DISSERTATIONES MEDICINAE UNIVERSITATIS TARTUENSIS
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CROSS-SECTIONAL IMAGING FOR PRETREATMENT EVALUATION AND FOLLOW-UP OF PELVIC MALIGNANT TUMOURS

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To my family

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LIST OF ORIGINAL PUBLICATIONS

The present study is based on the following papers, which will be referred by their Roman numerals

I Järv V, Blomqvist L, Holm T, Ringertz H, Jacobsson H. Added value of CEA scintigraphy in the detection of recurrence of rectal carcinoma. Acta Radiologica. 2000; 41: 629–633.

II Järv V, Blomqvist L, Ringertz H, Sjövall A. Single sequence screening for liver metastases as addition to high resolution pelvic MRI. Manuscript submitted to Eur J Radiol.

III Sjövall A, Järv V, Blomqvist L, Cedermark B, Glimelius B, Singnomklao T, Holm T. The potential for improved outcome in patients with hepatic metastases from colon cancer: a population-based study. Eur J Surg Oncol. 2004; 30 (8): 834–841.

IV Järv V, Leht M, Timberg G, Kotsar A, Samarin A, Hirmo J, Kulla A. MR staging of prostate cancer (in Estonian). Eesti Arst. 2004; 83(6): 364–370.

ABBREVATIONS

APR	Abdomino-perineal rectum excision
BW	Behringwerke
CEA	Carcinoembryonic antigen
CEMRI	Contrast-enhanced magnetic resonance imaging
CT	Computed tomography
CRM	Circumferential resection margin
DRE	Digital rectal examination
ECE	Extracapsular extension
ETL	Echo train length
EUS	Endorectal ultrasound
FLL	Focal liver lesion
FN	False negative
FOV	Field-of-view
FP	False positive
FSE	Fast spin-echo
Gd	Gadolinium
GE	General Electric
IOUS	Intraoperative ultrasonography
IORT	Intraoperative radiotherapy
IS	Immunoscintigraphy
KI	Karolinska Institute
LAR	Low anterior resection
LR	Local recurrence
MD-CT	Multi-detector row spiral CT
MR	Magnetic resonance
MRI	Magnetic resonance imaging
ms	milliseconds
NPV	Negative predictive value
PPV	Positive predictive value
PET	Positron emission tomography
PSA	Prostate-specific antigen
RFA	Radiofrequency ablation
SI	MR signal intensity
SPECT	Single-photon emission computed tomography
Tc	Technetium
TE	Echo time
TME	Total mesorectal excision

TR	Repetition time
TRUS	Transrectal ultrasonography
TU	Tartu University
TUC	Tartu University Clinics
US	Ultrasonography
USPIO	Ultrasmall superparamagnetic iron oxide
3D	Three-dimensional

1. INTRODUCTION

Malignant tumours are the second most common cause of death and are responsible for more than 12% of all deaths worldwide (World Health Organization, 1998). Colorectal cancer is a potentially lethal disease and the second cause of cancer-related death in the United States and Europe (Boyle and Langman, 2000). It is associated with a poor prognosis because of the high risk both for local recurrence (LR) and for metastases (Beal *et al*., 1956; Abdel-Nabi *et al*., 1988; Morgan-Parkes, 1995; Sagar *et al*., 1996; Adam *et al*., 2001). Of other common pelvic tumours, prostate cancer is the second leading cause of cancer death in American men (American Cancer Society, 2004). In the last decade prostate cancer has become the second most common diagnosed cancer in Estonian men (Estonian Health Statistics, Ministry of Social Affairs of Estonia, 2003).

Improvement in the preoperative assessment of the tumour extent, as possible early detection and detailed characterisation of cancer spread or recurrence during follow-up help both the planning of the surgical treatment as well as the choice of adjuvant treatment and has influence on management of the patient and treatment outcome. Despite the progress in cancer imaging during the last decades major difficulties still exist in tumour pre- and posttreatment diagnostic work-up (D'Amico *et al*., 1996; Perrotti *et al*., 1996). Diagnosis of LR is often difficult, because most LR occur extraluminally and conventional follow-up fails to detect them at early stage (Quirke *et al.,* 1986; Adam *et al*., 1994; Sagar *et al*., 1996; Minsky, 1999; Lohnert *et al*., 2000). Liver metastases in 20–25% of colorectal cancer patients could be potentially curatively resected, which allows the five-year survival rate 30–40% (Scheele *et al*., 1995; Minagawa *et al*., 2000; Adam *et al*., 2002; Choti *et al*., 2002). However there are few population-based series and knowledge is lacking on treatment strategies and results for colorectal cancer patients with liver metastases in unselected patient populations. Considering effectiveness of diagnostic work-up, a simple and fast imaging technique would be useful for upper abdomen screening purposes. For the treatment planning of prostate cancer, accurate local staging is essential, since radical prostatectomy is method of choice if the disease is intracapsular (T1/T2 stage) (McNeal *et al*., 1990; Epstein *et al*., 1993). However, clinical staging and conventional radiological methods used for this purpose until today have shown local underestimation of the disease in up to 40% cases (D'Amico *et al*., 1996; Perrotti *et al*., 1996).

Cross-sectional imaging techniques have been increasingly used for pretreatment staging and follow-up. During last decade they have become available for Estonian patients too. Ultrasonography (US) and computed tomography (CT) are the first-line modalities for many abdominal applications. US is widely used and has showed its effectiveness also for selected oncological problems, e.g. liver metastases (Cervone *et al*., 2000; Solbiati *et al*., 2001). However due

to inherent limitations of the method, it can in many situations not be used for a detailed evaluation of the total intra-abdominal extent of a malignant disease. Although endorectal ultrasonography (EUS) remains the most accurate staging tool for superficial rectal cancer it is not always applicable or as useful for staging of LR (Solomon *et al*., 1993; Garcia-Aguilar *et al.,* 2002). CT is in this respect robust and reproducible for abdominal oncological staging and became shortly after its introduction an imaging modality of choice for staging of abdominal cancers. Although CT is an excellent method for imaging tissues with high differences in X-rays absorption values, despite the help of contrast agents it has limitations in terms of contrast resolution when imaging soft tissues (Giess *et al*., 1998; Hopper *et al*., 2000). CT is limited in the diagnosis of malignancy by a reliance on unspecific size criteria and comparison with normal anatomy, which could be markedly distorted by radiation and/or surgery in the pelvic region (Quirke *et al* 1986; Minsky, 2001). Rapid developments of magnetic resonance imaging (MRI) showed its diagnostic potential in many areas, in last decade it was introduced for abdominal studies as well (Blomqvist *et al*., 1998; Outwater *et al*., 1999; Semelka *et al*., 1999; Low, 2000; Blomqvist *et al*., 2002). However, all these techniques mainly give imaging information, thus exhibit a restricted specificity. It has been reported that, occult tumours that escape detection with standard radiological imaging techniques can be identified using antibody imaging methods giving biologically based information (Patt *et al*., 1990). Nevertheless, there is still need to study the significance of the diagnostic information obtained by these biological methods additionally to anatomical imaging.

Cancer imaging remains the area of the continuous development. All the diagnostic methods currently in use have limitations and still exists urgent need for the further clinical research.

2. REVIEW OF THE LITERATURE

2.1. Radiological diagnosis of recurrence of rectal cancer

Treatment for rectal cancer

Important for the treatment of rectal cancer was the the standardization of the surgical technique with introduction of total mesorectal excision (TME) (Heald *et al.,* 1986). With this surgical technique, the overall recurrence rate has been reported to be well below 10%, even without radiation therapy (Heald *et al.,* 1986).

Because of results of large European randomized trials, there has been renewed interest in preoperative radiation therapy for patients with mobile rectal cancer (Minsky, 2001). A Scandinavian randomized trial showed that short course preoperative radiation therapy reduces the LR rate from 27% to 11% (Swedish Rectal Cancer Trial, 1997).

The relative merits of both strategies, TME and preoperative radiation therapy, have recently been tested in a Dutch randomized trial (Colorectal Cancer Collaborative Group, 2001) in which TME with a preoperative short course of radiation therapy was compared with TME without radiation therapy. The results of the trial showed that a short course of preoperative radiation therapy reduces the LR rate from 8.2% to 2.4% at 2 years, which indicated that even with 'standardised surgery', preoperative radiotherapy is beneficial.

2.1.1. Detection of local recurrence (LR) of rectal cancer

After curative surgery for rectal cancer, if a surveillance program is employed, an important goal is detection of recurrent disease at an early and potentially curable stage. LR refers to tumor recurrence in the previous operative field where curative resection was performed. The surgical field includes the tumor bed, the anastomosis, the surgical scars, the perirectal fat, the regional mesentery, the adjacent pelvic structures, and the peritoneum. More than a decade ago, reported curative colorectal cancer resection rate varied from 50% to 90% (Turk *et al.,* 1993). One concern after rectal cancer surgery was the high rate of LR. Adam and coworkers showed that the risk of LR was highly linked to the presence of tumour in the lateral resection margin of the surgical specimen (Adam *et al.*, 1994). Sagar *et al.* stated that after curative resection of the rectum for rectal cancer, LR rates varied as much as between 3% to 32% (Sagar *et al.,* 1996).

Incomplete removal of the lateral spread of the tumour is now accepted as major historical cause of these recurrences. Quirke *et al*., (1986) demonstrated that microscopically positive resection margins resulted in a LR rate of as high

as 83%. Besides incomplete lateral removal, LR may also be caused by tumour cell implantation during previous surgery, tumour spread through vessels, metastatic lymph nodes, peritoneal implants and possibly cell hyperplasia on the anastomotic suture line (Reinbach *et al.*, 1993; Reinbach *et al.*, 1995; Watanabe *et al.*, 1995).

Clinically, LR is often debilitating with severe pain, immobility, prolonged and multiple hospital admissions for surgery, radiation and chemotherapy but still a poor prognosis. For this reason, help to improve therapeutic management of rectal cancer is a challenging task for radiologists. To allow adequate radiological assessment, information about previous treatment as well all available relevant clinical, histopathological, surgical and previous radiological information is important. The radiological findings of LR are variable and largely depending its cause, presence and degree of mucus production, necrosis, associated fibrotic changes and pattern of spread.

For patients with LR alone (in 30–50% of patients this is the only manifestation of disease [Olson *et al.,* 1980; Holm *et al.,* 1994]) following initial attempted curative resection, aggressive local therapy with repeat low anterior resection and coloanal anastomosis, abdominoperineal resection, or posterior or total pelvic exenteration can lead to long-term disease-free survival (Ogunbiyi *et al.*, 1997). If available, intraoperative radiation therapy (IORT) in patients who received previous external beam radiation may also improve local control of LR (Haddock *et al.,* 2001).

Accurate and detailed anatomic information on tumour extent is essential not only for the selection of patients for neoadjuvant chemotherapy and radiation therapy to achieve tumor shrinkage but also for planning of the optimal surgical procedure (Quirke *et al.,* 1986; Adam *et al.*, 1994; Sagar *et al.,* 1996; Minsky, 2001). At early stages, the diagnosis of LR of rectal cancer is often difficult, because most LR occur extraluminally and conventional follow-up fails to detect them at this stage (Lohnert *et al.,* 2000). In this respect, cross sectional imaging modalities have an important role.

Endorectal ultrasonography (EUS)

For local staging of the primary tumour, EUS is still widely used for assessment of tumour growth into the rectal wall layers with accuracies for T staging varying between 69% and 97% (Akasu *et al.*, 2000; Gualdi *et al.*, 2000; Kim *et al.,* 2000; Garcia-Aguilar *et al.,* 2002). Although EUS remains the most accurate staging tool for superficial rectal cancer is it not as useful for staging of advanced rectal cancer as it was demonstrated in a meta-analysis (Solomon *et al.,* 1993) of 11 studies, sensitivity was shown to be affected by T stage because the limited depth of acoustic penetration. A recent large study on EUS (Garcia-Aguilar *et al*., 2002) in 1,184 patients with rectal tumors confirmed these findings. Another reason for the discrepant results of that study was the operator-dependent nature of US and substantial interobserver variability, which was also reported in previous studies (Solomon *et al.*, 1994; Gold *et al.*, 1999;

Garcia-Aguilar *et al.*, 2002). However, with EUS, an advantage of being able to identify one-third of asymptomatic LR that were missed by DRE or proctoscopic examination and opportunity of using guided needle biopsy for tissue verification of pararectal masses was shown (Lohnert *et al.,* 2000). By experienced users, EUS is a valuable tool in the detection of LR and could be used for follow up of patients after surgery for rectal cancer (Rotondano *et al*., 1997). However, EUS is not applicable after rectal amputation, in case of stenotic tumours and due to the limited FOV it can not adequately describe the full extraluminal extent of malignant disease.

Computed tomography (CT)

CT has been used for more than two decades to evaluate the rectal cancer, in particular for metastases screening but also for evaluation of local tumour extent. It has often been used in the follow-up of rectal cancer patients for early detection of LR, as well distant metastases (Thoeni *et al.*, 1981; Grabbe *et al.*, 1983; Hodgman *et al.*, 1986; Rotte *et al.*, 1989; Thoeni, 1997). Regarding local staging of rectal cancer, optimistic initial results obtained with conventional CT showed high accuracies for T staging varying between 79% and 94% (Butch *et al.*, 1986; Rifkin *et al.*, 1989; Shank *et al.*, 1990; Goldman *et al.*, 1991; Cova *et al.*, 1994; Zerhouni *et al.*, 1996; Thoeni, 1997; Kim *et al.*, 1999) but these works mainly focused on locally advanced rectal cancer and later studies that included less advanced tumors have shown accuracies that were not as high as anticipated, ranging between 52% and 74% (Kwok *et al.*, 2000). The most recent breakthrough in CT technology; multidetector row spiral CT (MD-CT) scanners with superior multiplanar and spatial resolution, are expected to provide better performance than earlier generations of CT scanners. For detection of local recurrence of rectal cancer, some of the first reports show promising results (Horton *et al.,* 2000; Chiesura-Corona *et al.,* 2001), but Stuckle (2004) report after examining 83 patients for LR suspicion with MD-CT and administration of contrast media no statistically significant difference in diagnostic performance compared to noncontrast study. Results of further studies are awaited to assess if new-generation CT scanners can compete with MR imaging for diagnosis of local tumour recurrence. CT would have the advantage that a single investigation could be used to combine local, regional, and distant staging. With that capability and the addition of fast acquisition time and relatively low cost, staging with CT would be beneficial for both the patient and the health care system. The possibility to confirm the diagnosis by CT-guided needle biopsy is an undebatable advantage of this method.

Magnetic Resonance Imaging (MRI)

The successful introduction of MR imaging for pelvic diseases has, in recent years, led to the gradual replacement of CT by MR imaging for local and regional staging of rectal cancer staging and for detection of LR because initial MR studies with a conventional body coil techniques showed a resolution that

was still insufficient. For local staging of the primary tumour overall accuracies in T-staging reported for MR imaging with a body coil was not any better than those reported for CT, with values ranging from 59% to 88% (Butch *et al.,* 1986; Hodgman *et al.,* 1986; Guinet *et al.*, 1990; Okizuka *et al.*, 1993; Cova *et al.*, 1994; Zerhouni *et al.*, 1996).

Endorectal coils

The introduction of endoluminal coils facilitated improved spatial resolution and made a more detailed evaluation of the layers of the rectal wall feasible (Chan *et al.*, 1991; Schnall *et al.*, 1994; Indinnimeo *et al.*, 1996; Zagoria *et al.* 1997; Pegios *et al.,* 1996; Gualdi *et al.*, 2000). However, some problems remained with endorectal MR imaging. Besides the invasiveness and limited availability, MR imaging with an endoluminal coil, especially when used in isolation, has a limited FOV. Like endorectal US, the mesorectal fascia and surrounding pelvic structures are difficult to visualize owing to the sudden signal drop-off at a short distance from the coil (Maldjian *et al.*, 2000). Furthermore, the positioning of an endoluminal device can be difficult or impossible in patients with high and/or stenosing tumors, and failed insertion rates of as high as 40% have been reported in patients with rectal cancer (Hunerbein *et al.*, 2000). Endorectal coils are also not applicable after rectum amputation.

Phased-array surface coils

Improvement in MR imaging performance with the introduction of dedicated external coils, especially phased-array coils because the advantages of high spatial resolution with a large FOV of was shown to make MR imaging suitable for staging rectal tumours (Blomqvist *et al.*, 1997).

Immunoscintigraphy (IS)

Carcinoembryonic antigens have been in focus of colorectal and gastric cancer research since the beginning of 1980-s (Karesen *et al*., 1980; Iwamatsu *et al.,* 1983). Results of several authors indicate that IS improves detection of extra-hepatic abdominal recurrence of colorectal cancer. Lechner and coworkers (Lechner *et al.,* 2000) found in their study of 40 patients that CEA immuno-scintigraphy enables to disclose LR of rectal cancer at a stage that allows surgical salvage therapy, therefore could it be recommended for serial monitoring of these patients. However the authors stress that after this pilot study further larger prospective studies should be undertaken.

