Chapter 2

Diagnostic Modalities in Colorectal Cancer –Endoscopy, Ct and Pet Scanning, Magnetic Resonance Imaging (Mri), Endoluminal Ultrasound and Intraoperative Ultrasound

Valentin Ignatov, Nikola Kolev, Anton Tonev, Shteryu Shterev, Elitsa Encheva, Tanya Kirilova, Tsvetelina Teneva and Krassimir Ivanov

Additional information is available at the end of the chapter

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1. Introduction

Colorectal cancer (CRC) is the third most diagnosed cancer in men, next to prostate and lung cancer. In women it is the second most diagnosed cancer, next to breast cancer. In a time of limited resources in health care, there has been considerable debate which imaging modality offers the best non-invasive examination of colorectal cancer, offering both detection and characterization. The use of multiple diagnostic modalities is both costly and time-consuming. Clinical evidence amassed over the last several decades indicates that routine colorectal cancer (CRC) screening, compared to no screening, detects CRC at an earlier stage, reduces the incidence of CRC or the progression early CRC through polypectomy, and reduces CRC mortality.

2. Endoscopy

The first complete examination of the colon using a flexible fiber optic endoscope is reported by Wolff and Shinya in 1971 [42]. Nowadays colonoscopy is the gold standard for evaluation of the entire colonic mucosa with therapeutic capability of resecting detected malignancies.

In the last years the colonoscopy is the modality of choice to detect and correct the adenomatous polyps and colorectal cancer. The diagnosis CRC can be confirmed after biopsy in a known

malignant pathology and by obtaining more tissue sampling and/or a second opinion from a consulting pathologist in none diagnostic, highly suspected colon lesion. Besides the role as a diagnostic tool in CRC, colonoscopy identifies subsequent lesions at the time of surgery, which is called preoperative endoscopic marking. It is performed through metallic clip placement and endoscopic tattooing.

The colonoscopic equipment consists of camera and four-way tip controls [43]. The camera can produce images of high-definition quality. The four way tip controls include (1) examination of a found patch to confirm an abnormal growth; (2) insufflating air to dilate the lumen for mucosal inspection and relieving air after examination, (3) irrigating a suspected region; (4) suctioning to avoid missing lesions under fluid, and (5) inserting biopsy devices.

The patient must undergo bowel preparation - taking clear liquid diet and ingesting laxative solutions for colon cleansing the day before examination. Sedation is needed to relieve the discomfort during the procedure, but it increases the costs. The complication of sedation are different cardiac disturbances such as hypotension, arrhythmias,oxygen desaturation, and others. The preparation with purgatives may cause abdominal discomfort, nausea, and other symptoms. The colonoscopy continues from 30 minutes to an hour. The risk during colonoscopy consists in colonic perforation in 0,1 % of cases. Colonoscopy fails to visualize the entire colon in 10–15% and it may miss up to 10–20% of polyps fewer than 10 mm.

Colonoscopy is golden standard for diagnosing of CRC but there are more symptoms which could be evaluated and appreciated by endoscopic examination, for example- abdominal pain, unexplained gastrointestinal bleeding, diarrhea of unexplained origin, chronic inflammatory bowel disease, etc. It is also the most common interventional modality for polypectomy, hemostasis, balloon dilation, foreign body removal, palliative treatment of neoplasms, etc. Colonoscopy could be the best screening option for all none specific underdiagnosed gastrointestinal symptoms.

Colonoscopy removes all detected polyps, regardless of histology type- adenomatous or hyperplastic. Not all of them must undergo resection. The polyps vary in size and polyps under 5 mm are not detected endoscopic. For detection of polyps smaller than 5 mm the virtual colonospcopy is the alternative to the conventional colonoscopy.

3. Virtual colonoscopy

Virtual Colonoscopy uses computed tomography (CT) imaging virtual- reality technology for the purpose of screening the entire colon which is reconstructed from abdominal CT images.

The technique starts after cleansing of the colon with oral laxatives with inflation of air or CO2 introduced through rectal tube [71]. Then abdominal CT images are taken during a single breath holding with sub mm resolution in axial and transverse directions. The volume model of the colon is constructed from the spiral CT images. Image segmentation is necessary for the reconstruction of an accurate colon model [72]. Computer graphics navigate inside the 3D colon model, the navigation is called fly through model. For validating the detection in the 3D

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colon model, interpretation of the 2D image slices at transverse, sagital and coronal directions is often included in the procedure.

The virtual colonoscopy achieves higher sensitivity and specificity rates compared to conventional colonoscopy for detecting polyps, which are 8 mm and larger by the same bowel preparation, and for polyps larger than 10 mm they have a comparable performance. CTC can be a potential screening tool to supplement OC for colorectal cancer. CTC is refused to be included in Medicare coverage because of its radiation risk- in about 50 mAs or 2 rads. Reducing the radiation could be achieved by decreasing of the mAs level optimization of kVp value, X-ray flux beam collimation, filtering, etc. The low-mAs strategy will lead to higher noise in the acquired data which results in steak artifacts. The significant amount of X-ray radiation exposure and the data noise cannot be disregarded and allowed to the CTC to be a preferred screening modality.

An alternative method to minimize the radiation is to use magnetic resonance imaging (MRI), i.e., MR colonography (MRC). However, this MRC has several limitation compared to CTC-high costs, sensitiveness to motion and other artifacts, and has lower spatial resolution. Modern CT can reach sub-millimeter spatial resolution and acquire a volumetric image of the abdomen, detecting polyps which are smaller than 5mm.

There are other reasons responsibe for missing small polyps.

The main reason is due to the partial colon cleansing and air/CO2 inflation and this will not generate a good interface between the colon wall and the lumen. Others include loss of image information in post-imaging processing, different anatomical characteristics in the bowel mucosa, residual fluid or stool covering the polyps. The solution could be virtual or electronic colon cleansing (ECC) - special type of software programming for virtually cleansing of the colon. It consists of three main components - (1) fecal tagging, (2) image segmentation for classifying the tagged image voxels, and (3) post-segmentation operation for cleansing the colon. ECC works virtually on the residual faecal materials with or without adequate bowel preparation with purgatives (the so called cathartic-free CTC). The ECC must handle with the partial volume (PV) effect and with the non-uniformly altered image intensity distribution. Partial volume (PV) effect is the interface between the colon wall and the fecal materials with heterogeneously enhanced image intensities. The PV effect blurs the interface over several image voxels, causing the loss of details about the interface what results in the misdetection of small polyps. A dual energy scans of a modern CT device or a dual X-ray source scanner is a new challenging imagining modality. Two volumetric images can be acquired simultaneously at two energy levels. It is expected that the polyps would have different image contrasts in the two scans and if the contrasts are insufficient for segmenting the image voxels, oral contrast media may be utilized to increase the density of the polyps. The ECC role in this dual energy strategy is to segment the colonic materials from multi-spectral CT images. After ECC-cleansing the colon lumen could be easily inspected for abnormalities and polyps along the long colon during the fly-through navigation.

Variation among readers with different experience has been noticed. Computer-aided detection (CAD) can minimize the variation among readers' assessments. CAD system's

disadvantages are many false positives (FPs), such as partial bowel cleansing, image noise, motion artifacts, colon fold structures, etc. High sensitivity CAD with minimal number of FPs and development of various texture features and virtual biopsy features remains an innovative research goal.

