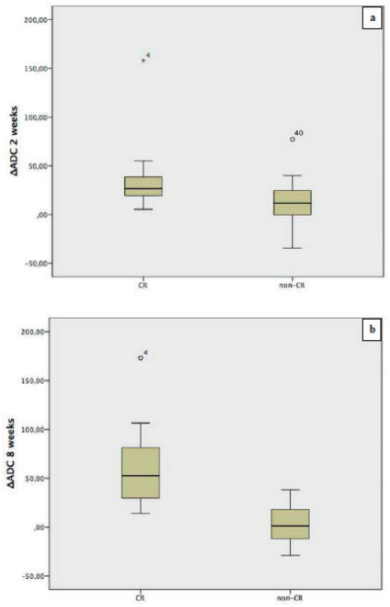
[1]SS. Annunziata Hospital- "G. D'Annunzio" University, Department of Radiation Oncology, Chieti, Italy
[2]"G. D'Annunzio" University, Department of Neuroscience- Imaging and Clinical Sciencies, Chieti, Italy

Purpose or Objective
Diffusion-weighted MR imaging (DWI), used to measure apparent diffusion coefficient (ADC), provides biological information related to tumor cellularity and integrity of cell membranes and it is sensitive to intratumoral changes induced by chemoradiation therapy (CRT). Previous studies showed a potential role of DWI in predicting tumor response during and after CRT in locally advanced rectal cancer (LARC) patients. The purpose of this study was to determine whether changes in ADC values of LARC, obtained 2 weeks after the beginning of CRT, allow to predict response to treatment and whether they correlate with tumor histopathologic response.
Material and Methods
Forty-three patients affected by LARC were tr eated with CRT and received a 3.0T MRI with diffusion-weighted sequences before, 2 weeks during and 8 weeks after CRT. ADC values were calculated at each time point. The percentage of ADC changes at 2 weeks (ΔADC during) and after 8 weeks (ΔADC post) were then assessed. All data were correlated to histopathologic tumor regression grade (TRG), according to Mandard classification. The ADC values and ΔADCs of complete responders (CR=TRG1) and non-complete responders (non-CR=TRG 2-5) were compared. A receiver-operating characteristic curve (ROC) analysis was used to assess the diagnostic accuracy of ΔADC for differentiating CR from non-CR. The correlation with TRG was investigated using Spearman rank test.
Results
In 21 out of 43 (48.8%) patients no residual tumor cells were found after CRT and surgery (TRG1) and were considered complete responders. The remaining 22 patients were classified as non-complete responders (4 TRG2, 13 TRG3, 5 TRG4). Both ΔADC at 2 weeks (Figure 1a) and post treatment (Figure 1b) were significantly higher in CR (33.9% and 57%, respectively) compared to non-CR (13.5% and 2.2%, respectively) group (p=0.006 and p<0.001, respectively). A significant moderate and good negative correlation was found between ΔADC during and ΔADC post and TRG (r=-0.418, p=0.007; r=-694, p≤0.001, respectively). In addition, ROC analysis revealed the following diagnostic performances: ΔADC at 2 weeks: AUC 0.78 (0.08 standard error), p=0.004, cut-off 20.6% (sensitivity 75% and specificity 76.5%); ΔADC post treatment: AUC 0.94 (0.04 standard error), p≤0.001, cut-off 22% (sensitivity 95% and specificity 82.4%).



Conclusion
ΔADC at 2 weeks after the beginning of CRT resulted a reliable tool to early assess treatment response, with an appreciable level of sensitivity and specificity. This can allow to perform surgery before or after 8 weeks interval-to-CRT, according to MRI tumor response.