Previous literature comparing both CT/MRI with CEA-scintigraphy for detection of LR and disease staging was lacking and for this reason an aim of this thesis was to perform such a comparison and to find out the additional diagnostic value of IS to cross-sectional anatomical imaging.

2.1.2. Detection of liver metastases

Metastasis is the most common neoplasm in an adult liver, and the liver is the second most common site for metastatic spread, after the lymph nodes. Analysing the data from 9700 consecutive autopsies in patients with 10,736 primary cancers, Pickren *et al.,* (1982) found that liver metastases were present in 41%. Because the liver is often the only metastatic site in colorectal carcinoma, the curative potential of liver resections in these patients has been shown by several authors (Scheele *et al*., 1995; Moore *et al*., 2002; Penna *et al*., 2002). Although a large number of local or regional treatments for liver metastases are now available, including several minimally invasive techniques, at present, liver resection is considered the gold standard and possible curative treatment for metastases from colorectal cancer that are organ confined. Surgery offers the best results, with 5-year and 10-year survival rates of up to 45% and 21%, respectively. By comparison, 5-years survival is less than 5% and median survival about 6 to 9 months if surgery is not possible (Bengtsson *et al.,* 1981). Imaging plays a vital role in the diagnosis of liver metastases and in the assessment of the response to treatment (Zerhouni *et al*., 1996; Cervone *at al*., 2000; Kwok *et al*., 2000; Solbiati *et al*., 2001).

Ultrasonography (US)

US is widely used in the investigation of suspected liver metastases. The specificity of US in detecting liver metastases from older studies was poor, with overall false-negative (FN) rate 50%. However, US technology has evolved considerably and IOUS of the liver has a high sensitivity for the detection of focal liver lesions (FLL), with 96% accuracy versus 84% for transabdominal US (Cervone *at al.,* 2000). The high accuracy of IOUS is due to the contact scanning possible with a high-frequency transducer and color flow Doppler imaging; with this technique, the complete organ can be covered with high spatial resolution. Duplex and color flow image provide additional aids to the localization of lesions, the differentiation between ducts and blood vessels, the documentation of vascular invasion and/or occlusion, and the assessment of the degree of vascularity of liver metastases. Although color Doppler study is of limited value in adding specificity to a US diagnosis, it can be valuable in localizing areas of vascularity to optimize the site for biopsy. Late-phase pulse-inversion harmonic imaging is a useful technique for characterizing hepatic lesions and for demonstrating both greater numbers of liver metastases and smaller liver metastases. Contrast-enhanced US is promising and improves the detection of hepatic metastases, relative to non-enhanced conventional US (Solbiati *et al*., 2001). US is especially valuable since it is inexpensive, quick, portable and lesions as small as or even lower than 1 cm can be depicted. US can also be used to guide access to FLL for biopsy.

Computed tomography (CT)

CT is a commonly used method for evaluating liver metastases due to the short examination time, robustness of the technique, standardised examination protocols and the wide availability of the equipment. The use of intravenous contrast agents is included when CT of the liver is performed. This is largely attributable to the dual blood supply of the liver and the enhancement characteristics of metastases compared with normal liver parenchyma. The accuracy of CT for detection of metastases varies with the technique used, the underlying primary lesion, and the degree of vascularity. The majority of colorectal liver metastases are hypovascular. Hypovascular lesions are routinely detected by using contrast-enhanced techniques. The rate of contrast administration and the timing of the acquisition must be precise to avoid FN results. The recent introduction of MD-CT have improved CT in hepatic imaging (Hopper *et al.*, 2000). Several authors give CT sensitivity for liver metastases detection between 80–85% (Zerhouni *et al*., 1996; Cervone *at al*., 2000; Kwok *et al*., 2000). Some authors report over 90% CT accuracy in liver metastases detection achieved during arterial portography (CTAP) and CT hepatic arteriography (CTA) (Inaba *et al*., 2000; Valls *et al*., 2001). However both techniques are highly invasive, therefore not in wide use.

Magnetic Resonance Imaging (MRI)

MRI in liver imaging is usually reserved as a problem solving modality because of cost and limited availability. However, the high spatial resolution and excellent soft-tissue contrast make MR imaging an ideal tool for the detection of parenchymal liver lesions. As with CT and US, liver metastases have a variety of appearances on MRI. Most liver tumors benign or malignant appear as hypointense lesions on T1-weighted images and hyperintense lesions on T2-weighted images. Heavily T2-weighted images are useful in differentiating hemangiomas and cysts because the T2-weighted signal intensity is usually higher in these benign lesions as compared with liver metastases. However, differentiating benign lesions from malignant lesions on the basis of signal intensity characteristics on heavily T2-weighted images alone may not always be conclusive, and combining the signal intensity changes with the morphologic changes with pattern of contrast enhancement in the lesion is even more useful. Morphologic characteristics on T2-weighted images that suggest metastatic liver disease include the following: heterogeneous signal intensity with irregular and indistinct outer margins, and a smooth or irregular central area of high signal intensity with a surrounding ring of signal intensity lower than that of the central focus but higher than that of the adjacent normal liver (Danet *et al.,* 2003). Hemangiomas are often reliably diagnosed with MRI, and more importantly, they are usually easily differentiated from metastases. Intravenous non-specific extracellular contrast agents improve characterization and to some extent also the detection of focal liver lesions (Robinson, 2002). Metastases enhance heterogeneously and occasionally show central nonenhancing areas due

to tumor necrosis. Gadolinium-enhanced MRI of the liver should include T1-weighted gradient-echo sequences during hepatic arterial, portal venous, and delayed phase of contrast enhancement. A contrast-enhanced study is preferably performed in the phase that shows the greatest differences in the distribution of contrast agent between normal and abnormal tissues. In liver metastases from colorectal cancer, this is the portal venous phase. Therefore, a time limit exists during which imaging can be performed with gadolinium-based and other extracellular contrast agents. This time window limitation can be avoided using contrast agents targeted to the liver. A previous report from Said and co-workers (Said *et al*., 2000) showed that no additional hepatic metastases and no better performance than unenhanced MRI in detecting small hepatic metastasis was achieved with Ferumoxide-enhanced MRI. However, recent studies showed higher sensitivity and specificity in metastases detection with liver specific contrast agents in MR-imaging, Resovist compared to biphasic CTAP and intraoperative US (Vogl *et al*., 2003).

The so far limited FOV restricting coverage to a single body region must be considered as a major limitation of conventional MR imaging techniques. Recently, whole-body MR imaging has been proposed for evaluation of the presence of metastases and/or for the evaluation of primary cancers. This concept was showed to surpass CT for detection of hepatic metastases and compared to scintigraphy for detection of skeletal metastases (Hawighorst *et al.,* 1999; Ruehm *et al*., 2000; Barkhausen *et al.,* 2001; Goyen *et al*., 2002; Lauenstein *et al.,* 2002*,* Lauenstein *et al.,* 2004).

General remarks

Tumor staging plays a key role for further treatment options in patients with malignant tumors- mortality rates and the success of therapeutic approaches depend mainly on the type of cancer, but they also depend on the presence of metastases. The recognition of a liver lesion as a metastatic focus may significantly influence the patient's treatment and prognosis. In addition, work-up should also be able to exclude extrahepatic disease. Today patients have to undergo several examinations, such as CT, MR imaging, US, and scintigraphy, for staging of metastases.

Considering, that the staging process is often both time-consuming and expensive, and that the diagnostic accuracy limitations still remains (Van den Brekel, 2000), we in this thesis evaluated the use axial T2 weighted FSE MR as a simple screening of liver metastases, performed as an additional sequence to a dedicated pelvic MR exam in patients with pelvic malignant tumors. Although colorectal cancer metastases to the liver is stage IV disease, the results with surgical resection suggest that perhaps we should begin to look at this subset of patients with "curative" intent rather than relegate them to "palliative" therapy. Therefore our III study aimed to evaluate the unused potential to substantially prolong survival in patients with liver metastases from colon cancer.

2.2. Local staging of the prostate cancer

Prostate cancer is the most common cancer and the second leading cause of cancer death in American men. The American Cancer Society estimates that in 2004, 230,110 new cases of prostate cancer will be diagnosed in the United States and 29,900 people will die of the disease, increases of 4.5% and 3.5%, respectively, compared with 2003 data (American Cancer Society, 2004). There are signs of a similar trend in European countries and in Estonia as well. In the last decade, prostate cancer has become the second most common diagnosed cancer site in Estonian men. This may be attributed to the increasing age of the population and early diagnosis with the measurement of prostate-specific antigen (PSA). We register in Estonia annually about 400 new cases, with an incidence of 58/100 000 inhabitants (Estonian Health Statistics, Ministry of Social Affairs of Estonia, 2003). Controversy exists with regard to the appropriate management of prostate cancer. The choice of treatment depends on the patient's age at diagnosis, the stage and aggressiveness of the tumor, the potential side effects of the treatment, and patient comorbidity (Cookson *et al*., 1997; Johansson *et al.,* 1997; Lu-Yao GL *et al*., 1997; Kattan *et al*., 1998; Holmberg *et al*., 2002; Physician Data Query (PDQ) of the National Cancer Institute, 2004). The stage distribution is affected substantially by PSA testing, and most of the cases (up to 70%) are diagnosed in the absence of symptoms (Miller *et al*., 2003). Prostate cancer is a multifocal and histologically heterogeneous disease (Cookson *et al*., 1997; Steinberg *et al*., 1997). Although biopsy is considered a gold standard for diagnosing prostate cancer, it is limited in defining all cancer sites and grades. Estimates suggest that with a threshold PSA value of 4.1 ng/mL, 82% of cancers in men younger than 60 years and 65% of cancers in men older than 60 years could be missed by this procedure alone (Punglia *et al*., 2003). When biopsy results were compared with those from radical prostatectomy for sextant tumor localization, the positive predictive value (PPV) of biopsy was 83.3% and the negative predictive value (NPV) 36.4% (Wefer *et al*., 2000). For the treatment planning of prostate cancer, accurate local staging is essential, since radical prostatectomy is indicated when disease is defined to the gland (T1/T2 stage) (McNeal *et al.*, 1990; Epstein *et al.*, 1993). Patients with local prostate cancer have the best prognosis after radical prostatectomy. Those with focal extracapsular extension (ECE) (Epstein *et al*., 1996), extensive ECE, extension to the seminal vesicles (D'Amico *et al*., 1996), or nodal extension have the second best prognosis. However, clinical staging and diagnostic methods previously used have not been accurate to define these stages of the disease. According to the literature underestimation of T3-disease in up to 40% cases compared to histopathology is not unusual (D'Amico *et al.,* 1996; Perrotti *et al.*, 1996).

Transrectal ultrasonography (TRUS)
Transrectal ultrasonography is used for examination of the prostate gland, because it well differentiates zonal anatomy and allows biopsy guiding. For cancer detection and staging the diagnostic performance has limitations (Epstein *et al*., 1993; Beyersdorff *et al*., 2002). Among the well-known shortcomings of ultrasonography include limited field of view (FOV) due to the low penetration of the high-frequency ultrasound and user-dependance.

Computed tomography (CT)
CT is widely in use as a method for the examining many regions of the human body, and it is sufficient for the detection of the many local tumours and distant metastases. However CT can not demonstrate the internal structure of the prostate gland and is presently unable to delineate the glandular cancerous tissue. Therefore it has not much been used for prostate imaging. However, recent prospective investigations for prostate cancer detection with MD-CT have shown some promising results (Prando *et al*., 2000).

Magnetic Resonance Imaging (MRI)
Today, MRI is state-of-the-art modality for imaging soft tissues, and it has also been used for prostate cancer imaging. Some studies report 85–92% accuracy (Jager and Ruijter *et al*., 1996; Engelbrecht *et al*., 2002; Akin *et al.*, 2004) for endorectal MRI in determining the local extent of prostate cancer. Although MRI findings in the detection of prostate cancer does not have a good anatomic correlation with biopsy and most of the tumours below 5 mm in size remain undetected, it has proven surpass the accuracy of the DRE and rectal ultrasonography (Jager *et al*., 2000; Beyersdorff *et al*., 2002).

Familiarity with the normal anatomy of the prostate gland is crucial for image interpretation. Although the zones of the prostate gland were first described in the 1960s, the terms were not commonly used in clinical practice until the 1980s (McNeal, 1981). The zones are not only defined histologically; many prostatic diseases have a zonal distribution. For example, 70% of adenocarcinomas arise in the peripheral zone, 20% in the transition zone, and 10% in the central zone. MR imaging depicts the zonal anatomy of the prostate with exquisite detail because of its high spatial and contrast resolution (Ogura *et al*., 2001; Engelbrect *et al*., 2003). Clinical T-staging (American Joint Committee on Cancer, 2002) is largely dependant on imaging findings. Compared to CT, US, and DRE, MR imaging has a higher accuracy in the assessment of uni- or bilobar disease (stage T2), extracapsular extension and seminal vesicle invasion (stage T3), and invasion of adjacent structures (stage T4). The literature, however, shows a wide range (50%–92%) in the accuracy of local staging with MR imaging (Jager and Barentsz *et al*., 1996; Engelbrecht *et al*., 2002). Despite its high specificity in the identification of organ-confined disease and extracapsular extension, owing to lower sensitivity and substantial interobserver variability, the routine use of MR imaging in the local staging of prostate cancer

remains controversial. Increased experience in interpretation and a better understanding of morphologic criteria used to diagnose extraprostatic disease are keys to wider implementation of MR imaging in prostate cancer staging.

Clinical assessment is based on PSA level and Gleason score, which are derived from the nomograms of Partin *et al.*, (1993). It is feasible to categorise patients into three subgroups with low (PSA level <10 ng/mL and biopsy Gleason score of 2–5), moderate (PSA level of 10–20 ng/mL and biopsy Gleason score of 5–7), and high (PSA level > 20 ng/mL or biopsy Gleason score of 8–10) risk of having extracapsular disease. In addition to ECE, seminal vesicle invasion is an important prognostic clinical parameter because it is associated with the highest rates of treatment failure-second only to lymph node metastases (Catalona *et al*., 1999; Hull *et al*., 2002). MR imaging is also helpful for diagnosing invasion of adjacent organs. In the evaluation of lymph node metastases, efficacy data for MR imaging and CT are similar, both modalities having low sensitivity. Results of a recent investigation (Harisinghani *et al*., 2003) showed that high-resolution MR imaging with lymphotropic superparamagnetic nanoparticles holds considerable promise in the detection of occult lymph node metastases. Needle biopsy, with or without transrectal US guidance, is the method most commonly used for making the histologic diagnosis of prostate cancer. To avoid under- or overestimation of tumor location and extent, MR imaging should be delayed for at least 4–6 weeks after prostate biopsy (White *et al*., 1995; Ikonenen *et al*., 2001). The use of dynamic contrast material–enhanced MR imaging is an option that is reported to improve its accuracy by some groups (Barentsz *et al*., 1999; Engelbrecht *et al*., 2003). A number of different ^{1}H MR spectroscopic techniques and chemical shift imaging have also been described. The combined use of MR imaging and MR spectroscopy improves detection of tumors within the peripheral zone (Star-Lack *et al*., 1997; Obek *et al*., 1999; Scheidler *et al*., 1999; Males *et al*., 2000; Zakian *et al*., 2002). MR imaging and/or MR spectroscopy are not used as a first approach to diagnose prostate cancer but may be useful for targeted biopsy, especially in patients with PSA levels indicative of cancer but negative results from previous biopsies (Zakian *et al*., 2003; Beyersdorff *et al*., 2002). Radionuclide bone scanning is the initial imaging modality recommended for detecting bone metastases. Concerning skeletal imaging, a higher number of osseous metastases have been detected with MR imaging than with skeletal scintigraphy probably due to the inherent high sensitivity for detection of bone marrow changes (Algra *et al.,* 1991; Eustace *et al.,* 1997). Although MR imaging is more sensitive than radionuclide scanning, evaluation of the entire skeletal system has not been critically analysed. Reported cut off values of PSA level used to identify patients at high risk for lymph node and bone metastases are around 15 ng/mL and 20 ng/mL, respectively; however, there is considerable variation in cut off values among different series in the literature (Wymenga *et al*., 2001; Naya and Babaian, 2003). Endorectal MR imaging has been used to predict the ECE of clinically localized tumors since 1991 (Schnall *et al*., 1991).

