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Y90 radioembolization of colorectal cancer liver metastases: response assessment by contrast-enhanced computed tomography with or without PET-CT guidance☆,☆☆,★

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ABSTRACT

Purpose: To compare various computed tomography (CT) parameters to the positron emission tomography with computed tomography (PET-CT) response, with or without PET guidance for the response assessment of colorectal cancer (CRC) metastases treated by Y90 radioembolization.
Methods: Thirty-six CRC metastases were retrospectively evaluated on 18F-Fluoro-Deoxy-Glucose PET-CT and contrast-enhanced computed tomography (CECT) performed at baseline and 2–3 months after Y90 radioembolization.
Results: Median SUVmax values decreased from 11.39 to 6.71 after radioembolization ($P<.001$), and 23/36 (64%) metastases were categorized metabolic responses according to European Organisation for Research and Treatment of Cancer criteria. Only a decrease of the mean attenuation in the structural ($P<.001$) and metabolic active volume ($P<.001$) was observed. The change in these criteria was correlated with the change of SUVmax.

1. Introduction

Classically, response to therapy of liver metastases secondary to colorectal cancer (CRC) is assessed by Response Criteria in Solid Tumors (RECIST) methodology on contrast-enhanced computed tomography (CECT) [1,2]. RECIST consists in summing tumor maximal diameters (MDs) measured in the axial plane. These evaluation criteria face criticism because of frequent discrepancy with glucose metabolism changes observed on 18F-Fluoro-Deoxy-Glucose (FDG) positron emission tomography (PET), a reliable technique for response assessment for CRC hepatic metastases treated by liver-directed therapies (LDTs) [3–7]. Treatment options of hepatic metastases in patients not candidates for surgery, including ^{90}Yttrium (Y90) radioembolization, should be discussed in multidisciplinary consultation on a lesion-by-lesion basis [8,9].

The lack of sensitivity and specificity of RECIST criteria in the response assessment of hepatic tumors after Y90 radioembolization is explained by their necrotic, edematous, or hemorrhagic presentation after treatment; these can lead to an increase in size despite effective therapy [10,11]. A critical number of beneficial treatment responses are thereby underestimated, particularly when metastases develop in altered liver parenchyma due to previous surgery, systemic chemotherapy, or locoregional treatments. Nevertheless, a reliable response assessment to therapy is essential, particularly if supplementary curative or palliative treatment options are discussed. As a result, new radiologic evaluation criteria have been proposed during recent years, such as changes in tumor volume and intratumoral attenuation [12–14]. Studies evaluating intratumoral attenuation are promising [10,14,15].

Abbreviations: CEA, carcinoembryonic antigen; CRC, colorectal cancer; CECT, contrast-enhanced computed tomography; EORTC, European Organisation for Research and Treatment of Cancer; FDG, 18F-Fluoro-Deoxyglucose; HU, Hounsfield unit; IQR, interquartile range; LDT, liver directed therapies; MAMAV, mean attenuation in the metabolic active volume; MASV, mean attenuation in the structural volume; MD, maximal diameter measured in the axial plane; PET(−CT), positron emission tomography (with computed tomography); RECIST, response criteria in solid tumors; S.D., standard deviation; SPECT, single photon emission computed tomography; SUVmax, maximal standardized uptake value; SV, structural volume; ^{99}Tc-MAA, ^{99}Technetium-macroaggregated albumin; VOI, volume of interest; Y90, ^{90}Yttrium.

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The aim of this study was to evaluate, on a lesion-by-lesion basis, CECT-based parameters and to evaluate the ability of FDG-PET response to increase the accuracy of CECT interpretation. For this, we tested a new evaluation methodology in which residual metabolically activity was used for delineating the lesions seen on CECT.

2. Material and methods

2.1. Patient and lesion sample

This retrospective study consisted of a review of computed tomography (CT) and PET CT scans of patients treated between October 1, 2008 and November 9, 2009 at the J. Bordet Institute (Brussels) by Y90 radioembolization for metastases secondary to CRC. Studied patients were not candidates for surgical resection because of tumor (unresectability) or patient (inoperability) characteristics. Exclusion criteria consisted of (a) time between the concordant examinations (CECT and PET-CT assessment before or after treatment) longer than 4 weeks; (b) additional antitumoral treatment administered between the imaging examinations; (c) the lack of one or more imaging examinations; and (d) the presence of unacceptable imaging artifacts. Patients with bilobar disease underwent bilobar treatment, whether by sequential or concomitant fashion (if liver function was considered acceptable). Twelve patients fulfilled initial inclusion criteria. Of the 12 patients, 5 were excluded for the following reasons: 3 because of missing of data (one or more imaging examination not available), 1 with unacceptable delay between baseline CECT and the PET-CT (>4 weeks) and 1 because of suboptimal contrast injection on the pretreatment CECT. This last patient was excluded because of a portal vein thrombosis, which delays the contrast uptake in the liver, reducing the depiction of metastases, at the portal venous phase.