PO-0798 High dose IMRT for locally advanced rectal cancer - late toxicity and patient-reported outcomes
A.L. Appelt[1,2], B.M. Havelund[2], H.S. Rønde[3], J. Pløen[2], I.R. Vogelius[4], A. Jakobsen[2]
[1]University of Leeds & St James's University Hospital, Leeds Institute of Cancer and Pathology & Leeds Cancer Centre, Leeds, United Kingdom
[2]Vejle Hospital & University of Southern Denmark, Danish Colorectal Cancer Centre South & Institute of Regional Health Research, Vejle, Denmark
[3]Vejle Hospital, Department of Medical Physics, Vejle, Denmark
[4]Rigshospitalet- University of Copenhagen, Department of Oncology, Copenhagen, Denmark

Purpose or Objective
Clinical data on late toxicity and patient reported outcomes after intensity-modulated radiotherapy (IMRT) for neoadjuvant treatment of rectal cancer are severely lacking. Here, we report on a prospective study of high-dose IMRT for locally advanced rectal cancer aiming to examine late toxicity and patient-reported outcomes (PROs).
Material and Methods
Patients with locally advanced (T3-4N0-2M0) rectal cancer were prospectively enrolled in this single-institution study. They were treated with IMRT to 50Gy in 30 fractions to elective pelvic lymph nodes with a simultaneous integrated boost (60Gy) to the primary tumour. Plans were optimized for target coverage, while sparing organs at risk. 5Gy brachytherapy or 6Gy external beam was delivered as further sequential tumour boost. Concomitant chemotherapy (UFT or capecitabine) was given on treatment days. TME surgery was scheduled 8 weeks after end of radiotherapy. Clinical outcomes and toxicity (CTCAE v4.0) and PRO (EORTC QLQ CR29) were recorded at baseline, during treatment, and at 3, 6, 9, 12, 16, 20, 24, 30 and 36 months follow-up. Overall survival (OS) and progression-free survival (PFS) were

evaluated using Kaplan-Meier estimates; toxicity and PROs were compared to baseline using paired Wilcoxon tests.

Results

Fifty-five patients (35 men / 20 women) were included; majority cT3 disease (42 patients) with cN+ (49 patients). Fifty-four patients received full external beam radiotherapy; median PTV for tumour and elective lymph nodes were 214cm^3 and 1457cm^3, respectively. Acute clinician scored side effects were mild, with only nine patients experiencing grade ≥2 bowel toxicity. Overall PRO scores were significantly worse at end of treatment compared to baseline (median 22.22 vs 13.89, p<0.0001). Surgery was conducted as planned in 51 patients. Thirteen patients (24%) had complete response of primary tumour to treatment (11 with pathological complete regression, two declined surgery after clinical complete response). All patients were followed for at least 2 years (median clinical follow-up 3.3 years, survival 4.8 years), excepting patients with disease progression (n=10 at 2 years) or withdrawing consent for further study participation (n=9). OS and PFS at 3 years were 92.7% (95% CI 86.1-99.9%) and 68.4% (95% CI 56.7-82.6%), respectively. 64% of patients had a stoma at 2 years. Figure 1 shows clinician-scored toxicities (n=35) and patient-reported symptoms (n=30) at 2-year follow-up. Clinician-scored urinary urgency (p=0.01) and frequency (p<0.001) as well as patient-reported incontinence for gas (p=0.001) were significantly increased from baseline. Generally, patients reported more symptoms than clinicians across most symptom domains. However, overall PRO scores at late follow-up were lower (i.e. better) than at baseline, see Figure 2.

