FDG-PET AS A RESPONSE MONITOR IN RADIATION THERAPY FOR LUNG CANCER

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Glucose is an essential nutrient for viability and proliferation of tumor cells. Changes in glucose metabolism in tumor as a result of radiation therapy (RT) or chemo-radiotherapy (CT+RT), which occur earlier than anatomical changes, may be a useful monitor for therapy response and guiding RT. Cessation of glucose uptake by tumor cells after CT+RT or RT is a reflection of cell's inability to continue its vital function, i.e., glycolysis. Residual glucose uptake after CT+RT depends upon the number and metabolic activity of the remaining tumor and host cells. No uptake is strong evidence for no residual cells. Residual uptake could reflect the presence of reproductively dead but metabolically intact cells (in full or part) admixed with reproductively intact cells. Therefore, among the biologic markers resulting from genetic lesions in lung cancer, enhanced glucose utilization measured with FDG-PET may be a useful marker for therapy response to RT and CT, and also for the definition of biological tumor volume as opposed to anatomic tumor volume by computed tomographic scan.

Glucose analog, 2-fluoro-2-deoxy-D-glucose (FDG) allows a measurement of regional glucose utilization by quantitative study of 18F-FDG and positron emission tomography (PET). Three-dimensional (3-D) information of glucose utilization in tumor mass can be obtained with FDG-PET study. This information can be coregistered with chest CT scan for a fused image, which provides biochemical (biological) property of tumor within the anatomical landmark of tumor. Fifty patients have been studied with FDG-PET before and after RT or CT+RT in a pilot study at our institution with the following goals: (1) to determine the relationship between probability of pathologic tumor control (pTCP) and the gradient of residual glucose metabolic rate (MRGlc) in response to RT or CT + RT, (2) to define the levels of residual MRGlc that correspond to 100%, 90%, 80%, 50% and 0% probability of pTCP (FDG-pTCP 100% FDG-pTCP 0%) and (3) to define biologic tumor volume (BTV) corresponding to the gradient of residual MRGlc and the BTV as target for intensity modulated radiotherapy (IM RT).

Quantitative and dynamic 18F-FDG-PET was performed initially in 13 patients with stage III NSCLC to measure regional glucose utilization by primary tumor and involved regional lymph nodes. A modified kinetic method was developed subsequently as a simplified method from the initial dynamic study and used in the subsequent 37 patients for a correlation between residual MRGlc and pTCP. In the modified kinetic method, MRGlc was measured from a single static image at 45 minutes after injection with a correction for blood 18F-FDG activity and glucose concentration. Patients who were free of tumor progression after RT or CT + RT were subjected to surgery. The degree of residual MRGlc in tumor was correlated with histopathologic tumor response.

Among these 50 patients, 29 patients with 30 primary lesions were evaluable for a correlation between residual MRGlc and histopathologic tumor response. The baseline value (mean) of maximum MRGlc was 0.250 ± 0.086 mol/min/gm, and it was reduced to 0.1044 ± 0.058 mol/min/gm by CT + RT. The correlation between residual MRGlc and pTCP was as follows: Pathologic complete response was obtained in 6/6 patients with residual MRGlc 0.048 mol/min/gm, 3/4 with 0.064, 3/6 with 0.077, 2/8 with 0.127 and 0/6 with 0.131 mol/min/gm respectively. An inverse dose response relationship was found between the gradient of residual MRGlc after CT + RT and pTCP. From this relationship, MRGlc 0.048 mol/min/gm was determined to represent FDG-pTCP 100%. From this inverse dose response relationship, residual MRGlc corresponding to 100%, 90%, 80%, 50% and 0% probability of pathologic tumor control (FDG-pTCP 100% FDG-pTCP 0%) can be determined. Using this dose-response data, biological tumor volume (BTV) with different degree of biological activity can be outlined in 3-D fashion and 3-D iso-dose map representing the required dose for pTCP 50%, 80% and 95% can be generated.

CONCLUSION

Biological target volume (BTV) defined by FDG-PET decreases with an increase in radiation dose. A concept of 3-D BTV, 3-D iso-biological tumor volume (3-D iso-BTV) and 3-D iso-dose map aimed for pTCP >90%, which are derived from the dose-response relationship and coregistered FDG-PET and chest CT scan, are put forward for further studies in an attempt for optimization of RT.

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