PURPOSE: The purpose of this study was to evaluate prospectively, whether integrated 2-deoxy-2-[(18)F]fluoro-D-glucose positron emission tomography-computed tomography (FDG-PET-CT) is more accurate for determination musculoskeletal tumors compared with separate interpretation of CT and FDG-PET, because most of the current clinical data come from patients studied with PET. METHODS: Eighty patients with newly diagnosed musculoskeletal tumors underwent FDG-PET-CT. CT, FDG-PET, and FDG-PET-CT were interpreted separately to determine the performance of each imaging modality. RESULTS: Assuming that equivocal lesions are benign, performance of diagnostic tests was as follows: sensitivity, specificity and accuracy for CT alone was 81, 84, 83%, for PET 71, 82, 76, and for PET-CT 80, 83 and 86%. Assuming that equivocal lesions are malignant, sensitivity, specificity, and accuracy for CT was 61, 100, 70%, for PET 69, 100, 79, and for PET-CT 69, 100 and 79%. CONCLUSIONS: Combined FDG-PET-CT reliably differentiates soft tissue and bone tumors from benign lesions. The value of the information provided by FDG-PET-CT for planning surgical procedures must be evaluated in further studies.