	Univariate		Multivariate	
	Hazard ratio	P-value	Hazard ratio	P-value
Gender (baseline male)	1.54 (0.71–3.3)	0.3	2.70 (0.85 – 8.50)	0.09
Age	1.04 (0.99–1.10)	0.1	1.001 (0.94 – 1.09)	0.7
ECOG performance status (baseline PS 0)	1.31 (0.68–2.51)	0.4	1.50 (0.48– 4.67)	0.5
GTV volume (cubic cm)	1.0008 (1.0 – 1.002)	0.2	1.0 (0.997 – 1.001)	0.4
Rate of change of first order interquartile range	0.42 (0.18-0.98)	0.04	0.44 (0.15-1.35)	0.2
Rate of change of first order maximum	2.33 (1.09-4.98)	0.03	1.81 (0.62 – 5.27)	0.3
Rate of change of shape spherical disproportion	0.26 (0.11-0.611)	0.002	0.12 (0.03 – 0.46)	0.002
Rate of change of GLCM contrast	2.43 (1.09-5.43)	0.03	1.63 (0.33 – 7.89)	0.5
Rate of change of GLCM dissimilarity	2.11 (1.0-4.5)	0.05	1.50 (0.21-10.72)	0.7
Rate of change of GLCM inverse variance	2.81 (1.29-6.12)	0.009	2.41 (0.56 – 10.44)	0.2
Rate of change of GLRLM run variance	0.47 (0.22-0.99)	0.05	1.63 (0.45-5.92)	0.5
Rate of change of GLSZM intensity variability normalized	0.41 (0.19-0.88)	0.02	0.33 (0.07 – 1.57)	0.2

Table 1 - Cox regression hazard ratios (95% confidence interval) and significance of clinical factors and the rate of change of radiomic features.

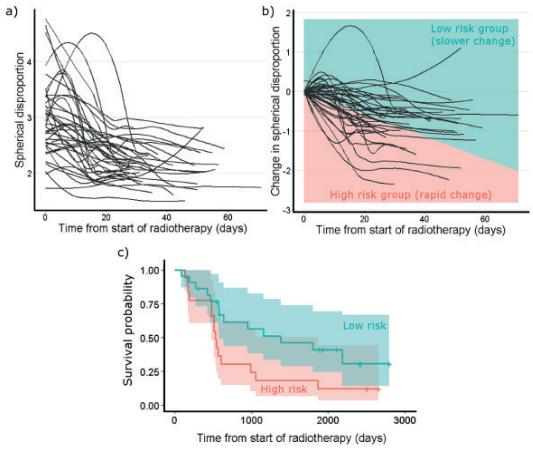

Figure 1 - Change in GTV spherical disproportion during radiotherapy of 46 SCLC patients (a). Patients were stratified into high (pink) and low (blue) risk groups based on the rate of change of the feature (b). The survival advantage of the low risk group is shown in (c) (log rank p = 0.04).

Conclusion

We have shown for the first time that the rate of change of tumour radiomic features in IGRT data relates to overall survival in SCLC patients. If validated in larger cohorts, the ubiquity of IGRT would facilitate rapid clinical translation to assist personalized therapy in SCLC. Work is on-going to refine the methodology (e.g. contour propagation validation, non-linear analysis of rate of change) and to roll the analysis out to larger routinely treated patient cohorts.

PO-0752 Isotoxic Intensity Modulated Radiotherapy in stage III NSCLC – A feasibility study

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Purpose or Objective

The majority of stage III patients with NSCLC are unsuitable for concurrent chemoradiotherapy (cCRT). As the rate of local failure for sequential chemoradiotherapy is high, there is a rational for treatment intensification.

Material and Methods

Isotoxic intensity modulated radiotherapy (IMRT) is a multicentre feasibility study combining different intensification strategies; dose escalation, acceleration and hyperfractionation, facilitated by IMRT. Patients with inoperable stage III NSCLC, ECOG PS 0-2, unsuitable for cCRT were recruited. A mandatory ≥2 cycles of chemotherapy was given before RT. Radiation dose was increased until ≥ 1 of the organs at risk (OAR) met predefined constraints or maximum dose of 79.2Gy was reached. RT was delivered twice-daily in 1.8Gy fractions. A RT quality assurance programme was in place. Primary end point was feasibility, with acute/late toxicity (CTCAE version 4.0), local control and overall survival as secondary end points.

Results

Between 06/14 – 03/16, 37 patients enrolled from 7 UK centres. Median age = 67 years (range 46-86). Male:female ratio = 18:19. ECOG PS=0, 5 (13.51%), PS=1, 29 (78.38%), PS=2, 3 (8.11%). Stage IIIa:IIIb ratio 23 (62.16%):14 (37.84%). Out of 37 patients, 2(5.4%) failed to achieve EQD2 >60Gy and received standard RT, due to large tumour size/inability to meet OAR constraints. Median prescribed tumour dose was 77.4Gy (61.2 – 79.2Gy). Maximum dose of 79.2Gy was achieved in 14 (37.84%) patients. All patients completed RT as scheduled except one due to disease progression. Acute and late toxicities are summarised in Table 1. There were two G5 events: radiation pneumonitis and bronchopulmonary haemorrhage, both likely treatment related. At time of analysis median follow-up was 12.8 months for 20 survivors. Overall survival and progression-free survival at 1 year was 75% and 59% respectively.

Conclusion

Isotoxic IMRT is a feasible and well tolerated ap proach to treatment intensification. This regime will be tested alongside other intensified treatments against standard sequential chemoradiotherapy in the ADSCAN study.

PO-0753 Phase I trial evaluating MEK inhibitor selumetinib with concomitant thoracic radiotherapy in NSCLC

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