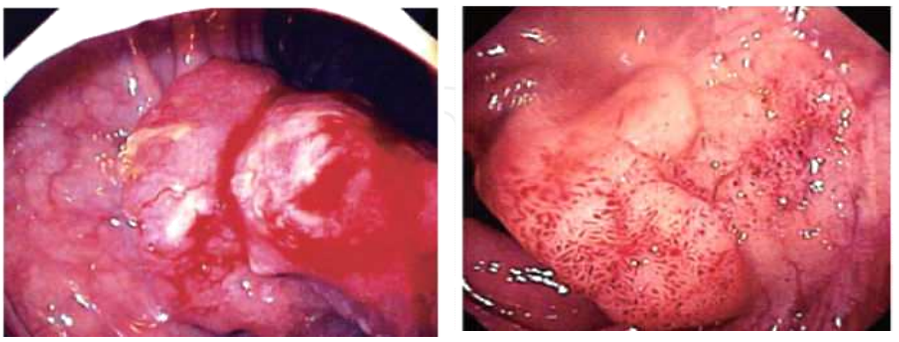

Figure 1. Endoscopic view of corectal tumor – conventional endoscopy

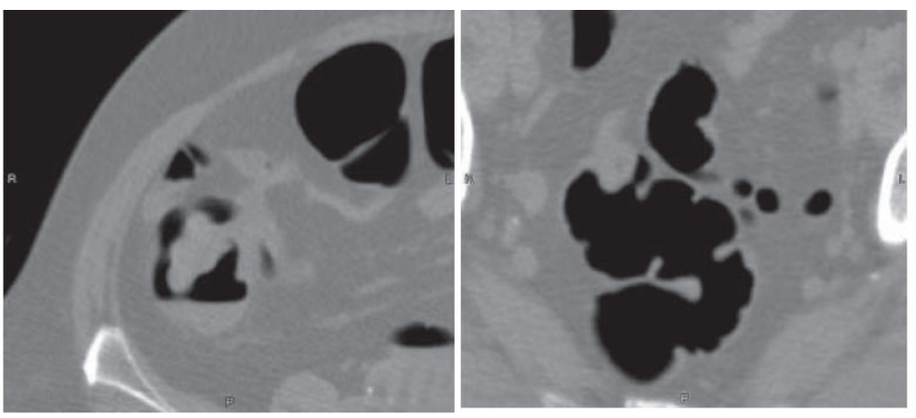

Figure 2. Virtual colonoscopy – a view of pediculaneted polypus and a small carcinoma - CT images.

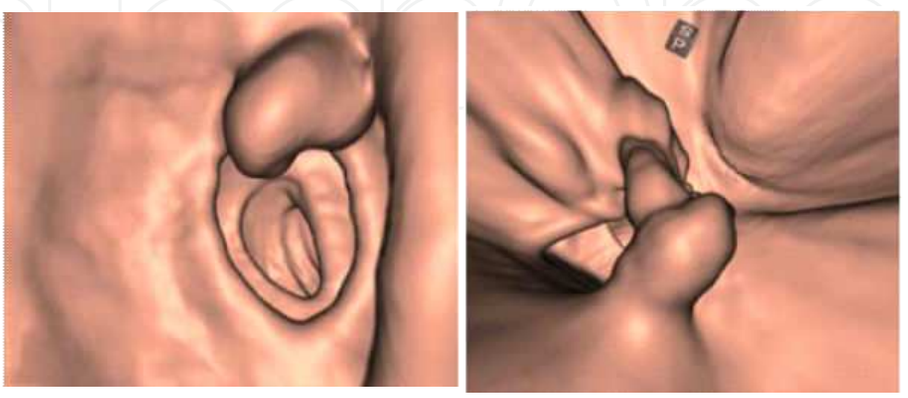

Figure 3. Virtual colonoscopy – a view of pediculaneted polypus and a small carcinoma - a 3-D reconstruction after software rendering.

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4. Imaging diagnostics in rectal cancer

Staging of rectal cancer is of great importance before the surgical treatment, because staging predicts the management, prognosis, recurrence and/or metastatic disease risk (13). Staging is divided into local and distant staging. Local staging points at wall invasion, resection margin involvement and the nodal status for metastasis and distant staging refers to presence or absence of metastatic disease. Rectal examination using proctoscopy may be considered as an important tool for newly diagnosed rectal cancers. Proctoscopy may determine better visualization, localization and fixity of the tumor, including taking biopsy, which may affects positively the staging of the rectal cancer.

Nowadays several imaging modalities or combination of these are available for evaluating preoperative staging of colorectal cancer- computed tomography (CT), magnetic resonance imaging (MRI), and/or endorectal ultrasonography (EUS). EUS and MRI of the pelvis are used to appreciate the local dissemination while CT defines systemic dissemination. PET is indicated when there is clinical, biochemical or radiological suspicion of local recurrence or systemic disease. Functional imaging such as diffusion weighted MRI imaging (DWI) and CT/PET are used to distinguish fibrosis from tumor [33].

The T staging accuracy in more advanced cancer is achieved by using MR imaging modality because MRI can distinguish between mesorectum and mesorectal fascia. The N staging accuracy is also provided by MRI particularly using superparamagnetic iron oxide particles.

4.1. Endorectal ultrasound

The advancing of imaging technologies has made endoscopic ultrasound a modality of choice in gastrointestinal diseases, regarding diagnosis, staging and prognosis stratification. These novel techniques assign excellent to rectal tumors.

Endorectal ultrasound (EUS) is useful in evaluating early rectal cancers (T1 and T2 lesions) and post transanal surgery. EUS can visualize the rectal wall without distinguishing of mesorectal fascia, peritumor inflammation, or faeces collections. The accuracy of the T stage evaluation varies from 60%-90% [45].

In comparison to MRI EUS was found to be highly accurate in early lesions (for T1 and T2 the accuracy can reach to 100%), as well as for nodal metastases. For evaluation of metastatic disease neither MRI nor EUS enable reliable diagnosis.

Besides the misleading lymph node assessment, EUS has its disadvantages in detecting T3 lesions (advanced, stenotic, bulky lesions) or tumors after neoadjuvant therapy, and the technique is operator dependent.

Hypoechoic appearance, size > 5 mm, round shape, peritumoral location are characteristics suggestive of malignant involvement of lymph nodes [45,46,51-53]. EUS-guided fine-needle aspiration can be carried out from the lesion or suspiciously looking lymph nodes.

An newer technique is the three-dimensional ERUS (3D-ERUS). It consists of transverse, coronal and sagittal scan and has been found to be more reliable in staging colon cancer to

two-dimensional EUS and CT. The accuracy of 3D-ERUS for assessing the depth of cancer infiltration and for nodal involvement is with 10% more than the other imaging modalities. 3D images have proved a better visualization of the mesorectal margins. With 3D-ERUS the surgeon can perform endoscopic mucosal resections of early tumors. A reliable predictor for response after chemoradiation therapy are the accurate volumetric measurements achieved by 3D-ERUS. Using Doppler signal enhancers tumor perfusion can be determine, coming to better results in neoadjuvant therapy and antiangiogenesis treatment.

3D-ERUS, elastography, and contrast enhancement might bring additional information, increasing diagnostic accuracy of ERUS and amplifying its roles in the complex management in rectal cancer.

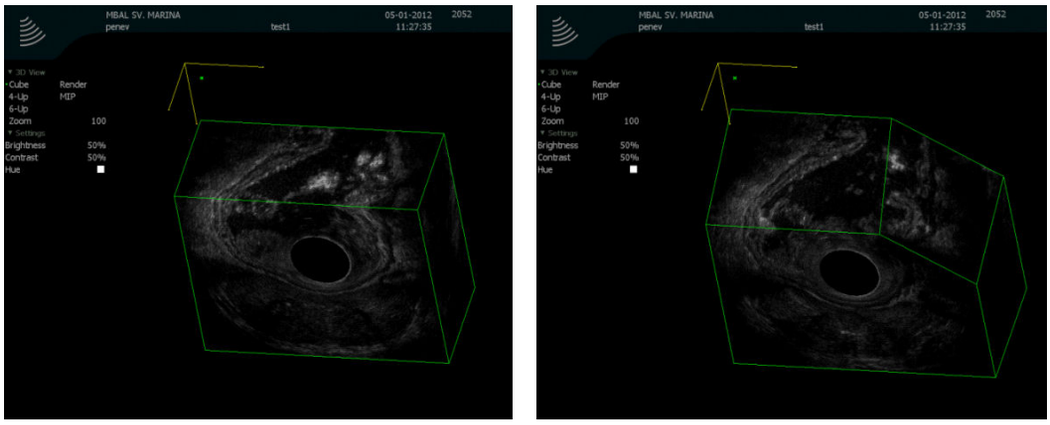

Figure 4. Endorectal ultrasonography – a view of T-3 carcinoma - 3-D reconstruction after real-time software rendering.

