

mean dose comparisons (T-pair and Kruskal-Wallis tests), log rank tests on event-free survivals, and probit analyses. The highest graded event, or in cases of similar grade the earliest, was considered for analyses.

Results: One hundred and fifteen patients were eligible. Of them, 94.8% received concomitant chemoradiotherapy; 12.2% extended-field radiotherapy, and 32.2% nodal sequential boost. Their mean age was 47.5 years. The median follow-up was 35.5 months. A total of 522 events was reported. Focusing on the highest grade per patient: 17 had grade 0, 75, grade 1, 20, grade 2 and 3, grade 3. The prevalence of grade 1 events appeared stable during the study period, ranging between 31.2 and 50%. The one of grade 2 events tended to worsen: 2.2% at 6 months, 4.5% at 1 year, 6.9% at 2 years, and 7.0% at 3 years. Incidences of grade 2-4 events were 0.9% at 6 months, 6.6%, 19.0%, and 27.2% at 1, 2, 3 years respectively. The mean D2cm3 and D0.1cm3 were respectively 68.7 ± 13.6 Gy and 85.8 ± 33.1 Gy and did not differ according to grade ($p=0.47$ and $p=0.52$). Comparisons of mean D2cm3 and D0.1cm3 according to grade 0-1 versus 2-4 were not significant (68.0 ± 12.4 vs 71.4 ± 17.7 Gy, $p=0.38$ and 83.7 ± 26.4 vs 94.5 ± 51.9 Gy, $p=0.33$ respectively). Log rank tests were performed after splitting patients into 4 groups according to D2cm3 levels: > 80 Gy, 70 to 79 Gy, 60 to 70 Gy and < 60 Gy. No difference was observed for grade 1-4 ($p=0.52$), grade 2-4 ($p=0.52$) or grade 3-4 ($p=0.21$). Probit analyses showed no correlation between both dosimetric parameters and the probability of small bowel events grade 1-4, 2-4, or 3-4 (p ranging from 0.19 to 0.48).

Conclusion: No significant dose-volume effect relationships were demonstrated between the D2cm3 and D0.1cm3 and the probability of late small bowel morbidity. These two parameters should not limit the optimization process.

OC-0352

The high doses employed in brachytherapy of cervical cancer counteract hypoxia - a modelling study

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Purpose or Objective: Brachytherapy is a well-established radiotherapy treatment modality that has been employed in treatments of several cancer types for more than a century. One of the most common treatment strategies for cervical cancer today is a combination of external beam radiotherapy, chemotherapy and brachytherapy. Similar to other forms of radiation therapy, pre-treatment imaging of hypoxia is rarely done for cervical cancer. Nevertheless, the clinical outcome is highly positive, despite the fact that hypoxia has been repeatedly confirmed in cervical tumours. It was therefore the purpose of this study to investigate whether the success of brachytherapy in these tumours, seemingly regardless of oxygenation status, could be explained by the characteristics of the brachytherapy dose distributions in comparison to external beam radiotherapy.

Material and Methods: A previously used *in silico* model of tumour oxygenation and radiation response was further developed to simulate the treatment of cervical cancer employing the combination of external beam radiotherapy and intracavitary brachytherapy. Based on the local clinical protocol and using a clinically derived brachytherapy dose distribution and assuming a homogeneous dose delivered by external radiotherapy, survival was assessed on voxel level taking into account the dose-modifying effect of the oxygenation as well as the effects of repair and repopulation of tumour cells during treatment. Two scenarios were considered for brachytherapy: one in which the high dose region was highly conformal to the hypoxic region in the target and one in which they were displaced relative to each other. Overall-response was assessed as Poisson-based

tumour control probability (TCP). The interplay between tumour oxygenation and the heterogeneous high-dose distribution was also studied by simulating different spatial and temporal patterns of hypoxia. The results were compared to the case when irradiation was performed only with external beams delivering a homogeneous dose to the target.

Results: Predicted values of D50 with respect to the external treatment and assuming reoxygenation were in agreement with the clinically observed high cure rates. Assuming fast reoxygenation, the D50 was similar for the different cases of overlap between the brachytherapy dose distribution and the tumour, regardless if the hypoxic fraction was 10% or 25% (Table 1). To achieve 50% control with external RT only, a total dose of more than 70 Gy in 25 fractions would be required for both cases of hypoxic fraction assuming reoxygenation (Figure 1).

