demonstrating a significant association between intensity of neoadjuvant chemotherapy received and pathological complete response rates.[1] It is definitely possible that chemotherapy related complications in some patients have the potential to cause harm by introducing prolonged delays in cystectomy in individuals who may not harbor distant metastases.

Due to the fact that many patients in our cohort received chemotherapy from their local oncologists, we are unable to fully characterize the specific reasons for patients receiving less than full neoadjuvant treatment intensity. We are not suggesting that neoadjuvant chemotherapy harbors no risks to the patient. However, we were unable to find a significant association between time to cystectomy and overall survival in our cohort, of whom all received neoadjuvant chemotherapy. This finding suggests that the level of risk related to timing of surgery may be different in patients with bladder cancer receiving systemic chemotherapy compared to those who remain untreated from the date of transurethral resection of bladder tumor until definitive cystectomy. Our report presents initial data on this issue, and certainly additional data sets need to be analyzed before any definitive statements can be made. We merely propose that our data do not support the notion that neoadjuvant chemotherapy associated delays in cystectomy leading to a missed potential for curative intervention are common.

In our cohort 124 patients had clinical T2,N0 disease at initiation of neoadjuvant chemotherapy. The therapy received in this group was consistent with the data for the overall cohort, with a median of 3 cycles of neoadjuvant chemotherapy, a median time to cystectomy of 195 days and a pathological complete response rate of 24% (30 patients). Median overall survival for this group was 22.4 months. However, nearly half of the patients in this group (58, 47%) underwent cystectomy in 2012 or later. Hence, followup for this group is immature. We will continue to follow this cohort closely and report any new findings that come to light with longer followup.

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Re: Critical Analysis of Early Recurrence after Laparoscopic Radical Cystectomy in a Large Cohort by the ESUT

S. Albisinni, L. Fossion, M. Oderda, O. M. Aboumarzouk, F. Aoun, T. Tokas, V. Varca, R. Sanchez-Salas, X. Cathelineau, P. Chlosta, F. Gaboardi, U. Nagele, T. Piechaud, J. Rassweiler, P. Rimington, L. Salomon and R. van Velthoven

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To the Editor: The authors critically analyze a large cohort by the European Association of Urology Section of Uro-Technology and assess early recurrences after laparoscopic radical cystectomy and evaluation of risk factors, including the impact of pneumoperitoneum. They focus their analysis on patients with favorable pathology (pT2 N0 R0 disease), finding that 27 of 311 patients (8.7%) experienced recurrences during the following 24 months. Surgical negligence was observed in only 1 patient, which was associated with the endo bag rupturing during transvaginal extraction with subsequent vulvar and peritoneal tumor metastasis after 4 months. Among the 27 patients with recurrence a shorter recurrence-free survival was significantly predictive of cancer specific death (HR 0.86, 95% CI 0.78–0.94, $p = 0.001$) as well as carcinoma in situ on pathological examination (HR 3.68, 95% CI 1.07–12.7, $p = 0.039$). While analyzing causes of early recurrence, the authors suggest that the continuous insufflation-desufflation and leakage of gas around the ports—with consequent aspiration of tumor cells via a chimney effect—may promote tumor seeding (TS).[1]

The hypothesis correlating a cause and effect relationship of their findings with CO_2 pneumoperitoneum conditions is coherently founded and extensively studied by implementation of animal models, in vitro experiments, case reports and a prospective study.[2,3] A model of

desufflation during laparoscopic surgery was designed by means of in vitro cell culture tools. The impact of desufflation on survival and invasion capacities of cancer cells was tested compared to continuous CO_2 insufflation by means of an in vitro pneumoperitoneum gas box model.[4] Survival and invasion capacities of cancer cells were superior in the desufflation model and were associated with oxidative stress. In that study desufflation during CO_2 pneumperitoneum was highlighted as the triggering factor of postoperative cancer cell survival and invasion.

However, the impact of CO_2 pneumoperitoneum desufflation cannot be considered the only triggering factor associated with port site metastasis (PSM) and TS. Indeed, in an Italian survey on laparoscopic cystectomy an interesting aspect was the absence of tumor seeding in 83 cases despite the longer operative time compared to open surgery (520 vs 330 minutes).[5] This finding suggests that respect of surgical oncologic principles is important to prevent TS.