T and LN staging

In colon cancer patients it is essential to correctly determine the TNM stage. The modalities of choice are CT, MRI and, as mentioned above, the novel technique ERUS.

ERUS shows high sensitivity and specificity in T-staging and is prior to CT and MRI for staging superficial rectal tumors, with accuracy in evaluating rectal wall invasion to 97% [23,24]. For T1, T2, T3 and T4 staging accuracy of ERUS is more than 80%. One common finding is a lower accuracy for T2 tumors, because the impossibility in distinguishing those tumors that have deep invasion into the muscularis propria from those with microscopic invasion into the perirectal fat.

Transanal endoscopic microsurgery (TEM) and endoscopic submucosal dissections are novel important strategies which directs the mode of surgery because of the ability to visualize the submucosa. This can lead to down- or upstaging of the detected rectal cancer. Besides ERUS can detect recurrence at the anastomosis site and to differentiate between postoperative scars and local recurrences. Unfortunately assessment for nodal metastases is less accurate than that for tumor depth and reaches 75%. For rectal cancer in particular, over half of the metastatic

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nodes are less than 5 mm and are located within 3 cm of the primary tumor [31]. Metastatic disease was shown to predict local recurrence.

The sensitivity of ERUS in detecting LN metastasis ranges from 50% to 83%, because small lymph node (less than 5mm) is not observed with ERUS and it has limited field of view. Factors for malignancy in lymph node besides node size, echogenicity, shape, border, include: hypoechogenicity, short axis ≥ 5 mm, long axis length greater than 9 mm.

Detecting of iliac adenopathy is crucial because it goes after total mesorectal excision. This is possible through flexible not rigid probes. In general, ERUS is better at detecting lymph nodes in the distal and middle thirds of the rectum [21,33]. The reactive swollen lymph nodes, small blood vessels, urethra, and seminal vesicle often are mistaken for malignant lymph nodes and these results in over staging of the disease. On the other hand, the major reason for nodal status under staging is misdetecting of very small involved nodes (less than 2 mm) and nodes outside the perirectal tissue [21,33].

Preoperative chemoradiation is a limiting factor affecting accurate staging of rectal cancer. There are associated reactive and inflammatory changes in the rectum wall after radiotherapy. However, radiotherapy affects the wall thickness but does not change the five-layered image.

The 3D reconstruction allows improved T and N staging through direct visualization of subtle protrusions of tumors infiltrating into adjacent tissues and organs.

Limitations of ERUS are several. Firstly it is operator's experience dependent; it varies after partial excision or neoadjuvant chemoradiation. It has poor patient acceptability and it has limited depth of penetration; Another disadvantages are those that it cannot be performed in obstructive tumors [16,21]; it is unable to visualize tumors located higher with a rigid probe. It is insufficient in detecting lymph nodes outside the range of the transducer, or visualize mesorectal fascia because of its limited field of view. In addition, accuracy is affected by villous or pedunculated tumors, inflammation, hemorrhage [22,31].

MRI

MRI obtain image identification of the distance of the CRM to the tumor, the relation to pelvic floor and anal sphincter complex, differentiation between mucinous and none mucinous neoplasia. T staging accuracy of MRI is 52% when compared to histology, because of the interface between muscularis propria, perirectal fat and mesorectal fascia. MRI cannot distinguish between T1 and T2 lesions, as well as between T2 and T3 cancer.

T staging

The depth of invasion through the muscle wall is one important element seen on MRI that can help guide clinical decision making for patients with rectal cancer. Not only does the incidence of nodal involvement increase with increasing tumor penetration [19,20], but clinical studies have shown that patients with stage ⊚ (T1-2 N0) rectal cancer do not benefit from neoadjuvant radiotherapy [21] and may be amenable to a less than radical surgical treatment [22]. Patients with clinically staged T3-4 tumors typically require preoperative CRT since it reduces the rates of local recurrence more effectively than either postoperative CRT or preopera-

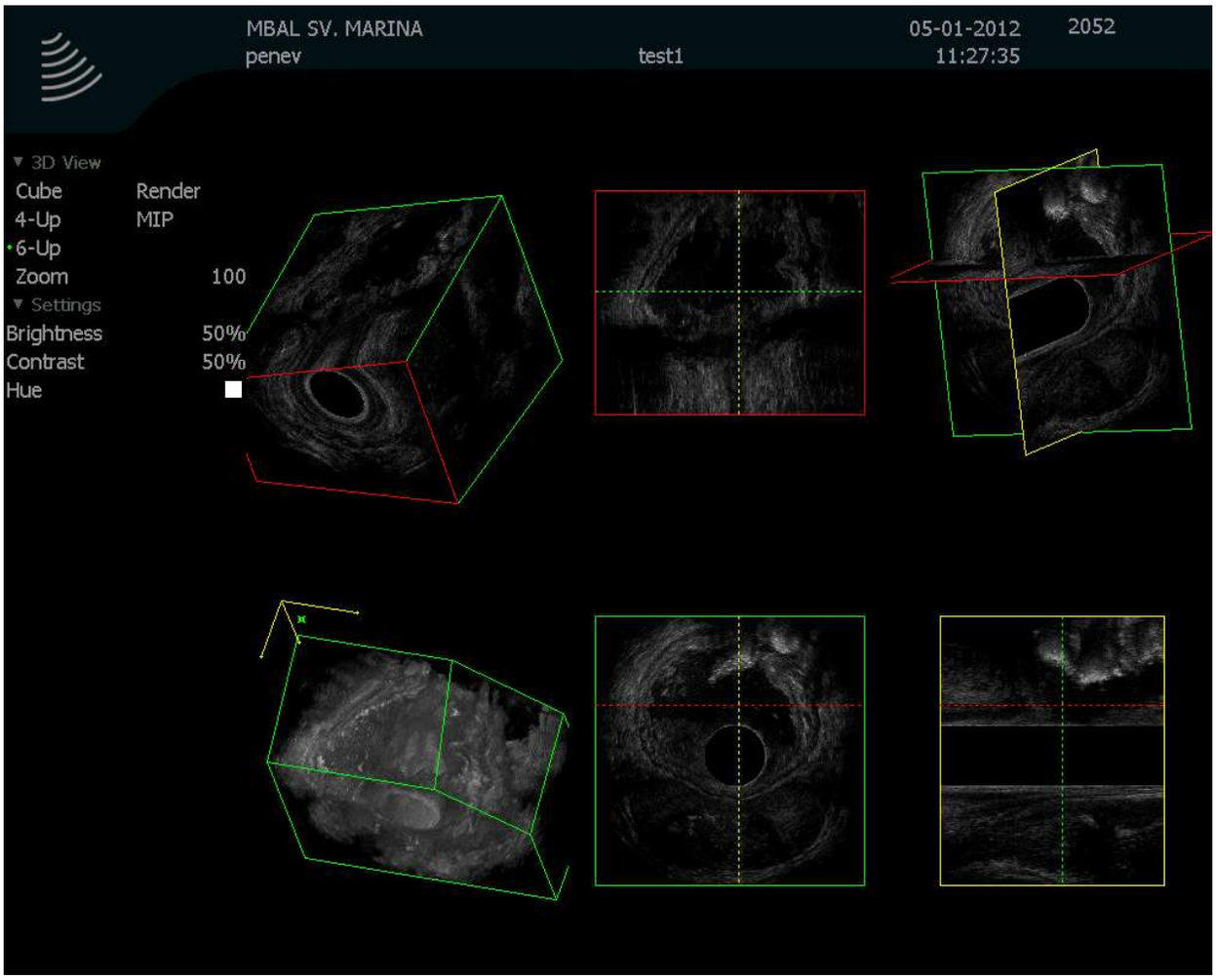

Figure 5. Endorectal ultrasonography – a real time 3-D reconstruction with different options for endorectal evaluation of the tumor process.

tive radiotherapy alone [23-25]. However, some problems remain with T stage determination on MR imaging. Overall, the agreement between MRI and histology for T staging has ranged from 66%-94% [18,26-28]. One of the main problems of T staging on MRI is the distinction between T2 and T3 tumors. In fact, investigators have shown that the negative predictive value for invasion beyond the muscularis propria varied from 93% (expert reading) to 76% (general radiologist reading) [26]. This difficulty is attributed to the presence of desmoplastic reactions around the tumor. This reaction makes it difficult to distinguish between spiculation in the perirectal fat caused by fibrosis alone from that caused by fibrous tissue that contains tumor cells [26]. In contrast, MRI has been shown to be more accurate in imaging the more advanced tumors (T4) [27,29]. According to a metaanalysis, MRI for T4 lesions has a specificity of 96% [30].