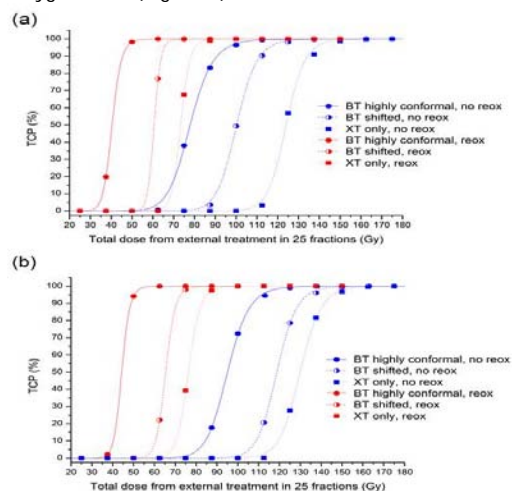


Figure 1. TCP curves for external RT given in 25 fractions for various scenarios for the brachytherapy (BT) dose distribution: highly conformal or shifted relative to the hypoxia area and the corresponding curves for the external RT (XT) only, for a simulated tumour with 10% hypoxia in (a) and 25% hypoxia in (b).

Hypoxic fraction	Oxygenation pattern	D ₅₀ (Gy)		
		BT highly conformal	BT shifted	XT only
10%	No reoxygenation	77.9	100.3	124.1
	Fast reoxygenation	40.4	60.6	73.4
25%	No reoxygenation	95.1	118.7	129.9
	Fast reoxygenation	44.3	65.4	76.2

Table 1. Values of D₅₀ for external RT given in 25 fractions for various scenarios for the brachytherapy (BT) dose distribution: highly conformal or shifted relative to the hypoxia area and the corresponding values for the external RT (XT) only.

Conclusion: Assuming fast reoxygenation, the dependence on the degree and extent of hypoxia has little impact on the outcome and therefore the high doses delivered in brachytherapy could counteract the negative impact of hypoxia.

OC-0353

EBRT and interstitial brachytherapy for recurrent vault carcinomas: Factors influencing the outcomes

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Purpose or Objective: Post hysterectomy vaginal vault recurrences have poor outcomes with pelvic control rates ranging from 50-60%. We conducted this prospective study at our centre with an aim to determine the factors influencing

the outcomes of these patients treated with external beam radiotherapy (EBRT) and interstitial brachytherapy.

Material and Methods: Ninety patients were accrued between October 2008 and May 2014. All the patients underwent prior hysterectomy and were diagnosed to have recurrent vault cancers with squamous cell carcinomas. Only patients with minimum gap of 6 months between the hysterectomy and recurrence were accrued in the study. All underwent EBRT of 50Gy (2Gy/fraction) to pelvis and simultaneous boost to the pelvic nodes of (10 Gy/5 fraction) if present, using Intensity Modulated Radiotherapy with concurrent chemotherapy of weekly cisplatin (40mg/mt2) followed by HDR Interstitial brachytherapy boost of 20Gy (4Gy/fraction b.i.d).

Results: Eighty (88%) patients were post simple hysterectomy and 20(22%) had Wertheim's hysterectomy, 16 (18%) had pelvic nodes and 46(51%) had parametrial extension upto the pelvic side walls. All the patients completed EBRT and concurrent chemotherapy and 28 (31%) patients had gross residual disease at the time of interstitial brachytherapy. Post brachytherapy 5 patients continued to have persistent disease, 6 had local relapse, 2 had local + distant relapse and 9 patients had only distant relapse. At the median follow up of 42 months for the surviving patients the local control rate was 86% and the 5-year actuarial disease-free survival (DFS) and overall survival (OAS) was 75%, 71%. In univariate analysis OAS was influenced by tumor involving the pelvic side wall (55% vs 84% p=0.004) and large pelvic nodes >1cm (44% VS.73% P=0.01) at presentation and partial vs. complete tumor response to EBRT at the time of brachytherapy (40% vs. 83% p=0.001). On multivariate analysis pelvic nodes at presentation and the tumor response to EBRT were significant factors affecting DFS and OAS. Other factors such as age, disease volume, and vaginal extension did not impact the survivals. Grade III/IV rectal toxicity was seen in 5 (5%) patients, bladder toxicity in 3 (3%) patients, whereas none of the patients developed Grade III small bowel toxicity.

