Gleason Score Discrepancies Between Needle Biopsies and Radical Prostatectomy Specimens in an African Men: Clinical Implication

Abdellatif Janane[1,*], Fouad Hajji[1], Youssef Dakkak[1], Mohamed Ghadouane[1], Ahmed Ameur[1], Mohamed Abbar[1] and Abderhman Albouzidi[2]

[1]*Department of Urology, Universitary Military Hospital Mohamed V. Rabat, Morocco*

[2]*Department of Pathology, Universitary Military Hospital Mohamed V. Medical University Med V. Rabat, Medical Faculty Mohamed V. Rabat, Morocco*

Abstract: *Objective*: Gleason scores, as determined by 18-gauge core needle biopsies (NB), were compared with both Gleason scores and the pathological staging of corresponding radical prostatectomy(RP) specimens. The goal was to evaluate the clinical implication and the prognostic impact of these discrepancies.

Methods: Records of 234 consecutive patients undergoing a radical retro pubic prostatectomy between 2001 and 2012 were reviewed. In total, all our patients were enrolled, al1 of whom had been diagnosed with adenocarcinoma by transrectal needle biopsies using an 18-gauge automated spring-loaded biopsy gun.

Results: Grading errors were greatest with wel1-differentiated tumors. The accuracy was 18 (23%) for Gleason scores of 2-4 on needle biopsy. Of the 108 evaluable patients with Gleason scores of 5-7 on needle biopsy, 84 (78%) were graded correctly. All of the Gleason scores of 8-10 on needle biopsy were graded correctly. 54 of 162 patients (33%), with a biopsy Gleason score of < 7 had their cancer upgraded to above 7. Tumors in 18 patients (60%) with both a Gleason score < 7 on the needle biopsy and a Gleason score of 7 for the prostatectomy specimen were confined to the prostate.

Conclusion: The potential for grading errors is greatest with well-differentiated tumors and in patients with a Gleason score of < 7 on the needle biopsy. Predictions using Gleason scores are sufficiently accurate to warrant its use with all needle biopsies, recognizing that the potential for grading errors is greatest with well-differentiated tumors.

Keywords: Prostate adenocarcinoma, needle biopsy, radical prostatectomy, Gleason score correlation, prognostic significance.

INTRODUCTION

Originally described in the 1960s, The Gleason score (GS) remains the most widely accepted grading system in the evaluation of adenocarcinoma of the prostate [1]. Given the inherent sampling error of diagnostic needle biopsy (NB) and the frequently multifocal nature of prostate cancer, discrepancy between the GS of NB specimens and RP is a common finding [2, 6]. One review summarized 11 series with over 2620 cases, in which an exact match in grading was seen in an average of only 42% of the time [3]. Accurate prediction of the biological potential of prostate cancer remains important to clinicians treating patients with this disease. A separate interrogation that has received less critical study in the literature is whether these commonly noticed discrepancies in grade assignment between NB and RP GS may provide intrinsic prognostic information. It's generally accepted that the RP GS represents the "true" grade of the cancer, to the extent that the specimen is reviewed in its entirety [4].

Histological grading separates cancers of the prostate into groups with markedly different rates of progression and dissemination over time. Gleason's system is popular because it is easy to learn and reproduce, and has been shown to correlate well with the c1inical course in groups of patients [1, 5]. We compared the Gleason score determined by 18-gauge core needle biopsies with both the Gleason score and pathological staging of radical prostatectomy specimens.

MATERIAL AND METHODS

The records of 234 consecutive patients who underwent a radical retro pubic prostatectomy for prostate cancer between 2001 and 2012 were retrospectively reviewed. Patient and tumor characteristics are shown in Table **1**.

In all 234 cases, a radical retro pubic prostatectomy for clinically localized prostatic carcinoma was performed after negative frozen sections came back from bilateral pelvic lymphadenectomies. All of the patients had initially been diagnosed with an adenocarcinoma using an 18-gauge biopsy gun. The age, preoperative and postoperative PSA levels, and

*Address correspondence to this author at the Urology Department, Universitary Military Hospital Med V. Hay Ryad, Rabat, Morocco; Tel: 00212 61 21 93 21; Fax: 00212 5 37 71 68 10; E-mail: a.janane@yahoo.fr

ISSN: 1927-7210 / E-ISSN: 1927-7229/13

Table 1: Patient and Tumor Characteristics

Number of patients	234
Mean age in years (range)	60.4 (48·75)
No. at a tumor stage (%)	96(41%)
T1c	78(33%)
T2a	42(18%)
T2b	9(3.8%)
T3a	9(3.8%)
T3b	5.9
PSA (ng/ml)	10.2
T1c	14.9
T2a	18.1
T2b	23.2
T3a	13.7
T3b	
Mean PSA (ng/ml)	

Abbreviations: PSA: prostate specific antigen.

