Radiology of colorectal cancer with emphasis on imaging of liver metastases

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Summary and Conclusion

SUMMARY

In this chapter the studies in this thesis are briefly summarized. As mentioned in **chapter 1**, colorectal cancer is the third leading cause of worldwide cancer deaths. Mortality is directly related to the presence of liver metastases. Radiology of both primary and secondary colorectal cancer has tremendously changed and expanded over the past two decades. The purpose of this thesis is:

1. to compare established and new magnetic resonance (MR) sequences, both T1- and T2-weighted for the detection of focal liver lesions,
2. to investigate the quantitative analysis of focal liver lesions on MR imaging and its use in the development of MR sequences,
3. to evaluate the use of computer tomography (CT) and its read-out type in the diagnosis and follow-up of colorectal liver metastases.

In **chapter 2** a study is described in which two respiratory-triggered T2-weighted MR sequences, the inversion-recovery gradient- and spin-echo (IR GRASE) and the fast spin-echo (SE), in the diagnosis of liver metastases are compared. In this prospective study, two radiologists independently identified focal hepatic lesions on respiratory-triggered IR GRASE and respiratory-triggered fast SE MR images in 28 consecutive patients with 186 (135 malignant and 51 benign) proven focal liver lesions. A combination of findings at surgery, intra-operative ultrasonography (IOUS), and histologic examination served as the standard of reference. Contrast-to-noise ratios (CNRs) were obtained from 86 lesions larger than 10 mm. The sensitivity in the detection of liver metastases was, independent of lesion size and observer, higher for IR GRASE imaging (55%) than for fast SE imaging (44%-50%) (observer 1, $P = .014$; observer 2, $P = .21$). Confidence levels with IR GRASE imaging were higher, but not significantly so, than those with fast SE imaging ($P < .098$). Both observers characterized liver lesions better with IR GRASE than with fast SE imaging (observer 1, $P = .04$; observer 2, $P = .48$). The metastasis-liver CNR was significantly higher ($P = .012$) with IR GRASE imaging. It is concluded that the respiratory-triggered IR GRASE sequence is a fast alternative to the respiratory-triggered fast SE sequence in the evaluation of suspected liver metastases.

In **chapter 3** a thick-slice breath-hold (BH) and a thin-slice respiratory-triggered (RT) T1 magnetization-prepared gradient-echo (MPGE) are compared in the detection of colorectal liver metastases. 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 IOUS. The observers subjectively scored, liver coverage, the amount of breathing motion and image contrast per sequence in each patient. 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. In conclusion, the 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.

Since spleen-liver CNR was found to be similar to those of metastases-liver on conventional SE sequences, the so-called spleen-liver model has been used in studies with healthy volunteers to optimize various T1-weighted sequences. More recently, this model has also been used in newer more complicated pulse sequences. The predictive value of spleen-liver CNR for metastases-liver CNR has, however, been challenged in other reports using modern state-of-the-art sequences. In **chapter 4**, the value of the spleen-liver model in optimizing seven pulse sequences is evaluated statistically. Optimization of conventional SE, breath-hold T1-MPGE and fat frequency-selective presaturation inversion-recovery fast SE can be done using the spleen-liver model. CNR of spleen-liver and metastases-liver, however, differed significantly ($P \leq .04$) on our T1 gradient-echo and T2-weighted fast SE images, with and without fat-selective saturation. It is concluded that the spleen-liver model is of limited value, especially in the newer and often more complex sequences, since contrast mechanisms are subject to many parameters.

During the study into the spleen-liver model different quantitative methods were encountered in the literature. The use of different formulas to calculate contrast and the use of non-uniform technology prohibits comparison of data presented in the literature. In **chapter 5** the effects of changing analytic method variables on signal intensity difference-to-noise ratios (SDNRs) between lesions and background organ depicted on MR images are assessed. Furthermore, a standardized analytic method for the quantitative analysis of focal masses seen at MR imaging is proposed. The signal intensities (SI) of 48 liver metastases (originating from colorectal cancer) in 20 patients, the surrounding liver parenchyma and the background noise were measured on T2-weighted MR images. All 2000 and 2001 issues from the American Journal of Roentgenology, Journal of Magnetic Resonance Imaging, Magnetic Resonance Imaging and Radiology were searched for articles describing quantitative analyses. SDNRs were calculated by using formulas from these articles and various region-of-interest (ROI) locations to measure metastasis and background noise SIs. In 34 articles in which quantitative analysis of focal masses are described, the reported SDNRs were calculated with four different formulas. The SDNRs for our study material calculated with the four formulas reported in the literature differed grossly in both number and unit. The SDNRs for ROIs encompassing the entire metastasis differed significantly (P = .034) from the SDNRs for ROIs in a homogeneous area of the metastasis margin. Differences in SDNRs between various noise ROI locations were significant ($P \leq .022$). It is concluded that apparently slight changes in the variables of the quantitative analysis of focal masses had marked effects on reported SDNRs. To overcome these effects, the use of a standardized method involving one formula, a lesion ROI in a homogeneous area at the metastasis margin, and a background noise ROI along the phase-encoding axis in the air (including systematic noise) is proposed for the quantitative analysis of findings on magnitude MR images.