Endorectal MR imaging seems to be indicated in carefully selected patients-specifically, those with three or more positive biopsy specimens, a palpable tumor, and/or a PSA level greater than 10 ng/mL (O'Dowd *et al.,* 1998; Cornud *et al*., 2002). Several authors (Jager and Ruijter *et al*., 1996; Yu *et al*., 1996) have reported the conditions in which MR imaging should be used — that is, to yield the best specificity. Literature data regarding usage of MR for the low-risk group show it is cost-effective by some authors (Laupacis *et al*., 1992) and unnecessary by others (Lu-Yao *et al*., 1994; O'Dowd *et al*., 1998). For patients at intermediate and high risk is the common opinion is that MR staging lowers costs because it is a valuable procedure to avert unnecessary surgery (Partin *et al*., 1993; D'Amico *et al*., 1996).

To our knowledge there have not been published comparative studies about local MR staging for prostate cancer with usage the latest dedicated phased-array coils and histopathology. Therefore our aim in study IV was to evaluate the diagnostic performance of the new and best locally available technique: MR imaging with dedicated flexible phased-array coil for the local staging of prostate cancer if decisive in the preoperative selection for radical prostatectomy, which has became in the last few years treatment of choice for T1/T2 prostate cancers.

3. THE AIMS OF THIS THESES

The aim of this theses was to explore the diagnostic potential of currently available radiological methods: CT, MRI and IS with CEA-antibodies in some challenging situations during work-up of pelvic malignant tumours.

Specific questions addressed for this purpose were following:

- Can functional imaging modality provided by CEA-scintigraphy give additional information to the anatomical imaging modalities, CT and/or MRI, in the detection and determination of the extent of malignant disease as examplified by local recurrence of rectal cancer? (I)
- Is a single unenhanced axial T2 weighted FSE MR sequence, performed additionally to the dedicated pelvic multicoil MR examination, effective to use for the screening of the upper abdomen for liver metastases? (II)
- Can the decision-making and the clinical management of colon cancer patients with liver metastases potentially be improved? (III)
- Is MR imaging with dedicated flexible external phased array coil reliable in the preoperative local staging of prostate cancer? (IV)

4. PATIENTS AND METHODS

4.1. Patients

The whole study is based on data of four separate groups of patients examined with cross-sectional imaging modalities (CT, MRI, IS) for specific purposes. The patient material in the four publications is presented in Table 1.

Table 1.

Study type	Study site	Study period	No of patients male/female	Goals of the study	Publication
Retrospective	K	1993–1995	46 (31/15)	Diagnosis of local recurrence	I Acta Radiologica 2000
Prospective and retrospective	K	1996–1998	111(58/53)	Detection of liver metastases	II Manuscript
Population study	K	1996–1999	2280 (1096/1184)	Manageme nt of liver metastases	III European Journal of Surgical Oncology
Prospective and retrospective	TUC	2001–2003	26 males	Local staging of prostate cancer	IV Eesti Arst 2004

K — Karolinska University Hospital Solna
TUC — Tartu University Clinics

Publication I provides assessment of 46 consecutive patients who met the following criteria: previous surgery for rectal cancer, clinical suspicion of LR, examined with CEA scintigraphy, CT or MRI between 1993–1995 at Karolinska Hospital. Low anterior resection was performed in 26 patients, abdomino-perineal resection in seventeen and in three patients subtotal colectomy was performed. Thirty-one patients had been operated on once, twelve twice and three patients had three or more surgical events. The time interval from previous surgery till examinations in question varied from 1 month to 7 years (mean 16 months). CT and MRI were performed in 38 patients, only CT in 7 and only MRI in one patient. The study group included 15 females and 31 males (mean age 60 years, ranging between 28 and 2 years) twenty-two of those received preoperative radiotherapy.

Publication II is based on the data of 111 patients (53 women and 58 men, (median age 64 years (14–92)) with primary pelvic malignant disease examined with pelvic and upper abdomen MR imaging at Karolinska Hospital between January 1996 and December 1998. The clinical diagnoses in the series are presented in the Table 2.

Table 2. Clinical diagnoses in the study group

Diagnoses	Number of patients
Recto-sigmoid carcinoma	84
Ovarian carcinoma	5
Ovarian teratoma	2
Uterine rhabdomyosarcoma	3
Endometrial carcinoma	3
Cervical carcinoma	5
Carcinoma of the urinary bladder	5
Prostate cancer	2
Perianal rhabdomyosarcoma	1
Hodgkin lymphoma	1
Total	**111**

Fifty-five examinations were performed preoperatively as a part of the initial staging and other 56 examinations were part of the post-treatment follow-up.

Publication III is related to a population based study including data of all 2280 patients diagnosed with an invasive adenocarcinoma of the colon in the Stockholm-Gotland region between 1996 and 1999. Hepatic metastases until December 31, 2001 were diagnosed in 537 (24%) of these patients. In all, 177 patients were eligible for a review of CT and/or MRI. Of these, 38 patients were diagnosed with liver metastases at laparotomy or by ultrasonography and could thus not be re-evaluated. In the 139 patients who were diagnosed by CT or MRI of the liver, images were available in 114.

In publication IV, we aimed to study the accuracy of MRI in local staging of prostate cancer in 26 radically operated patients. These were selected from 66 consecutive patients with histologically verified prostate cancer. Examinations were performed between December 2001 – September 2003 at Tartu University Clinics (TUC) on a 1,5 T MR unit with a dedicated flexible phased array coil. The age of the patients was 49–74 years (median 64,3 y). The time between the examination and subsequent surgery was from seven days to four months (median 49 days). The study group consisted of patients belonging to a “median risk group” which have high probability of ECE, T3 stage. That group is clinically characterised by PSA 10–20 ng/ml, Gleason score 5–7, tumour finding at DRE and absence of known distant metastases.

4.2. Methods

4.2.1. Radiological methods

For the radiological examinations cross-sectional (tomographic) functional techniques (CEA-scintigraphy) and/or anatomical (CT, MR) imaging methods were used.

4.2.1.1. CEA-scintigraphy

In paper I, CEA-scintigraphy was performed for diagnosis of LR of rectal cancer. IS was performed with a gamma camera (400 AZ Maxicamera [GE] or a BIAD XLT double-headed camera [Trionix]) equipped with low-energy high resolution collimators. After i.v. injection of 1000 Mbq mouse anti-CEA monoclonal antibodies labeled with ^{99m}Tc (Scintimun CEA, BW) AP and PA registrations of at least the lower abdomen and pelvis and a tomographic examination of the pelvis were acquired 18–24 hours later. Before the IS the urinary bladder was catheterised and emptied.

4.2.1.2. Computed tomography

CT examinations were performed for diagnosis of LR of rectal cancer in paper I, as part of the radiological follow-up of patients with pelvic malignant tumours in paper II, and for the detailed examination of liver metastases in colon cancer patients — paper III. In paper I, examinations were carried out on Toshiba TCT 600S or Siemens Somatom HiQ scanners, which both were single detector-ring scanners. CT scanning of the upper abdomen was performed in supine position one hour after oral administration of contrast medium (50 ml Urographin 30%, Shering AG, diluted to 1000 ml with water). The pelvis (paper I) was examined after at least 6 hours delay from drinking of 1000 ml of the same contrast agent, prior the scanning the second portion of contrast was administered as for the upper abdomen study. The abdomen and pelvis were scanned with 10 mm continuous slices after injection of intravenous contrast medium. In paper III, either conventional or helical CT-scanners were used for liver metastases detection.

4.2.1.3. Magnetic resonance imaging

MR scanning was performed with a super-conductive high-field 1.5 Tesla (T) MR system (Signa Advantage [General Electric] in paper I and II. In paper IV, a 1.5 T Magnetom Somphony, [Siemens] scanner was used. In the first study, the examinations were performed in supine position using a pelvic phased-array surface coil. T2-weighted FSE sagittal and axial images were obtained, when necessary supplemented with oblique images. T1-weighted transaxial scans were performed and when considered valuable repeated using intravenous gadolinium chelates. Slice thickness of 5 mm and 0–2.5 mm interslice distance was used. In the second study, high-resolution images of the pelvis with a multicoil array all patients were examined with an axial T2-weighted FSE sequence of the upper abdomen using the body coil. The slice thickness was 10 mm and interslice gap 2,5 mm. A standard protocol (Table 3) was established for the pelvic MR examination in paper IV

Table 3. MR protocol for local staging of prostate cancer

Sequence/ parameters	Plane	Region	TR (ms)	TE (ms)	FOV (mm)	Slice (mm)
T1	axial	from sypmhyses till aortic bif.	500	13	250x100	7
T2	axial	pelvis	4000	101	200x200	3
T2	coronar	pelvis	4000	101	200x200	3
T2	sagital	pelvis	4000	101	200x200	3
T2 fat sat	axial	pelvis	4180	101	200x200	3
STIR	coronar	pelvis	5000	26	380x380	3

fat sat – fat saturation

4.2.2. Clinical verification

In the first study, surgical verification was obtained in 31 patients. In seven patients diagnostic correlation was based on endoscopic biopsy or fine needle aspiration cytology guided by CT or ultrasound, in the remaining eight patients by follow-up during the 4-24 (medium 12) months period. In the second study, findings of fifty-five MR examinations were correlated with data of surgery and 56 had convincing radiological follow-up during at least 1.5 years. For the population based study in paper III clinical decision-making and verification of metastases was based on prospective CT/MR diagnoses and the potential of improvement was assessed based on a review of these images and the clinical records. MR findings in paper IV were all correlated to the histopathology and

surgery data. Beside the local tumour spread the correlation between pathology „cancer maps" and corresponding axial T 2 weighted images as well as the accuracy of MRI for the detection of the ECE, involvement of the seminal vesicles and regional lymph nodes was also studied.

4.2.3. Image interpretation

Images were evaluated independently by two experienced radiologists who were only aware about suspicion of LR (I study), verified liver metastases (III study) and suspicion of ECE (IV study), without any knowledge of other diagnostic or clinical data. Results of two observes were combined and the consensus reached. In study II, image evaluation was performed by one radiologist who was only aware about pelvic malignancy, and compared the findings with those of prospective study.

Diagnosis of LR and metastases on CT and MR images were based on earlier (Ellert and Kreel, 1981; Granfield *et al*., 1992; Kelvin *et al*., 1983) described signs: 1) bowel wall thickening, 2) suspect masses and growth of masses 3) any predominantly hyperintense and inhomogeneous FLL on T2-weighted MR-imaging with indistinct, irregular borders, 4) serosal masses or ascites and 5) enlarged lymph nodes. Ascites was judged as suggesting presence of peritoneal tumour implants. Lymph nodes measuring at least 1 cm in the short axis diameter relative to adjacent vessels or that showed growth on follow-up CT/MR examinations were considered metastatic.

In the population based study, the number and sizes of the metastases in each segment and hepatic tumor infiltration into adjacent organs were recorded. Patients with less than five hepatic metastases were regarded as having potentially respectable hepatic disease and their medical records were analyzed in detail to assess whether they had been evaluated for a possible hepatic resection.

For the prostate cancer staging were used diagnostic criteria (Table 4) known from the literature (Outwater *et al*., 1994; Yu *et al.*, 1996; Jager *et al.*, 2000; Beyersdorff 2002).

CEA-scintigraphy images were analysed by one nuclear medicine physician experienced in the field. Any focus of activity outside the normal distribution of the tracer including urine and faecal activity on CEA scintigraphy images was considered characteristic for recurrence.

Table 4. MR diagnostic criteria for prostate cancer staging

Carcinoma detection	Extracapsular spread	Involvement of the seminal vesicles	Lymph node metastases.	Skeletal metastases.
Decreased SI in T2-weighted images	1. broad-based capsular contact 2. contour deformity 3. obliteration of the recto-prostatic angle 4. asymmetry of the neurovascular bandle 5. irregular capsular bulging 6. extracapsularar tumour mass	SI decrease, contour irregularity	Diameter >1 cm in short axis	1. osteobl. mts.-SI decrease in T1, T2 2. osteolytic and mixed mts.-T1,T2 mixed SI

Osteobl.,osteol. – osteoblastic, osteolytic; mts. – metastases

4.2.4. Statistical analysis

Descriptive statistics were applied for assessment of accuracy of cross-sectional techniques for LR detection in paper I, for liver metastases detection in paper II and for ECE diagnosing in paper IV. In paper IV, cumulative proportion survival Kaplan-Meier analyses was used in population study. Students *t*-test was used in paper I for evaluation of additive value of IS. Differences were considered statistically significant for p values less than 0.05. Statistical analysis in paper III was performed using the statistical software package “Statistica”.

5. RESULTS

5.1. Added value of CEA scintigraphy in the detection of recurrence of rectal carcinoma (publication I)

In 24 patients examined by CEA-scintigraphy, 25 patients examined by CT and in 27 patients examined by MRI, the diagnosis of local recurrence correlated with follow-up (Table 5).

Table 5. Matrix analysis of CT, MR, and CEA scintigraphy in the detection of local tumour recurrence of rectal cancer

Modality (positives+/negatives-)	True-positive*	True-Negative*	False-Positive*	False-Negative*
CT (37+/18-)	25	4	4	12
MR (33+/6-)	27	3	3	6
CEA scintigraphy (38+/8-)	24	6	2	14

* The figures correspond to number of patients

A total 33 of 38 LR's were diagnosed by either CEA scintigraphy or by CT/MRI. All three methods agreed in 23 patients in the diagnosis of LR that correlated with follow-up. Fourteen LR's were missed by CEA scintigraphy. The detection of LR by IS was significantly ($p<0.05$) related to tumour size. None of LR's measuring 3 cm or less were detected by CEA scintigraphy. In three other patients, all three diagnostic methods failed to diagnose tumour recurrece. In these patients, only extensive fibrosis was found at surgery but histopathological analysis of surgical biopsy specimen showed malignancy.

Although an indwelling catheter was inserted, interpretation of CEA scintigraphy images was disturbed by residual bladder and bowel activity, which appeared in several cases.

With the limited number of patients in study I, CEA scintigraphy had a higher specificity (75%, 6 of 8 patients) than CT/MRI (50%, 4 of 8 patients by CT and 3 of 6 patients by MRI) in the diagnosis of LR. The complementary role of CEA scintigraphy to CT/MRI in diagnosing distant metastases and metastatic lymph nodes was not significant. Twelve of 16 patients (75%) with proven distant metastases were detected by CT/MRI. Liver metastases were detected in 2 patients by CEA scintigraphy. In both, the metastases were 4 cm or more in diameter. In 10 patients, liver metastases were not diagnosed by CEA scintigraphy.

Lymph node metastases were found by CEA-scintigraphy in five patients and by CT/MRI in 9 of 15 proven cases. One false positive diagnosis of tumour on CEA-scintigraphy occurred in a patient where metastases to lymph nodes were interpreted as possible soft tissue metastases.

Our data demonstrated no additive value of immunoscintigraphy to CT/MRI in detection of LR of rectal cancer.

5.2. T2-weighted fast spin-echo screening for liver metastases as addition to pelvic MRI in patients with pelvic malignant tumours (publication II)

According to radiological and surgical follow-up, eighteen patients proved to have liver metastases. Liver metastases were detected with the T2-weighted MR sequence in fifteen of these eighteen patients (Table 6).

Table 6. Presence of liver metastases according to the T2-weighted screening sequence, radiological and surgical follow-up

		MR		
		LM	No LM	Total
FU	LM	15	3	18
	No LM	3	90	93
Total		**18**	**93**	**111**

FU = Radiological or surgical follow-up, LM = Liver metastases

In eleven patients, liver metastases were found at surgery and in seven patients proved on the radiological follow-up no later than three months after MR. In two patients, liver metastases were found at surgery but preoperative MR imaging was FN. With knowledge of surgical information, one possible liver metastasis could be found at a second review. In one patient, liver metastases below 2 cm in diameter were found at US examination two months after the MR screening. These metastases were interpreted as cysts during review of the MR images and this finding was considered FN.

Hyperintense focal liver lesions on the T2-weighted sequence were falsely interpreted as liver metastases in three patients. One hyperintense lesion proved to be a small haemangioma and the two other cysts; all with typical US appearance and no change in lesion size or structure during 1,5 years follow-up. Altogether 27 metastatic sites in 23 patients confirmed by either surgery or radiological follow-up were found. Additionally benign FLL (cysts and haemangiomas) were found in 28 patients.

16 patients had additional CT (n=11) or US (n=5) examinations of the upper abdomen performed within 10 days–11 months (median 2 months) before the MR screening. MR screening confirmed liver metastases suspected by CT in two of these patients. In two other patients, liver metastases were suspected on CT but were proven to be liver cysts on MR and on follow-up. In one of these patients, retroperitoneal lymph node metastases where also present, which were detected by both methods.

Our results obtained with axial T2-weighted fast spin-echo screening sequence showed its feasible for liver metastases screening, though all liver metastases can not be detected with this method alone.