Gleason scores from the trans rectal needle biopsy and radical prostatectomy specimens were examined. the protocol included sextant biopsies, 3 additinnal posterolateral biopsies in each peripheral zone, and 3 biopsies in the midline peripheral zone. All suspicious hypo echoic lesions were considered to be positive ultrasound findings and the basis for biopsy. A minimum of 12 cores were collected. According to standard procedures, all available biopsy materials were reviewed, and representative histological slides were assigned a Gleason score by the same uro pathologist at our institution. Two pathologic stages where recognized: (1) disease confined to the prostate (tumors that were confined to the parenchyma of the prostate or that had invaded but did not penetrate the capsule of the prostate) and (2) extracapsular extension. To obtain a Gleason score, the primary and secondary patterns were combined for a number score of from 2 to 10. Grouping the Gleason scores into 3 categories can be helpful, with well- (Gleason scores of 2-4), moderately (Gleason scores of 5-7), and poorly (Gleason scores of 8-10) differentiated disease. A comparison was made between the Gleason scores of the needle biopsies and prostatectomy specimens. Overall accuracy was evaluated using the sensitivity, specificity, and positive and negative predictive values. The accuracy of the needle biopsy was compared to the Gleason scores and clinical staging using chi-square analysis. A value of $p<0.05$ was considered statistically significant.

RESULTS

Gleason scores for needle biopsy specimens and radical prostatectomy specimens were compared in 234 patients. Patient ages ranged from 48 to 75 (mean: 60.4 years). Preoperative serum PSA ranged from 2.0

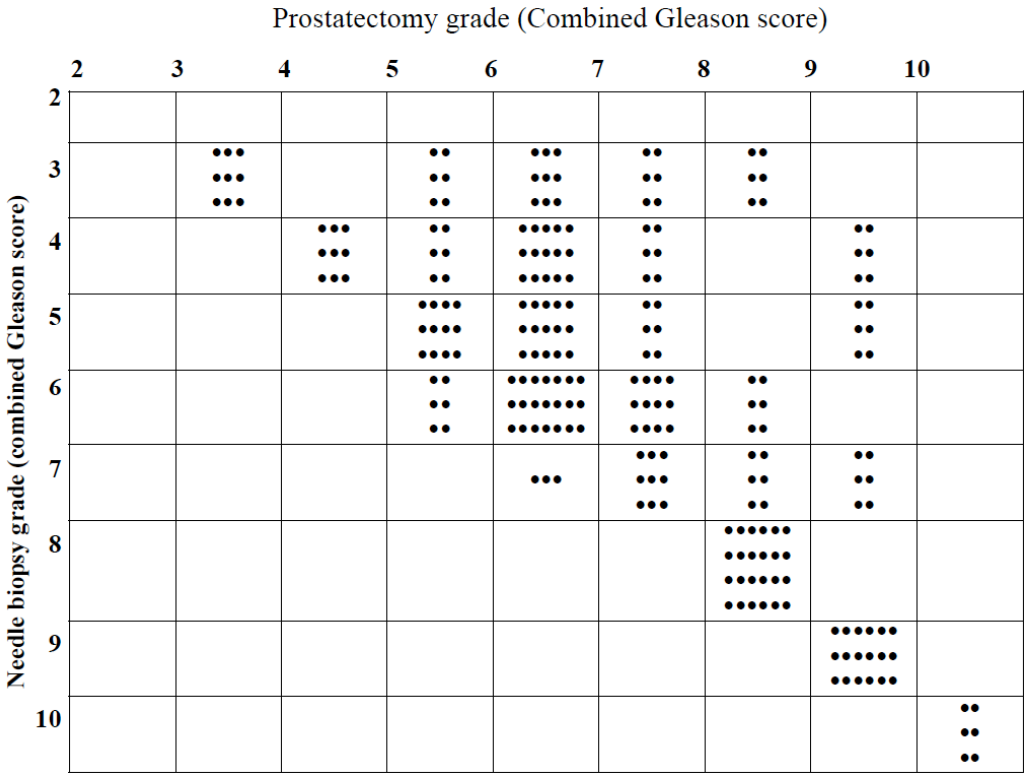

Figure 1: Comparison of Gleason score from needle biopsies and radical prostatectomy specimens.