Another important factor associated with TS and PSM is the origin of the tumor and its malignant and metastatic potential. Transitional cell carcinoma is one of the most malignant urinary tract tumors with a high grade of dissemination. Most of the published data on TS and PSM in the urological literature are related to transitional cell carcinoma.[5] Albisinni et al suggest that tumor stage is an important prognostic factor for TS but we believe that tumor grade is another important predictor of worse prognosis. Tumor grade usually follows tumor stage, and patients with high grade carcinoma have higher stage disease.[6] In a recent survey Micali et al showed that in all patients with TS the histological features demonstrated a high grade status.[7]

PSM is suggested as a rare complication of robotic and laparoscopic minimally invasive surgery.[8,9] We believe that superior laparoscopic surgical skills and broad oncologic expertise should be well consolidated to perform challenging procedures such as cystectomy. In this era of worldwide expanded laparoscopic technologies and use of laparoscopic approaches in patients with advanced cancer TS and PSM should be considered when planning such treatment, and desufflation should be avoided during laparoscopic procedures.

Respectfully,

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2. Sultania M, Pandey D, Sharma J et al: Delayed isolated port-site metastasis of gallbladder cancer following laparoscopic cholecystectomy: report of two cases. J Gastrointest Cancer, suppl., 2014; **45:** 188.
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9. Song J, Kim E, Mobley J et al: Port site metastasis after surgery for renal cell carcinoma: harbinger of future metastasis. J Urol 2014; **192:** 364.

Reply by Authors: We agree with the points highlighted by Mynbaev et al. We wish to emphasize that most of the recurrences observed were due to hematogeneous spread, thus advancing the hypothesis that the cancerous cells spread through the venous system rather than in the peritoneal cavity as a consequence of bladder pedicle squeezing in the Batson plexus. We want to stress the need for further studies exploring the effect of pneumoperitoneum on urothelial cancer dissemination, challenging the adequacy of minimally invasive surgery in the management of such a lethal disease.

Re: Consensus Guidelines for Reporting Prostate Cancer Gleason Grade

A. Zietman, E. Klein, M. J. Droller, P. Dasgupta, J. Catto and J. A. Smith, Jr.

J Urol 2016; ***195****: 1723.*

To the Editors: It was with some surprise that we read the Commentary by the editors of the *International Journal of Radiation Oncology, Biology and Physics; Urology; Urologic Oncology; BJU International; European Urology;* and *The Journal of Urology*® regarding the recently defined grading system for prostate cancer.[1–6] For clarification the Commentary published in *The Journal of Urology* is titled "Stage Grouping," which would appear to be an error.

In the Commentary it was noted that the modifications to the Gleason grading systems have been endorsed by the International Society of Urological Pathology (ISUP). In reality this is not the case. The consensus conference held in Chicago on November 1, 2014 was convened under the auspices of the ISUP but the attendees were selected and, unlike other ISUP consensus conferences, attendance was not open to the full membership of the society. The modifications to the Gleason grading system published in the *American Journal of Surgical Pathology* have never been formally endorsed by either the Council or the membership of the ISUP. What has been discussed is the terminology that has been applied to the grading system and the ISUP Council has unanimously endorsed the name ISUP Grade as the meeting was coordinated under the auspices of the ISUP.

The Commentary refers to the new system as Grade Groups rather than ISUP Grade. This terminology appears in the latest edition of the World Health Organization (WHO) classification.[7] However, it should be noted that this was not adopted by consensus but, rather, was a stop-gap measure proposed by the chair of the WHO Prostate Cancer Committee. While the final sentence of the definitive grading paper is "The new grading system and the terminology Grade Groups 1-5," has also been accepted for volume 8 of the 4th edition of the WHO series on histological and genetic typing of human tumors,[7] the phrase and the terminology "Grade Groups 1-5" were added to the proof of the article without the knowledge of at least some of the authors. As such, this statement is not endorsed by the ISUP. It should be noted that the term Grade Group is entirely inappropriate as the new grading system is a combination of Gleason scores and Gleason grades, and indeed is primarily score based.

Interestingly, there has been much debate in the pathology literature concerning the terminology and content of the new grading system, and it is clear that the grading system requires modification. We have recently outlined some of these concerns regarding grading terminology and criteria elsewhere, including a commentary in *BJU International*,[8–11] although this appears to have been overlooked by the authors of the Commentary. Such is our concern that we have made recommendations regarding a re-working of the system.[9–11]

Over the years the ISUP has endorsed recommendations regarding issues relating to prostate and renal cancer reporting.[12,13] However, these have never been the subject of a directive in the literature with respect to their implementation. We believe to do so is inappropriate and this has the effect of stifling academic debate. No such encouragement/requirement in relation to prostate cancer grading has appeared in the pathology literature and we believe that this is