# Radiology of colorectal cancer with emphasis on imaging of liver metastases
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# Detection of Colorectal Liver Metastases with T1-Weighted Magnetization-Prepared Gradient-Echo: Breath-Hold Thick Slice versus Respiratory-Triggered Thin Slice

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**ABSTRACT**

**Purpose:** To compare a thick-slice breath-hold (BH) and a thin-slice respiratory-triggered (RT) T1 magnetization-prepared gradient-echo (MPGE) in the detection of colorectal liver metastases.

**Materials and Methods:** Two observers independently identified focal hepatic lesions, in 16 patients, on a BH and RT T1-MPGE sequence with slice thicknesses of 13 and 5 mm, respectively. BH and RT T1-MPGE acquisition time were 19 seconds versus approximately 5 minutes. The standard of reference in all patients was the combination of surgical findings and intra-operative ultrasound. The observers subjectively scored liver coverage, the amount of breathing motion and image contrast per sequence in each patient.

**Results:** No significant differences were noted between the BH and RT T1-MPGE sequence in both observers for sensitivity and specificity of the detection of liver metastases. The observers rated the presence of breathing motion similar for each sequence. Liver coverage ($P \leq .046$) and image contrast ($P \leq .023$) were superior for the BH sequence.

**Conclusion:** Sensitivity and specificity for the detection of colorectal liver metastases were similar for thin-slice RT and thick-slice BH T1-MPGE. The acquisition time of BH T1-MPGE is 15 times shorter than that of the RT sequence. Thus, the BH T1-MPGE is preferred in clinical practice.

## INTRODUCTION

T1-weighted magnetization-prepared gradient-echo imaging, such as in T1-weighted TurboFLASH (Siemens Medical Systems, Erlangen, Germany), inversion-recovery-prepared fast GRASS (GE Medical Systems, Milwaukee, Wis.) or T1-weighted TFE (Philips Medical Systems, Best, The Netherlands) [1], uses a fast pulse sequence enabling breath-hold (BH) imaging. The addition of a slice-selective 180º inversion magnetization pulse to a T1 gradient-echo (GE) sequence increases its T1 weighting and subsequently improves lesion to liver contrast in the image. Furthermore, the slice-selective 180º inversion magnetization pulse results in images where vessels are bright and lesions dark. Studies by de Lange et al [2,3] have shown its ability to image the entire liver in one breath-hold with adequate detection rates, localization and characterization of focal hepatic lesions.

The T1-weighted magnetization-prepared gradient-echo (T1-MPGE) is an important sequence in our magnetic resonance (MR) imaging liver protocols because of its good overall image quality, detection rates and short acquisition time. The limited BH period, however, does not allow optimization of spatial resolution in relation to coverage. Both in the literature [2,3] and in the T1-MPGE sequence used in our hospital the section thickness of the 2D T1-MPGE is quite large (10 mm or more). As more frequently used in T2-weighted sequences we wanted to use respiratory-triggering (RT) to lengthen the available time window, enabling acquisition of thinner slices and subsequently improve lesion detection [4].

The purpose, therefore, of our study was to compare a thick-slice BH and a thin-slice RT 2D T1-MPGE in detecting colorectal liver metastases.

## MATERIALS AND METHODS

### PATIENTS

In a 18 month period, 30 consecutive patients suspected, or known, to have liver metastases, referred to our hospital to undergo partial liver resection or isolated liver perfusion with melphalan (Alkeran®; GlaxoSmithKline, Zeist, The Netherlands) [5], were eligible for this study. The diagnosis at the time of referral was, in most cases, established by an increased serum level of tumor markers and findings at ultrasound. The Institutional Review Board of our hospital did not require specific approval and informed consent for this study, because MR imaging of the liver is part of the clinical protocol in these patients.