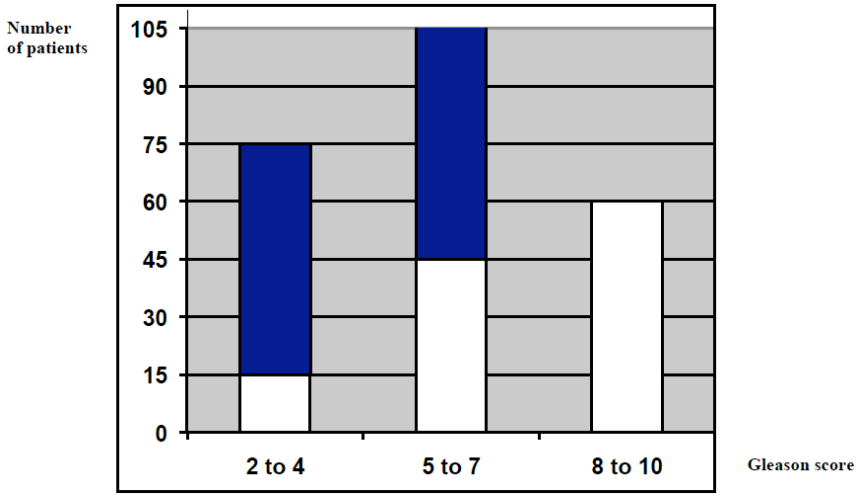

Figure 2: Effect of biopsy grade on grading accuracy. Shaded areas represent cases in which biopsy specimens were accurately graded. Biopsy grading improved for higher Gleason scores.

to 29.9 ng/ml (mean: 13.7 ng/ml). There were 96 patients with T1c, 78 with T2a, 42 with T2b, 9 with T3a, and 9 with T3b. Gleason score ranged from 3 to 10 for both needle biopsy and radical prostatectomy specimens. The relationship between Gleason score for needle biopsy and for prostatectomy specimens was shown in Figure **1**.

Gleason scores ranged from 3 to 10 for both needle biopsies and radical prostatectomy specimens. The Gleason score from the needle biopsy was identical to that of the prostatectomy specimen in 60 (25.6%) patients. One hundred and eight (46%) and 132 (56%) patients had Gleason scores of 5-7 (moderately differentiated tumor) on needle biopsy and prostatectomy specimens, respectively, whereas only 48 (21%) needle biopsies and 84 (36%) prostatectomy specimens had Gleason scores of 8-10 (poorly differentiated tumor). The relationship between clinical under-staging of the primary tumor and discrepancies between the Gleason scores of the biopsies and prostatectomy specimens are shown in Figure **2**. Among the 26 patients with Gleason scores of 2-4 on needle biopsy, 60 (77%) were under-graded, with 48 (80%) of the 60 having moderately differentiated (Gleason scores of 5-7) tumors, giving an accuracy of 23% (18/78) for Gleason scores of 2-4.

Of the 108 patients with Gleason scores of 5-7 on needle biopsy, 84 (78%) were graded correctly. In the remaining 24 (22%) patients, the tumors were graded incorrectly on the needle biopsy, with 8 having poorly differentiated tumors. All tumors with Gleason scores of 8-10 on needle biopsy were graded correctly.

Overall, needle biopsies were under-graded in 117 (50%) cases, over graded in 9 (3.8%), and correctly graded in 108 (46.2%). The positive predictive value of a Gleason score on needle biopsy was only 54.8%.

Clinical staging predominantly revealed T2 lesions: There were 96 patients with T1c, 78 with T2a, 42 with T2b, 9 with T3a, and 9 with T3b. Otherwise, the pathology of radical prostatectomy specimens identified pT2 in 75 patients (29%), PT3a in 99 men (39.5%) and PT3b in 60 cases (31.5%).