Conclusion: Using EBRT with concurrent chemotherapy and interstitial brachytherapy a majority of the recurrences can be salvaged. An excellent local control and survival is achievable using this technique and 28 (31%) patients had gross residual disease at the time of interstitial brachytherapy.

OC-0354

Artificial neural network for bladder dose interfractional variation prediction in GYN brachytherapy

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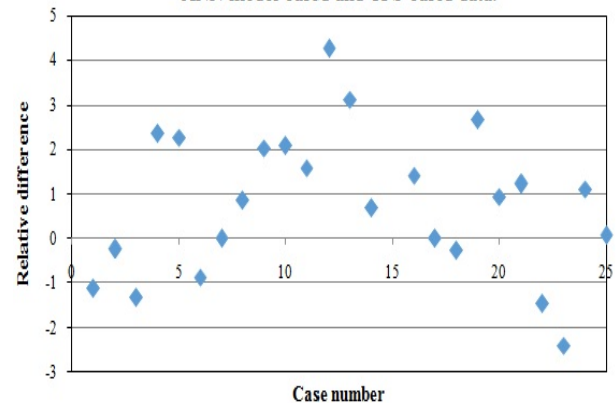
Purpose or Objective: Introducing a fast technique to estimate bladder dose due to interfractional variations.

Material and Methods: 30 cervical cancer patients treated with HDR intracavitary brachytherapy were selected. After applicator insertion all cases pelvic CT scans were performed twice; pre- and post-treatment (15-30 min after dose delivery), with applicator in situ and identical bladder filling protocol. A 3D treatment planning software (TPS) (Flexiplan®, version 2.6, Isodose control, the Netherlands) was used. Applicator (Rotterdam tandem-ovoid) reconstruction and organs contouring were done by the same physicist and physician on both image series. Planning was performed on the pre-treatment CT. Fractional prescription dose was calculated for each patient based on the EQD2 and defined planning aims: 80-90 Gy for D90 of the high-risk clinical target volume and D2cm³ of bladder, rectum, and sigmoid less than 85, 75, and 75, respectively. DVH parameters (D2cm³, D0.1cm³, D10, D30, and D50) were

recorded after each planning. 192Ir dwell times were copied manually to the post-treatment CT in the TPS. The recalculations of the DVH parameters showed the interfractional OAR dose variations. Images and structures of each pre- and post-treatment plan were exported in DICOM format to an in-house MATLAB written code. An artificial neural network (ANN) based on the 'back-propagation algorithm' was developed to predict the OARs dose variations. ANN input data was based on the changes of OAR wall distance-to-dwell positions along the applicators, that were extracted from two images series of each case. 25 cases were randomly selected as the training and model validation set (20 cases for training and 5 for validation), and the last 5 one for the resulted ANN model testing. Testing was performed by comparing the interfractional dose variations obtained from TPS calculated DVH and that obtained from ANN-based computing. The performance of the ANN was analyzed by root mean square error (RMSE).

Results: RMSE of the designed ANN was 0.28. RMSE of the testing cases was 0.72. TPS-based interfractional variations for D2cm³ were -2.9% ± 18.7%. As an example of the model performance, relative differences of TPS-calculated and ANN-based interfractional variations for D2cm³ of the training + validation cases (just the first 25 ones) are presented schematically in the Figure 1. It can be seen that these relative differences are almost less than 3%.

Figure 1: Relative difference of D_{2cm³} interfractional variations of ANN model-based and TPS-based data.



Conclusion: An ANN-based model was introduced which can give a fast prediction of bladder interfractional dose variations during cervical cancer intracavitary brachytherapy independent from TPS based dose calculations. This can serve as a basis for online verification tools in brachytherapy dose delivery.

OC-0355

Long term analysis of electron vs. HDR boost in breast conservation - an Indian experience

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Purpose or Objective: Last decade has witnessed a revolution in breast conservation (BCS) in India as a consequence of sustained awareness campaigns and detection of early cases. But success of BCS demands not only local control but cosmetic excellence as well. Radiotherapy plays a major role in this treatment and selected high risk cases require boost also. This retrospective analysis aims to