In 14 patients no standard of reference became available, because of advanced disease (extra-hepatic tumor or end-stage liver involvement). Finally, 16 patients (nine men, seven women) aged 36-69 years (median age, 52 years) were included in this study. The primary malignancy was colorectal adenocarcinoma in all patients. At least one metastasis in the liver in each patient was histologically proven. In none of the patients relevant coexistent morbidity of the liver (e.g., cirrhosis or steatosis) was diagnosed and none had previous liver surgery. The median interval between preoperative MR imaging and surgery was eight weeks (range, 3-12 weeks).

MR IMAGING

We used on our 1.5-T system (Gyroscan ACS or NT15; Philips Medical Systems, Best, The Netherlands) a dedicated phased-array coil for signal transmission and reception. In two patients the system's body coil was used due to a faulty phased-array coil. The BH MPGE sequence was acquired during one breath hold after full expiration. A belt around the upper abdomen generated the signal used for respiratory triggering of the RT MPGE. During the acquisition of this sequence, patients were not given special breathing commands. Image acquisition was started just before end expiration, allowing data acquisition during a period of reduced respiratory motion.

Both sequences were optimized for our MR system. The following parameters were identical for both sequences: two-dimensional, axial orientation, slice-selective pre-pulse, anterior-posterior phase-encoding direction, flip angle of 10 degrees and 128 x 256 matrix. The BH T1-MPGE had a repetition time (TR) of 9.3 msec, an echo time (TE) of 4.6 msec and an inversion time (TI) of 634 msec (based on preliminary studies). With one signal average per data line 15 sections of 13 mm, with a 1.2 mm intersection gap, were acquired in 19 seconds for the BH MPGE. The RT T1-MPGE had a TR, TE and TI of respectively 9.9, 4.6 and 679 msec (based on preliminary studies). With three averages per data line up to 40 sections of 5 mm, with a 0.5 mm intersection gap were acquired in approximately 5 minutes for the RT MPGE. The number of sections was planned into accordance with the craniocaudal size of the liver. Due to different breathing frequencies among the patients, minor variations in imaging time of the RT MPGE were noted. The field-of-view and rectangular field-of-view were 430 mm and 100%, and 375 mm and 91% for the BH and RT sequence respectively.

STANDARD OF REFERENCE

The standard of reference for all patients was based on the combination of findings at surgery, intra-operative ultrasound (IOUS), and histology. After inspection of the entire abdomen and complete mobilization of the liver, the surgeon palpated the liver bimanually. A radiologist, having full knowledge of the pre-operative data, performed IOUS, using an Aloka 2000 system (Aloka, Tokyo, Japan) with a 7.5-MHz transducer tailored for IOUS procedures.

Using the defined standard of reference we categorized lesions based on histologic findings, consistency at palpation, characteristic appearance and compressibility at IOUS, either as malignant or benign. Firm, irregular lesions at palpation with one or more of the following ultrasound features [6] were considered malignant: irregular shape, irregular margin, bull's eye appearance and/or amorphic calcifications. Lesions that did not meet benign criteria (hemangioma: soft, compressible, hyperechoic, geographically defined; or cyst: firm, sharply defined, thin-walled and echolucent with post-acoustic enhancement) were considered potentially malignant, and were either resected or a per-operative fine needle aspiration biopsy was performed. Thus, we identified 104 focal hepatic lesions: 93 malignant and 11 benign (two hemangioma, eight cysts, one granulomatous nodule). The median number of metastases per patient was five (range, 1-20). Using the Bismuth system [7] the location of each lesion was specified.

According to the Bismuth system [8] the liver consists of nine segments. We identified in our 16 patients, therefore, 144 liver segments. In 74 (51%) out of these 144 segments no metastases were detected with the standard of reference. The remaining 70 (49%) segments contained one or more metastases.

The largest diameter of all metastases was assessed by IOUS; 46 of 93 (49%) metastases were smaller or equal to 10 mm and 47 metastases were larger than 10 mm. Median diameter was 11 mm (range, 3-100 mm).


DATA ANALYSIS

Hard-copy images from all 16 patients were randomized and independently reviewed by two MR radiologists (M.E.J.P., M.N.J.M.W.). Each reader individually evaluated each of the two MR sequences separately, blinded to all other test results, during several sessions.