When the preoperative Gleason score was less than 7, 60 (37%) patients had organ-confined lesions. Otherwise, when the preoperative Gleason score was

Table 2: Comparison of Gleason Scores of < 7 and ≥ 7 for Needle Biopsies and the Pathological Staging of Prostatectomy Specimens

Needle biopsy	Prostatectomy stage: No. (%)			Total	p
Gleason score	**pT2**	**pT3a**	**pT3b**		
<7	60 (37)	75 (46)	27 (17)	162	
≥7	15 (21)	24(33)	33(46)	72	
Totals	75	99	60	234	< 0.001*

*Chi-square was used between Gleason score and tumor staging.

≥ 7, 15 patients (21%) had tumors confined to the prostate (Table **2**).

DISCUSSION

The Gleason grading is a powerful tool to prognosticate and aid in the treatment of men with prostate cancer. The needle biopsy Gleason score correlates with virtually other pathologic parameters, including tumor volume, margin status, seminal vesicle invasion and lymph node extension. Four decades after its initial description, The Gleason grade remains one of the most powerful prognostic predictors for adenocarcinoma of the prostate [1]. In light of the inherent sampling error of needle biopsy and the frequently multifocal nature of prostate cancer, discordance in grade between biopsy and prostatectomy specimen is common finding, with rates of 32-71% reported in the literature [2, 15]. Because of the prostatectomy GS is based on review of the entire gland submitted for pathological analysis and evaluation, it is intuitive that this grade more accurately reflects the underlying biology of the neoplasm. Indeed, when both the NB and RP GS are included in multivariate analyses to predict biochemical recurrence, RP GS has been shown to be a superior and strong predictor in auguring PSA outcome compared with the NB SG [3, 7].

The histological grade of prostate cancer indicates its aggressiveness and may predict the prognosis, thereby influencing treatment decision-making. Since prostate cancer is characterized by histopathological heterogeneity and is frequently multicentric, it is important to understand the relationship between the grade obtained from needle biopsies and the grade identified on direct examination of the tumor. Muller *et al*. found a uniform pattern in 12 of 100 total prostatectomy specimens. Potentially, a greater amount of biopsy material could reduce sampling errors in heterogeneous tumors. Accordingly, a larger number of biopsy specimens could reduce sampling errors in heterogeneous tumors [8] Currently, the magnitude of reported differences in Gleason scores between biopsy and prostatectomy specimens is generally not large. There are multiple factors that might account for potential differences in accuracy seen between studies using Gleason's grading system. Müntener *et al.* examined 6625 men treated by multiple surgeons at a tertiary referral center [9]. This study was the largest series addressing the issue of Gleason grade discrepancies and the first to systematically evaluate the prognostic significance of this phenomen. The authors found consistently lower risks of PSA progression among patients with a lower NB GS and significantly increased risk of PSA recurrence among men with a higher NB GS, within and across RP strata, relative to cases with equal NB and RP GS. Real differences in tumor homogeneity exist, so that the number of biopsy samples and prostatectomy specimen blocks examined may affect the final interpretation. Recent papers have showed that the anticipated incidence of regional lymph node metastasis is not measurably affected by grading errors [10, 11]. In our experience, the Gleason histologic scoring system for prostatic adenocarcinoma is one of the strongest predictors of biologic behavior, including invasiveness and metastatic potential, but it is not sufficiently reliable when used alone in predicting pathologic stage. The grade should be inc1uded among other prognostic factors in therapeutic decision-making, such as patient age and health, clinical stage, and serum PSA level. The likelihood of a large difference between the biopsy and prostatectomy specimen Gleason scores is greatest when only a single microscopic focus of the tumor is present in the biopsy specimen, and the tumor in the biopsy specimen is of low grade.

Other studies in the field shed light on potential explanatory hypotheses for GS discrepancies, including pathology error, borderline cases (in which an NB may be graded in two different, but not necessarily incorrect, ways), sampling error (in which a major component of the tumor in the RP is not present in the NB), and reverse sampling error (in which a minor component of tumor in the RP is sampled in NB), and reverse sampling error (in which a minor component of tumor in the RP is sampled in NB) [9, 12]. Pathology error is self-explanatory; consensus NB reading may reduce somewhat, but certainly not eliminate, the frequency of grade discrepancies [13]. Borderline cases are inherent to any grading system because grade is a continuum and there will inevitably be some cases in which the grade straddles two strata. Reverse sampling error can explain some cases of 3+4=7 or 4+3=7 on needle biopsy in which the RP has such little pattern 4 that the RP GS is called 3+3=6 with tertiary pattern 4, resulting in an apparent discrepancy when the tertiary pattern is dropped in the simplified reporting of RP GS [14, 15].