CRM

The CRM (lateral, radial) is defined as the surgical cut surface of the connective tissues (i.e. lymphovascular, fatty and neural tissue) that circumferentially encase the rectum. It equates to the mesorectal fascia that forms the plane of dissection in rectal cancer surgery. It is assessed

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by marking the outer surface (i.e. the CRM) with ink, taking serial cuts through the specimen and examining the macroscopic and microscopic relations between the tumor and the inked margin. The CRM gives significant information not only about the quality of the performed operation but also prognosis of the disease. Indeed, in a recent study based on the data from a randomized clinical trial, Nagtegaal *et al* [31] demonstrated in a multivariate model that the CRM is more important than the T stage for the prognosis of rectal cancer. The definition of a positive CRM remains a matter of debate. A review of the literature in 2006 showed that the majority of studies that dealt with CRM status used the ≤ 1 mm definition for positive CRM (91.1%; 7373 of 8094 patients) [32].

Six distinct types of CRM involvement have been described; direct tumor spread which occurs in 18% to 29% of cases; discontinuous tumor spread in 14% to 67% of cases; lymph node metastases in 12% to 14% of cases; venous invasion in 14% to 57% of cases; lymphatic invasion in 9% of cases; and perineural tumor spread in 7% to 14% of cases [32]. In approximately 30% of patients, there is more than one type of margin involvement. In contrast to direct tumor spread, the involvement of the CRM by lymph node metastases is not associated with local recurrence [32]. MRI is highly accurate and reliable for prediction of the CRM [33,34]. In their most recent study of 98 rectal cancer patients, Brown *et al* [27] reported a 92% agreement between MRI images and histologic findings for prediction of CRM involvement. In another study assessing the tumor relationship to the mesorectal fascia, two observers independently scored the tumor stage and the distance to the mesorectal fascia on MRI and compared these observations with the final histological findings [26]. For twelve tumors with involved mesorectal fascia, and thus, a CRM of 0 mm, the accuracy in predicting the CRM was 100% for both readers. In 29 patients with a wide CRM (10 mm), the accuracy for predicting the negative margin was 97% (27 of 28) for one reader and 93% (26 of 28) for the other [26]. It is relevant to point out that 5 mm of mesorectal tissue surrounding the lateral tumor edge on MRI was shown to equal a CRM of 2 mm in the surgical specimen [26]. In the report by Nagtegaal *et al* [35], a linear regression curve showed that the crucial distance of at least 2 mm could be predicted with 97% confidence when the distance on MRI is at least 6 mm. Therefore, the safe rule to predict CRM involvement on MRI is considered to be an MRI measurement minus 4 mm due to shrinkage of the specimen with fixation [6]. Of note, the CRM becomes more difficult to identify in low, anterior tumors and in patients with a limited amount of perirectal fat [36]. In a recent study by Frasson *et al* [37], the 5-year local recurrence rates for patients with a preoperative CRM of < 2 mm on MRI or EUS who did not receive preoperative chemoradiation was 19.4% compared to 5.4% for patients with a non-threatened margin. It is important to realize that a short course of preoperative radiotherapy has limited ability to control positive CRM. An analysis of more than 17 500 pathologic specimens by Nagtegaal *et al* [32] revealed that the chance of local recurrence was higher for patients with a positive CRM after neoadjuvant treatment (both radiotherapy and radiochemotherapy) than those with a positive CRM following immediate surgery (Hazard ratio 6.3 *vs* 2.0, respectively). Similar results have been reported following postoperative treatment [38]. In the MRC CR-07 trial, patients with positive radial margins who were selected to receive postoperative chemoradiation had a 21% local recurrence rate [39]. Thus, in cases where the tumors are close (< 2 mm) or through the mesorectal margin on preoperative MRI, a more aggressive treatment regimen is required with

neoadjuvant CRT or an upfront regimen of chemotherapy before chemoradiation prior to operation. In contrast, patients with a free margin > 2 mm from mesorectal fascia may undergo surgery [total mesorectal excision (TME)] alone, avoiding preoperative chemoradiation. Interestingly, MRI-based therapy for CRM positive tumors was able to reduce the frequency of neoadjuvant therapy for rectal carcinoma by 35% without the risk of worsening the oncological results [40]. However, omitting preoperative chemoradiation for all CRM-negative tumors on MRI needs to be further investigated in prospective clinical trials before it is adopted as standard therapy.

N staging

The presence of involved lymph nodes is an indicator for the likelihood of systemic disease and local recurrence [41]. Therefore node-positive disease is generally an indication for preoperative chemoradiation. However, radiological evaluation of lymph node metastatic involvement remains a challenge. Results of anatomic studies show that over half of the metastatic nodes from rectal cancer are within 3 cm of the primary tumor and are smaller than 5 mm in size [42]. With a standard TME, the perirectal nodes are removed with the primary tumor, but the internal iliac and obturator nodes are left in place. Moriya *et al* [43] reported that as many as 28% of lymph node-positive distal rectal cancers have involvement of lateral nodes and in 6% of cases, these were the only nodes involved. This means that in 6% of patients, the disease was incorrectly staged postoperatively as node-negative at TME. For pre-operative lymph node imaging, MRI at present is only moderately accurate, although this could change with advances in new MR techniques. Currently, the reported accuracy rate of MRI for nodal staging ranges from 71% to 91% [42]. On MRI, lymph nodes typically have lower signal intensity than the perirectal fat but higher signal intensity than arteries and veins. In patients with mucinous carcinoma, metastatic lymph nodes are visualized as hyperintense nodules alone or as hyperintense areas within hypointense nodules. A node is considered enlarged if the major axis length is more than 5 mm (mesorectal), 7 mm (internal iliac), 10 mm (external iliac), or 9 mm (common iliac) [44]. However, the morphological features or signal intensity of the nodes on MRI may more accurately determine metastatic involvement rather than measurement of size. Brown *et al* [45] demonstrated that an irregular border or mixed signal intensity of lymph nodes on MRI improved the specificity of predicting nodal status from 68% (based on size alone) to 97%. One of the more promising advances of MRI may be the use of new lymphographic agents that help assess tumor spread to lymph nodes. In a recent study, gadofosveset-enhanced MRI improved the specificity of nodal staging from 82% achieved with standard MRI to 97% [46]. Fusion of diffusion-weighted MR with T2-weighted images improves identification of pelvic lymph nodes compared with T2-weighted images alone. Using fusion images, 29% additional nodes were detected compared with T2-weighted images alone [47]. The improved nodal identification may aid in treatment planning.

For the vast majority of rectal carcinomas, MRI is currently the most accurate modality on which to base treatment decisions for patients with rectal cancer. Traditionally, the decision to apply preoperative treatment for rectal cancer patients has been based on the T- and N-stage. Lately, other MRI findings such as the radial distance of the tumor to the CRM and extramural vascular invasion score have been identified as important risk factors for local

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failure and survival. Every center that treats patients with rectal cancer should develop a multidisciplinary team featuring a description of the MRI findings and their implementation in the treatment strategy with the aim of increasing resectability, reducing the local recurrence and treatment morbidity, and improving the quality of life.

