Radiology of colorectal cancer with emphasis on imaging of liver metastases

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Introduction

This chapter is based on

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1.1 COLORECTAL CANCER AND LIVER METASTASES

EPIDEMIOLOGY

Virtually 98% of all cancers in the large intestine are carcinomas; 95% of all colorectal carcinomas are adenocarcinomas [1]. The other types of malignant tumors are beyond the scope of this study. The terms colorectal cancer and adenocarcinoma are alternately used.

Colorectal cancer is the second most common malignancy of both genders in industrialized countries [2] and, with an estimated 437,000 deaths annually, is the third leading cause of worldwide cancer deaths [3]. Currently, the approximate incidences of colon and rectal cancer in The Netherlands are 5,200 and 3,000 new cases each year. Both incidences have increased from 1989 to 1998, especially in men [4].

Mortality of colorectal cancer is related to the development of liver metastases. The liver is the most common site of metastases from colorectal cancer [5]. Liver metastases will develop in approximately one-half of all patients, who have colorectal cancer [6]. In 25% of patients, liver metastases are present at the time of diagnosis of colorectal cancer (synchronous metastases), an additional 25% will develop liver metastases within three years (metachronous metastases) [7,8]. Without treatment, the median survival of patients with colorectal liver metastases is between six and 11 months, mainly depending on the amount of liver parenchyma involved. Some subgroups of patients survive for more than two years; 5-year survival without treatment is anecdotal [9].

IMAGING PRIMARY COLORECTAL CANCER

Both colorectal adenocarcinoma and, its precursor, colorectal adenoma can be detected with a barium enema examination. Single- and double-contrast barium enema (DCBE) have similar sensitivity for clinically important lesions, polyps over 10 mm and colorectal cancers [10,11]. The reported sensitivity of DCBE for polyps over 10 mm is 33-100% [12-14] and for colorectal cancer 62-100% [10,12-15]. In up to 95% of patients, the entire colon can be examined with DCBE, an obviously important feature, in view of synchronous presence of cancer and/or its precursors. Five percent of patients have a synchronous colon cancer, and more than one-third have additional adenomatous polyps [16].

Transabdominal ultrasound is generally not used for the detection of colon cancer. In the detection, but more importantly staging of rectal cancer transrectal ultrasound (TRUS) is an

important tool, since TRUS enables the distinction of the various layers of the rectal wall [17-19]. The reported tumor staging accuracy of TRUS ranges between 67% and 93% [17,18,20].

The value of computer tomography (CT) in the initial work-up of colorectal cancer is limited. Accuracy rates, reported for pre-operative tumor staging of colorectal cancer, range between 48% and 77% [21,22]. In selected groups of patients suffering from rectal cancer the accuracy is reported to be as high as 82% [23]. These disappointing numbers are mainly due to the inability of CT to determine the depth of tumor bowel wall invasion and to differentiate malignant from reactive lymph nodes.

Virtual colonoscopy or CT colonography is an encouraging new method for assessing the colon. Following image acquisition, the CT data can be viewed using a variety of techniques, for example two-dimensional axial CT images at lung window settings and three-dimensional endoluminal images. Studies published from Boston Medical Center (BMC) [24], the Mayo Clinic [25] and the University of California in San Francisco (UCSF) [26] reported results on relatively large patient populations (Table 1). In these series all colorectal cancers were accurately detected with CT colonography (three in the BMC series and eight in the UCSF series). The challenge remains to reproduce these favorable results in clinical practice.

Table 1. Polyp Detection with CT Colonography.

Study	Patients	Polyps	Per Polyp Sensitivity		Per Patient Sensitivity	
		> 5 mm	Subc.[#]	≥ 10 mm	Subc.[#]	≥ 10 mm
BMC [24]	100	58	82%	91%	92%	96%
Mayo Clinic [25]	180	263	47%	75%	88%	85%
UCSF [26]	300	223	80%	90%	93%	100%

[#] Subc. = subcentimeter, and resembles 6-9 mm for the Boston Medical Center (BMC) study, and 5-9.9 mm for the Mayo Clinic and University of California in San Francisco (UCSF) study.

