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DELINEATION OF GROSS TUMOR VOLUME (GTV) FOR RADIATION TREATMENT PLANNING OF LOCALLY ADVANCED RECTAL CANCER USING INFORMATION FROM MRI OR FDG-PET/CT: A PROSPECTIVE STUDY

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Purpose: Accurate delineation of target volumes is important to maximize radiation dose to the tumor and minimize it to nontumor tissue. Computed tomography (CT) and magnetic resonance imaging (MRI) are standard imaging modalities in rectal cancer. The aim was to explore whether functional imaging with F-18 fluorodeoxyglucose (FDG) positron emission tomography (PET), combined with CT (FDG-PET/CT) gives additional information to standard pretreatment evaluation and changes the shape and size of the gross tumor volume (GTV).

Methods and Materials: From 2007 to 2009, 77 consecutive patients with locally advanced rectal cancer were prospectively screened for inclusion in the study at two university hospitals in Sweden, and 68 patients were eligible. Standard GTV was delineated using information from clinical examination, CT, and MRI (GTV-MRI). Thereafter, a GTV-PET was defined in the fused PET-CT, and the target volume delineations were compared for total volume, overlap, and mismatch. Pathologic uptake suspect of metastases was also registered.

Results: The median volume of GTV-MRI was larger than that of GTV-PET: 111 cm^3 vs. 87 cm^3 ($p < 0.001$). In many cases, the GTV-MRI contained the GTV defined on the PET/CT images as subvolumes, but when a GTV total was calculated after the addition of GTV-PET to GTV-MRI, the volume increased, with median 11% (range, 0.5–72%). New lesions were seen in 15% of the patients for whom PET/CT was used.

Conclusions: FDG-PET/CT facilitates and adds important information to the standard delineation procedure of locally advanced rectal cancer, mostly resulting in a smaller GTV, but a larger total GTV using the union of GTV-MRI and GTV-PET. New lesions were sometimes seen, potentially changing the treatment strategy.

^{18}F fluorodeoxyglucose positron emission tomography, Computed tomography, Radiotherapy, Delineation, Gross tumor volume, Locally advanced rectal cancer.

INTRODUCTION

Accurate delineation of target volumes is essential for optimal radiation treatment of any tumor, including locally advanced rectal cancer (LARC). The main goal is a high dose of radiation to the tumor, maintaining an acceptable dose to adjacent tissues. Positron emission tomography (PET) can visualize functional alterations, thereby facilitating early diagnosis. The commonly used radiopharmaceutical for this purpose is 2-^{18}F-fluoro-2-D-deoxyglucose (FDG). FDG-PET, especially when combined with anatomic imaging, such as computed tomography (CT) (FDG-PET/CT), gives information on molecular and morphologic characteristics, thereby potentially providing the most accurate information for staging of many malignancies (1).

Anatomic imaging like CT and magnetic resonance imaging (MRI) have been the most commonly used pretreatment modalities for LARC, and today MRI of the pelvis is internationally perceived to be the gold standard in local tumor staging of rectal cancer (2).

Over the past few years, FDG-PET/CT has become an additional modality in tumor mapping. CT still remains the clinical standard for volume definition and dose calculation, although one limitation is the lack of contrast resolution for soft-tissue structures, leading to noticeable inter- and intraobserver variations in the delineation of gross tumor volume (GTV) (1, 3). PET/CT has the potential to better define limits and thus minimize dose to organs at risk. More recently, diffusion-weighted MRI (4) has been documented as

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a potential tool for response prediction and assessment, generating image contrast based on differences in water mobility, and it could potentially also be integrated in the delineation of the target.

The scientific documentation focusing on PET and radiotherapy planning has rapidly increased over the past 10 years, especially in head-and-neck cancer (5, 6) and lung cancer (7). The literature describing rectal cancer, PET/CT, and GTV delineation is, however, sparse.

