Early response assessment by PET scan in chemoradiotherapy for nasopharyngeal carcinoma

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Background:

Local control is still a problem in T3/4 NPC. Local recurrence can occur in up to one third of patients with conventional radiotherapy (RT). With intensity modulated radiotherapy (IMRT) and chemotherapy, reports of early results shows ≥90% local control. However, recent large series with long follow up, reported 5 years local control of 82.9-86.8% only in locally advanced tumors. For locally advanced NPC, adequate dose and coverage of target volumes are limited by adjacent critical structures. There is a dose response relationship in tumor control and IMRT allows dose escalation but at the expense of increased toxicity. Induction chemotherapy (IC) before RT may shrink tumor and allow smaller target volumes.

In RT planning, the gross tumor volume (GTV) and planning target volume (PTV) of primary is contoured according to baseline imaging without assessment of response or adjustment of target volumes during treatment. Skull base invasion usually remains unchanged on MRI after chemotherapy. PET scan reflects the biological activity within tumor and high uptake in tumor is associated with higher stage of disease and poorer prognosis

In tumors like GIST and Hodgkin's disease, it was found that biological response shown on PET scan may occur before the change in size of tumor. Rapid decrease in tumor uptake correlates with good response to treatment and better outcome. Thus, PET scan may be used as biological imaging for in-vivo response assessment and treatment may be adjusted according to tumor response.

Objectives:

A pilot study was performed to observe tumor response on PET scan during chemoRT and to test out the feasibility of IMRT boost to residual biological target volume (BTV).

Methods and Materials:

Patients with T3/4, N0-3, M0, histologically proven NPC are eligible for study. All patients had IC followed by concurrent chemoRT (CRT). IC was either PF (cisplatin 100mg/sqm D1 and 5 FU1G/sqm D1-5) or GP (gemcitabine 1G/sqm D1, D8 and cisplatin 100mg/sqm D1) every 3 weeks for 3 cycles . CRT was cisplatin 100mg/sqm given on D1, D22, D43 of RT. PET/CT were performed at baseline, after IC and at around 30Gy RT. CT were performed with cast for IMRT planning. GTV-NP was localized according to baseline MRI and received 70Gy in 35 fractions. The BTV-NP was delineated on PET scan. Complete response on PET scan (CR-PET) was defined as SUVmax<2.5 or SUVmean <1.25 of liver background. For patients with incomplete response, the residual BTV-NP received an additional 6Gy in 3 fractions. Histological response was assessed by endoscopy and NP biopsies at 10 weeks after completion of RT. Post-RT imaging was performed at 3 months.

Results:

18 patients were treated between 9/2011 to 4/2013. T Stage was T3 in 10 and T4 in 8 patients. Overall stage was stage III in 8 patients and stage IV in 10 patients. Induction chemotherapy was GP in 6 patients and PF in 12 patients. All patients completed IC and RT with at least 1 cycle of CRT. Median follow up after completion of RT was 8 months (4-21 months). All patients were alive at time of analysis and completed post-RT assessment.

Table 1 shows the change in PET scan uptake during chemoradiotherapy compared with baseline before treatment:

PET scan uptake in primary	Baseline (range)	After induction chemotherapy (range)	After 30Gy RT (range)
Mean SUV max	13.4 (6.53-22.12)	5.31 (1.77-12.33)	4.63 (1.98 – 10.8)
Mean BTV (cc)	45.3 (10.9-147.77)	41.72 (18.33-131.84, 12 cases)	31 (11.42 – 72.1, 11 cases)
Mean SUV mean	6.8 (2.9-10.89)	2.93 (1.81-5.03, 12 cases)	2.76 (1.95 – 4.53, 11 cases)

Six patients achieved CR-PET after IC and another patient achieved CR-PET after 30Gy RT. Compared with baseline, the mean drop in SUVmax after IC and at 30Gy were 56.2% and 61.4% , respectively. Two patients had persistent disease in NP after RT. Both had incomplete response after IC and at 30Gy. The decrease in SUV max after IC was lower than the group's average (30% and 46%).

Conclusion:

PET scan can be used for early response assessment during treatment. CR-PET is achieved early after 3 cycles of IC and allows selection of incomplete responder for intensified treatment. Further study is required to correlate early response with outcome. RT boost to residual BTV is feasible. Randomized trial is required to see if the strategy of dose escalation in incomplete responder will improve local control.