Does dose-escalated neo-adjuvant radiotherapy improve pathological response in rectal cancers?

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Purpose or Objective: Neoadjuvant chemoradiotherapy (CRT) is considered a standard approach for locally invasive rectal cancer. Several phase 3 studies have shown an improvement in local control with combined radiotherapy and capcitabine / 5-fluorouracil. There is good evidence that increased dose of radiotherapy is associated with both better pathological response and survival in many malignancies, although the data in rectal cancer is less convincing. In this study we assessed the impact of dose-escalated radiotherapy on pathological outcome.

Material and Methods: We evaluated all patients who received chemoradiotherapy for rectal cancer and subsequently had an anterior resection/ abdominoperineal resection with a total mesorectal excision (TME) between February 2012 and December 2014. Patients received 50.4Gy 1.8Gy fractions, and more recently those who have T3/4 disease with a threatened circumferential margin had a simultaneous integrated boost of the primary tumour to a total dose of 53.2Gy, with concurrent capcitabine chemotherapy (825mg/m2 BD) daily throughout treatment. Treatment was initially using 3-D conformal radiotherapy but more recently has been using a VMAT technique with cone beam CT used during treatment. Surgery was performed 8-12 weeks after completion of CRT. The primary end point was pathological response (Dworak score 0-4) of the operative specimen. Scores of 0-2 were considered to be non-pathological responders and scores of 3-4 were considered to be pathological responders.

Results: A total of 73 patients received neoadjuvant chemoradiotherapy. 61 patients were treated with a standard radiotherapy fractionation of 50.4Gy in 28 fractions (Group A) and 12 patients were treated with a dose escalated fractionation to the primary tumour of 53.2Gy in 28 fractions (Group B). The rate of pathological response was 39.3% in Group A and 86.7% with Group B (t=3.55, p<0.001).

Conclusion: This study demonstrates the beneficial effects of dose-escalated radiotherapy and we therefore recommend this regime be considered for inclusion in future phase 2 studies.

EP-1287
Radiation-induced rectal toxicity in prostate cancer: a proctoscopy evaluation
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Purpose or Objective: Early proctoscopy (1 year) can predict late rectal mucosa changes and therefore can be used as surrogate end-point for late rectal toxicity. The aim of this study was to retrospectively analyze data of patients treated at a single institution, consecutively enrolled in different prospective clinical trials, trying to determine a correlation between treatment parameters and VRS (Vienna Rectoscopy Score) recorded at 1-year proctoscopy.

Material and Methods: Patients with prostate adenocarcinoma treated with curative or adjuvant RT underwent endoscopy one year after RT; 195 patients were included in this analysis. Correlations between VRS > 2 and several treatment parameters were investigated by univariate and multivariate logistic analysis.

Results: Patients treated with an EQD2 dose > 75 Gy with hypofractionated schedule and radiosurgery boost had a higher incidence of VRS > 2 (p < 0.001). On the contrary, previous surgery and 3D-conformal radiotherapy (vs IMRT) were associated with a lower incidence of rectal mucosal changes (p < 0.001; p < 0.003, respectively). At multivariate analysis radiosurgery boost was associated with the highest odd ratios for the risk of developing a VRS > 2 (OR: 4.14; CI: 1.24-13.81; p<0.001). Even surgery showed a significant correlation with VRS > 2 (OR: 0.39; CI: 0.17-9.94; p=0.037, Table 1).

Conclusion: Prolonged patients follow-up is needed to “clinically” confirm the increased rectal toxicity produced by radiosurgery boost.

EP-1288
Sphincter function and dose of radiation in rectal cancer. A Single-Institutional study
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Purpose or Objective: The objective of the study is to determine the correlations among the variables of dose and the sphincter function (SF) in patients with locally advanced rectal cancer treated with preoperative capcitabine/radiotherapy followed by Local Anterior Resection(LAR) +TME.

Material and Methods: We have retrospectively reviewed 92 consecutive patients with LARC treated at our center with LAR from 2006 and more recently 1 year free from disease. We re-contoured the anal sphincters (AS) of patients with the help of the radiologist. SF was assessed with the Wexner scale (0-20 points, being punctuation inversely proportional to SF). All questionnaires were filled out between January 2010 and December 2012. Dosimetric parameters that have been studied include: V20 V30, V40, V50, mean dose (Dmean), minimum dose (Dmin), D90 (dose received by 90% of the sphincter) and D98 Statistical analysis: the correlations

Conclusion: Prolonged patients follow-up is needed to “clinically” confirm the increased rectal toxicity produced by radiosurgery boost.
among the variables of dose and SF were studied by the Spearman correlation coefficient. Differences in SF related to maximum doses to the sphincter were assessed by the Mann-Whitney test.