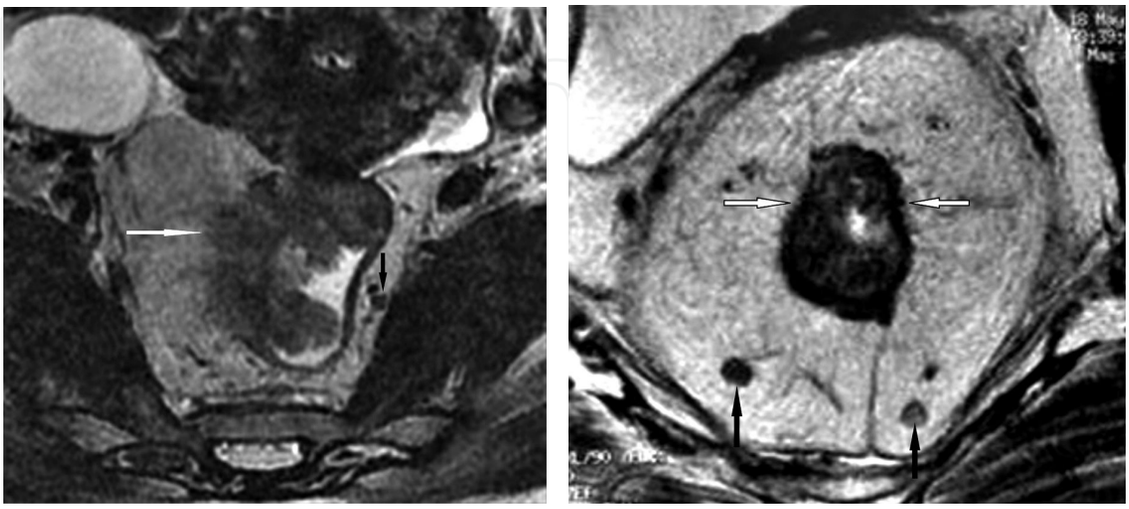

Figure 6. MRI – a view of T-3 carcinoma - 3-D reconstruction after real-time software rendering.

CT, MRI and intraoperative ultrasound for evaluation of the systematic progression in colorectal cancer

The morbidity rate for patients with cancer depends on the early detection of liver metastases. The presence of liver metastases makes of the primary tumour non-resectable for oncologic reasons, except for tumour palliative treatment (for example resection for obstruction of the gastrointestinal tract). For a few malignancies, as in colorectal carcinoma, resection of liver metastases has been shown to improve the survival of the patients. The hepatic metastases are divided into synchronous (i.e. occurring at the time of diagnosis of the primary tumour) and metachronous (occurring after diagnosis of the primary tumour). The surgical resection of the metastases depends on the division, number, size, regional distribution and all clinical parameters of the patient, which makes resectable only 30% of all colorectal patients with metastases. The 5-year survival rate of these patients is more than 30% in comparison to a survival of less than 5% of patients with liver metastases not amenable to liver surgery [1–4].

The goal of imaging modalities is to assess the presence or absence of liver metastases in surgical candidates. Different studies indicate ferumoxide-enhanced magnetic resonance (MR) imaging as more sensitive and specific than contrast-enhanced computed tomography (CT) in detection of hepatic metastases. The different MR pulse sequences and MR contrast media agents makes MRI the modality of choice for non-invasive lesion characterization.

Preoperative assessment of surgical candidates

Preoperative assessment of metastatic liver involvement should be performed for all surgery candidates. This preoperative staging is conceivable by contrast-enhanced CT and/or MRI in

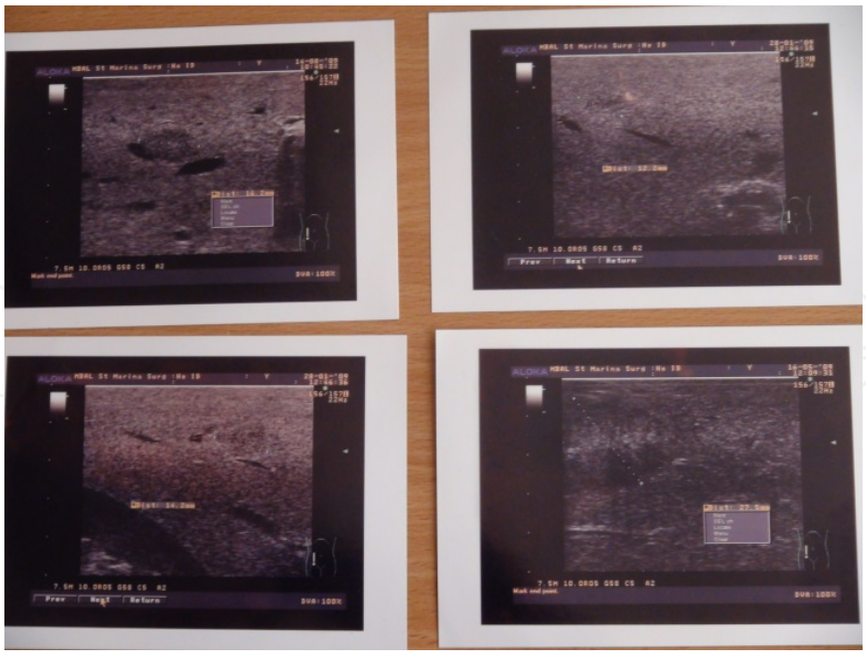

Figure 7. Intraoperative ultrasound of the liver

most oncologic centers. All imaging modalities present different false-positive or false-negative diagnoses- for helical CT- in 42%, intraoperative US- in 22.8%, mangafodipir-enhanced MRI- in 10%, ferumoxide-enhanced MRI technique is accurate as CT during arterioportography (CTAP)- in 19%. Another study found that FDG-PET CT is the most sensitive method for detection of metastases. There is no firm statement which is the best imaging modality, further more the choice depends on local equipment, availability, and operator expertise. MDCT is preferred as a screening method for hepatic lesions because of its ability to reduce respiration-related artifacts, to shorten scan time, to perform multiphase scanning. The disadvantage is the high radiation exposure.

Clinical Role of Intraoperative US

Intraoperative US provide more diagnostic and staging information to the surgeon during hepatic resection. Intraoperative US supplies 35% more information about the lesion type, localization and expansion to adjacent tissues, relation to vascular structures, providing more specificity in the evaluation of liver lesions. In addition intraoperative US represent 25% more lesions than did preoperative US, CT, or angiography. This results in correction in disease staging, which affects the surgical management and postoperative treatment. The intraoperative US has a positive effect on patient care, surgical planning, and clinical outcome.

Magnetic resonance imaging

The standard phased array MRI produces good quality images with good contrast resolution and a relatively large field of view, so it is the modality of choice for preoperative staging of rectal primary tumor. MRI is reliable for assessment of the tumor and its locoregional extension, for identifying recurrence and for planning radiation therapy. The disadvantage of MRI is impossibility in evaluation nodal metastases.

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Deciding in management of rectal cancer is the differentiation of the mesorectal fascia-circumstance, which is possible using phased-array coils (confirmed from the multicentre European MERCURY study)(21,23).

MRI may not be the examination of choice for every patient. Patients with contraindications to MRI (e.g. implantable pacemakers), or unable to tolerate MRI (e.g. due to claustrophobia) would preferably undergo preoperative imaging with CT. Motion related imaging artifacts that can severely dampen the diagnostic quality of MRI will occur in patients who are unable to breath hold for longer than 20 seconds.

FDG PET in the Initial Staging of CRC

FDG PET is not a routine investigation for primary cancer due to its limited spatial resolution. PET cannot define the T-category of the primary tumor, but PET is superior to other imaging modalities in detecting of lymph node and distant metastases- an important prognostic factor. After PET-CT investigation the patient could be upstaged in 17% because of identifying unsuspected systemic and lymph node metastases. But the specificity of PET in nodal staging does not be higher than multi-detector CT scan (MDCT).