For each patient, the observers subjectively scored liver coverage, the amount of

breathing motion and image contrast, per sequence. Liver coverage was qualified as complete (entire liver imaged) or incomplete (cranial and/or caudal part of the liver not imaged) at a two-point scale: 0, no; 1, yes. The amount of image degradation secondary to breathing motion was scored by using a four-point scale: 1, very much; 2, much; 3, some; 4, none. As discussed by Semelka et al [9] position inconsistencies between the volume of tissue undergoing excitation by the pre-pulse and the subsequently imaged slice of tissue can result in loss of contrast in that particular image. To quantify this phenomenon, per sequence, the number of images subjectively lacking the anticipated contrast were counted and divided by the total number of images. This resulted in a four-point scale for image contrast: 1, poor (= less than 25% of the images having the anticipated contrast); 2, fair (= between 25-50% of the images having the anticipated contrast); 3, moderate (= between 50-75% of the images having the anticipated contrast); 4, good (= more than 75% of the images having the anticipated contrast).

The observer noted the location, size, and suspected nature of each lesion. The suspected nature of each lesion was graded with a five-point scale on the basis of signal intensity, morphology, and conspicuity, where 1 was definitely benign and 5 was definitely malignant. Subsequently, for the 104 lesions identified with the standard of reference, the presence, location, and suspected nature were compared to the findings of each observer for each sequence.

STATISTICAL ANALYSIS

The Wilcoxon signed-rank test was used to compare liver coverage, the absence of breathing motion and image contrast of both sequences.

Sensitivity calculations and interobserver variability analysis were performed on a segment-by-segment basis, so if a segment contained one of more metastases it was graded positive and if no metastases were present negative. Furthermore, for sensitivity calculations and interobserver variability analysis, a lesion detected on MR images was considered malignant if an observer rated it definitely malignant (score of 5) or probably malignant (score of 4).

The sensitivity and specificity for the detection of colorectal liver metastases of the thick-slice BH and thin-slice RT T1-MPGE sequences were compared by using the McNemar test. The study of interobserver variability was restricted to liver metastases proven with the

standard of reference and was analyzed by means of κ statistics. Kappa values of 0.00-0.40 were considered to indicate poor correlation, values of 0.41-0.75 were considered to indicate good correlation, and values greater than 0.75 were considered to indicate excellent correlation.

For all tests used, a *P* value of less than .05 was considered statistically significant.