Over-grading tends to occur much less frequently than under-grading, and patients are rarely denied potentially curative surgery based on an incorrect Gleason score determined from a biopsy [9, 16]. In this

study, grading errors were found to be greatest in tumors with Gleason scores of 2-4, for which the positive predictive value of needle biopsy was approximately 23%. Among the 78 evaluable patients with Gleason scores of 2-4 on needle biopsy, 77% had been under-graded, with 48 patients having moderately differentiated tumors. All needle biopsy specimens with Gleason scores of 8-10 were graded correctly. The concordance between needle biopsy and radical prostatectomy Gleason scores improved with higher values for the Gleason score. We correlated the biopsy Gleason score with the final pathological stage and found that when the combined preoperative Gleason score was <7, 37% of patients had organ-confined lesions, while only 21% had tumors confined to the prostate when the preoperative score $\geq$ 7.

The mainstream use of the tumor grade as a prognostic indicator may have major ramifications for patients being treated for prostate carcinoma. Evaluation of Gleason scores in patients with well-differentiated tumors and Gleason scores of < 7 may eventually lead to guidelines regarding how management decisions in patients with prostate carcinoma should be considered. Before such protocols are implemented, further study is required to establish to what degree tumor grade affects prostate carcinoma needle biopsy efficacy [7, 9]. Overall, Gleason grades from needle biopsies produced accurate predictions in only 108 (46%) patients when compared with prostatectomy specimens. Accuracy was best for poorly differentiated biopsy specimens. The predictive value of the Gleason score is sufficient to warrant its use with a1l needle biopsies, recognizing that the potential for grading error is greatest with well-differentiated tumors. This awareness affects treatment policy, particularly the watchful waiting criteria. These parameters can at least serve as useful, specific tools which, when used with biopsy-derived Gleason scores, can provide information concerning the treatment and prognosis of a patient with prostate carcinoma. Determining a more-precise definition of the minimum number of specimens to reliably predict tumor grade in subsequent prostatectomies requires further study [10, 17].

The frequently multifocal nature of prostate cancer complicates the classification of architectural heterogeneity within and between tumor nodules. We did not specifically address the issue of multifocality because we could not tell whether our discrepancies were due to grade heterogeneity in a single- tumor nodule versus discrete tumor nodules. Ones series specifically examined this issue, finding the rate of upgrading to be twice as common among the over 80% of cases with heterogeneity in the topographical distribution of Gleason grades versus those cases with homogenous grade [9]. The results of the present study are consistent with that earlier work, even with stricter definitions of the comparison groups to patients consonant NB and RP GS, compared within and across multiple GS strata, and multivariate analyses adjusting for differences in PSA and pathological stage between the groups. Our results have the limitation inherent to any retrospective study. Given the referral nature of our practice, we have incomplete data on any biopsies that may been performed in addition to the index biopsy, the number of cores sampled in each case, and indices of the extent of involvement in particular cores. In addition, the volume of radical prostatectomy at our institution is too large for a single pathologist review all cases. Biopsy and prostatectomy Gleason were assigned by a small group of pathologists with extensive experience in urological pathology.

CONCLUSION

Grade discrepancy between needle biopsy and prostatectomy is a very common finding. In light of the inherently more comprehensive sampling, the Gleason score of the surgical specimen is widely held to be the “true” pathological grade of surgically treated patients. The potential for grading errors is greatest with well-differentiated tumors and in patients with a Gleason score of < 7 on the needle biopsy. The predictive value of the Gleason score is sufficient to warrant its use with a1l needle biopsies, recognizing that the potential for grading error is greatest with well-differentiated tumors. These potential discrepancies can provide information concerning the treatment and prognosis of a patient with prostate carcinoma.

REFERENCES

[1] Cookson MS, Fleshner NE, Soloway SM, Fair WR. Corre1ation between Gleason score of needle biopsy and radical prostatectomy specimen: accuracy and clinical implications. J Urol 1997; 157: 559-62. http://dx.doi.org/10.1016/S0022-5347(01)65201-7

[2] Gonzalgo ML, Bastian PJ, Mangold LA, *et al*. Relationship between primary Gleason pattern on needle biopsy and clinicopathologic outcomes among men with Gleason score 7 adenocarcinoma of the prostate. Urology 2006; 49: 820-26.

