Early assessment of therapy response in malignant lymphoma with the thymidine analogue [18F]FLT.

Abstract:

PURPOSE: The aim of this study was to determine whether the thymidine analogue 3'-deoxy-3'-[(18)F]fluorothymidine ([(18)F]FLT) is adequate for early evaluation of the response of malignant lymphoma to antiproliferative treatment in a mouse xenotransplant model. METHODS: Immunodeficient mice bearing a follicular lymphoma xenotransplant were treated with high-dose chemotherapy (cyclophosphamide, n = 10), immunotherapy (CD20 mAb, ibritumomab-tiuxetan, n = 10) or radioimmunotherapy ([(90)Y]CD20 mAb, Zevalin, n = 10). Forty-eight hours after treatment, antiproliferative effects were assessed with [(18)F]FLT. Ninety minutes after i.v. injection of 5-10 MBq [(18)F]FLT, mice were sacrificed and radioactivity within the tumour and normal organs was measured using a gamma counter and calculated as % ID/g. The proliferation fraction in tissue samples derived from treated and untreated tumours was evaluated by Ki-67 immunohistochemistry, which served as the reference for proliferative activity. RESULTS: In untreated lymphoma, the mean proliferation fraction was 83.6%. After chemotherapy, the mean proliferation fraction decreased to 39.3% (p = 0.0001), after immunotherapy to 77.6% (p = 0.0078) and after radioimmunotherapy to 78.8% (p = 0.014). In none of the animals was a
significant change in tumour size observed. In untreated lymphoma, tumoural [(18)F]FLT uptake was 5.4% ID/g, after chemotherapy it was 1.5% (p = 0.0005), after immunotherapy, 3.9% (non-significant), and after radioimmunotherapy, 5.8% (non-significant). CONCLUSION: In a lymphoma xenotransplant model, [(18)F]FLT detects early antiproliferative drug activity before changes in tumour size are visible. These findings further support the use of [(18)F]FLT-PET for imaging early response to treatment in malignant lymphoma.