Bassi *et al.* (8) studied 25 patients with rectal cancer who were candidates for preoperative radiotherapy. The GTV and the clinical target volume (CTV) were delineated on the basis of CT and PET/CT. In 24% of the patients, PET/CT affected tumor staging or the treatment purpose; in 12%, PET/CT showed an uptake in the regional lymph nodes and in one case also in the liver. The PET/CT-GTVs were statistically significantly larger than were the CT-GTVs; the mean difference was 25%. Roels *et al.* (9) investigated three different ^{18}F PET tracers: FDG, ^{18}F-fluoromisinidasol, and ^{18}F-fluorothymidine for radiotherapy planning. They concluded that FDG and ^{18}F-fluorothymidine corresponded best when used for delineation of GTV and were less variable over time. Another study (10) compared delineation of GTV using FDG-PET/CT and MRI before, during, and after long-course radiation for a group of 15 patients. Two segmentation algorithms were used to automatically delineate PET-GTV: a modified threshold-based method and a gradient-based method. In general, MRI showed larger GTVs than did FDG-PET/CT. There was a mismatch of approximately 50% between the PET-GTV and the MRI-GTV at baseline and during chemoradiotherapy (CRT). They concluded that the integration of MRI and FDG-PET diagnostics into radiotherapy planning seems feasible and that the spatial variance between MRI and FDG-PET GTVs should be taken into account for target definition. Ciernik *et al.* (11) also studied automated segmentation of the PET-derived GTV in rectal cancer and concluded that this method is effective, fast, and less prone to interobserver variation than is standard CT-based delineation.

The main aim of the present prospective study was to explore whether and how often imaging with FDG-PET/CT could give additional information to standard pretreatment evaluation (including CT of the thorax/abdomen/pelvis and MRI of the pelvis) and change the shape and size of GTV. FDG-PET/CT adds extra costs and should be used only if it adds clinically meaningful information often enough.

METHODS AND MATERIALS

Patients and inclusion criteria

Between November 2007 and December 2009, 77 consecutive patients diagnosed with LARC were discussed by a multidisciplinary team at Karolinska University Hospital, Solna, Stockholm, or Uppsala University Hospital, Uppsala, after standard clinical and radiologic examination. LARC was defined as clinical (c) Stage cT4a (12), cT3 with involvement of the mesorectal fascia (mrf+) or with radiologically malignant lateral lymph nodes outside the mesorectum (to be covered in a standard radiation target). The patients consented to undergo PET/CT investigation, and 68 patients were eligible.

All patients were planned for treatment according to the standard guidelines in the actual institution, independently of inclusion in this study. Most patients went through long-course preoperative CRT (50.4 Gy with capecitabine to GTV, 45 Gy to noninvolved lymph nodes at risk), but some started up-front combination chemotherapy because of synchronous metastases. Otherwise, they would have received the same CRT.

Image acquisition

Magnetic resonance imaging. Patients were referred from several hospitals in the counties of Stockholm, Uppsala, and Dalecarlia. In 41 of 68 patients, MRI was performed at the referring hospital; the remaining 27 patients were examined at Karolinska or Akademiska Hospitals. All examinations were evaluated by the multidisciplinary teams to be of sufficient quality for staging. All patients in the study were examined at 1.5 Tesla. All MRI protocols included at least transversal and sagittal T2-weighted fast spin-echo sequences and transversal T1-weighted images of the pelvic area. The patients were in supine position, and slice thicknesses were between 3 mm and 5 mm. The transversal T2-weighted images and the existing radiologic report were used as a basis for tumor delineation.

FDG-PET/CT. The patients were instructed to fast for 6 hours before examination. The blood glucose level was always measured. The patients were injected with 4 MBq/kg body weight of ^{18}F-FDG intravenously 60 minutes before examination. Scanning that covered at least the skull base to the proximal aspect of the thighs was performed with a Siemens Biograph 64 (45 patients) (Siemens Medical Solutions), a GE Discovery STE (20 patients) or a GE Discovery ST (3 patients) (both GE Medical Systems). All PET/CT datasets included transversal, sagittal, and coronal reformations of the PET, CT, and fused PET/CT images with a slice thickness of 3.75 to 5 mm.

Tumor delineation

Two physicians (M.B. and C.R.), both specialists in clinical oncology including radiotherapy, and one radiologist (K.H.), took part in the GTV delineation of all patients. Delineation of the CTV, including areas potentially containing subclinical disease, was not part of this study. The anatomic and biologic imaging datasets were transferred to, and registered in, the treatment planning system (Aria™) as Digital Imaging and Communications in Medicine (DICOM) datasets. The MRI images were not matched with the CT images and were reviewed on a separate screen. The CT examination from the PET/CT, done in supine position and in the radiation treatment position, was used as CT simulation to define the active tumor and target volumes. The GTV-MRI was delineated using information from clinical examination, CT, and MRI. Thereafter, a GTV-PET was defined with additional information from the fused PET/CT, using axial images and the window and level settings found most appropriate for each patient. No autocontouring was used. We adjusted the background intensity to what we considered normal on the basis of general FDG uptake in the liver. Areas with elevated FDG uptake not explained by normal anatomic structures were considered to be tumor tissue. No adjustment of the GTV-MRI was done after the incorporation of FDG-PET information. The target volume delineations were subsequently compared for overlap, or the union and intersection volumes as demonstrated,