5.3. The potential for improved outcome in patients with hepatic metastases from colon cancer in the Stockholm-Gotland region (publication III)

From 537 of the 2280 patients (24%) with liver metastases were synchronous metastases found in 343 (15%) and metachronous in 194 (9%) patients. The diagnosis of hepatic metastases was based on findings on either ultrasound, CT scan, examination during primary laparotomy or by a combination of these methods. In 29 patients the hepatic metastases were found at autopsy which excluded them from follow-up analysis.

Thus, 316 patients with synchronous and 192 patients with metachronous metastases were available for follow-up. In 167 (53%) of the 316 patients with synchronous hepatic metastases the liver was the only site of residual disease. In 51 patients additional metastases in extrahepatic locations were detected and in 98 patients an incomplete removal of the primary tumour was performed. Metachronous liver metastases were found after a median follow-up time of 14 (3-60) months. In 99 patients (52%) hepatic disease was the only detected tumour manifestation. In the remaining 93 patients other metastases, LR or an incomplete resection of the primary tumour was present concomitantly. Remaining 177 patients were eligible for a review of CT and/or MRI. Additionally 38 patients where liver metastases were diagnosed at laparotomy or by ultrasonography were excluded. In the 139 patients who were diagnosed by CT or MRI of the liver, images were available in 114 (Table 7).

Sixty-six (58%) of the 114 patients had less than five metastases and 44 (67%) of those had been evaluated by a hepatic surgeon. Patient assessments and hepatic resections were performed by seven different hepatobiliary surgeons in six different hospitals. Nineteen of the 44 patients underwent hepatic surgery but 25 did not.

Table 7. Distribution of hepatic metastases in the 114 patients according to review of CT/MRI

Number of metastases	Right lobe	Left lobe	Bilobar
1	17	5	5*
2	6	3	9
3	6	2	4
4	2		9
5			2
6	6		1
8			1
>9			41
Total	32	10	72

* Solitary metastases with overgrowth on segment in the other lobe

A potentially curative hepatic resection was performed in 21 out of the 266 patients (8%). All hepatic resections were considered curative by both the surgeon and the pathologist. The median age was 59 (37–78) years. Eleven (52%) out of the 21 resected patients were alive after a median follow-up time of 29 (13-45) months, eight without evidence of disease. Of the ten patients who died during the follow-up time, two died from complications related to the hepatic surgery. The other eight all had recurrent metastatic disease in the liver.

Symptomatic treatment alone was given to 152 (57%) of 266 patients with isolated hepatic metastases. The median age in this group was 79 (44–94) years and the median survival time 3 (0-32) months. No patient was alive at follow-up. In 242 patients with syn- or metachronous hepatic metastases and concomitant extrahepatic disease, chemotherapy was given to 84 (35%); three in combination with stereotactic radiation and one in combination with intrahepatic ethanol injections. One patient had stereotactic radiation alone towards the hepatic metastasis. The remaining 157 patients received only symptomatic treatment. The median age in this group was 72 (34–95) years and the median survival time was 3 (0–51) months.

According to our results in this population-based study, significant improvement in survival rate of surgically treated patients was achieved.

5.4. MRI for local staging of prostate cancer by a flexible phased-array coil (publication IV)

According to the data from surgery and pathology (Table 8), 19 of twenty-six (73%) patients examined at MRI had stage T1/T2 prostate cancer. In seven cases ECE was detected and in three of these, the tumour had only involved the prostate capsule or had a little involvement of the neurovascular bundle (T3a stage). In three other patients, involvement of the seminal vesicles was present according to pathology. In seven patients, ECE was found. In three of them, the tumour was assessed as T3a stage-minor involvement of the capsule or neurovascular bundle. In the other three men, additional cancerous involvement of the seminal vesicles was present according to histopathology.

Table 8. MRI and histo-pathological correlation in prostate cancer staging in 26 operated patients

MRI	**HISTOPATHOLOGY**			
	T1/T2 (19)	T3 (7)	N0 (26)	N1 (0)
T1/T2	16	3		
T3	3	4		
N0			25	
N1			1	

The accuracy of MRI for detection of extracapsular growth was in initial interpretation 64%. Retrospectively achieved consensus between two radiologists was more accurate- 74%. In three patients both, the initial and final diagnoses were FP regarding the detection of the ECE. One possible reason for false positive diagnoses was diminished image quality due to movement artifacts. Diagnosing suspected seminal vesicles involvement was correctly performed in two from three verified cases. On the other hand, FP involvement was assessed in six patients.

Similarly to “classical” signs we observed in our material also mostly hypointense appearance of the malignant tissue and hyperintense normal peripheral gland on T2-weighted and T2-weighted fat saturated MR images. Isointense prostate cancer, which is believed to be mucin-producing, was only present in two of the operated patients in our group. However, we observed cancer-mimicking picture caused by the adenomatous or inflammatory-dystrophic reasons in 18 patients. Subjective opinion of radiologist in cross-correlation between MR images and histological slices showed a good correlation in 62% cases. Twelve patients with extensive local spread and lymph node metastases and skeletal metastases according to pretreatment

investigations were not operated on. In one patient, enlarged lymph nodes, detected by MRI were morphologically proved to be caused by synchronous Hodgkin lyphoma.

Our data demonstrate 74% accuracy and 84% specificity for MR examination with dedicated phased array coil for local staging of prostate cancer ECE, thus pelvic MR examination with flexible phased array coil is effective tool for local staging of prostate cancer.

6. DISCUSSION

6.1. CEA scintigraphy, CT and MR imaging in detection of LR of rectal cancer

Can functional (biological) imaging improve cancer staging and recurrence detection? Already in 1983 a report of antibody imaging in cancer patients using monoclonal anti-CEA antibodies in vivo was published (Mach *et al*., 1983). However this technique is not currently in wide use. CT and MRI provide large amounts of detailed morphological information that is based on physical properties. The yield of information by CEA-scintigraphy is less detailed but since this diagnostic modality is based on biological properties, it is potentially complementary to radiological examinations. Earlier studies have shown that results of IS with technetium-labelled antibodies in the diagnosis of LR are better than on CT (Abdel-Nabi *et al*., 1990; Patt *et al*., 1990; Serafini *et al*., 1998) having an accuracy and sensitivity which is similar to that of MR-imaging, and higher specificity (Mach *et al*. 1983; Abdel-Nabi *et al*., 1988; Abdel-Nabi *et al*., 1990).

In our study, CEA scintigraphy showed a limited potential in demonstrating presence and location of LR. The size seemed to be important for detection of recurrent tumour on CEA-scintigraphy. Our results support earlier studies (Stomper *et al*., 1995) that IS adds neither sensitivity nor specificity to CT alone. Additionally, according to our data, CEA scintigraphy had no additive diagnostic value to CT and MRI in the detection of metastatic lymph nodes and other distant metastases. Our results are confirmed also by later studies (Fuster *et al*., 2003). However, the specificity of CEA scintigraphy in the diagnosis LR in our study seemed to be higher than that of CT and MRI. Therefore CEA scintigraphy, where it is an available technique, could be used for diagnosing and localising recurrent disease in patients with equivocal or negative CT and MR investigations when there is still strong clinical suspicion for LR.

Limitations in our study were that results of CEA scintigraphy were influenced by residual bladder and bowel activity, which was a disturbing factor in several cases. Furthermore, our study group consisted of consecutive patients not selected by serum CEA-levels.

Some authors still suggest the use of IS for diagnosing of colorectal LR (Lechner *et al*., 2000; Baulieu *et al*., 2001). Although it has a limited usefulness in the detection of distant metastases, it may be helpful in the diagnosis of suspected LR in patients with non-conclusive CT findings, when FDG-PET is not available (Abdel-Nabi *et al*., 1998; Behr *et al.,* 1997; Baulieu *et al*., 2001; Fuster *et al*., 2003).

More recently, functional data of fluorine 18 (18F) fluorodeoxyglucose (FDG) positron emission tomography (PET) has reported to have an important complementary role in the detection of distant metastases and local recurrence

(LR), in the differentiation of tumoral and nontumoral masses in patients with colorectal cancer (Kalff *et al*., 2002; Lonneux *et al*., 2002; Pijl *et al*., 2002). Unprecedented results have been shown using the last technical achievement: PET/CT which allows functional information superimposed on the anatomical images, combining morphology and physiology. Usage of PET/CT has started in many directions, especially in the field of cancer imaging. In the pelvis it was used to distinguish benign and malignant presacral abnormalities with a sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of 98%, 96%, 90%, 97%, and 93% respectively (Even-Sapir et. al., 2004). However, both PET and especially PET/CT are high-cost examinations with limited availability.

In paper I, MR imaging had the highest diagnostic potential for detection of LR of rectal cancer with accuracy 77% and 82% sensitivity, which confirms the opinion of other authors (Beets-Tan *et al*., 1999) that MRI is the modality of choice for imaging of locally recurrent rectal tumours. In the literature opinions whether to use intravenous contrast agents for this purpose has been studied (Vliegen *et al.,* 2002; Torricelli *et al.,* 2003), but this was not the aim of the present work.

6.2. Role of imaging for liver metastases detection and for pretreatment decision-making in colorectal cancer patients with liver metastases

If pelvic MR is increasingly performed- what is the role of MR screening sequences for liver metastases detection? In these days of spiraling costs and limited resources, there is considerable debate regarding the choice of the ideal noninvasive imaging modality for the detection of liver metastases. The use of multiple modalities is both time-consuming and costly.

Although comprehensive body MR examinations in 10 minutes has been reported (Outwater, 1999) MR-imaging has limitations as a screening method due to complexity of combining dedicated protocols for different anatomic areas such as the pelvis and upper abdomen, especially when dedicated surface coils and contrast media are used.

In our study, T2-weighted MR imaging showed a potential as a sole sequence for detection of liver metastases with sensitivity 82% and specificity 97%. However, it was found that all later verified metastases can not be detected with this sequence alone. Despite the limited protocol, MR screening was able to give additional information to CT in four cases. Suspected liver metastases on CT in two patients were showed by axial T2-weighted MR as liver cysts and in two other patients MR confirmed metastases suspected by CT. Only two cases were present, where MR did not detect small liver metastases.

A high specificity (97%) for detection of liver metastases was reached with screening MR. However, lesion characterization by a sole T2-weighted sequence was not completely accurate and our reference methods and follow-up also had limitations. In general practice MR imaging still has limitations as a screening tool due to complexity of combining dedicated protocols for different anatomic areas such as pelvis and upper abdomen, especially when dedicated surface coils and contrast media are used. For this reason only one single sequence of the upper abdomen was performed in this patient series not to compromise the quality of the pelvic examination. In our study, the average additional time needed for a T2–weighted transaxial FSE MR sequence of the upper abdomen prolonged the examination insignificantly, in average 16%.

Skeletal metastases are more common in breast and prostate cancer than in colorectal cancer. We encountered only two patients with prostate cancer in our study group, the majority of patients had colorectal cancer and MR screening or follow-up did not detect any skeletal metastases. Axial T2-weighted FSE images alone is not an effective way for detection of these metastases and in these cases. For this purpose, skeletal screening with coronal/sagittal short tau inversion recovery or T1-weighted images have to be additionally considered (Ohlsson *et al*., 1993). In the future, MRI may increasingly become an alternative to CT and US for screening of abdominal metastases. Developments of scanner hardware and refinements in imaging sequences, particularly in respect to fast standardised imaging techniques and new surface coils that potentially enable complete coverage of large body areas in one examination as well as increased availability of scanners will affect the role of MR in this respect.

Our results demonstrate that axial T2-weighted FSE MR imaging of the upper abdomen using the body coil as adjunct to high resolution pelvic MRI can be used as screening of liver metastases in patients with pelvic malignancies, it cannot, however, be a substitute for dedicated liver imaging.

The curative potential of liver resections in patients with metastatic disease of colorectal carcinoma has been shown by several other authors (Scheele *et al*., 1995; Wade *et al*., 1996; Penna *et al*. 2002; Moore *et al*., 2002). Results of our population based study (paper III) showed, that after review of CT/MR images less than five liver metastases were found in 66 (58%) of the 114 patients who's CT and MR images were reviewed. Thus, 66 (13%) out of all 508 patients had liver metastases amenable to liver resection according to the used criteria for resectability. It must be remembered, however, that in Sweden these criteria were not commonly adopted in the late nineties when bilobar disease was usually regarded as a contraindication to surgery. Unilobar disease was found in 42/114 (37%) patients. If we instead consider that these 42 patients could have been eligible for resection, about 8% of all 508 patients could have been potential candidates for hepatic resection. However, during the study period only 21 patients (4%) had a liver resection which constitutes half of the potentially resectable patients. The lack of routine follow-up protocols may also contribute as many patients had advanced disease when the liver metastases

were detected. Intensive follow-up after curative resection for colorectal cancer may improve survival, due to an earlier detection of isolated recurrences, as shown in two recent meta-analyses (Sheele *et al*., 1990; Adam *et al*. 2001). Despite this, there is no consensus regarding follow-up strategies in patients operated on for colon cancer. This study also revealed that information on treatment decisions for individual patients were often unavailable in the medical records and that there was a lack of structure in treatment strategies. The great variability in the treatment modalities used, the timing and the combinations of treatments indicates that there were no commonly used, standardized protocols for the management of these patients. Although colorectal cancer metastases to the liver is stage IV disease, the results with surgical resection suggest that perhaps we should begin to look at this subset of patients with "curative" intent rather than relegate them to "palliative" therapy. This is responsible role for radiology since decision-making for treatment selection in this patient category is based on cross-sectional imaging. Situation in this field in Estonia has not been specifically studied. We assume, that this is rather similar as in Sweden and further local research could possibly help to improve it.

6.3. Pelvic MRI with flexible phased-array coil in local staging for prostate carcinoma

Rectal ultrasonography is routinely used for the radiological examination of the prostate gland, because it well differentiates zone anatomy and allows biopsy guiding. For the cancer detection and staging is diagnostic performance of this modality insufficient (Epstein *et al*., 1993; Beyersdorff *et al*., 2002).

Today, MRI is state-of-the art for imaging soft tissue structures, and it has been increasingly used for the several oncological purposes. Some studies report even about 97% accuracy and 83% sensitivity for the endorectal MRI in the localising of the known prostate cancer. Although MRI finding in the detection of the prostate cancer does not have a good matching correlation with biopsy and most of the tumours below 5 mm in size remain undetected it has proven surpass the accuracy of the DRE and rectal ultrasonography (Jager *et al*., 2000; Beyersdorff *et al*., 2002).

Recently, MRI became available at Tartu University (TU) Clinics. This modality, using dedicated phased-array coil allows images of the pelvic anatomy with excellent soft-tissue contrast resolution, therefore it was introduced for local staging of prostate cancer. Our results show that MRI examination of the pelvis using the dedicated flexible phased array coil gives valuable information about stage of the disease in operated patients. In these patients, MR imaging showed a good potential for preoperative staging of known prostate cancer in the pre-selected subgroup of patients with moderate or high prior probability of extracapsular disease. For the detection of the involvement of neighboring

structures and the metastatic lymph nodes, none of the operated patients had the inoperable disease-considerable involvement of the neighboring structures, nor unremovable tumour. Despite the preoperative selection, this is promising data for the future preoperative selection of patients and avoiding unnecessary nonradical surgery. Accuracy 74% achieved in this study is confirming the results obtained by Cornud *et al*., (2002).

We consider it noteworthy, that in one of our patients, where several repeated biopsies were negative a positive biopsy was achieved after using the MR information for guidance. This case is supporting the opinions of some authors, who believe that MRI could be an alternative to rectal ultrasonography for prostate cancer screening and biopsy guiding (Hata *et al*., 2001). Results of the radiological examinations depend on the availability of the clinical information and on the co-operation of radiologists and clinicians (Getty *et al*., 1997). In our study group we initially observed cases, with suboptimal imaging quality due to post-biopsy haematoma in six cases. Prolonging the post-biopsy period allowed us to eliminate this disturbing factor. Rather moderate, 62% correlation for the malignant tissue location on the MR images and corresponding pathology specimen is confirming the main shortcut in this field — low specificity for MRI in detection of prostate cancer within the gland. Furthermore, other situations that may cause staging difficulties are after transurethral resection (TUR), in cases of large adenomas and in centrally located tumours within the gland. In addition to the information about the local tumour extent, we were able to diagnose enlargement of pelvic lymph nodes and bone metastases in twelve patients. Patients did then not need to have a CT for this purpose. The only decisive criteria for the detection of malignant lymph nodes by MRI was size criteria with its limitations in separating reactive from malignant infiltrations.