## RESULTS

### SEQUENCE QUALITY

None of the three image quality parameters of the RT T1-MPGE was ever judged to be superior to the BH sequence by both observers. In only two studies observer 2 rated the BH sequence superior to RT for the absence of breathing motion; the other 30 studies were scored to be of equal quality with regard to breathing motion. Liver coverage with the BH MPGE was rated superior to the RT version in four patients ($P = .046$) by observer 1 and in five patients ($P = .025$) by observer 2. Image contrast was judged to be superior on the BH sequence compared to the RT version in seven patients ($P = .014$) by observer 1 and in six patients ($P = .023$) by observer 2, as demonstrated in Figure 1.
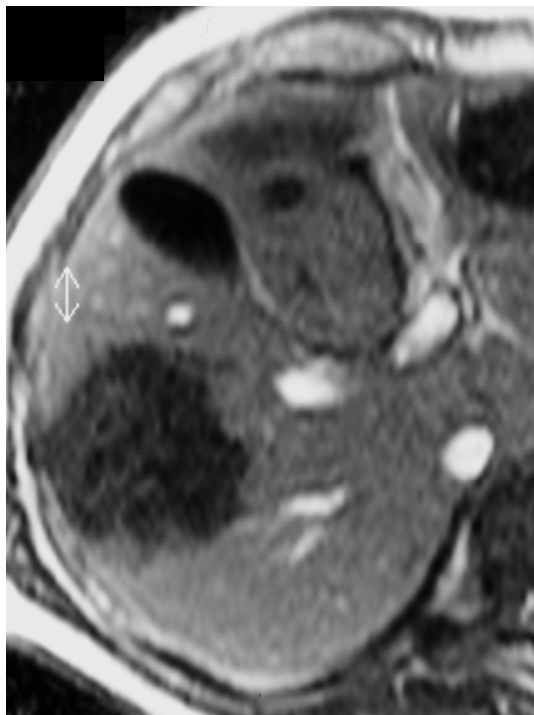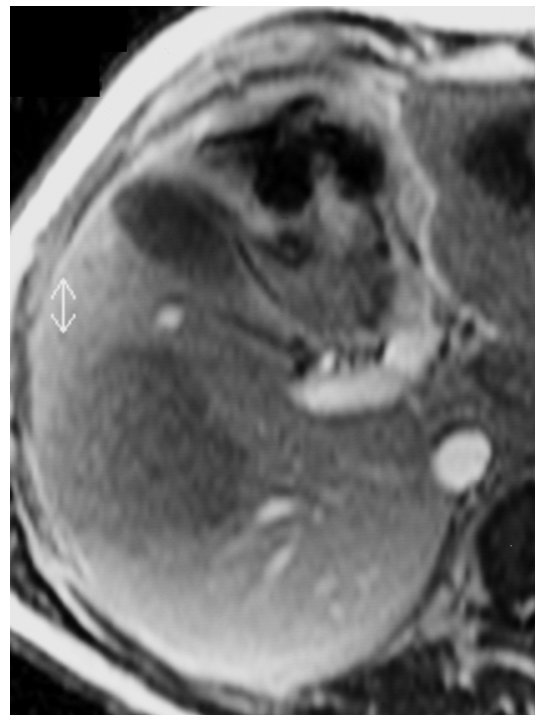


**a.**                                    **b.**
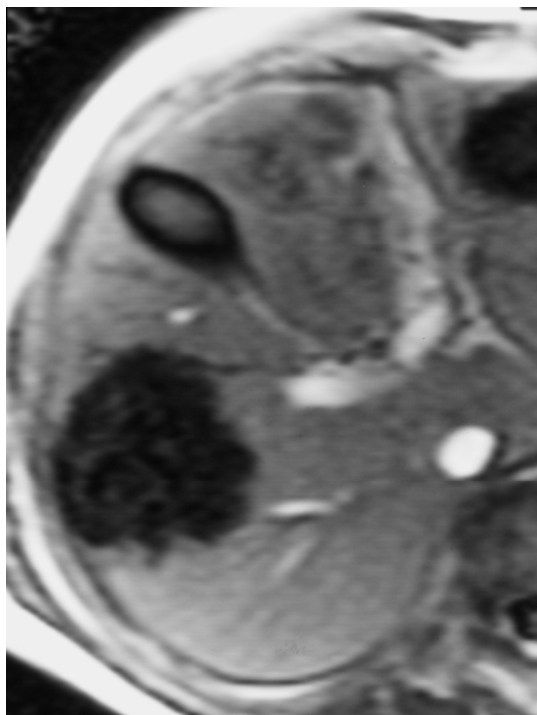
**c.**

**Figure 1.** T1-MPGE images show a colorectal liver metastasis in the right liver lobe. (**a,b**) Two subsequent thin-slice respiratory-triggered T1-MPGE images demonstrate the variation in contrast. Lesion-liver contrast is good at **a.**, but poor at **b.**, seriously degrading conspicuity of this large metastasis. (**c**) The breath-hold T1-MPGE image demonstrates good lesion-liver contrast, but suffers from blurring due to the 13 mm slice thickness. Note the absence of motion artifacts at all images.

SEGMENTAL ANALYSIS

No significant differences were noted between the thick-slice BH and thin-slice RT T1-MPGE sequence in both observers for sensitivity (Table 1) and specificity (Table 2) in the detection of colorectal liver metastases.