All hypermetabolic metastases on the pretreatment PET-CT were considered as target lesions. Non hypermetabolic metastases and metastases exhibiting maximal standardized uptake value (SUVmax)≤2 times the liver background (mean SUV) were excluded from analysis. Target lesions defined on the pretreatment PET-CT were identified on the corresponding CECT. An abdominal CT expert radiologist (DDB, >20 years of experience) reviewed the matching. Lesions were considered measurable if their MD in the axial plane was ≥1.0 cm. Patient and lesion selection is summarized in Fig. 1.

2.2. Imaging methodology

Our standard timeline of events of Y90 radioembolization includes baseline PET-CT and CECT within days before the planning angiography, during which ^{99}Technetium-macroaggregated albumin (^{99}Tc-MAA) are infused, immediately followed by a single photon emission computed tomography with computed tomography (SPECT-CT); Y90 radioembolization is performed 10 days following the planning angiography; the response assessment including laboratory (toxicity), CECT, and PET-CT (efficacy) is performed within 6–8 weeks following therapy.

CECT were performed on a SOMATOM Definition AS 40-slices machine (Siemens, Erlangen, Germany) with an iodinated contrast agent (Iomeron 400, Bracco Imaging, Italy) administered by a power injector (Ulrich Medical, and Ohio Tandem, Ulm, Germany). A triphasic injection protocol was used: initial unenhanced CT followed by 25-ml NaCl 0.9% 2-ml/s contrast (bolus test), 100-ml contrast agent bolus 2 ml/s then 30-ml NaCl 0.9% 2 ml/s (saline flush) to determine the arterial phase. The delay for the portal venous phase between beginning of injection and acquisition was 75 s, the acquisition time was about 15 s and the slice thickness of 1 mm. Image reconstructions were performed on a Syngo Acquisition Workplace station (Siemens, Erlangen, Germany) and included 1.5- and 3.0-mm automated postprocessing reconstructions.

PET-CT acquisitions were systematically obtained 1 h (±15 min) after injection of ^{18}F-FDG (260 to 330 MBq, according to the body mass index) and with a normal glycemia (80–110 mg/dl). Patients were fasting 4 h prior to FDG administration. All PET-CT scans were performed on a PET acquisition module coupled to a multidetector helical CT module (Discovery LightSpeed, General Electric, Fairfield, CT, USA). The CT acquisition was obtained with low-dose irradiation (62 mAs, 120 Kv) without intravenous contrast agent injection. PET-CT scans were acquired prior to radioembolization, and then 6 weeks after radioembolization in the same conditions. Images were reconstructed with an Ordered Subset Expectation Maximization (OSEM) algorithm (two iterations, 28 subsets, Gaussian postfilter 5.45 mm). PET-CT images were stored and processed using dedicated imaging software (PMOD Technologies Ltd, Zurich, Switzerland).

2.3. Y90 radioembolization and dosimetry

Treatments were preceded by a planning angiography permitting hepatic and tumor vasculature mapping, optimal catheter tip positioning,

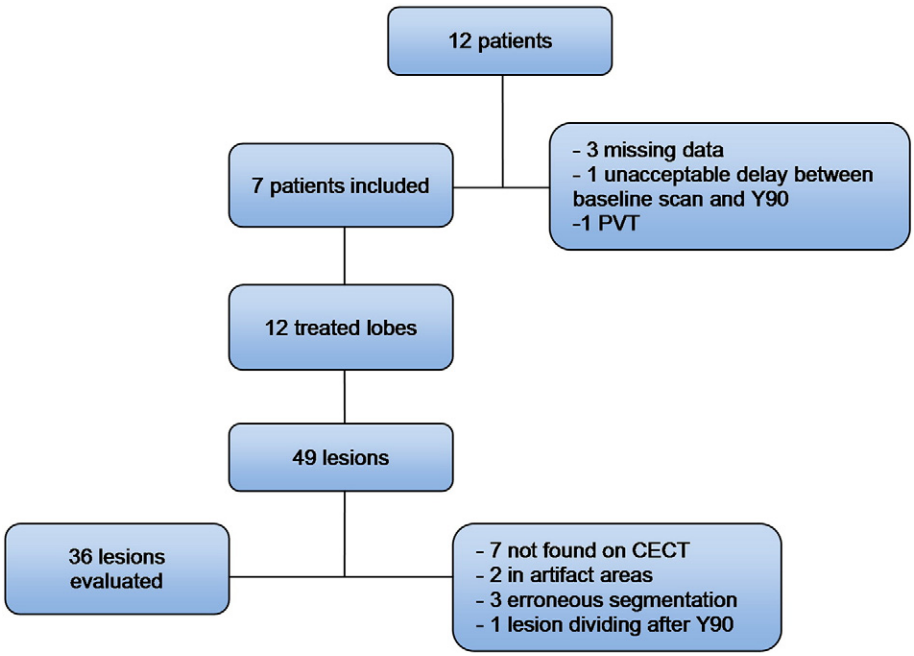

Fig. 1. Study flow chart.