Until today MRI has not been widely used for prostate examinations. High cost, low availability and moderate specificity for cancer detection are main reasons. Hopefully new methods as PET and MR-spectroscopy, with promising report of about 100% accuracy and 94% specificity in prostate cancer detection will further increase the role of preoperative prostate imaging (Coakley *et al*., 2003; Swindle *et al*., 2003). Accurate diagnosis and staging of prostate cancer to ascertain effective therapy is essential. Although MR imaging has a limited role in prostate cancer detection it may be helpful for patients with a high index of suspicion and negative initial biopsy. MR staging results should be interpreted in combination with clinical findings. Reader experience plays an important role in the ability to interpret prostate MR images and is an important contributor to interobserver variability. Diagnostic performance of MRI as the best locally available radiological tool for prostate cancer staging could maybe be improved using and endorectal coil which was not separately studied in this work. Future developments could be achieved using MR spectroscopy which provides functional information combined to anatomical image and allows better tissue characterisation.

7. CONCLUSIONS

CEA-scintigraphy has no additive diagnostic value to anatomical imaging with CT/MRI in detection and evaluation of LR of rectal cancer. However, usage of CEA scintigraphy could be considered for diagnosing recurrent disease in selected patients with equivocal or negative CT and MRI when there is still a strong clinical suspicion of LR (I).

Axial T2-weighted FSE MR imaging of the upper abdomen as adjunct to high resolution pelvic MRI is a reasonably sensitive way of screening for liver metastases in patients with pelvic malignancies. It cannot, however, replace a dedicated liver examination (II).

There is a potential for improvement in outcome for patients with liver metastases of colon cancer. The review of CT/MR images showed that 10% of the colon cancer patients with liver metastases likely had resectable metastases, but only 4% of all patients with hepatic metastases underwent a hepatic resection. Thus, less than 50% of immediately potentially resectable patients were actually resected (III).

Pelvic MR imaging used for local staging of prostate cancer is effective tool for diagnosing of ECE but is not accurate for the detection of the early capsular involvement (stage 3 a). Further MRI could be helpful for deciding biopsy-site in patients with clinically high index of suspicion and negative initial biopsies (IV).

8. REFERENCES

Abdel-Nabi H, Doerr R, Chan H. In-111-labeled monoclonal antibody immunoscintigraphy in colorectal carcinoma: Safety, sensitivity, and preliminary clinical results. Radiology. 1990; 175: 163–171.

Abdel-Nabi H, Doerr R, Lamonica D. Staging of primary colorectal carcinomas with fluorine-18 fluorodeoxy-glucose whole-body PET: correlation with histopathologic and CT findings. Radiology. 1998; 206: 755–760.

Abdel-Nabi H, Schwartz A, Goldfogel G, Ortman-Nabi J, Matsuoka D, Unger M, Wechter D. Colorectal tumors: scintigraphy with In-111 anti-CEA monoclonal antibody and correlation with surgical, histopathologic, and immunohistochemical findings. Radiology. 1988; 166: 747–752.

Adam A. Interventional radiology in the treatment of hepatic metastases. Cancer Treat Rev. 2002; 28: 93–99.

Adam I, Mohamdee M, Martin I. Role of circumferential margin involvement in the local recurrence of rectal cancer. Lancet. 1994; 344: 707–711.

Adam R, Avisar E, Ariche A, Giachetti S, Azoulay D, Castaing D. Five-year survival following hepatic resection after neoadjuvant therapy for nonresectable colorectal. Ann Surg Oncol. 2001; 8: 347–353.

Akasu T, Kondo H, Moriya Y. Endorectal ultrasonography and treatment of early stage rectal cancer. World J Surg. 2000; 24: 1061–1068.

Akin O, Nessar G, Agildere A, Aydog G. Preoperative local staging of rectal cancer with endorectal MR imaging: comparison with histopathologic findings**.** Clin Imaging. 2004; 28: 432–438.

Algra P, Bloem J, Tissing H, Falke T, Arndt J, Verboom L. Detection of vertebral metastases: comparison between MR imaging and bone scintigraphy. Radiographics. 1991; 11: 219–232.

American Cancer Society. Cancer facts and figures 2004. Publication No 5008.04. Atlanta.

American Joint Committee on Cancer. Prostate. AJCC cancer staging manual. 6th ed., NY: Springer. 2002; 309–316.

Barentsz J, Engelbrecht M, Jager G. Fast dynamic gadolinium-enhanced MR imaging of urinary bladder and prostate cancer. J Magn Reson Imaging. 1999; 10: 295–304.

Barkhausen J, Quick H, Lauenstein T, Goyen M, Ruehm S, Laub G, Debatin J, Ladd M. Whole-body MR imaging in 30 seconds with real-time true FISP and a continuously rolling table platform: feasibility study. Radiology. 2001; 220: 252–256.

Baulieu F, Bourlier P, Scotto B, Mor C, Eder V, Picon L, De Calan L, Dorval E, Pottier J, Baulieu J. The value of immunoscintigraphy in the detection of recurrent colorectal cancer. Nucl Med Commun. 2001; 22: 1295–1304.

Beal J, Cornell G. A study of the problem of recurrence of carcinoma of the anastomotic site following resection of the colon for carcinoma. Ann. Surg. 1956; 143: 165–173.

Beets-Tan R, Beets G, van der Hoop A. High-resolution magnetic resonance imaging of the anorectal region without an endocoil. Abdom Imaging. 1999; 24: 576–581; discussion 582–584.

Behr T, Goldenberg D, Scheele J, Wolf F, Becker W. Clinical relevance of immunoscintigraphy with 99mTc-labelled anti-CEA antigen-binding fragments in the follow-up of patients with colorectal carcinoma. Assessment of surgical resectability

with a combination of conventional imaging methods. Dtsch Med Wochenschr. 1997; 122: 463–470.
Bengtsson G, Carlsson G, Hafstrom L, Jonsson P. Natural history of patients with untreated liver metastases from colorectal cancer. Am J Surg. 1981; 141(5): 586–589.
Beyersdorff D, Taupitz M, Winkelmann B. Patients with a history of elevated prostate-specific antigen levels and negative transrectal US-guided quadrant or sextant biopsy results: value of MR imaging. Radiology. 2002; 224: 701–706.
Blomqvist L, Holm T, Nyren S, Svanstrom R, Ulvskog Y, Iselius L. MR imaging and computed tomography in patients with rectal tumors clinically judged as locally advanced. Clin Radiol. 2002; 57: 211–218.
Blomqvist L, Holm T, Rubio C, Hindmarsh T. Rectal tumors: MR imaging with endorectal and/or phased-array coils, and histopathological staging on giant sections — a comparative study. Acta Radiol. 1997; 38: 437–444.
Blomqvist L, Fransson P, Hindmarsh T. The pelvis after surgery and radio-chemotherapy for rectal cancer studied with Gd-DTPA-enhanced fast dynamic MR imaging. European Radiology. 1998; 8: 781–785.
Boyle P, Langman J. ABC of colorectal cancer: epidemiology. BMJ. 2000; 321:805–808.
Butch R, Stark D, Wittenberg J. Staging rectal cancer by MR and CT. Am J Roentgenol. 1986; 146: 1155–1160.
Catalona W, Ramos C, Carvalhal G. Contemporary results of anatomic radical prostatectomy. Cancer J Clin. 1999; 49: 282–296.
Chan T, Kressel H, Milestone B. Rectal carcinoma: staging at MR imaging with endorectal surface coil — work in progress. Radiology. 1991; 181: 461–467.
Cervone A, Sardi A, Conaway G. Intraoperative ulstrasound (IOUS) is essential in the management of metastatic colorectal lesions. Am.Surg. 2000; 66: 611–615.
Chiesura-Corona M, Muzzio P, Giust G, Zuliani M, Pucciarelli S, Toppan P. Rectal cancer: CT local staging with histopathologic correlation. Abdom Imaging. 2001; 26: 134–138.
Choti M, Sitzmann J, Tiburi M, Sumetchotimetha W, Rangsin R, Schulick R. Trends in long-term survival following liver resection for hepatic colorectal metastases. Ann Surg. 2002; 235: 759–766.
Coakley FV, Qayyum A, Kurhanewicz J.Magnetic resonance imaging and spectroscopic imaging of prostate cancer. J Urol. 2003 ;170: 69–75.
Cookson M, Fleshner N, Soloway S, Fair W. Correlation between Gleason score of needle biopsy and radical prostatectomy specimen: accuracy and clinical implications. J Urol. 1997; 157: 559–562.
Colorectal Cancer Collaborative Group. Adjuvant radiotherapy for rectal cancer: a systematic overview of 8,507 patients from 22 randomised trials. Lancet 2001; 358: 1291–1304.
Cornud F, Thierry F, Chauveinc L, Hamida K, Chrétien, Y, Vieillefond A, Hélénon O, Moreau F. Extraprostatic Spread of Clinically Localized Prostate Cancer: Factors Predictive of pT3 Tumor and of Positive Endorectal MR Imaging Examination Results. Radiology 2002; 224: 203–210.
Cova M, Frezza F, Pozzi-Mucelli R. Computed tomography and magnetic resonance in the preoperative staging of the spread of rectal cancer: a correlation with the anatomicopathological aspects. Radiol Med. 1994; 87: 82–89.

D'Amico A, Whittington R, Malkowicz S. Critical analysis of the ability of the endorectal coil magnetic resonance imaging scan to predict pathologic stage, margin status, and postoperative prostate-specific antigen failure in patients with clinically organ-confined prostate cancer. J Clin Oncol. 1996; 14: 1770–1777.

Danet I, Semelka R, Leonardou P, Braga L, Vaidean G, Woosley J, Kanematsu M. Spectrum of MRI Appearances of Untreated Metastases of the Liver. AJR. 2003; 181: 809–817.

Ellert J, Kreel L. The value of CT in malignant colonic tumors. J Comput Assist Tomogr. 1981; 4: 225–231.

Engelbrecht M, Huisman H, Laheij R. Discrimination of prostate cancer from normal peripheral zone and central gland tissue by using dynamic contrast-enhanced MR imaging. Radiology. 2003; 229: 248–254.

Engelbrecht M, Jager G, Laheij R, Verbeek A, van Lier H, Barentsz J. Local staging of prostate cancer using magnetic resonance imaging: a meta-analysis. Eur Radiol. 2002; 12: 2294–2302.

Epstein J, Carmichael M, Pizov G, Walsh P. Influence of capsular penetration on progression following radical prostatectomy: a study of 196 cases with long-term follow-up. J Urol. 1993; 150: 135–141.

Epstein J, Partin A, Sauvageot J, Walsh P. Prediction of progression following radical prostatectomy: a multivariate analysis of 721 men with long-term follow-up. Am J Surg Pathol. 1996; 20: 286–292.

Estonian Health Statistics. Ministry of Social Affairs of Estonia. Department of Statistics and Analysis. Tallinn. 2003.

Eustace S, Tello R, DeCarvalho V. A comparison of whole-body turboSTIR MR imaging and planar 99mTc-methylene diphosphonate scintigraphy in the examination of patients with suspected skeletal metastases. AJR. 1997; 169: 1655–1661.

Even-Sapir E, Parag Y, Lerman H, Gutman M, Levine C, Rabau M, Figer A, Metser U. Detection of recurrence in patients with rectal cancer: PET/CT after abdominoperineal or anterior resection. Radiology. 2004; 232(3): 815–822.

Fuster D, Maurel J, Muxi A, Setoain X, Ayuso C, Martin F, Ortega M, Fuertes S, Pons F. Is there a role for (99m)Tc-anti-CEA monoclonal antibody imaging in the diagnosis of recurrent colorectal carcinoma? Q J Nucl Med. 2003; 47: 109–115.

Garcia-Aguilar J, Pollack J, Lee S. Accuracy of endorectal ultrasonography in preoperative staging of rectal tumors. Dis Colon Rectum. 2002; 45: 10–15.

Getty D, Seltzer S, Tempany C, Pickett R, Swets J, McNeil B. Prostate cancer: relative effects of demographic, clinical, histologic, and MR imaging variables on the accuracy of staging. Radiology. 1997; 204(2): 471–479.

Giess C, Schwartz L, Bach A , Gollub M, Panicek D. Patterns of neoplastic spread in colorectal cancer: implications for surveillance CT studies. AJR. 1998; 170: 987–991.

Gold D, Halligan S, Kmiot W, Bartram C. Intraobserver and interobserver agreement in anal endosonography. Br J Surg .1999; 86: 371–375.

Goldman S, Arvidsson H, Norming U, Lagerstedt U, Magnusson I, Frisell J. Transrectal ultrasound and computed tomography in preoperative staging of lower rectal adenocarcinoma. Gastrointest Radiol. 1991; 16: 259–263.

Goyen M, Quick H, Debatin J. Whole-body three-dimensional MR angiography with a rolling table platform: initial clinical experience. Radiology. 2002; 224: 270–277.

Grabbe E, Lierse W, Winkler R. The perirectal fascia: morphology and use in staging of rectal carcinoma. Radiology. 1983; 149: 241–246.
Granfield C, Charnsangavej C, Dubrow R. Regional lymph node metastases in carcinoma of the left side of the colon and rectum: CT demonstration. AJR. 1992; 159: 757–764.
Gualdi G, Casciani E, Guadalaxara A, d'Orta C, Polettini E, Pappalardo G. Local staging of rectal cancer with transrectal ultrasound and endorectal magnetic resonance imaging: comparison with histologic findings. Dis Colon Rectum. 2000; 43: 338-345.
Guinet C, Buy J, Ghossain M. Comparison of magnetic resonance imaging and computed tomography in the preoperative staging of rectal cancer. Arch Surg. 1990; 125: 385–388.
Haddock M, Gunderson L, Nelson H. Intraoperative irradiation for locally recurrent colorectal cancer in previously irradiated patients. Int J Radiat Oncol Biol Phys. 2001; 49 (5): 1267–1274.
Harisinghani M, Barentsz J, Hahn P. Noninvasive detection of clinically occult lymph-node metastases in prostate cancer. N Engl J Med. 2003; 348: 2491–2499.
Hata N, Jinzaki M, Kacher D, Cormak R, Gering D, Nabavi A, Silverman S, D'Amico A, Kikinis R, Jolesz F, Tempany C. MR imaging-guided prostate biopsy with surgical navigation software: device validation and feasibility. Radiology. 2001; 220(1): 263–268.
Hawighorst H, Schoenberg SO, Knopp MV, Essig M, Miltner P, van Kaick G. Hepatic lesions: morphologic and functional characterization with multiphase breath-hold 3D gadolinium-enhanced MR angiography. Radiology. 1999; 210: 89–96.
Heald R, Ryall R. Recurrence and survival after total mesorectal excision for rectal cancer. Lancet. 1986; 1: 1479–1482.
Hodgman C, MacCarty R, Wolff B. Preoperative staging of rectal carcinoma by computed tomography and 0.15T magnetic resonance imaging: preliminary report. Dis Colon Rectum. 1986; 29: 446–450.
Holm T, Cedermark B, Rutqvist L. Local recurrence of rectal adenocarcinoma after curative surgery with and without preoperative radiotherapy. Br J Surg. 1994; 81: 452–455.
Holmberg L, Bill-Axelson A, Helgesen F. A randomized trial comparing radical prostatectomy with watchful waiting in early prostate cancer. N Engl J Med. 2002; 347:7 81–789.
Hopper K, Singapuri K, Finkel A. Body CT and oncologic imaging. Radiology. 2000; 215 (1): 27–31.
Horton K, Abrams R, Fishman E. Spiral CT of colon cancer: imaging features and role in management. Radiographics. 2000; 20: 419–430.
Hull G, Rabbani F, Abbas F, Wheeler T, Kattan M, Scardino P. Cancer control with radical prostatectomy alone in 1,000 consecutive patients. J Urol. 2002; 167: 528–534.
Hunerbein M, Pegios W, Rau B, Vogl T, Felix R, Schlag P. Prospective comparison of endorectal ultrasound, three-dimensional endorectal ultrasound, and endorectal MRI in the preoperative evaluation of rectal tumors: preliminary results. Surg Endosc. 2000; 14: 1005–1009.
Ikonen S, Kivisaari L, Vehmas T. Optimal timing of post-biopsy MR imaging of the prostate. Acta Radiol. 2001; 42: 70–73.

Inaba Y, Arai Y, Kanematsu M, Takeuchi Y, Matsueda K, Yasui K. Revealing hepatic metastases from colorectal cancer: value of combined helical CT during arterial portography and CT hepatic arteriography with a unified CT and angiography system. AJR. 2000; 174: 955–961.

Indinnimeo M, Grasso R, Cicchini C. Endorectal magnetic resonance imaging in the preoperative staging of rectal tumors. Int Surg. 1996; 81: 419–422.

Iwamatsu M, Saito T, Matsuguchi T, Tamada R, Soejima K, Inokuchi K. Early detection of recurrence of gastric cancer by serial plasma carcinoembryonic antigen assays. Gastroenterology. 1983; 84(3): 651–653.

Jager G, Barentsz J, Oosterhof G, Witjes J, Ruijs S. Pelvic adenopathy in prostatic and urinary bladder carcinoma: MR imaging with a three-dimensional TI-weighted magnetization-prepared-rapid gradient-echo sequence. AJR. 1996; 167: 1503–1507.