**Table 1.** Segmental Sensitivity for the Detection of Liver Metastases.

| Observer | Sensitivity BH[#] | Sensitivity RT[#] | *P* Value |
|----------|-------------------|-------------------|-----------|
| 1 | 42 (60) | 47 (67) | .36 |
| 2 | 50 (71) | 46 (66) | .45 |

[#] Data are number of segments containing one or more metastases (total number of segments containing one or more metastases is 70). Numbers in parentheses are percentages.
BH = breath-hold T1-MPGE; RT = respiratory-triggered T1-MPGE.

**Table 2.** Segmental Specificity for the Detection of Liver Metastases.

| Observer | Specificity BH[#] | Specificity RT[#] | *P* Value |
|----------|-------------------|-------------------|-----------|
| 1 | 58 (78) | 57 (77) | .99 |
| 2 | 60 (81) | 55 (74) | .30 |

[#] Data are number of segments without metastasis (total number of segments without metastasis is 74). Numbers in parentheses are percentages.
BH = breath-hold T1-MPGE; RT = respiratory-triggered T1-MPGE.

INTEROBSERVER VARIABILITY

Interobserver agreement for both sequences was good with κ values of 0.50 for the breath-hold T1-MPGE sequence and 0.58 for the respiratory-triggered version.

**DISCUSSION**

The sensitivity and specificity in the detection of colorectal liver metastases are similar for the thick-slice breath-hold T1-MPGE and thin-slice respiratory-triggered T1-MPGE. The breath-hold sequence, however, was rated significantly better for liver coverage ($P \leq .046$) and image contrast ($P \leq .023$) compared to the respiratory-triggered version. The presence, or rather absence, of breathing motion was almost equal for both sequences.

Although, we expected, as demonstrated by Pauleit et al [4], that scanning with thinner slices would improve sensitivity for the detection of liver metastases we could not confirm this. We assume that the inferior image contrast ($P \leq .023$) of the RT sequence neutralizes the gain of thin slices. We believe that the inferior image contrast at the respiratory-triggered version is caused by minor breathing excursions, which results in position inconsistencies between the volume of tissue undergoing excitation by the slice selective pre-pulse and the subsequently imaged slice of tissue. Semelka et al [9] discuss that this phenomenon will be seen when substantial motion occurs, but apparently this can be noted with only minor breathing motions regarding the high subjective score for absence of breathing motion.

The entire liver was always imaged with the BH T1-MPGE in contrast to the RT T1-MPGE; this difference reached significancy in both observers ($P \leq .046$). Apparently, either the cranial or caudal portions of the liver were not always imaged on respiratory-triggered sequence. This can be explained by position changes of the liver between scout images and the diagnostic sequence, due to variations in breathing.

We feel that this study has two limitations. First, the slice thickness of the BH T1-MPGE, 13 mm, is obviously much thicker than used for 2D breath-hold T1-GE sequences at presence, often in the order of 7 or 8 mm [10-12]. Despite these thick slices, sensitivity for detection of liver metastases (60-70%) is in accordance with data in the literature [13], especially considering the large amount of small metastases (49% smaller than or equal to 10 mm). Second, image contrast of the respiratory-triggered sequence was often disturbed due to reasons explained above.

Recently, development of parallel acquisition techniques like sensitivity encoding (SENSE) or simultaneous acquisitions of spatial harmonics (SMASH) [14] has enabled significant reduction in examination times without penalty in resolution. With use of parallel imaging it is likely that the slice thickness in breath-hold imaging can be significantly reduced [15]. Further studies are required to evaluate the use of parallel imaging in T1-MPGE imaging, and if breath-hold scanning with thinner slices will improve detection of focal liver lesions.

In conclusion, the sensitivity and specificity for the detection of colorectal liver metastases are similar for the thick-slice BH and a thin-slice RT T1-MPGE. Apparently the disadvantage of thick slices in the BH T1-MPGE sequence is balanced by significantly better image contrast ($P \leq .023$) and liver coverage ($P \leq .046$). Since acquisition time of the BH version is 15 times shorter than that of the RT sequence we still prefer the BH version for daily clinical practice.

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