



Factsheet for the Press (Clinical)

PROTON COMPARED TO X-IMRT COMPARED TO 3D IN LOCALLY ADVANCED NSCLC (Non-small-cell lung carcinoma)

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Context: With this study, it was shown that use of intensity-modulated (X-ray) RT (X-IMRT) can further reduce the risk of treatment-related pneumonitis, but not that of esophagitis, relative to 3D CRT. Hypothesizing that the physical dose characteristics of protons will allow proton beam therapy (PBT) to spare critical structures such as esophagus, lung, and bone marrow from incidental irradiation to a greater extent than X-ray therapy, the team evaluated the rates of severe esophagitis, pneumonitis, and bone marrow suppression in patients with locally advanced NSCLC (Non-small-cell lung carcinoma) treated with concurrent chemotherapy with either PBT or X-IMRT.

Purpose: We have compared severe pneumonitis, esophagitis and bone marrow toxicity rates among patients with locally advanced NSCLC treated by IMRT or PBT and concurrent chemotherapy.

Patients and Methods: From January 2003 to June 2008, 128 patients with locally advanced NSCLC were treated with chemotherapy and PBT (62 patients) or chemotherapy and X-IMRT (66 patients); all had concurrent chemotherapy, none had had prior thoracic RT, and all were treated to at least 60 Gy (for X-IMRT) or 60 CGE (cobalt-⁶⁰Gy-equivalent) (for protons). Patients who had both IMRT and 3D CRT or PBT were excluded. Toxicity was graded according to the Common Terminology Criteria for Adverse Events version 3.0.

Results

Our preliminary analysis of patients with locally advanced NSCLC suggests that treatment with concurrent chemotherapy and PBT leads to less bone marrow toxicity compared with concurrent chemotherapy and X-IMRT, which could allow the use of more aggressive systemic regimens for such patients. This supposition needs to be tested prospectively in a randomized trial. The considerable reduction in esophageal reactions after PBT is consistent with the predicted sparing of normal tissues. The ongoing reductions in severe treatment-related pneumonitis (from 32% after 3D CRT to 9% after X-IMRT to 2% after PBT) are consistent with the ability of advanced technologies to spare normal lung. These findings have led to the development of a prospective randomized comparative trial of PBT vs. X-IMRT (funded by the U.S. National Cancer Institute) conducted jointly at MD Anderson and Massachusetts General Hospital. Both arms of the study will involve high-dose radiation (66 Gy to 74 Gy) with concurrent carboplatin and paclitaxel chemotherapy. The endpoints are local tumor control and severe treatment-related pneumonitis. Tumor motion is being accounted for by using 4D CT simulation to develop internal target volumes for use with breath-hold or gating techniques. Future developments in PBT such as discrete spot scanning and intensity-modulated proton therapy must await resolution of tumor motion issues when these advanced techniques are to be used for proton delivery.



Findings:

1. Reducing severe pneumonitis
2. Reducing bone marrow toxicity by using PBT.
3. Increasing the dose to the tumor to 74 CGE

Impact: This trial became the base of prospective randomized study of stage III NSCLC treated by chemotherapy and concurrent IMRT vs. PBT

Indicative of a bigger trend in oncology? Our standard treatment for Stage III non-small-cell lung cancer (NSCLC) is combined chemoradiotherapy. Because of increase of normal tissue toxicity from 3DCRT and chemoradiotherapy, we have started to treat patients with stage III NSCLC by IMRT and chemotherapy. Proton Beam Treatment (PBT) and concurrent chemotherapy started to treat stage III NSCLC at MDACC in May 2006. We have compared normal tissue toxicity between those who were treated by IMRT and PBT with concurrent chemotherapy. There was significant reduction of normal tissue toxicity by PBT compared to IMRT and concurrent chemotherapy. This study suggested that PBT and concurrent chemotherapy is more tolerable for stage III NSCLC patients and we have developed a prospective randomized trial to compare IMRT vs. PBT for stage III NSCLC treated with concurrent chemotherapy. Now we have more than 100 patients enrolled to this study. If this randomized trial will show that PBT with concurrent chemotherapy for patients with stage III NSCLC would be less toxic to normal tissue, it will change our standard practice.