[3] Makhlouf AA, Krupski TL, Kunkle D, Theodorescu D. The effect of sampling more cores on the predictive accuracy of pathological grade and tumor distrubition in the prostate biopsy. BJU Int 2004; 93: 271-74. http://dx.doi.org/10.1111/j.1464-410X.2004.04600.x

[4] King CR, Mc Neal JE, Gill H, Presti Jr JC. Extended prostate biopsy scheme improves reliability of Gleason grading: implication of radiotherapy patients. Int J Radiat Oncol Biol Phys 2004; 59: 386-61. http://dx.doi.org/10.1016/j.ijrobp.2003.10.014

[5] Koksal T, Ozcan F, Kadiog1u TC, Esen T. Klcaslan J, Tunc M. Discrepancy between Gleason scores of biopsy and radical prostatectomy specimens. Eur Urol 2000; 37: 670-4. http://dx.doi.org/10.1159/000020216

[6] Chun FK-H, Steuber T, Erbersdobler A. Development and internal validation of a nomogram predicting the probability of prostate cancer Gleason sum upgrading between biopsy and radical prostatectomy pathology. Eur Urol 2006; 49: 820-26. http://dx.doi.org/10.1016/j.eururo.2005.11.007

[7] King CR. Patterns of prostate cancer biopsy grading: trends and clinical implications. Int J cancer 2000. http://dx.doi.org/10.1002/1097-0215(20001220)90:6<305::AID-IJC1>3.0.CO;2-U

[8] Epstein JI, Allsbrook Jr WC, Amin MB, Egevad LL. The 2005 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of prostatic carcinoma. Am J Surg Pathol 2005; 29: 1228-42. http://dx.doi.org/10.1097/01.pas.0000173646.99337.b1

[9] Mûntener M, Epstein JI, Hernandez DJ, Gonzalgo ML, *et al*. Prognostic significance of Gleason Score discrepancies between needle biopsy and radical prostatectomy. Eur Urol 2008; 53: 767-76. http://dx.doi.org/10.1016/j.eururo.2007.11.016

[10] Stephen A, Boorjian R, Jeffrey Karnes R, *et al*. The impact of discordance between biopsy and pathological Gleason scores on survival after radical prostatectomy. J Urol 2009; 181: 95-104. http://dx.doi.org/10.1016/j.juro.2008.09.016

[11] Rauf Taner D, Asken Erog L, Sahen A. Increasing the number of biopsies increases the concordance of Gleason scores of needle biopsies and prostatectomy specimens Urol Oncol 2007; 25: 276-82.

[12] Yang CW, Lin TP, Huang YH. Does extended prostate needle biopsy improve the concordance of Gleason score between biopsy and prostatectomy in the Taiwanese population? J Chin Med Ass 2012; 75: 97-101. http://dx.doi.org/10.1016/j.jcma.2012.02.001

[13] Davies JD, Aghazadeh MA, Phillips S, Salem S. Prostate size as a predictor of Gleason upgrading in patients with low risk prostate cancer. J Urol 2011; 186: 2221-27. http://dx.doi.org/10.1016/j.juro.2011.07.104

[14] Audenet F, Comperat E, Seringe E, *et al*. Patient risk stratification using Gleason concordance and upgrading among men with prostate biopsy Gleason score 6 or 7. Urol Oncol 2011; 29: 602-607. http://dx.doi.org/10.1016/j.urolonc.2009.09.011

[15] Isariyawongse BK, Sun L, Banez LL, Robertson C, *et al*. Significant discrepancies between biopsic and pathologic Gleason sums in prostate cancer. The predictive role of Age and prostate specific antigen. Urology 2008; 72: 882-86. http://dx.doi.org/10.1016/j.urology.2008.02.021

[16] Kuroiwa K, Shiraishi T, Naito S. Gleason score correlation between biopsy and prostatectomy specimen and prediction of high grade Gleason patterns: significance of central pathologic review. Urology 2011; 77: 407-11. http://dx.doi.org/10.1016/j.urology.2010.05.030

[17] Gershman B, Dahi DM, Olumi AF, *et al*. Smaller prostate gland size and older age predict Gleason score upgrading. Urol Oncol 2011; 28: 11-16.

Received on 24-11-2012 Accepted on 03-05-2013 Published on 31-07-2013

http://dx.doi.org/10.6000/1927-7229.2013.02.03.6