Magnetic resonance (MR) imaging for detection and tumor staging is most useful in colorectal cancer located in the rectosigmoid, because image quality is only minimally degraded by respiratory motion and peristalsis, in this relatively fixed part of the colon. The superior demonstration of rectal wall layers achieved by endoluminal MR does not improve tumor staging accuracy (approximately 80%) of rectal cancer compared to phased array MR [27]. Beets-Tan et al [28] published that the clinically more important circumferential

resection margin in rectal cancer can be predicted very accurately and consistently with phased array MR.

Positron emission tomography (PET) with [^{18}F]flouro-2-deoxyglucose (FDG) has not been explored extensively in the diagnosis of primary colorectal cancer. While PET can show primary colorectal cancers with high sensitivity, the substantial FDG activity in the normal gut due to intestinal flora and uptake of FDG in muscle, etc., makes detection of small lesions challenging. PET has been used to some extent for primary tumor staging of colorectal cancer.

RADIOLOGY OF COLORECTAL LIVER METASTASES

Simultaneously with the evolution in imaging primary colorectal cancer over the past two decades, radiology, in general, of colorectal liver metastases has also changed tremendously. Liver metastases of colorectal cancer are, nowadays, imaged with ultrasound (US), helical or multi-slice CT, MR, and PET. Imaging of colorectal liver metastases with CT and MR is the subject of this thesis, as stipulated below. Before addressing aim and outline of the thesis, I would like to mention three important and relatively new issues: PET, image fusion, and image-guided minimally invasive treatment.

In the setting of a rising carcinoembryogenic antigen (CEA) serum level after “definitive” treatment for colorectal adenocarcinoma, PET can be very useful in locating the source of recurrence, with over half of the patients having a source of the rising tumor marker identified [29,30].

One of the largest direct comparative trials of conventional and helical CT versus PET for accuracy in colorectal cancer in 105 patients [31], showed the overall sensitivity of PET to be 87% versus 68% for CT, and the sensitivity for liver metastases superior to that of CT (89% versus 71%). Results from two meta-analyses showed similar results [32,33].

One of the exciting opportunities in PET at present is the fusion of cross-sectional anatomic imaging methods and PET into hybrid images (Figure 1). This can be done by software methods (anato-metabolic fusion) or by dedicated hardware devices, in which PET and for instance CT are performed in the same instrument, a “PET-CT” scanner. These devices will allow us to combine the best in anatomic and functional imaging, although it is not yet proven that they improve diagnostic accuracy.

Radiology, once a primarily diagnostic profession has expanded its therapeutic modalities, and not only in the cardiovascular system. Since surgical resection of colorectal