Jager G, Ruijter E, van de Kaa C. Local staging of prostate cancer with endorectal MR imaging: correlation with histopathology. AJR.1996; 166: 845–852.

Jager G, Severens J, Thornbury J, de La Rosette J, Ruijs S, Barentsz J. Prostate cancer staging: should MR imaging be used? A decision analytic approach. Radiology. 2000; 215: 445–451.

Johansson J, Holmberg L, Johansson S, Bergstrom R, Adami H. Fifteen-year survival in prostate cancer: a prospective, population-based study in Sweden. JAMA. 1997; 277: 467–471.

Kalff V, Hicks R, Ware R. The clinical impact of 18F-FDG PET in patients with suspected or confirmed recurrence of colorectal cancer: a prospective study. J Nucl Med. 2002; 43: 492–499.

Karesen R, Hertzberg J, Johannesen J, Thoresen B, Orjasaeter H. Carcinoembryonic antigen in the diagnosis and follow-up of colorectal carcinoma. Am J Proctol Gastroenterol Colon Rectal Surg. 1980; 31(11): 18–22.

Kattan M, Eastham J, Stapleton A, Wheeler T, Scardino P. A preoperative nomogram for disease recurrence following radical prostatectomy for prostate cancer. J Natl Cancer Inst. 1998; 90: 766–771.

Kelvin F, Korobkin M, Heaston D. The pelvis after surgery for rectal carcinoma: Serial CT observations with emphasis on nonneoplastic features. AJR. 1983; 141: 959–962.

Kim H, Kim T, Sung K. CT during Hepatic Arteriography and Portography: An Illustrative Review. Radiographics. 2002; 22(5): 1041–1051.

Kim N, Kim M, Yun S, Sohn S, Min J. Comparative study of transrectal ultrasonography, pelvic computerized tomography, and magnetic resonance imaging in preoperative staging of rectal cancer. Dis Colon Rectum. 1999; 42: 770–775.

Kwok H, Bissett I, Hill G. Preoperative staging of rectal cancer. Int J Colorectal Dis. 2000; 15: 9–20.

Lauenstein T, Goehde S, Herborn C. Three-dimensional volumetric interpolated breath-hold MR imaging for whole-body tumor staging in less than 15 minutes: a feasibility study. AJR. 2002; 179: 445–449.

Lauenstein T, Goehde S, Herborn C, Goyen M, Oberhoff C, Debatin J, Ruehm S, Barkhausen J. Whole-body MR imaging: evaluation of patients for metastases. Radiology. 2004 233(1): 139–148.

Laupacis A, Feeny D, Detsky A, Tugwell P. How attractive does a new technology have to be to warrant adoption and utilization? tentative guidelines for using clinical and economic evaluations. CMAJ. 1992; 146: 473–481.

Lechner P, Lind P, Goldenberg D. Can postoperative surveillance with serial CEA immunoscintigraphy detect resectable rectal cancer recurrence and potentially improve tumor-free survival? J Am Coll Surg. 2000; 191(5): 511–518.
Lohnert M, Doniec J, Henne-Bruns D. Effectiveness of endoluminal sonography in the identification of occult local rectal cancer recurrences. Dis Colon Rectum. 2000; 43(4): 483–491.
Lonneux M, Reffad A, Detry R, Kartheuser A, Gigot J, Pauwels S. FDG-PET improves the staging and selection of patients with recurrent colorectal cancer. Eur J Nucl Med Mol Imaging. 2002; 29: 915–921.
Low R. Magnetic Resonance Imaging of the Abdomen: Applications in the Oncology Patients. Oncology. Suppl. 3. June 2000.
Lu-Yao G, Greenberg E. Changes in prostate cancer incidence and treatment in USA. Lancet. 1994; 343: 251–254.
Lu-Yao G, Yao S. Population-based study of long-term survival in patients with clinically localised prostate cancer. Lancet. 1997; 349: 906–910.
Mach J, Chatal J, Lumbroso J, Buchegger F, Forni M, Ritschard J, Berche C, Douillard J, Carrel S, Herlyn M. Tumor localization in patients by radiolabeled monoclonal antibodies against colon carcinoma.Cancer Res. 1983; 43(11): 5593–5604.
Maldjian C, Smith R, Kilger A, Schnall M, Ginsberg G, Kochman M. Endorectal surface coil MR imaging as a staging technique for rectal carcinoma: a comparison study to rectal endosonography. Abdom Imaging. 2000; 25: 75–80.
Males R, Vigneron D, Star-Lack J. Clinical application of BASING and spectral/spatial water and lipid suppression pulses for prostate cancer staging and localization by in vivo 3D 1H magnetic resonance spectroscopic imaging. Magn Reson Med. 2000; 43: 17–22.
McNeal J, Villers A, Redwine E, Freiha F, Stamey T. Capsular penetration in prostate cancer. Significance for natural history and treatment. Am J Surg Pathol. 1990; 14(3): 240–247.
McNeal J. The zonal anatomy of the prostate. Prostate. 1981; 2: 35–49.
Miller D, Hafez K, Stewart A, Montie J, Wei J. Prostate carcinoma presentation, diagnosis, and staging: an update from the National Cancer Data Base. Cancer. 2003; 98: 1169–1178.
Minagawa M, Makuuchi M, Torzilli G, Takayama T, Kawasaki S, Kosuge T. Extension of the frontiers of surgical indications in the treatment of liver metastases from colorectal cancer: long-term results. Ann Surg. 2000; 231(4): 487–499.
Minsky B. Adjuvant radiation therapy for rectal cancer: is there finally an answer? (editorial). Lancet. 2001; 358: 1285–1286.
Minsky B. Role of adjuvant therapy in adenocarcinoma of the rectum. Semin Surg Oncol. 1999; 17: 189–198.
Moore K, Bokey L, Chapuis P, Tait N. How are we treating patients with hepatic colorectal metastases in Sydney? ANZ J Surg. 2002; 72: 125–130.
Morgan-Parkes J. Metastases: mechanisms, pathways, and cascades. AJR. 1995; 164: 1075–1082.
Naya Y, Babaian R. The predictors of pelvic lymph node metastasis at radical retropubic prostatectomy. J Urol. 2003; 170: 2306–2310.
Obek C, Louis P, Civantos F, Soloway M. Comparison of digital rectal examination and biopsy results with the radical prostatectomy specimen. J Urol. 1999; 161: 494–498.

O'Dowd G, Veltri R, Orozco R, Miller M, Oesterling J. Update on the appropriate staging for newly diagnosed prostate cancer. J Urol. 1998; 158: 687–698.
Ogunbiyi O, McKenna K, Birnbaum E. Aggressive surgical management of recurrent rectal cancer-is it worthwhile? Dis Colon Rectum. 1997; 40 (2): 150–155.
Ogura K, Maekawa S, Okubo K. Dynamic endorectal magnetic resonance imaging for local staging and detection of neurovascular bundle involvement of prostate cancer: correlation with histopathologic results. Urology. 2001; 57: 721–726.
Ohlsson B, Tranberg KG, Lundstedt C, Ekberg H, Hederstrom E. Detection of hepatic metastases in colorectal cancer: a prospective study of laboratory and imaging methods. Eur J Surg. 1993 May; 159(5): 275–281.
Okizuka H, Sugimura K, Ishida T. Preoperative local staging of rectal carcinoma with MR imaging and a rectal balloon. J Magn Reson Imaging. 1993; 3: 329–335.
Olson R, Perecevich N, Malcolm A, Chaffey J, Wilson R. Pattern of recurrence following curative resection of adenocarcinoma of the colon and rectum. Cancer. 1980; 45: 2969–2974.
Outwater E. Ultrafast MR imaging of the pelvis. Eur J Radiol. 1999; 29: 233–234.
Outwater E, Petersen R, Siegelman E, Gomella L, Chernesky C, Mitchell D. Prostate carcinoma: assessment of diagnostic criteria for capsular penetration on endorectal coil MR images. Radiology. 1994; 193:333–339.
Partin A, Borland R, Epstein J, Brendler C. Influence of wide excision of the neuro-vascular bundle(s) on prognosis in men with clinically localized prostate cancer with established capsular penetration. J Urol. 1993; 150: 142–148.
Patt Y, Lamki L, Shanken J, Jessup J, Charnsangavej C, Ajani J. Imaging with Indium 111-labelled anticarcinoembryonic antigen monoclonal antibody ZCE-025 of recurrent colorectal or carcinoembryonic antigen-producing cancer in patients with rising serum carcinoembryonic antigen levels and occult metastases. J. Clin. Oncol. 1990; 8: 1246–1251.
Pegios W, Vogl J, Mack M. MRI diagnosis and staging of rectal carcinoma. Abdom Imaging. 1996; 21: 211–218.
Penna C, Nordlinger B. Surgery of liver metastases from colorectal cancer: new promises. Br Med Bull. 2002; 64: 127–140.
Perrotti M, Kaufman R, Jennings T. Endo-rectal coil magnetic resonance imaging in clinically localized prostate cancer: is it accurate? J Urol. 1996; 156: 106–109.
Physician Data Query (PDQ) of the National Cancer Institute. treatment options for health professionals — prostate cancer 2004. Available at: *http://www.cancer.gov/*.
Pickren J, Tsukada Y, Lane W. Liver metastasis. In: Weiss L, Gilbert HA, eds. Analysis of Autopsy Data. Boston: GK Hall and Company. 1982: 2–18.
Pijl M, Chaoui A, Wahl R, van-Oostayen J. Radiology of colorectal cancer. Eur J Cancer. 2002; 38: 887–898.
Punglia R, D'Amico A, Catalona W, Roehl K, Kuntz K. Effect of verification bias on screening for prostate cancer by measurement of prostate-specific antigen. N Engl J Med. 2003; 349: 335–342.
Quirke P, Durdey P, Dixon M, Williams N. Local recurrence of rectal adenocarcinoma due to inadequate surgical resection: histopathological study of lateral tumor spread and surgical excision. Lancet. 1986; 2: 996–999.
Reinbach D, Mc Gregor J, Dahill S, Docherty J O'Dwyer P. Collagen promotes perianastomotic tumour growth in an experimental animal model. J Surg Oncol. 1995; 60: 112–115.

Reinbach D, Mc Gregor J, Docherty J O'Dwyer P. Effect of suture material on tumour cell adherence at sites of colonic injury. Br J Surg. 1993; 80: 774–776.
Rifkin M, Ehrlich S, Marks G. Staging of rectal carcinoma: prospective comparison of endorectal US and CT. Radiology. 1989; 170: 319–322.
Robinson P**.** The early detection of liver metastases. Cancer Imaging. 2002; 2: 1–3.
Rotondano G, Esposito P, Pellecchia L, Novi A, Romano G. Early detection of locally recurrent rectal cancer by endosonography . BJR. 1997;70: 567–571.
Rotte K, Kluhs L, Kleinau H, Kriedemann E. Computed tomography and endosonography in the preoperative staging of rectal carcinoma. Eur J Radiol. 1989; 9: 187–190.
Ruehm S, Goyen M, Quick H. Whole-body MRA on a rolling table platform (Angio-SURF). Rofo Fortschr Geb Rontgenstr Neuen Bildgeb Verfahr. 2000; 172: 670–674.
Sagar P, Pemberton J. Surgical management of locally recurrent rectal cancer. Br J Surg.1996; 83: 293–304.
Said B, McCart J, Libutti S, Choyke P. Ferumoxide-enhanced MRI in patients with colorectal cancer and rising CEA: surgical correlation in early recurrence. Magn Reson Imaging. 2000; 18(3): 305–309.
Scheele J, Stang R, Altendorf-Hofmann A, Paul M. Resection of colorectal liver metastases. World J Surg. 1995; 19(1): 59–71.
Scheidler J, Hricak H, Vigneron D. Prostate cancer: localization with three-dimensional proton MR spectroscopic imaging — clinicopathologic study. Radiology. 1999; 213: 473–480.
Schnall M, Furth E, Rosato E, Kressel H. Rectal tumor stage: correlation of endorectal MR imaging and pathologic findings. Radiology. 1994; 190: 709–714.
Schnall M, Imai Y, Tomaszewski J, Pollack H, Lenkinski R, Kressel H. Prostate cancer: local staging with endorectal surface coil MR imaging. Radiology. 1991; 178: 797–802.
Semelka R, Balci N, Op De Beeck B, Reinhold C Evaluation of a 10 — minute comprehensive MR Imaging Examination of the upper abdomen. Radiology. 1999; 211: 189–195.
Serafini A, Klein J, Wolff B, Baum R, Chetanneau A, Pecking A, Fischman A, Hoover H, Wynant G, Subramanian R, Goroff D, Hanna M. Radioimmunoscintigraphy of recurrent, metastatic, or occult colorectal cancer with technetium 99m-labeled totally human monoclonal antibody 88BV59: results of pivotal, phase III multicenter studies. J Clin Oncol. 1998; 16(5): 1777–1787.
Shank B, Dershaw D, Caravelli J, Barth J, Enker W. A prospective study of the accuracy of preoperative computed tomographic staging of patients with biopsy-proven rectal carcinoma. Dis Colon Rectum. 1990; 33: 285–290.
Sheele J, Stangl R, Altendorf-Hofmann A. Hepatic metastases from colorectal carcinoma: impact of surgical resection on the natural history.Br J Surg. 1990; 77: 1241–1246.
Solbiati L, Tonolini M, Cova L. Goldberg S. The role of the contrast-enhanced ultrasound in the detection of focal liver lesions. Eur Radiol. 2001; 11 Suppl 3: 15–26.
Solomon M, McLeod R, Cohen E, Simons M, Wilson S. Reliability and validity studies of endoluminal ultrasonography for anorectal disorders. Dis Colon Rectum. 1994; 37: 546–551.
Solomon M, McLeod R. Endoluminal transrectal ultrasonography: accuracy, reliability, and validity. Dis Colon Rectum .1993; 36: 200–205.

Star-Lack J, Nelson S, Kurhanewicz J, Huang L, Vigneron D. Improved water and lipid suppression for 3D PRESS CSI using RF band-selective inversion with gradient dephasing (BASING). Magn Reson Med. 1997; 38: 311–321.

Steinberg D, Sauvageot J, Piantadosi S, Epstein J. Correlation of prostate needle biopsy and radical prostatectomy Gleason grade in academic and community settings. Am J Surg Pathol. 1997; 21: 566–576.

Stomper P, D'Souza D, Bakshi S, Rodriguez-Bigas M, Burke P, Petrelli N. Detection of pelvic recurrence of colorectal carcinoma: prospective, blinded comparison of Tc-99m-IMMU-4 monoclonal antibody scanning and CT. Radiology. 1995; 197(3): 688–692.

Stuckle C. Recurrent rectal cancer: diagnosis by contrast enhancement in MD-CT. Radiologe. 2004 Dec 31; (Epub ahead of print).

Swedish Rectal Cancer Trial. Improved survival with preoperative radiotherapy in resectable rectal cancer. N Engl J Med. 1997; 336: 980–987.

Swindle P, McCredie S, Russell P, Himmelreich U, Khadra M, Lean C, Mountford C.Pathologic characterization of human prostate tissue with proton MR spectroscopy. Radiology. 2003; 228(1): 144–151.

Thoeni R, Moss A, Schnyder P, Margulis A. Detection and staging of primary rectal and rectosigmoid cancer by computed tomography. Radiology. 1981; 141: 135–138.

Thoeni R. Colorectal cancer: radiologic staging. Radiol Clin North Am. 1997; 35: 457–485.

Torricelli P, Pecchi A, Luppi G, Romagnoli Gadolinium-enhanced MRI with dynamic evaluation in diagnosing the local recurrence of rectal cancer. Abdom Imaging. 2003; 28(1): 19–27.

Turk P, Wanebo H. Results of surgical treatment of nonhepatic recurrence of colorectal carcinoma. Cancer. 1993; 71: 4267–4277.

Valls C, Andia E, Sanchez A, Guma A, Figueras J, Torras J. Hepatic metastases from colorectal cancer: preoperative detection and assessment of respectability with helical CT. Radiology. 2001; 218: 55–60.

Van den Brekel M. Lymph node metastases: CT and MRI. Eur J Radiol. 2000; 33: 230–238.

Vliegen R, Beets G, Kessels A. Magnetic resonance imaging in staging rectal cancer: is gadolinium helpful? Radiology. 2002; 205: 244–245.

Vogl T, Schwarz W, Blume S, Pietsch M, Shamsi, Franz K. Preoperative evaluation of malignant liver tumours: comparison of unenhanced and SPIO (Resovist)-enhanced MR imaging with biphasic CTAP and intraoperative US. Eur Radiol. 2003; 13: 262–272.

Wade T, Virgo K, Li M, Callander P, longo W, Johnson F. Outcomes after detection of metastatic carcinoma of the colon and rectum in a national hospital system. J Am Surg. 1996; 182: 353–361.

