171 POSTER

Vaginal cuff irradiation using ovoids: The benefit of treatment planning and dose calculation in each fraction

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Aim: To investigate the interfractional geometric and dose variations of ICRU 38 rectal (R) and bladder (BL) doses in patients receiving vaginal cuff irradiation.

Methods: Brachytherapy (BT) was done using Ir192 High Dose Rate (HDR). two ovoids were used and both fixed to each other and the coach. Orthogonal x-ray films were taken, treatment planning and optimisation were done in each fraction. Vaginal cuff, R and BL doses were calculated. In order to obtain the changes of applicators positions, pelvic bony landmarks were accepted as constant points, applicators, BL and R points were accepted as an inconstant points. The distances between constant and inconstant points were measured in x, y and z axes. The differences of distances between fractions were calculated. Furthermore, the magnitudes of the displacements in three planes were used to calculate the resultant vector and the relation between the ovoid diameter and the magnitude of resultant vectors were examined. To see whether the change of applicator position to bony pelvis has an effect on calculated R and BL doses, active source position and calculated durations of treatment time of first fraction was repeated for subsequent fractions, pertaining hypothetical R and BL doses were obtained. Then, R and BL reference doses and the difference first and subsequent hypothetic R and BL doses were calculated. Changes in subsequent hypothetic R and BL doses were compared with ovoid diameter. The relation between applicators displacement and the hypothetic doses were examined.

Results: Average magnitude of displacement of inconstant points in x, y and z axes were between 3,2 and 12,1mm. Resultant vectors of displacement were between 12,2 and 17,1mm. There was no significant relation between the ovoid size and the magnitude of resultant vectors of LO, RO, R and BL ($p>0.05$). The mean differences for calculated BL and R doses were 64-75cGy, and 47-58cGy respectively. No relation was seen between changes in subsequent hypothetical R, BL doses and ovoid diameter. Magnitudes of resultant vectors and changes in calculated doses showed no correlation ($p>0.05$).

Conclusion: There were geometric variations in the applicators, BL and R positions, between the fractions. Although there were significant differences in R and BL doses among the fractions, the magnitudes were relatively small. The result of this study suggest that the benefit of treatment planning is not enough to support to repeat in each fraction.

172 POSTER

Phase I/II study of PLD and Carboplatin in patients with advanced gynaecological carcinomas. An interim analysis of the GYN II trial of the AGO ovarian cancer study group

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We want to evaluate the MTD and the DLT of the combination chemotherapy with different doses of PLD. Dose level 0 was 20 mg/m2 PLD up to dose level 3 with 50 mg/m2 in 10 mg/m2 steps with a fixed dose of carboplatin AUC 6 up to a maximum of 800 mg every 4 weeks. Three patients per dose level should be recruited. If there was no DLT observed another three patients were recruited into the next level. If one DLT was observed at this dose level another three patients were recruited into this dose level. If further DLT's within this dose level were observed the MTD was reached. With the dose level one step under the MTD level another 9 to twelve patients should be treated.

Patients: 36 Patients were recruited. In 17 patients it was the first line therapy and for 19 patients it was second line treatment. 15 patients with ovarian cancer, 13 with cervical or endometrial carcinoma and 8 patients with sarcoma were recruited. 16 patients received a platinum based chemotherapy as first-line treatment, two patients were treated earlier by radiation therapy and one patient received MPA.

In all dose levels 6 patients were recruited. DLT's were observed in all dose levels, and due to these results the LPK decided to recruit into level +2 corresponding 40mg/m2 PLD and carboplatinum AUC 6. Further 12 patients were recruited.

Results: A total of 121 courses of this combination chemotherapy is the data-source. There are no data regarding response and overall survival.

Haematological toxicities over all levels data of 26 patients were available (CTC-Grading worst case per patient)regarding haemoglobin grade I 9 (34,6%), grade II 11 (42,3%), grade III 1 (3,9%), grade IV 2 (7,7%). Leukocytes grade I 4 (15,4%), grade II 9 (34,6%), grade III 4 (34,6%), grade IV 2 (7,7%). Neutrophils grade I 4 (15,4%), grade II 3 (11,5%), grade III 11 (42,3%), grade IV 5 (19,2%), only two patients have had a febrile neutropenia and in both it was at the first course. Thrombocytes grade I 14 (53,9%), grade II 4 (15,4%), grade III 4 (15,4%), grade IV 1 (3,9%). Infection grade I 4 (15,4%), grade II 6 (23%) and grade III 2 (7,7%).

Non-haematological toxicities over all levels were moderate.

Discussion: PLD and Carboplatin is a feasible and well tolerated chemotherapy even in pretreated patients. The MTD is Carboplatin AUC 6 and PLD 50 mg/m2. The recommended dose for phase II trail for evaluation of efficacy is carboplatin AUC 6 and PLD 40 mg/m2.

173 POSTER

Clinical significance of E-cadherin, alpha catenin and gamma catenin immunoexpression in epithelial ovarian cancer

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Introduction: Epithelial cadherin, a calcium-dependent cell-cell adhesion molecule, plays a key role in the maintenance of tissue integrity. The function of this molecule is partly mediated by alpha, beta and gamma catenin. Loss or dysfunction of E-cadherin is associated with the invasive phenotype.

Aim: To analyze the immunohistochemical expression of E-cadherin, alpha catenin and gamma catenin in ovarian carcinomas with interest in its association with clinicopathological characteristics and patient survival.

Materials and Methods: E-cadherin, alpha catenin and gamma catenin was immunohistochemically evaluated in formalin-fixed, paraffin embedded samples of 104 patients with primary ovarian carcinomas.

Results: In 104 carcinomas, E-cadherin immunoreactivity was negative in 7 (7%) cases, and positive in 97 (93%). Immunoreactivity for alpha catenin was negative in 22 (21%) cases, and positive in 88 (79%). Immunoreactivity for gamma catenin was negative in 23 (22%) cases, and positive in 81 (78%). E-cadherin, alpha catenin, gamma catenin immunoreactivity categorized into negative *versus* positive immunoexpression did not correlate with any of the clinicopathological factors. Only the negative immunoexpression for E-cadherin significantly predicted poorer overall survival when compared with positive membranous expression of E-cadherin. Negative E-cadherin immunoexpression and presence of residual tumour retained their statistical significance in both univariate ($P=0.0089$, $P=0.0138$, respectively) and multivariate analyses ($P<0.001$, $P=0.0340$, respectively) as negative prognostic factors.

Conclusion: The presence of residual tumour and negative immunoexpression of E-cadherin seems to be a useful marker in patients with ovarian carcinomas likely to run a less favourable course.

The assessment of E-cadherin immunoreactivity may be a useful prognostic marker in ovarian cancer complementary to established prognostic factors. The negative E-cadherin expression in carcinomas and the strong impact on survival justifies further prospective studies.