The principle of positron emission tomography (PET) (and Fluoro-deoxy-glucose (FDG) used as tracer or enhancer) is based on the differential metabolic profile of tumors - higher metabolic activity, change in the tumor biology. FDG/PET is mainly useful in the assessment of local recurrence and metastases. Besides in neoplastic cells FDG accumulates in areas of inflammation, infection, in organs of increased metabolic activity such as brain, myocardium, liver or kidneys leading to false positive results. Interpretation of PET without anatomic correlation is difficult which results in necessity of fusing PET with CT images- PET-CT fusion scans are invented. This offers a detailed anatomical and functional imaging. The combination provides additional value to localize the hot spots. The false positive rates are due to other diseases and physiological processes. PET scans improve the management plan for rectal cancer. The addition of FDG-PET changes patient management in up to 30% of patients with potentially resectable liver metastases, mainly by detecting previously unknown extrahepatic disease. Furthermore, FDG-PET is useful in the follow-up of patients who underwent surgical procedures of the liver, since it is sensitive in detecting residual or relapse malignancy in scarred liver tissue following both resection and local ablative techniques. For follow-up during systemic therapy, early FDG-PET appears predictive for response to therapy. FDG-PET, computerized tomography and magnetic resonance imaging are complementary techniques in staging and restaging patients with advanced colorectal cancer. A combination of FDG-PET and CT scanning characteristics seems promising, and integrated PET/ CT is becoming more widely available, although the exact clinical value and efficacy is not yet fully established. In addition, assessment of these modalities in joint reading sessions with radiologist, nuclear medicine physician, medical and surgical oncologists significantly impacts upon patient management. This review evaluates the potential of FDG-PET and combined PET/CT in patients with colorectal liver metastases and discusses potential future possibilities.

Suggested investigations for tumor staging of rectal cancer

CT scanning is still the current standard for distant staging, but not to stage the local neoplasm. The combination of CT and PET offers both anatomical and functional imaging, so it is sufficient for recurrent rectal cancers. MRI and EUS should be considered as the initial modalities to stage the local tumor. For T1-T2 lesions EUS is more appropriate, whereas MRI is used in advanced rectal cancer. MRI has been shown to be highly accurate in predicting a clear circumferential resection margin in patients undergoing TME.

Suggested investigation for nodal staging of rectal cancer

Significant malignant lymph nodes (more than 1cm in diameter), in conjunction with size, shape and morphology, are identified through MRI, CT and EUS studies. The enlarged lymph node can be as a result of the inflammatory process but normal size nodes can have micrometastases. Moreover the halves of nodes less than 5 mm are proved to be malignant. One novel technique involves use of a contrast media containing superparamagnetic iron oxide particles SPIO which accumulates in normal lymph nodes, but not in malignant nodes due to poor uptake. Then, using T2 weighted imaging, these nodes can be identified. Initial studies are promising but further research is needed [35].

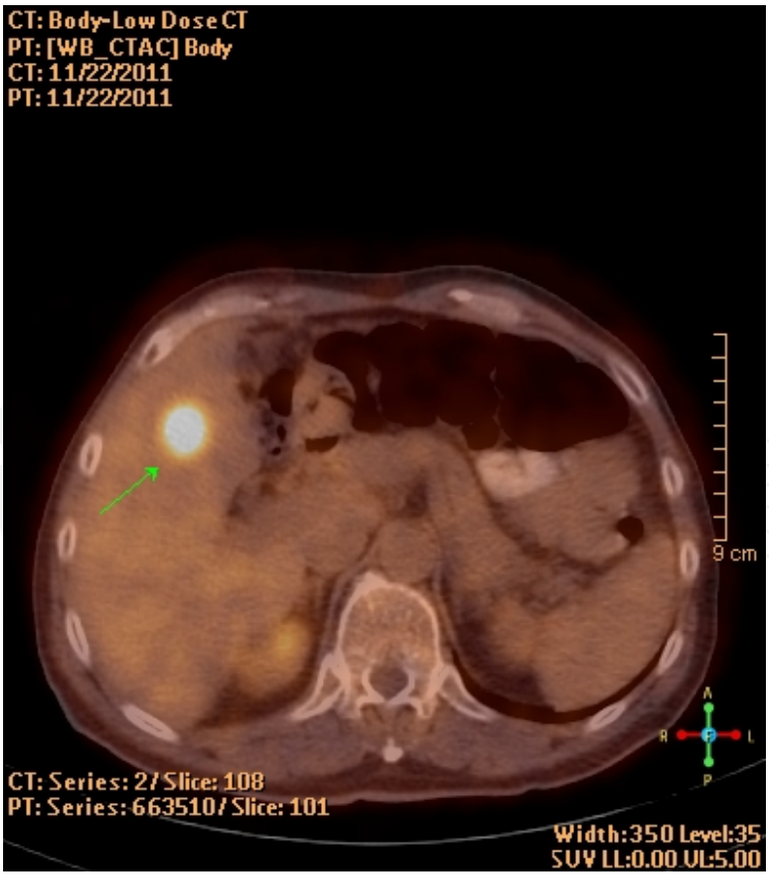

Figure 8. Positron emission tomography of the liver – an observation of metastasis from colorectal origin

http://dx.doi.org/10.5772/57508

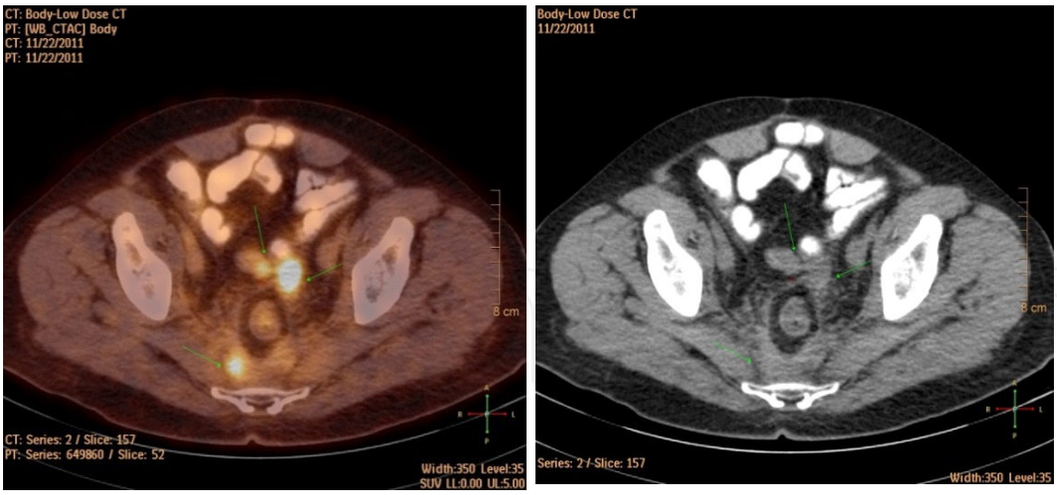

Figure 9. Positron emission tomography of the body – an observation of perirectal lymphadenopathy

5. Conclusion

Optical colonoscopy (OC) and virtual colonoscopy (VC) (i.e. CT colonoscopy and MR colonoscopy) are constantly developing and adapting to the new clinical needs. The optical colonoscopy has the advantage of being both diagnostic and therapeutic procedure for patients with positive findings on screening tests. The virtual colonoscopy is much less invasive method and can be used for mass screening because of the high prevalence of the colorectal cancer. As a screening test the VC has advantages over OC and other options such as FOBT, FIT, stool DNA testing, and DCBE. These methods can make a good combination of VC screening with OC follow-up on the positive findings. The current imaging modalities for VC are CT and MRI and in the future other modalities might be available.

The imaging standard for accurate diagnostics for colorectal cancer includes ultrasound (US), CT and MRI. The nuclear medicine has its role in finding extra-regional localization of the main disease by FDG-PET and FDG-PET/CT. The protocol for liver metastases includes CT as a first choice, which is followed by US. Lung-metastases are evaluated by X-ray or chest CT. The extrahepatic metastases are assessed by CT. The present guidelines could be adjusted by conducting comparative studies on different strategies for colon and rectal cancer, such as CT liver/abdomen vs. MRI liver/abdomen for liver and extrahepatic metastases, X-ray chest and CT chest for lung metastases.