In **chapter 6** the comparison of the soft- and hard-copy CT image interpretation with regard to evaluation time and detection rates for hepatic and extrahepatic colorectal metastases is described. The CT data sets of 20 patients with a history of colorectal carcinoma were evaluated independently by two radiologists. In each patient, soft-copy readouts and hard-copy printouts were compared for nonenhanced hepatic, contrast material-enhanced hepatic, and contrast-enhanced extrahepatic data sets. A stopwatch was used to document evaluation time. Ninety-two hepatic metastases and six extrahepatic metastatic recurrences were detected with the standard of reference – surgical, intra-operative ultrasonographic, and histologic findings. Both observers evaluated the contrast-enhanced hepatic data set significantly faster (P = .026 and .009) by using soft-copy readouts. The contrast-enhanced extrahepatic data set was also evaluated significantly faster (*P* = .010 and .006) with soft-copy readouts. Detection of hepatic and extrahepatic tumor with soft-copy readouts was not significantly superior to that with hard copies. Detection rates of hepatic metastases for nonenhanced and contrast-enhanced CT for both observers ranged from 50%-80% (46-74 of 92) for soft-copy readouts and 46%-75% (42-69 of 92) for hard copies. Interobserver agreement was highest for contrast-enhanced soft-copy readouts for hepatic metastases. It was concluded that soft-copy readouts of contrast-enhanced CT data sets for the detection of hepatic metastases and extrahepatic metastatic recurrences were evaluated significantly faster than were hard copies, with at least equal sensitivity and with excellent interobserver agreement.

In **chapter 7** the results of a phase II study of the isolated hepatic perfusion (IHP) in patients with colorectal metastases confined to the liver is reported. IHP involves a method of complete vascular isolation of the liver to allow treatment with doses that would be toxic if delivered systemically. Seventy-three patients with irresectable colorectal metastases underwent IHP with high-dose melphalan (200 mg) for one hour. Toxicity was graded according to the National Cancer Institute Common Toxicity Criteria and tumor response, as recorded on CT images, was assessed according to World Health Organization criteria. Seventy-one patients were perfused according to the protocol. Four patients died within 30 days after IHP, resulting in an operative mortality of 5.6%. Sixteen patients (22.5%) experienced grade 3-4 hepatotoxicity one week after IHP, which was transient and resolved within three months in all patients. The tumor response rate (complete or partial remission) was 59%. Median time to progression was 7.7 (range 2.3-31.4) months. Overall median survival after IHP was 28.8 months with a 3-year survival rate of 37%. It was concluded that IHP for irresectable colorectal metastases confined to the liver results in good response rates and long-time survival in a selected group of patients.

CONCLUSION

Imaging is crucial in the management and prognosis of patients with colorectal liver metastases. New MR sequences will continue to be developed, and need to be evaluated. The respiratory-triggered IR GRASE sequence is a fast alternative to the respiratory-triggered fast SE sequence in the evaluation of suspected liver metastases. Breath-hold T1-MPGE, despite its rather thick slices, is in clinical practice preferred over the respiratory-triggered T1-MPGE, since it performs equally well in a far shorter acquisition period.

Past, current and future imaging studies should all be critically judged, especially for their methods and used standard of reference. The spleen-liver model, as a predictor of metastases-liver SDNR, is of limited value, especially in the newer and often more complex sequences. The quantitative analysis of focal masses on magnitude MR images should be performed by using of a standardized method, involving one formula, a lesion ROI placed in a homogeneous area at the metastasis margin, and a background noise ROI along the phase-encoding axis in the air (including systematic noise).

CT is in the majority of hospitals around the world the “work-horse” for the evaluation of patients with liver metastases. Helical and multi-slice scanners generate an enormous amount of images that can be read significantly faster during a soft-copy readout compared to hard-copy readout, with at least equal sensitivity. CT is not just an important diagnostic imaging tool, but is also an accomplished method for the evaluation of various cancer treatments, in both surgery and medical oncology. At presence, CT has a third application, image guiding in the local ablative treatment, for example radio-frequency ablation, of liver tumors.

Finally, two clinically relevant items encountered in the management of patients with colorectal liver metastases should be mentioned. First, preoperative imaging asks for modalities with high spatial resolution, CT or MR, to delineate not only the extent of the disease but also the location of the metastasis in relationship to the hepatic anatomy in general and to the vessels and bile ducts in particular. Since [^{18}F]fluoro-2-deoxyglucose positron emission tomography (FDG PET) offers little information on anatomic structures, PET as a single modality does not provide sufficient information for adequate presurgical planning. The greatest impact of FDG PET in patients with hepatic metastases is in detecting extrahepatic disease that would preclude curative surgery, or change therapeutic management from a localized directed approach to a more systemic approach with chemotherapy [1].

Second, patients with colorectal liver metastases deserve to be treated on the basis of combined knowledge of dedicated surgeons, medical oncologists, gastroenterologists, nuclear medicine physicians and radiologists. The only approach to this disease is a multidisciplinary approach.

References

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