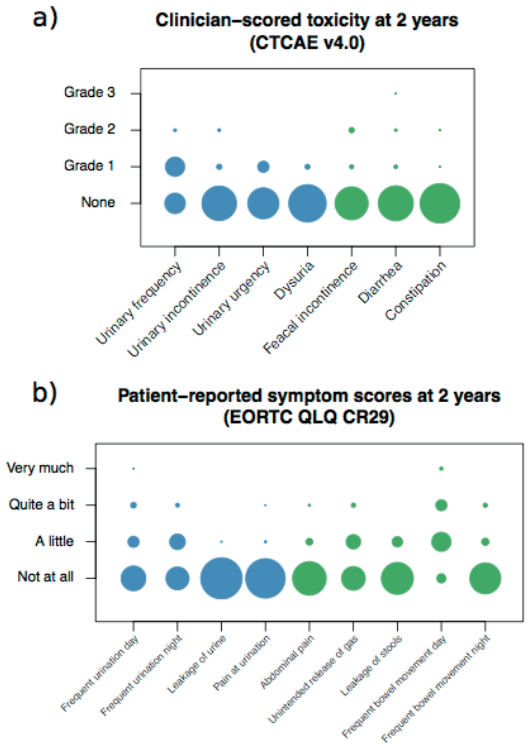


Figure 1: Clinician-scored toxicity (Fig 1a, n=35) and patient-reported symptoms (Fig 1b, n=30) at 2-year follow-up following neoadjuvant intensity-modulated chemoradiotherapy for locally advanced rectal cancer. Size of bubbles indicate the relative proportion of patients with the respective score / symptom. Blue bubbles are used for bladder-related side-effects, green bubbles for bowel-related side-effects.

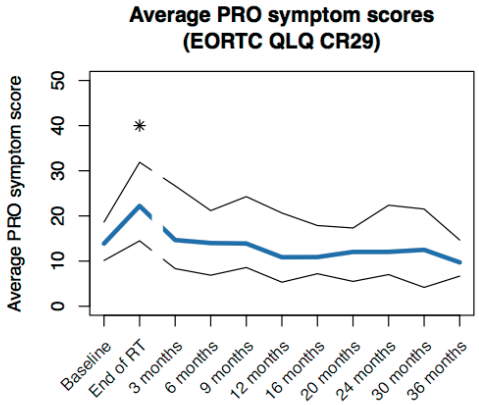


Figure 2: Average patient-reported symptom scores from EORTC QLQ CR29 before and after neoadjuvant intensity-modulated chemoradiotherapy for locally advanced rectal cancer. Bold line indicates patient cohort median, thinner lines interquartile ranges. Higher scores correspond to worse outcome. Only scores at end of radiotherapy were significantly worse than baseline scores.

Conclusion

Late outcomes of high dose IMRT for locally advanced rectal cancer appear promising, with low levels of toxicity. However, we observe under-reporting of toxicities by clinicians compared to PRO data.

PO-0799 An externally validated MRI radiomics model for predicting clinical response in rectal cancer

C. Masciocchi[1], E. Cordelli[2], R. Sicilia[2], N. Dinapoli[1], A. Damiani[1], B. Barbaro[3], L. Boldrini[1], C. Casà[1], D. Cusumano[4], G. Chiloiro[1], M.A. Gambacorta[1], R. Gatta[1], J. Lenkowicz[1], J. Van Soest[5], A. Dekker[5], P. Lambin[5], P. Soda[2], G. Iannello[2], V. Valentini[1]

[1]*Università Cattolica del Sacro Cuore - Fondazione Policlinico "Agostino Gemelli", Radiation Oncology Department, Roma, Italy*

[2]*Università Campus Bio-Medico, Computer Science and Bioinformatics- Engineering Department, Rome, Italy*

[3]*Università Cattolica del Sacro Cuore - Fondazione Policlinico "Agostino Gemelli", Radiology Department, Rome, Italy*

[4]*Università Cattolica del Sacro Cuore - Fondazione Policlinico "Agostino Gemelli", Physics Department, Rome, Italy*

[5]*Maastricht University Medical Center, Radiation Oncology MAASTRO-GROW School for Oncology and Development Biology, Maastricht, The Netherlands*

Purpose or Objective

Aim of this study was to extract a massive number of morphological(MP) and filtered Radiomic Features(RF) from pre-treatment T2 MRI in Locally Advanced Rectal Cancer (LARC) patients (pts) and select features able to predict pathological Complete Response (pCR).

Material and Methods

LARC pts were retrospectively enrolled from May 2008 to December 2014.

All pts underwent neoadijuvant chemotherapy(nCRT) followed by surgery: Tumor Regression Grade(TRG) was assessed on pathological specimens, considering TRG1 as pCR.

A pelvic MRI was performed in all pts before nCRT: Gross Tumor Volume(GTV) was delineated by 1 radiologist and 1 radiation oncologist on T2 staging images in each case. 61 RF(First-Order (FO), MP, and texture) were extracted using in-house Moddicom software.

