Mazzucchelli R. and Montironi R. (2006). Current practice of Gleason grading of prostate carcinoma. *Virchows Arch.* 448, 111-118.
- Melia J., Moseley R., Ball R.Y., Griffiths D.F.R., Grigor K., Harnden P., Jarmulowicz M., McWilliam Jr., Montironi R., Waller M., Moss S. and Parkinson M.C. (2006). A UK-based investigation of inter-and intra-observer reproducibility of Gleason grading of prostatic biopsies. *Histopathology* 48, 644-654.
- Mills S.E. and Fowler J.E. (1986). Gleason histologic grading of prostatic carcinoma. Correlations between biopsy and prostatectomy specimens. *Cancer* 57, 346-349.
- Mosse C.A., Magi-Galluzzi C., Tsuzuki T. and Epstein J.I. (2004). The prognostic significance of tertiary Gleason pattern 5 in radical prostatectomy specimens. *Am. J. Surg. Pathol.* 28, 394-398.
- Mostofi F.K., Sesterhenn I.A. and Davis C.J. (2002). Histological typing of prostate tumours In World Health Organization International histological classification of tumours. Springer Berlin Heidelberg New York.
- Pan C.C., Potter S.R., Partin A.W. and Epstein J.I. (2000). The prognostic significance of tertiary Gleason patterns of higher grade in radical prostatectomy specimens: a proposal to modify the Gleason grading system. *Am. J. Surg. Pathol.* 24, 563-569.
- Partin A.W., Kattan M.W., Subong E.N., Walsh P.C., Wojno K.J., Oesterling J.E., Scardino P.T. and Pearson J.D. (1997). Combination of prostate-specific antigen, clinical stage, and Gleason score to predict pathological stage of localized prostate cancer: a multi-institutional update. *J.A.M.A.* 277,1445-1451.
- Raagde H., Korb L.J., Elgamad A.A., Grado G.L. and Nadir B.S. (2000). Modern prostate brachytherapy: prostate specific antigen results in 219 patients with up to 12 years of observed follow-up. *Cancer* 89, 135-141
- Sakr W.A., Tefili M.V., Grignon D.J., Banerjee M., Dey J., Gheiler E.L., Tiguert R., Powell I.J. and Wood D.P. (2000). Gleason score 7 prostate cancer: a heterogeneous entity? Correlation with pathologic parameters and disease-free survival. *Urology* 56, 730-734.
- Steinberg D.M., Sauvageot J., Piantadosi S. and Epstein J.I. (1997). Correlation of prostate needle biopsy and radical prostatectomy Gleason grade in academic and community settings. *Am. J. Surg. Pathol.* 21, 566-576.
- Young R.H., Srigley J.R., Amin M.B., Ulbright T.M. and Cubilla A.L. (2000). Tumors of the prostate gland, seminal vesicles, male urethra, and penis. In: Atlas of tumor pathology. Rosai J. and Sobin L.H. (eds). A.F.I.P. Washington. pp 111-216.

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