The screening of asymptomatic patients is justified due to the high prevalence of colon carcinoma and the mortality can be effectively reduced by removing adenomatous polyps. Although effective, this method consumes large resources if applied to the whole target population. The currently available screening options have limitations. The VC has the option to identify patients with adenomatous polyps. The combination of VC screening and OC follow-up might prove as a cost-effective measure against colorectal cancer.

The challenges of VC are the associated radiation and the differentiation of the colonic materials from the colon wall. The MRI-based VC has no radiation and has better potential in differentiation of colonic materials from the colonic wall, but it has lower spatial resolution and is prone to motion artifacts. CT and MRI VC require sophisticated software processing to construct the colon model and real-time fly-through inside the lumen. More sophisticated image processing is important for the differentiation of adenomatous from hyperplastic ones. The extraction of the colon wall can be performed by the new method of electronic colon cleansing and analysis of texture features from image intensity of the wall. These processing methods are step toward computer-aided detection and diagnosis. Despite recent advances in chemotherapeutic agents, the prognosis for metastatic colon cancer remains poor. Over the past two decades, hepatic metastasectomy has emerged as a promising technique for improving survival in patients with metastatic colon cancer and in some cases providing long-term cure. To maximize safety and efficacy of metastasectomy, appropriate pre-operative imaging is needed. Advancements in computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET) have led to improved detection of occult lesions and better definition of surgical anatomy. While CT, PET and MRI have a comparable sensitivity for detection of large liver metastases, MRI excels at detection of subcentimeter liver metastases compared to CT and FDG-PET, especially with the combination of diffusion weighted imaging (DWI) and hepatocyte-specific contrast agents. CT may be useful as a screening modality or in preoperative planning such as volumetric estimation of the remnant liver size or in defining preoperative arterial anatomy for hepatic artery infusion pump placement. While technologic advancements have led to unprecedented image quality and clarity, this does not replace the need for a dedicated, competent radiologist with experience in hepatic imaging.

Author details

Valentin Ignatov[1], Nikola Kolev[1], Anton Tonev[1], Shteryu Shterev[1], Elitsa Encheva[4], Tanya Kirilova[2], Tsvetelina Teneva[3] and Krassimir Ivanov[1]

1 Department of General and Operative Surgery, University Hospital "St. Marina" – Varna, Bulgaria

2 Department of Gastroenterology, University Hospital "St. Marina"- Varna, Bulgaria

3 Department of Image diagnostics, University Hospital "St. Marina"- Varna, Bulgaria

4 Department of Radiology, University Hospital "St. Marina" – Varna, Bulgaria

References

[1] American Cancer Society. Cancer Facts & Figures 2008. Atlanta: American Cancer Society; 2008.

[2] Jemal A, Siegel R, Ward E, et al. Cancer Statistics – 2008. A Cancer Journal for Clinicians 2008;58 (1):71–96.

[3] Hill M, Morrison B, Bussey H. Etiology of Adenoma Carcinoma Sequence in the Large Bowel. Lancet 1978;1(2):245–247. [PubMed: 74668]

[4] Rickert R, Auerbach O, Garfinkel L, et al. Adenomatous Lesions of the Large Bowel – An autopsy survey. Cancer 1979;43(11):1847–1857. [PubMed: 445371]

[5] Grandqvist S. Distribution of Polyps of the Large Bowel in Relation to Age: A colonoscopic study. Scandinavian Journal of Gastroenterology (SJG) 1981;16(11):1025–1031.

[6] Stryker S, Wolff B, Culp C, et al. Natural History of Untreated Colonic Polyps. Gastroenterology 1987;93(5):1009–1013. [PubMed: 3653628]

[7] Winawer S, Zauber A, Diaz B. The National Polyp Study – Temporal sequence of evolving colorectal cancer from normal colon. Gastrointestinal Endoscopy 1987;33(2): 167.

[8] Fearon E, Vogelstein B. A Genetic Model for Colorectal Tumorigensis. Cell 1990;61(5):759–767. [PubMed: 2188735]

[9] Johnson D, Gurney M, Volpe R, et al. A Prospective Study of the Prevalence of Colonic Neoplasms in Asymptomatic Patients with an Age-Related Risk. American Journal of Gastroenterology (AJG) 1990;85(6):969–974.

[10] Simons B, Morrison A, Lev R, Verhoek-Oftendahl W. Relationship of Polyps to Cancer of the Large Intestine. Journal of the National Cancer Institute (JNCI) 1992;84(5): 962–966.

[11] Potter J, Slattery M. Colon Cancer: A review of the epidemiology. Epidemiologic Reviews 1993;15 (3):499–545. [PubMed: 8174669]

[12] Byers T, Levin B, Rotherberger D, et al. ACS Guidelines for Screening and Surveillance for Early Detection of Colorectal Polyps and Cancer: Update 1997, CA. A Cancer Journal for Clinicians 1997;47(1):154–160.

[13] Winawer S, Fletcher R, Mayer R. Colorectal Cancer Screening: Clinical guidelines and rational. Gastroenterology 1997;112(3):594–642. [PubMed: 9024315]

[14] Robbins D, Itzowitz S. The Molecular and Genetic Basis of Colon Cancer. Medical Clinics of North America (MCNA) 2002;86(6):1467–1495.

[15] Church J. Clinical Significance of Small Colorectal Polyps. Diseases of the Colon and Rectum 2004;47(4):481–485. [PubMed: 14994108]

[16] Lieberman D, Holub J, Eisen G, et al. Prevalence of Polyps Greater Than 9 mm in a Consortium of Diverse Clinical Practice Settings in the United States. Clinical Gastroenterology and Hepatology 2005;3(8):798–805. [PubMed: 16234009]

[17] Odom S, Duffy S, Barone J, et al. The Rate of Adenocarcinoma in Endoscopically Removed Colorectal Polyps. The American Surgeon 2005;71(12):1024–1026. [PubMed: 16447472]

[18] Jass J. Classification of Colorectal Cancer based on Correlation of Clinical, Morphological and Molecular Features. Histopathology 2007;50(1):113–130. [PubMed: 17204026]

[19] Yoo T, Park D, Kim Y, et al. Clinical Significance of Small Colorectal Adenoma Less Than 10 mm: The KASID study. Hepatogastroenterology 2007;54(74):418–21. [PubMed: 17523287]

[20] Smith L. Fibreoptic Colonoscopy: Complications of colonoscopy and polypectomy. Diseases of the Colon and Rectum 1976;11(1):146–150.

[21] Kronberg O, Fenger C, Olsen J, et al. Randomized Study of Screening for Colorectal Cancer with Fecal-Occult-Blood Test. Lancet 1996;348(12):1467–1471. [PubMed: 8942774]

[22] Mandel J, Church T, Bond J, et al. The Effect of Fecal Occult Blood Screening on the Incidence of Colorectal Cancer. The New England Journal of Medicine 2000;343(22): 1603–1607. [PubMed: 11096167]

[23] Allison J, Sskoda I, Ransom L, et al. Screening for Colorectal Neoplasms with New Fecal Occult Blood Tests: Update on performance characteristics. Journal of the National Cancer Institute 2007;99 (11):1462–1470. [PubMed: 17895475]

[24] Imperiale T, Ransohoff D, Itzkowitz S, et al. Fecal DNA verse Fecal Occult Blood for Colorectal Cancer Screening in an Average-Risk Population. The New England Journal of Medicine 2004;351 (26):2704–2714. [PubMed: 15616205]

[25] Ahlquist D, Sargent D, Loprinzi C, et al. Stool DNA and Occult Blood Testing for Screen Detection of Colorectal Neoplasia. Annals of Internal Medicine 2008;149(7): 441–450. [PubMed: 18838724]

[26] Fork F. Double Contrast Enema and Colonoscopy in Polyp Detection. Gut 1981;22:971–977. [PubMed: 7308852]

[27] Morosi C, Ballardini G, Pisani P. Diagnostic Accuracy of the Double-Contrast Enema for Colonic Polyps in Patients with or without Diverticular Disease. Gastrointestinal Radiology 1991;16(2):345–347. [PubMed: 1936780]