Watanabe M, Sugimura K, Kuroda S, Okizuka H, Ishida T. CT assessment of post-radiation changes in the rectum and perirectal region. Clin Imaging. 1995; 19: 182–187.

Wefer A, Hricak H, Vigneron D. Sextant localization of prostate cancer: comparison of sextant biopsy, magnetic resonance imaging and magnetic resonance spectroscopic imaging with step section histology. J Urol. 2000; 164: 400–404.

White S, Hricak H, Forstner R. Prostate cancer: effect of postbiopsy hemorrhage on interpretation of MR images. Radiology. 1995; 195: 385–390.

World Health Organization. Press release: cancer toll can be reduced dramatically. October 16, 1998; 72.

Wymenga L, Boomsma J, Groenier K, Piers D, Mensink H. Routine bone scans in patients with prostate cancer related to serum prostate-specific antigen and alkaline phosphatase. BJU Int. 2001; 88: 226–230.

Yu K, Hricak H, Alagappan R, Chernoff D, Bacchetti P, Zaloudek C. Detection of extracapsular extension of prostate carcinoma with endorectal and phased-array coil MR imaging: multivariate feature analysis. Radiology, 1996; 202: 697–702.

Zagoria R, Schlarb C, Ott D. Assessment of rectal tumor infiltration utilizing endorectal MR imaging and comparison with endoscopic rectal sonography. J Surg Oncol. 1997; 64: 312–317.

Zakian K, Eberhardt S, Hricak H. Transition zone prostate cancer: metabolic characteristics at 1H MR spectroscopic imaging — initial results. Radiology. 2003; 229: 241–247.

Zakian K, Sircar K, Hricak H. Correlation of proton MR spectroscopic imaging with Gleason score based on step-section pathology after radical prostatectomy. Radiology. 2002; 225: 628–629.

Zerhouni E, Rutter C, Hamilton S, Balfe D, Megibow A, Francis I, Moss A, Heiken J, Tempany C, Aisen A, Weinreb J, Gatsonis C, McNeil B. CT and MR imaging in the staging of colorectal carcinoma: report of the Radiology Diagnostic Oncology Group II. Radiology. 1996; 200 (2): 443–451.

SUMMARY IN ESTONIAN

Radioloogiline kihtdiagnostika vaagna pahaloomuliste kasvajate ulatuse ravieelsel määramisel ja ravijärgsel jälgimisel

Pahaloomulised kasvajad on surmapõhjustena sageduselt teisel kohal. Kirjanduse andmeil sageneb elanikkonnas haigestumus jämesoolevähki, ka eesnäärmevähi haigestumusnäitajad on tõusuteel. Vähi korral sõltub sobiva ravimeetodi valik ja haige prognoos suurel määral kasvaja levikuulatusest diagnoosimishetkel. Seetõttu on kasvaja staadiumi ravieelse määramise täpsus oluline. Ka ravijärgsel jälgimisel võimalikult vara avastatud metastaasid või retsidiiv võivad haiguse kulgu otsustavalt mõjutada.

Kasvaja staadiumi määramisel, metastaaside ja retsidiivi avastamisel ja hindamisel on laialdaselt kasutusel kihtdiagnostilised uurimismeetodid. Ultraheliuuring (UH) kui esmane kõhupiirkonna radioloogiline uuring on tõestanud oma efektiivsust paljude onkoloogiliste probleemide lahendamiseks, kuid ei saa oma mitmete puuduste tõttu olla abiks pahaloomulise haiguse leviku täpsel määramisel. Kompuutertomograafia (KT) on saanud suhtelise lihtsuse ja universaalsuse tõttu valikmeetodiks paljude kasvajapaikmete jaoks. KT-l ilmestuvad suurepäraselt suure tihedusediferentsiga koed, kuid vaatamata kontrastvahendite kasutamisele on pehmete kudede eraldusvõime kesine. Magnetresonantstomograafia (MRT) kiire areng on esile toonud selle suure potentsiaali mitmes piirkonnas, laieneb ka MRT kasutamine mitmesuguste vaagna piirkonna haiguste uurimisel. Ka isotoopdiagnostika on väga lootustandev radioloogiaharu, sellega saadav unikaalne bioloogilist laadi informatsioon võimaldab iseloomustada kudesid funktsionaalselt, mis võib anatoomilistele diagnostikameetoditele anda olulist lisateavet.

Peamised **soolevähi** ravitulemusi halvendavad tegurid on kalduvus lokaalretsidiividele (LR) ja sage metastaseerumine maksa. Et LR pole sugugi harv ja selle ravis on kõige tulemuslikum operatsioon koos intraoperatiivse radioteraapiaga võib radioloogilisel uurimisel olla kirurgilise ravi kandidaatide valikul otsustav osa. Pärasoolevähi LR diagnoosimine on üks keerulisemaid ülesandeid onkoloogilises diagnostikas. Vaagna komplitseeritud anatoomia on varjatud massiivse luulise ümbrisega ja raskelt uuritav. Veelgi keerulisemaks muutub olukord, kui on tekkinud olulisi muudatusi varasemast operatsioonist või kiiritusjärgsest fibroosist. Kuna anatoomiliste uurimismeetoditega on raske eristada fibroosi LR-st on suuri lootusi pandud funktsionaalsetele meetoditele, CEA-stsintigraafiale ja viimasel ajal ka positronemissioontomograafiale (PET-le), mis annavad teistlaadset- bioloogilist informatsiooni. Et funktsionaalsed uurimismeetodid ei ole seni laialdast kasutust leidnud seadsimegi üheks oma töö eesmärgiks uurida, kuivõrd olulist lisainformatsiooni KT-le ja/või MRT-le annab LR korral IS.

Teadaolevalt on maks mitmete pahaloomuliste kasvajate, sealhulgas **soolevähi**, sage metastaseerumispaik. Maksametastaaside võimalikult varajane avastamine on üks olulisemaid onkoloogilisi probleeme, kiire ja lihtsa meetodi otsingud selleks otstarbeks jätkuvad. MRT suurenev kättesaadavus ja pidev tehnoloogiline areng ahvatleb ette võtma järjest uusi diagnostilisi rakendusi. Ka meie seadsime oma uurimistöö üheks eesmärgiks hinnata üksiku MRT sekventsi sobivust maksametastaaside avastamiseks. Pidades silmas, et maksametastaasid on soolevähi korral sageli ainsaks metastaasipaikmeks ja nende radikaalse resektsiooni puhul paraneb valitud haigete prognoos oluliselt, tuleks operatsioonikandidaatide selektsioonile pöörata suuremat tähelepanu. Kuna valik põhineb suures osas radioloogilistel kihtdiagnostilistel uuringutel ja senini puuduvad ühtsed hindamis- ja valikukriteeriumid otsustasime oma uurimistöö ühes osas analüüsida taoliste kriteeriumite rakendatavust maksametastaasidega soolevähihaigetel.

Eesnäärmevähi lokaalne levikuulatus on määrava tähtsusega ravi valikul. Radikaalne operatiivne ravi on intrakapsulaarse protsessi korral saanud valikmeetodiks, kuid tänaseni kasutusel olnud kliinilised- ega radioloogilised uurimismeetodid pole staadiumi määramisel olnud piisavalt täpsed. Kaasaegse, 1,5 T magnetvälja tugevusega MRT seadme ja kliinilise vajaduse olemasolu ajendasid läbi viima uurimistööd eesnäärmevähi lokaalse levikuulatuse määramiseks MRT-l kasutades selleks uudset kehavälist faseeritud elastset mähist.

Uurimistöö eesmärgid

Uurimistöös seati eesmärgiks hinnata tänapäeval kasutatavate radioloogiliste meetodite KT, MRT ja CEA-antikehadega stsintigraafia diagnostilist väärtust mõnede vaagna levinenumate pahaloomuliste kasvajatega seotud probleemsetes lõikudes. Täpsustatult oli sihiks leida vastused järgmistele küsimustele:

- Kas funktsionaalne uurimismeetod CEA-stsintigraafia võimaldab pärasoolevähi LR näite põhjal anda diagnostilist lisainformatsiooni anatoomilistele uurimismeetoditele KT-le ja MRT-le pahaloomulise haiguse avastamisel ja selle staadiumi määramisel? (I)
- Kas üksik kontrastita aksiaalne T2 kaalutud FSE MRT sekvents, lisatult detailsele vaagna pahaloomulise kasvaja MRT uuringuprotokollile, on sobiv ülakõhu skriiningmeetodiks maksametastaaside avastamiseks? (II)
- Kas maksametastaasidega jämesoolevähihaigete ravi valikut ja kliinilist käsitlemist on võimalik parandada? (III)
- Kas elastse kehavälise faseeritud mähisega MRT uuring on usaldusväärne meetod eesnäärmevähi lokaalleviku operatsioonieelsel määramisel? (IV)

Patsiendid ja metoodika

Kogu uurimistöö põhineb nelja eraldioleva patsientide rühma andmetel. Esimeses publikatsioonis on hinnatud 46 kliiniliselt kahtlustatud pärasoolevähi LR-ga haige KT, MRT ja kartsinoembrüonaalsete antikehadega (CEA)-stsintigraafia uuringute tulemusi. Isotoopstsintigraafia (IS) uuring tehti gamma kaameraga (400 AZ Maxicamera [GE] või BIAD XLT [Trionix]) 18-24 h peale 1000 Mbq ^{99m}Tc (Scintimun CEA, BW) märgistatud hiire anti-CEA monoklonaalsete antikehade i.v. injektsiooni. MRT uuring viidi läbi 1,5 T väljatugevusega mitmemähiselisel seadmel (Signa Advantage [General Electric] ja KT uuringud kas Toshiba TCT 600S või Siemens Somatom HiQ skanneril. Eesmärk oli selgitada välja, kas IS-l saadav informatsioon annab olulist lisateavet KT-le ja MRT-le pärasoolevähi LR avastamisel ja levikuulatuse määramisel. Radioloogiliste uuringute tulemuste kontroll 38 verifitseeritud LR puhul viidi läbi operatsiooniandmete (25 haiget), biopsia (7patsienti) ning jälgimisel saadud andmete alusel (6 haiget).

II publikatsioonis hinnati 111 vaagna pahaloomulise kasvajaga (neist 84 rektumi või sigmasoole vähiga) patsiendi vaagna detailse MRT uuringu järel ülakõhust tehtud üksiku lisasekventsi diagnostilist väärtust. Eelkõige maksametastaaside, kuid ka teiste intraabdominaalsete siirete avastamiseks võeti 1,5 T väljatugevusega mitmemähiselisel seadmel (Signa Advantage [General Electric]) täiendavalt kasutusele T2 kaalutud aksiaalne *fast spin echo* (FSE) sekvents (TR 2500-12500 ms, TE 126 ms, ETL 8, kiht/interval 10/2,5 mm), selle täpsus määrati saadud tulemuste kõrvutamisega operatsioonileiuga (55 haiget) või ravijärgse jälgimise tulemustega (56 haiget).

Populatsioonipõhine uurimus (III publikatsioon) hõlmas 2280 maksametastaasidega soolevähihaige käsitlemist Stockholm-Gotlandi piirkonnas. Analüüsimisel võrreldi uuritute elunemusnäitajaid sõltuvalt rakendatud ravist. Metastaaside resektaabelsuse määramiseks ja kirurgilise ravi kandidaatide valikuks taashinnati KT ja MRT uuringukujutised kasutades kindlaksmääratud kriteeriume.

Neljandas uurimistöös analüüsisime kehavälise faseeritud mähisega MRT uuringu efektiivsust prostata kartsinoomi lokaalleviku määramisel, kusjuures eriline tähelepanu oli pööratud operatsiooniks olulisemate faktorite: ekstrakapsulaarse leviku, naaberkudede haaratuse ja regionaalmetastaaside diagnoosimisele. Publikatsioon põhineb 26 järjestikusel opereeritud ja MRT-l uuritud morfoloogiliselt verifitseeritud prostata kartsinoomi haige andmetel. Uuringunäidustusteks oli kõrge või keskmine risk T3 staadiumile (PSA 10–20 ng/ml, Gleason'i näit 5–7, palpeeritav tuumor ja teadaolevate kaugmetastaaside puudumine). MRT uuringud tehti kaasaegsel 1,5 T skanneril (Magnetom "Symphony") kasutades uudset elastset kehavälist faseeritud mähist ja standardiseeritud uuringuprotokolli, tulemused kõrvutati operatsiooni ja pato-histoloogia andmetega. Statistiliseks töötluseks sisestati saadud andmed arvuti

andmebaasi ("Statistica" programm), kasutati kirjeldavat statistikat, t-testi, Kaplan-Meier analüüsi.

Uurimistööst tulenevad järeldused

CEA- stsintigraafia ei anna pärasoolevähi LR avastamisel ja selle staadiumi määramisel olulist diagnostilist lisainformatsiooni anatoomilistele uurimismeetoditele KT-le ja MRT-le. Siiski võiks CEA-stsintigraafia kasutamist kaaluda sel osal haigetest, kellel on kliiniliselt oluline kahtlus LR-le, kuid KT/MRT uuring seda ei kinnita (I).

Aksiaalne T2-kaalutud FSE MRT uuring ülakõhust lisatuna vaagna kõrgeraldusvõimega MRT uuringule on arvestatava tundlikkusega meetod maksametastaaside avastamiseks vaagna pahaloomuliste kasvajatega haigetel, kuid ei asenda maksa eriuuringuid (II).

Maksametastaasidega jämesoolevähihaigete käsitlemist on võimalik parandada. KT/MRT kujutiste läbivaatamisel selgus, et 10% maksametastaasidega jämesoolelvähi haigetest olid metastaasid resetseeritavad, kuid ainult 4%-l kõigist maksametastaasidega haigetest tehti maksa resektsioon. Seega tehti maksa resektsioon alla 50% haigetest, kes uurimismomendil võinuks olla operatsioonikandidaadid (III).

Vaagna MRT uuring eesnäärmevähi lokaalleviku määramisel kehavälise faseeritud spetsiaalmähisega on efektiivne ekstrakapsulaarse leviku kindlakstegemisel, kuid pole piisavalt täpne avastamaks kapsli varajast haaratust (3a staadium). Lisaks võib MRT uuring olla kasuks biopsia juhtimisel juhul, kui varasemad biopsiad kliiniliselt olulise eesnäärmevähi kahtlusega haigel on olnud negatiivsed (IV).

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PUBLICATIONS

SINGLE SEQUENCE SCREENING FOR LIVER METASTASES AS ADDITION TO HIGH RESOLUTION PELVIC MRI

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Abstract

Objective: To investigate the diagnostic value of T2-weighted magnetic resonance (MR) imaging in the screening for liver metastases (LM).

Materials and Methods: In 111 consecutive patients with pelvic malignancy after pelvic imaging with a multicoil-array on a 1,5 T system, the upper abdomen was additionally examined with a single unenhanced axial T2-weighted fast spin-echo (FSE) sequence (TR 2500–12500 ms, TE 126 ms, echo-train length 8, slice thickness/interval 10/2,5 mm). All images were retrospectively evaluated and compared to surgical verification in 55 patients and with radiological follow-up for a minimum of 1,5 years in 56 cases.

Results: Verified LM was detected in 15 of 18 patients by the T2-weighted screening sequence. In two patients LM were not detected and in one patient a LM was misinterpreted as a benign liver cyst. Three false-positive diagnoses occurred where LM suspected by MR were proven to be benign liver cysts in two cases and haemangioma in one patient on radiological follow-up.

Conclusion: When performing pelvic MRI, screening for liver metastases with a single T2-weighted sequence of the upper abdomen with the body coil is feasible but all focal liver lesions (FLL) can not be detected or characterised with this single sequence.

Key words: liver; metastases; MR-imaging: fast spin-echo

Introduction

In the evaluation of patients with pelvic malignancy, the local tumour extent as well as distant tumour spread is needed for staging and to select appropriate treatment. Among malignant tumours within the pelvis, recto-sigmoid cancer is one of the most common. These tumours frequently metastasise to the liver and surgical removal of these metastases may in selected cases improve patient outcome.

Ultrasonography (US) and CT are both being used as first line methods for detection of metastases to the liver, retroperitoneum and abdominal cavity (6, 7).

MR imaging is becoming increasingly available and has evolved as a state-of-the-art imaging modality for patients with malignant tumours within the abdomen and pelvis (2, 9, 10, 11). Combining the evaluation of local tumour spread in the pelvis with evaluating for probable liver metastases (LM) in the same session would be of interest, but despite improvements in scanning techniques, such protocols have until recently not been feasible because of the design of pulse sequences, body phased-array surface coils and scanning table constructions. Some investigators have proposed dedicated short MR examination protocols in the screening of the upper abdomen for LM and other pathological findings (3, 5, 13).