Results: Wexner scaleMean Wexner score was 5.5 points higher in those patients with V20=0 compared to those for which V20=0 (p=0.008). In a multivariate regression model, results suggest that the effect of V20 on poor anal sphincter control is independent of the effect of distance, with an adjusted OR of 3.42 (1.09, 10.72).

Conclusion: In order to improve the SF, the maximum dose of radiation to the AS should be limited, when possible, to < 20 Gy

EP-1289
Anal squamous cell carcinoma; a retrospective case series
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Purpose or Objective: Anal cancer is a relatively rare cancer, making up approximately 0.4% of all new diagnoses of cancer. In 2011, there were 1,175 new cases of anal cancer diagnosed in the UK. The current standard treatment is radical chemoradiotherapy. We conducted a retrospective case series of anal squamous cell carcinoma treated in the regional radiation oncology network between 2008 and 2014 inclusive to examine recent management practice and outcome of anal squamous cell carcinoma.

Material and Methods: Patients were identified from the regional radiation oncology cancer database. Data was collected retrospectively from ARIA® oncology information system and patient charts. Information was collected in relation to demographic details, radiotherapy dose and regimen, chemotherapy regimen, persistence and recurrence of disease, salvage surgery rates, and survival analysis. Statistical analyses were carried out using IBM® SPSS® statistical software version 21.0.

Results: 79 cases of anal squamous cell carcinoma were identified. Mean age at commencement of radiotherapy was 60.2 years (+/-13.2 years). 29 patients were male (36.7%) and 50 (63.3%) were female. 8 (10.1%) patients had documented HIV infection. 74 (93.7%) patients were treated with radical chemoradiotherapy. The most common total radiotherapy dose delivered was 50.4 Gy in 28 fractions (H:58; 73.4%) (see table 1). The majority of patients (N=67; 84.8%) received combination chemotherapy with mitomycin C and 5-FU. 2 (2.5%) patients who received radical treatment had persistent disease following radiotherapy. 5 (6.3%) patients had loco-regional recurrence and 3 (3.8%) patients developed solid organ metastases following complete treatment response at the primary. 4 patients had salvage surgery. Survival was measured from the initiation of radiotherapy treatment using the Kaplan-Meier method. Overall survival was 98%, 90%, 83% and 83% at 1, 2, 3 and 4 years respectively. Disease free survival was 91%, 77%, 74% and 74% at 1, 2, 3 and 4 years respectively (see fig. 1).

Table 1 Total delivered radiotherapy dose and fractions

<table>
<thead>
<tr>
<th>Radiotherapy Dose (Gy)/Fraction</th>
<th>Number of Patient (%)</th>
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<tr>
<td>50.4/28</td>
<td>58 (73.4)</td>
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<tr>
<td>54/30</td>
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<tr>
<td>39.433</td>
<td>5 (6.3)</td>
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<td>54.831</td>
<td>1 (1.3)</td>
</tr>
<tr>
<td>50.25</td>
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</table>

Conclusions: Our study found that the majority of patients in our radiation oncology network were treated with chemoradiotherapy in line with international guidelines. In our study, chemoradiotherapy in the treatment of anal squamous cell carcinoma was associated with a high complete response rate and a low treatment failure rate. Treatment and outcomes in our study are consistent with international trial data.

EP-1290
A review of grade 3 bowel toxicity in patients treated with chemoradiotherapy for rectal cancer
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Purpose or Objective: Concurrent chemoradiotherapy (CRT) is the standard treatment for locally advanced rectal cancer to downstage disease prior to definitive surgery. Previous studies report grade 3 (G3) bowel toxicity of 3-4%; QUANTEC recommend small bowel V45 <195 cm3 to reduce G3 toxicity. We noted an increase in G3 bowel toxicity in the period Sept – Dec 2014 in our institution and aimed to determine the cause.

Material and Methods: We retrospectively identified patients who received pre-operative long-course CRT for rectal cancer between Sept - Dec cohort (n=28) was compared to Sept - Dec cohort (n=22). Both groups were similar for patient demographics, CRT treatment volumes and doses, patient positioning and XRT delivery technique. Two of 28 patients (9%) in Jan - April cohort had G3 bowel toxicity; both were admitted for symptom control. Six of 22 patients (27%) in Sept - Dec cohort developed G3 bowel toxicity; 5 (23%) required admission. G3 toxicity occurred after a minimum of 16 fractions (range 16-21). All patients had normal bowel function prior to

Results: Fifty patients were identified: Jan - April cohort (n=28) was compared to Sept - Dec cohort (n=22). Both groups were similar for patient demographics, CRT treatment volumes and doses, patient positioning and XRT delivery technique. Two of 28 patients (9%) in Jan - April cohort had G3 bowel toxicity; both were admitted for symptom control. Six of 22 patients (27%) in Sept - Dec cohort developed G3 bowel toxicity; 5 (23%) required admission. G3 toxicity occurred after a minimum of 16 fractions (range 16-21). All patients had normal bowel function prior to