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Measurement variability of liver metastases from neuroendocrine tumors on different magnetic resonance imaging sequences

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Liver metastasis;
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Interobserver variability

Abstract
Purpose: To assess dimension measurement variability of liver metastases from neuroendocrine tumors (LMNET) on different magnetic resonance imaging (MRI) sequences.
Material and methods: In this institutional review board-approved retrospective study from January 2011 to December 2012, all liver MRI examinations performed at our department in patients with at least one measurable LMNET according to response evaluation criteria in solid tumors (RECIST1.1) were included. Up to two lesions were selected on T2-weighted MR images. Three reviewers independently measured long axes of 135 hepatic metastases in 30 patients (16 men, 14 women, mean age 61 ± 11.4 (SD) years; range 28—78 years), during two separate reading sessions, on T2-weighted, diffusion-weighted MRI (DWI) (b; 50, 400, 800 s/mm^2) and arterial, portal and late phases after intravenous administration of a gadolinium chelate. Intraclass-correlation coefficients and Bland—Altman plots were used to assess intra-and interobserver variability.
Results: Intra- and interobserver agreements ranged between 0.87—0.98, and 0.88—0.97, respectively. Intersequence agreements ranged between 0.92 [95%CI: 0.82—0.98] and 0.98 [95%CI: 0.93—0.99]. 95% limits of agreement for measurements were −10.2%, +8.9% for DWI (b = 50 s/mm^2) versus −21.9%, +24.2% and −15.8, +17.2% for arterial and portal phases, respectively.

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Conclusion An increase < 9% in measurement and a decrease of −10% on DWI should not be considered as true changes, with 95% confidence, versus 24% and −22% on arterial and 17%, −16% on portal phases, respectively. DWI might thus be the most reliable MR sequence for monitoring size variations of LMNETs.

Neuroendocrine tumors (NETs) are rare tumors and when well differentiated, they are often slowly evolving [1]. Patients with NET can have very long survival, even when the disease is disseminated [2]. The most common metastatic site in NETs is the liver, with liver being involved by metastases in apparoximately 60% of patients with intestinal NET and liver burden is a major prognostic factor [3]. Computed tomography (CT) remains the reference technique for the initial evaluation and follow-up of NET-associated metastases [4]. However, magnetic resonance imaging (MRI) is now the optimal imaging modality to best detect liver metastases from NET [5]. Moreover, diffusion-weighted MR sequences have been recently shown to further improve overall detection of liver metastases in this specific context [6—8]. Furthermore, in these patients, who are often rather young, repeated exposure to radiation is an issue as they are likely to be followed-up with repeated examinations over time. Liver MRI is thus increasingly performed instead or in addition to CT, being radiation-free and the practice of performing repeated liver MRI for follow-up of patients with NETs metastases is currently emerging. Current evaluation of solid tumor response under therapy is still based on RECIST 1.1 criteria, despite their widely acknowledged limits [9,10].

According to RECIST, lesions must be measured using the same MRI sequence on subsequent examinations. However, to our knowledge, so far, there are no clear guidelines as to which MR sequence must be selected in order to ensure optimal reproducibility of measurements during follow-up. A recent study investigated the reproducibility of dimension measurements on MRI in liver metastases regardless of their origin and concluded that interobserver and intersequence agreement rates for measurements are high [11]. However, liver metastases from NETS are somewhat specific in that they are considered as hypervascular and thus, more prone to variation in their visibility among different MR sequences than the more common metastases from colorectal cancer [12,13]. Two recent papers suggested that diffusion-weighted (DW) MRI used alone for strict RECIST 1.1 evaluation resulted in excellent agreement with their reference standard defined as the hepatocyte phase after injection of a hepatocyte-specific contrast material [14,15].

The purpose of this study was to assess dimension measurement variability of liver metastases from NETs on the different MRI sequences that are used for the follow-up of these tumors during standard routine practice and according to RECIST 1.1 guidelines.

Materials and methods

Patients

In this institutional review board-approved retrospective study from January 2011 to December 2012, all liver MRI examinations performed at our department in patients with liver metastases from histologically proven NETs and with at least one measurable liver lesion according to RECIST 1.1 were included. Informed consent was waived.

All MRI examinations were performed on the same MRI equipment with the same MRI protocol. All patients with MRI examinations that showed at least one metastasis≥10 mm in long axis according to RECIST 1.1 criteria were kept in the final population [10].

The standard of reference for the diagnosis of liver metastases from NET was based on a combination of typical imaging appearances — mildly to moderately hyperintense on low *b*-value DW MRI and remaining hyperintense on higher *b*-value DW MRI; moderately or strongly hyperintense in relation to the surrounding liver parenchyma on T2-weighted MR images, but less than the signal intensity of liquid; hypervascular or peripherally enhanced without a globular pattern (whatever enhancement on delayed-phase imaging) on dynamic gadolinium chelate-enhanced T1-weighted MR images — as well as clinical follow-up and histopathology.

For all patients, we noted from the medical records the age, sex, primary location of the neuroendocrine tumor and its grade, its Ki 67 coefficient, the time of the MRI examination(s) relatively to diagnosis of tumor, as well as treatments (non-systemic chemotherapy, somatostatin analog, anti-angiogenic therapy or transarterial chemoembolization). Liver steatosis as evidenced with MRI was also noted.

MRI acquisition

Patients were examined in a supine position with a 1.5-T superconducting MR imaging system (Magnetom Avanto®; Siemens Healthineers, Erlangen, Germany) using a phased-array abdominal coil. The protocol included an axial T1-weighted dual fast gradient-recalled-echo sequence, T2-weighted fast spin-echo (FSE) sequence with spectral fat saturation, DW fat-suppressed single-shot spin-echo planar sequences with three diffusion factors (*b*-values of 50 s/mm^2, 400 s/mm^2 and 800 s/mm^2) and a transverse fat-saturated three-dimensional low-angle volumetric interpolated breath-hold (VIBE) T1-weighted gradient echo

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