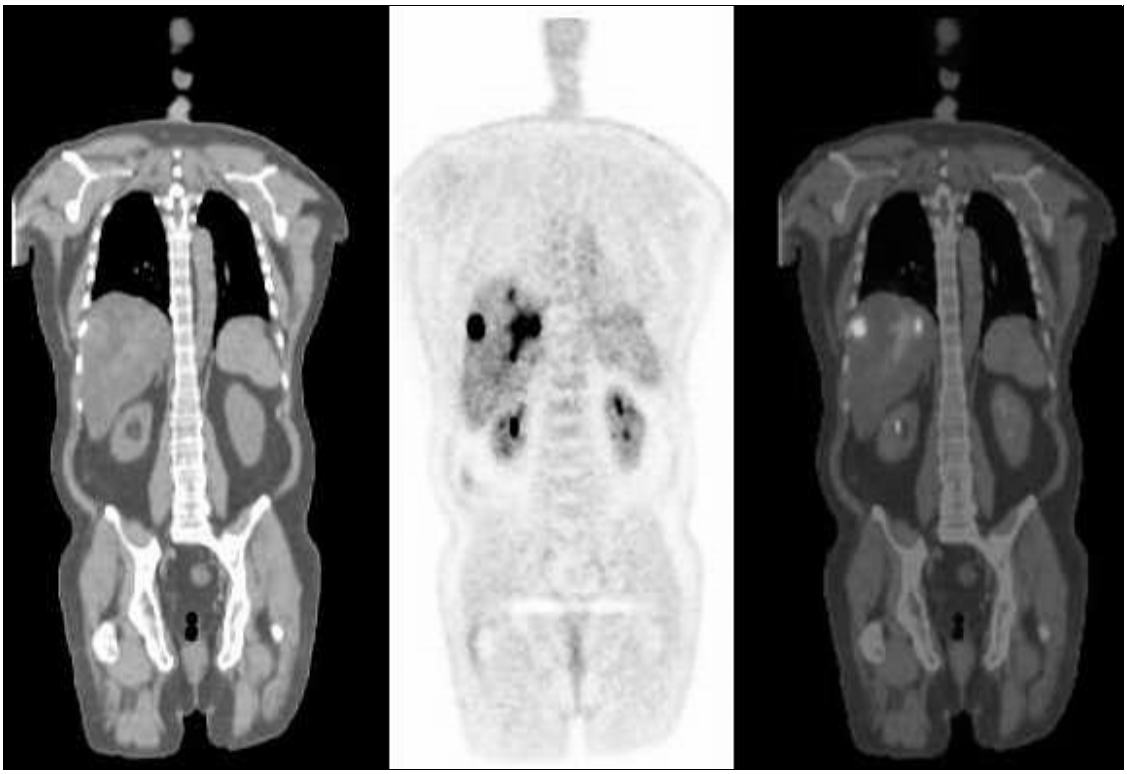

Figure 1. Coronal reformatted CT (left), PET (center) and fusion hybrid images (right) of multiple colorectal liver metastases. The metastases appear slightly hyperdens in a steatotic liver at the non-enhanced CT image, dark at the PET image and bright at the fused image.

metastases confined to the liver is only possible in 10-15% of patients, other means of controlling or potentially curing liver metastases are explored [34]. With continuing improvements in technology and increasing clinical experience, image-guided minimally invasive techniques may become a challenge for surgical resection [35,36]. Simultaneously performed, combined (surgical resection and local ablation) approaches will become increasingly important, and make inoperable patients liable for "surgery".

Several thermal ablation methods to destroy the liver metastases are in operation today: laser, microwave, radio-frequency, and cryo-ablation. They all rely on the principle of inflicting thermal damage to tissue by either heating to more than 50ºC or freezing below -30ºC. Ablations using laser, microwave and radio-frequency can be performed in a percutaneous approach, as well as open (via laparotomy). Cryo-ablation is virtually always performed as an open procedure. Correct placement of the thermal device in or at the metastasis is the hallmark of all methods and is virtually always image-guided (CT, transabdominal US or intra-operative US).

1.2 PURPOSE AND OUTLINE OF THE THESIS

Colorectal cancer is the third leading cause of worldwide cancer deaths, and 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. Our goal was to contribute to the continuing improvement and development of MR and CT techniques for the detection of colorectal liver metastases.

The purpose of this thesis is threefold: 1. Compare established and new MR sequences, both T1- and T2-weighted for detection of focal liver lesions; 2. Investigate the quantitative analysis of focal lesions, as seen on MR images and its use in the development of MR sequences; 3. Evaluate the use of CT and its read-out type in the diagnosis and follow-up of colorectal liver metastases.

In chapter 2 a newly developed T2-weighted sequence, inversion-recovery gradient- and spin-echo, is compared for speed and detection rates with a regular fast spin-echo and a standard of reference for detection and characterization of focal liver lesions. In chapter 3 the comparison of a respiratory-triggered and a breath-hold T1-weighted, magnetization-prepared gradient-echo sequence for detection of colorectal liver metastases and image quality is described. In chapter 4 the validity of the spleen-liver model, once developed for “simple” MR sequences, is addressed in the setting of new, complex pulse sequences. The wide variety of analytic methods, encountered in the literature search for chapter 4, created the idea of chapter 5. In chapter 5 apparently slight changes in the variables of the quantitative analysis of focal masses, as detected on MR images, and their effects on the signal intensity difference-to-noise ratios are described. Chapters 6 and 7 involve CT and colorectal liver metastases. In chapter 6 the soft- and hardcopy interpretation of helical CT in diagnosing colorectal cancer liver metastases are compared for sensitivity and speed. The evaluation of isolated hepatic perfusion, a novel treatment for diffuse liver metastases is described in chapter 7. A summary is provided in chapter 8.

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