The aim of this study was to retrospectively investigate the diagnostic performance of one single sequence T2-weighted FSE of the upper abdomen for the diagnosis of LM among patients examined with pelvic MRI for tumours within the pelvis..

Material and methods

Patients: One hundred and fifty one consecutive patient examined with pelvic MR imaging between January 1996 and December 1998 were included. Forty patients were excluded from the review: nine because examination of non-malignant pelvic disease, 14 patients with examination of the upper abdomen with more than an axial T 2-weighted sequence, 12 cases without surgical control or radiological follow-up and 5 patients that presented with LM later than three months after negative MR screening.

Thus 111 patients with primary malignant pelvic tumours, 53 women and 58 men with a median age 64 years (14–92) were evaluated. The clinical diagnoses in the series are presented in table 1.

Fifty-five examinations were performed preoperatively as a part of initial staging and 56 as post-treatment follow-up.

MR examination protocol: MRI was performed on a 1,5 T system (Signa Advantage, General Electric, Milwaukee, U.S.A.). After dedicated pelvic imaging with a multicoil array, all patients were additionally examined with

axial T2-weighted FSE sequence from diaphragm to the promontory using the body coil. The pulse sequence parameters for the sequence were: TR 2500–12500 ms depending on the number of sections necessary and the respiratory rate, TE 126 ms, echo-train length 8 and number of excitations 2–4. Matrix size was 256 × 192–224. Field-of-view (FOV) was adjusted according to patient size 320–430 mm × 240–320 mm (¾ FOV applied in the direction of the frequency encoded axis). The slice thickness was 10 mm and interslice gap 2,5 mm.

The average total scanning time calculated as a sum of the imaging sequences was 50 minutes and the time for the additional T2 weighted axial screening sequence was in average 7 minutes.

Image analysis: Axial T2 weighted images of the upper abdomen were retrospectively evaluated by one certified radiologist (V.J.) being informed only about the diagnosis of pelvic malignancy. The reviewer finally compared the findings with those in the prospective radiological report for each examination. If a disagreement was found, the reviewer reassessed these images to explore the reason for disagreement and changed the final report from his review based on his reassessment.

Imaging criteria

Diagnostic criteria for LM were any predominantly hyperintense focal lesion with indistinct, irregular borders, and inhomogeneous internal structure.

Liver haemangiomas or benign liver cysts were defined as round or lobulated lesions with sharp margins and high signal intensity on T2-weighted MR-images. Liver cysts were defined on CT as rounded lesions with sharp margins and no contrast enhancement and on ultrasound anechoic focal lesions within the liver. Liver haemangiomas were diagnosed in case of well defined lesions with characteristic fill-in pattern of contrast enhancement on CT and high echogenicity on ultrasound.

Extrahepatic metastases were defined as lymph nodes exceeding 10 mm in short axis diameter. Peritoneal tumour spread was defined as either intra-abdominal collections of increased fluid, nodules or other mass lesions within the peritoneal space.

Follow-up

The findings from the T2-weighted sequence were checked for the best possible verification available starting with histopathology to surgery followed by radiological follow-up with magnetic resonance imaging, contrast enhanced computed tomography or ultrasound in descending order. For verification of benign haemangiomas and cysts, typical appearance and no increase in size on follow-up ultrasound or CT was regarded as verification.

Results

Eighteen patients, fifteen of these with colorectal cancer, had LM verified at surgery and histology (11 patients), by fine needle biopsy (4 patients) or on radiological follow-up within up to 1,5 years after MR (3 patients).

These LM were diagnosed on the T2-weighted sequence in fifteen cases (table 2). In one patient with no LM found on the T2-weighted sequence but LM later verified at laparotomy, a possible LM could be detected at a second review with knowledge of the surgical findings (figure 1). LM below 2 cm in diameter were reported at US examination two months after the MR screening in another patient. This case was considered also false negative because these LM were interpreted as cysts during review of the MR images.

Hyperintense FLL on the T2-weighted sequence were misinterpreted as metastases in three patients. One of these lesions proved to be a small haemangioma (figure 2 a–c) and the two other were benign liver cysts; all with a typical US appearance and no change in lesion size or structure during 1,5 years follow-up.

However, the T2-weighted sequence enabled detection of extrahepatic metastases in 12 patients (table 3) later proven by follow up: in retroperitoneal lymph nodes (6 patients), peritoneal carcinomatoses with ascites (3 cases) and in solitary patients pleural, soft tissue, splenic and skeletal metastases .

Benign FLL (cysts in 21 and haemangiomas in 6 patients) were additionally detected in 27 patients on the T2-weighted screening MR sequence.

Discussion

Despite the limited upper abdominal MR-imaging protocol in this study, liver metastases could be demonstrated by a single T2-weighted sequence performed as an adjunct to pelvic MRI. LM were diagnosed in fifteen out of later totally verified 18 patients.

Magnetic resonance imaging protocols have traditionally been focussed on either the upper or the lower abdomen for oncologic staging. The purpose of this study was to find out what could be detected by one single MR-sequence of one abdominal region when performing a detailed examination of the other.

For detection of FLL multi-detector spiral CT with imaging at different delays after contrast media injection is today regarded as a golden standard. Short examination time, large anatomical coverage, technical robustness, standardised examination protocols and wide availability of equipment explain the wide usage of helical contrast enhanced multi-detector CT for cancer staging (7).

What is the performance of dedicated liver imaging? One study (12) showed 75% sensitivity in detection of LM from colorectal cancer by dual-phase contrast-enhanced CT compared to intra-operative ultrasonography (IOUS),

which for many years has been considered as a gold standard method for this purpose (4). Other investigators report overall LM detection rate of 85% correlated to IOUS and histopathology using portal-phase contrast-enhanced CT (17). Inaba *et al.* (8) used a unified CT and angiography system and achieved during arterial portography and CT hepatic arteriography in preoperative examinations of forty-five patients 87% relative sensitivity. Even higher sensitivity and specificity can probably be achieved with using liver specific contrast agents in MR-imaging (18) and contrast enhanced ultrasonography is also evolving as a very promising method for detection of hepatic metastases (15)

Is it possible to perform a comprehensive examination of the liver in a pelvic MR-imaging protocol? It is reported to be possible to perform comprehensive body MR examinations in 10 minutes (13). However, in general practice, MR-imaging still has limitations as a screening method due to complexity of combining dedicated protocols for different anatomic areas such as the pelvis and upper abdomen, especially when dedicated surface coils and contrast media are used. For this reason, only one single sequence of the upper abdomen was performed in this patient series not to compromise the quality of the pelvic examination. The additional sequence prolonged the pelvic examination time in average 16%.

When considering the detection of metastases with a T2-weighted sequence in our study one must take into consideration the heterogeneous follow-up methods available in the material which did not include dedicated liver examinations such as IOUS or contrast enhanced ultrasonography of the liver. For this reason, some small liver metastases may also have been unrecognised by follow-up used as our standard of reference. Furthermore, lesion characterisation by the T2-weighted sequence in our study was not accurate in all cases. According to follow-up data, one liver lesion diagnosed on MR as cyst appeared to be LM according to follow-up. In twenty-seven patients, benign FLL were correctly identified but in three patients, LM was suggested on the T2-weighted sequence, which later turned out to be benign focal liver lesions.

Our results must also be considered against the fact this group of patients was selected based the oncologic referrals we received during this time and may not reflect the distribution of patients in a general oncologic referral.

There are some further limitations. First, the number of patients with LM was too small to make valid statistical conclusions. We only attempted to find out how this sequence preformed based on data that became available from the time when it was used. Furthermore, ultrafast imaging sequences, such as half-fourier single shot turbo spin echo (HASTE) techniques may further reduce scanning times compared to FSE imaging (14). These sequences were not available at our institution by the time of the study. Using these sequences, especially in combination with phased-array coils with large anatomical coverage, thin-slice T1-weighted volume interpolated breath-hold gradient-echo sequences (16), and parallel imaging (19), MR imaging with phased-array coils

and a moving table (1) or phased-array coils with more extensive coverage, the efficacy of whole abdominal MR protocols may be improved. The slice thickness of 10 mm that was used in this study is rather thick which may leave small metastases undetected. Additional T2-weighted images of the liver with longer echo-time might also have further improved characterisation of cysts and haemangiomas in our study.

Magnetic resonance imaging should be regarded as a complementary examination to CT and US for screening of abdominal metastases. Developments of scanner hardware and refinements in imaging sequences, particularly in respect to fast standardised imaging techniques that potentially enable complete coverage of large body areas in one examination as well as increased availability of scanners, will affect the role of MR in this respect.

Our results demonstrate that axial T2-weighted FSE MR imaging of the upper abdomen using the body coil as adjunct to high resolution pelvic MRI can be used for screening of LM in patients with pelvic malignancies. It cannot, however, be a substitute for dedicated liver imaging.

REFERENCES

1. Barkhausen J, Quick H, Lauenstein T, Goyen M, Ruehm S, Laub G, Debatin J, Ladd M. Whole-body MR imaging in 30 seconds with real-time true FISP and a continuously rolling table platform: feasibility study. Radiology 220 (2001), 252–256
2. Blomqvist L, Hindmarsh T Magnettresonanstomografi av lilla bäckenet. Klinisk förankring i otakt med tekniken. Läkartidningen 94 (1997), 4765–4769
3. Bosmans H, Van Hoe L, Gryspeerdt S, Kiefer B, Van Steenberg W, Baert A, Marchal G. Single shot T2 — weighted MR imaging of the upper abdomen: preliminary experience with double-echo HASTE technique. AJR 169 (1997), 1291–1295
4. Cervone A, Sardi A, Conaway G Intraoperative ultrasound (IOUS) is essential in the management of metastatic colorectal liver lesions. Am Surg. 66 (2000), 611–615
5. De Jaegere, Van Hoe L, Van Steenbergen W, Van Cutsem E, Bosmans H, Heindryckx E, et al. Screening applications for MRI in the detection of upper abdominal disease: comparative study of non-contrast-enhanced single-shot MRI and contrast-enhanced helical CT. Eur Radiol 9 (1999), 853–861
6. Giess C, Schwartz L, Bach A, Gollub M, Panicek D. Patterns of neoplastic spread in colorectal cancer: implications for surveillance CT studies. AJR 170 (1998), 987–991
7. Nelson, R C. Spielmann, A L. Liver imaging with multidetector helical computed tomography. 27 Suppl 1 (2003), 9–16
8. Inaba Y, Arai Y, Kanematsu M, Takeuchi Y, Matsueda K, Yasui K, et al. Revealing hepatic metastases from colorectal cancer: value of combined helical CT during arterial portography and CT hepatic arteriography with a unified CT and angiography system. AJR 174 (2000), 955–61
9. Low R Magnetic Resonance Imaging of the Abdomen: Applications in the Oncology Patients. Oncology. Suppl. 3 (2000)

10. Outwater E Ultrafast MR imaging of the pelvis. Eur Radiol 29: (1999) 233–244
11. Scheidler J, Reiser M MRI of the female and male pelvis: current and future applications of contrast enhancement. Eur Radiol 34 (2000), 220–228
12. Scott DJ, Guthrie JA, Arnold P, Ward J, Atchley J, Wilson D, et al. Dual phase helical CT versus portal venous phase CT for the detection of colorectal liver metastases: correlation with intra-operative sonography, surgical and pathological findings. Clin Radiol. 56 (2001), 235–242
13. Semelka R, Balci N, Op De Beeck B, Reinhold C Evaluation of a 10 — minute comprehensive MR Imaging Examination of the upper abdomen. Radiology 211 (1999), 189–195
14. Semelka R, Kelekis N, Thomasson D, Brown M, Laub G HASTE MR imaging description of technique and preliminary results in the abdomen. J Magn Reson Imaging 6 (1996), 698–699
15. Solbiati L, Tonolini M, Cova L. Goldberg S The role of the contrast-enhanced ultrasound in the detection of focal liver lesions. Eur Radiol 2001; 11 Suppl 3:E 15–26
16. Rofsky N, Lee V, Laub G, Pollack M, Krinsky G, Thomasson D, et al. Abdominal MR imaging with a volumetric interpolated breath-hold examination. Radiology 212 (1999), 876–884
17. Valls C, Andia E, Sanchez A, Guma A, Figueras J, Torras J, et al. Hepatic metastases from colorectal cancer: preoperative detection and assessment of resectability with helical CT. Radiology. 218 (2001), 55–60
18. Vogl T, Schwarz W, Blume S, Pietsch M, Shamsi, Franz K, et al. Preoperative evaluation of malignant liver tumours: comparison of unenhanced and SPIO (Resovist)-enhanced MR imaging with biphasic CTAP and intraoperative US. Eur Radiol (13(2)) 2003 pp 262–272
19. Wang Y. Description of parallel imaging in MRI using multiple coils Magn Reson Med. 44 (2000), 495–499

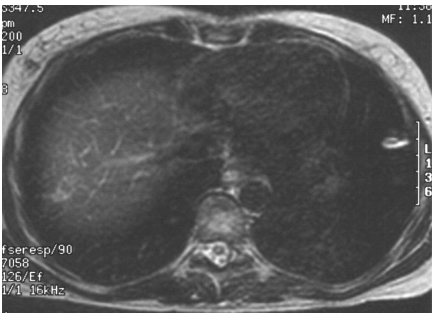

Figure 1. Axial unenhanced T2 weighted FSE image in a patient with rectal cancer examined preoperatively judged as free from LM. At subsequent surgery, LM close to the diaphragm were found. With knowledge of the surgical findings, one 8 mm moderately hyperintense lesion can be seen in the right liver lobe (black arrow).

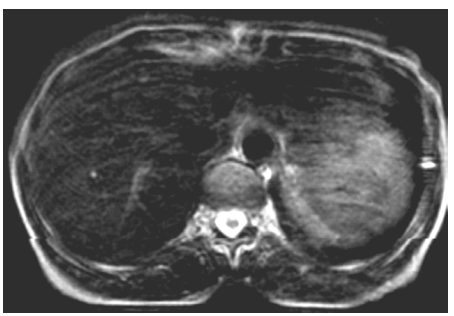

Figure 2a.

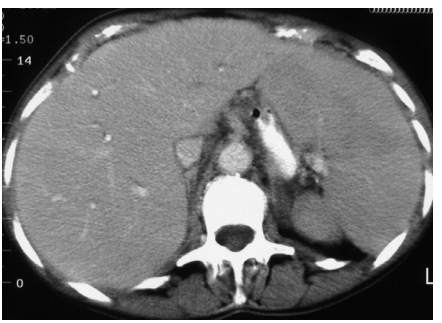

Figure 2b.

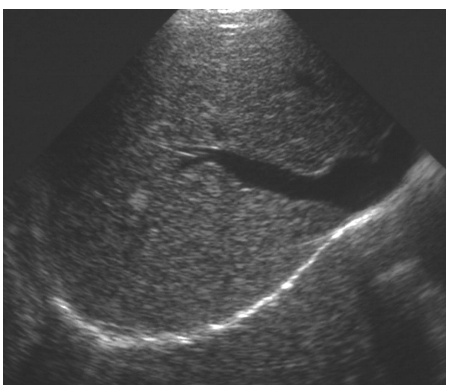

Figure 2c.

Figures 2 a–c. a) Patient with rectal cancer examined with MR. On an axial unenhanced T2 weighted FSE image, a 5 mm hyperintense lesion is found in the right liver lobe interpreted as LM. In this patient, image quality of the T2-weighted sequence was degraded by respiratory artefacts. b) On subsequent CT, no FLL are found c) On US performed three weeks after MR, a hyperechoic lesion corresponding to the lesion on MR is found. The lesion is characteristic for a haemangioma and did not change in size at a follow-up with (US) 18 months later.

Table 1. Clinical diagnoses in the study group

Diagnoses	Number of patients
Recto-sigmoid carcinoma	84
Ovarian carcinoma	5
Ovarian teratoma	2
Uterine rhabdomyosarcoma	3
Endometrial carcinoma	3
Cervical carcinoma	5
Carcinoma of the urinary bladder	5
Prostate cancer	2
Perianal rhabdomyosarcoma	1
Hodgkin lymphoma	1
Total	**111**

Table 2. Presence of liver metastases according to the T2-weighted 'screening' sequence, radiological and surgical follow-up

		MR		Total
		LM	No LM	
FU	LM	15	3	18
	No LM	3	90	93
Total		**18**	**93**	**111**

Note: FU = Radiological or surgical follow-up
LM = Liver metastases

Table 3. Metastases diagnosed on axial T2-weighted MR imaging in 111 patients

Metastases site	liver	lymph nodes	peritoneal	other
Number of patients	15	6	3	3

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Teadustegevus

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Kaksteist teaduspublikatsiooni.

Kuulun Eesti Radioloogia Ühingusse, olen Ameerika Röntgenoloogiaühingu korrespondentliige.