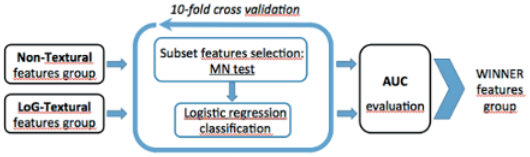
FO and textural features were calculated after filtering by Laplacian of Gaussian(LoG) using different settings(σ parameter range from 0,3 to 2,5 with a step of 0,01). 12,763 RF were extracted for each pt and were divided into two groups: "LoG-Textural" and "Non-Textural"(MO and LoG-FO features).

A Feature Selection(FS) for each separate group was performed(figure 1) using 10-fold Cross Validation(CV). For each folder a univariate correlation between outcome and each covariate at specific σ was evaluated using a Mann-Whitney(MN) test. We selected the statistically significant covariates (p-value < 0.05). If a feature was selected at different σ values, we chose the σ with the lowest p-value. A Logistic Regression Model(LRM) was applied on the resulting subset of features. The Area Under the ROC Curve(AUC) was evaluated and the group with the highest average value was selected.

From this group, the final predictors were determined using the same strategy(figure 1) but in leave-one-patient-out CV. The RF with an occurrence higher than 90% were selected.

Finally clinical features(cT and cN) were added and a LRM was applied on the external validation set(VS), computing the AUC value and the Hosmer-Lemeshow(HL) test.

Figure 1

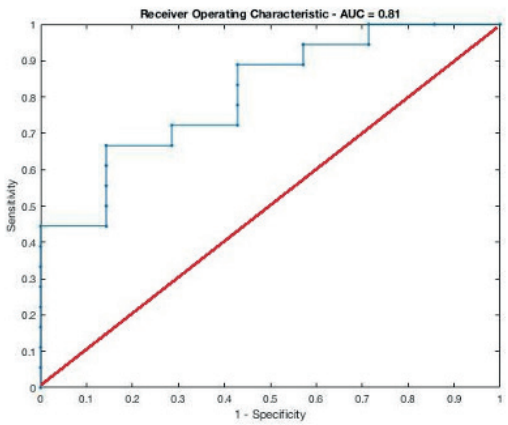


Results

173 pts were selected in the Training Set(TS); 25 pts in the VS. No significant differences were observed in the distribution of clinical and pCR characteristics. The overall pCR was similar between TS and VS(27% vs 28%). Using the PI and LoG filter, "Non-Textural" features were selected as the best predictors of pCR. The "Non-Textural" and "LoG-Textural" AUC values were 0,63 and 0,61 respectively.

Among all the final FR, the features with an occurrence >90% were 3: surface, volume, skewness (σ = 0,42). RF were finally combined with cT and cN. The final model consisted of cT(p<0,01), cN(p=0.72), surface (p=0,01), volume(p<0.01) and skewness(σ = 0,42) (p<0,01). The performance of the LRM was evaluated on external VS with an AUC of 81%(figure 2) and an HL of 0.85.

Figure 2



Conclusion

The model offered a promising performance with these settings.

The exclusion of textural RF might depend on the application of LoG filter. Further investigations on different filtering and a suitable normalization algorithm are ongoing.

PO-0800 Deep Neural Network predicts complete response in rectal cancer after neo-adjuvant chemoradiation

J.E. Bibault[1], P. Giraud[2], A. Burgun[3]

[1]*Georges Pompidou European Hospital, Radiation Oncology Department- INSERM UMR 1138 Team 22: Information Sciences to support Personalized Medicine, Paris, France*

[2]*Georges Pompidou European Hospital, Radiation Oncology Department, Paris, France*

[3]*Georges Pompidou European Hospital, Biomedical Informatics and Public Health Department- INSERM UMR 1138 Team 22: Information Sciences to support Personalized Medicine, Paris, France*

Purpose or Objective

Treatment of locally advanced rectal cancer involves chemoradiation, followed by total mesorectum excision (TME). Complete response after chemoradiation is an accurate surrogate for long-term local control. However,