[28] Brady A, Stevenson G, Stevenson I. Colorectal Cancer Overlooked at Barium Enema Examination and Colonoscopy: A continuing perceptual problem. Radiology 1994;192(2):373–378. [PubMed: 8029400]

[29] Selby J, Friedman G, Quesenberry C, Weiss N. A Case Control Study of Screening Sigmoidoscopy and Mortality from Colorectal Cancer. The New England Journal of Medicine 1992;326(10):653–657. [PubMed: 1736103]

[30] Elwood J, Sli G, Schlup M, et al. Flexible Sigmoidoscopy or Colonoscopy for Colorectal Screening: A randomized trial of performance and acceptability. Cancer Detection and Prevention 1995;19(4): 337–347. [PubMed: 7553676]

[31] Kewenter J, Breringe H, Engaras B, Haglind E. The Value of Flexible Sigmoidoscopy and Double Contrast Barium Enema in the Diagnosis of Neoplasms in the Rectum and Colon in Subjects with Positive Hemoccult: Results of 1,831 rectosigmoidoscopies and double contrast barium enemas. Endoscopy 1995;27(1):159–163. [PubMed: 7601048]

[32] Newcomb P, Storer B, Morimoto L, et al. Long-Term Efficacy of Sigmoidoscopy in the Reduction of Colorectal Cancer Incidence. Journal of the National Cancer Institute 2003;95(8):622–625. [PubMed: 12697855]

[33] Levin T, Farraye F, Schoen R, et al. Quality in the Technical Performance of Screening Flexible Sigmoidoscopy: Recommendations of an international multi-society task group. Gut 2005;54(6): 807–813. [PubMed: 15888789]

[34] Wolff W, Shinya H. Colonofiberoscopy. Journal of the American Medical Association (JAMA) 1971;217(11):1509–1512.

[35] Hafner M. Conventional Colonoscopy: Technique, indications, limites. European Journal of Radiology (EJR) 2007;61(2):409–414.

[36] Winawer S, Zauber A, Ho M, et al. Prevention of Colorectal Cancer by Colonoscopic Polypectomy. The New England Journal of Medicine 1993;329(27):1977–1981. [PubMed: 8247072]

[37] American Society for Gastrointestional Endoscopy. Appropriate Use of Gastrointestional Endpscopy. Gastrointestinal Endoscopy 2000;52(5):831–837.

[38] Seeff L, Richards T, Shapiro J, et al. How Many Endoscopies are Performed for Colorectal Cancer Screening? Results from CDC's survey of endoscopic capability. Gastroenterology 2004;127(6): 1670–1677. [PubMed: 15578503]

[39] Bartram C. Bowel Preparation – Principles and practice. Clinical Radiology 1994;49(2):365–367. [PubMed: 8045057]

[40] Ristvedt S, McFarland E, Weinstock L, Thyssen E. Patient Preferences for CTC, Conventional Colonoscopy, and Bowel Preparation. American Journal of Gastroenterology 2003;98(4):578–585. [PubMed: 12650790]

[41] "A Consensus Document on Bowel Preparation Prior to Colonoscopy," prepared by a Task Force from American Society of Colon and Rectal Surgeons (ASCRS), the American Society of Gastrointestinal Endoscopy (ASGE), and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) on April of 2006.

[42] Cai S, Zhang S, Zhu H, Zheng S. Barriers to Colorectal Cancer Screening: A case-control study. World Journal of Gastroenterology 2009;15(12):2531–2536. [PubMed: 19469005]

[43] Stevenson G, Wilson J, Wilkinson J, et al. Pain Following Colonoscopy: Elimination with carbon dioxide. Gastrointestinal Endoscopy 1992;38(3):564–567. [PubMed: 1397911]

[44] Steine S. Which Hurts the Most? A comparison of pain rating during double-contrast barium enema examinations and colonoscopy. Radiology 1994;191(1):99–101. [PubMed: 8134605]

[45] Orsoni P, Berdah S, Verrier C, et al. Colonic Perforation due to Colonoscopy: A retrospective study of 48 cases. Endoscopy 1997;29(1):160–164. [PubMed: 9201463]

[46] Weitzman E, Zapka J, Estabrook B, Goins K. Risk and Reluctance: Understanding impediments to colorectal cancer screening. Preventive Medicine 2001;32(6):502–513. [PubMed: 11394954]

[47] Rex D, Rahmani E, Haseman J, et al. Relative Sensitivity of Colonoscopy and Barium Enema for Detection of Colorectal Cancer in Clinical Practice. Gastroenterology 1997;112(1):17–23. [PubMed: 8978337]

[48] Bressler B, Paszat L, Vinden C, et al. Colonoscopic Miss Rates for Right-Sided Colon Cancer: A population-based analysis. Gastroenterology 2004;127(2):452–456. [PubMed: 15300577]

[49] Pickhardt P, Nugent P, Mysliwiec P, et al. Location of Adenomas Missed by OC. Archives of Internal Medicine 2004;141(2):352–359.

[50] Heresbach D, Barrioz T, Lapalus M, et al. Miss Rate for Colorectal Neoplastic Polyps: A prospective multi-center study of back-to-back video colonoscopies. Endoscopy 2008;40(4):282–290.

[51] Lieberman D, Moravec M, Holub J, et al. Polyp Size and Advanced Histology in Patients Undergoing Colonoscopy Screening: Implications for CTC. Gastroenterology 2008;135(4):1100–1105. [PubMed: 18691580]

[52] Kim D, Pickhardt P, Taylor A. Characteristics of Advanced Adenomas Detected at CTC Screening: Implications for appropriate polyp size thresholds for polypectomy versus surveillance. American Journal of Roentgenology 2007;188(6):940–944. [PubMed: 17377027]

[53] Lieberman D, de Garmo P, Fleischer D, et al. Colonic Neoplasia in Patients with Non-Specific GI Symptoms. Gastrointestinal Endoscopy 2000;51(6):647–651. [PubMed: 10840294]

[54] Gelfand D. Gastrointestinal Radiology: A short history and predictions for future. American Journal of Roentgenology 1988;150(4):727–730.

[55] Vining, D.; Gelfand, D.; Bechtold, R., et al. Technical Feasibility of Colon Imaging with Helical CT and Virtual Reality. Annual Meeting of American Roentgen Ray Society; New Orleans. 1994. p. 104

[56] Hong, L.; Kaufman, A.; Wei, Y.; Viswambharan, A.; Wax, M.; Liang, Z. IEEE Biomedical Visualization Symposium. IEEE CS Press; CA: 1995. 3D Virtual Colonoscopy; p. 26-32.

[57] Hara A, Johnson C, Reed J, et al. Detection of Colorectal Polyps by CTC: Feasibility of a novel technique. Gastroenterology 1996;110(2):284–290. [PubMed: 8536869]

[58] Hong L, Liang Z, Viswambharan A, et al. Reconstruction and Visualization of 3D Models of Colonic Surface. IEEE Transactions on Nuclear Science (TNS) 1997;44(11): 1297–1302.

[59] Reed J, Johnson C. Automatic Segmentation, Tissue Characterization, and Rapid Diagnosis Enhancements to the CTC Analysis Workstation. Journal of Digital Imaging 1997;10(1):70–73. [PubMed: 9268843]

[60] Wan, M.; Tang, Q.; Kaufman, A.; Liang, Z. Proc IEEE Computer Graphics and Applications. 1999. Volume Rendering Based Interactive Navigation within the Human Colon; p. 397-400.

[61] Coin C, Wollett F, Coin J, et al. Computerized Radiology of the Colon: A potential screening technique. Computed Radiology 1983;7(2):215–221.

[62] Shinners T, Pickhardt P, Taylor A, et al. Patient-Controlled Room Air Insufflation versus Automated Carbon Dioxide Delivery for CTC. American Journal of Roentgenology 2006;186(10):1491–1496. [PubMed: 16714635]

[63] Liang Z, Chen D, Li B, et al. On Segmentation of Colon Lumen for VC. Proc SPIE Medical Imaging 1999;3660:270–278.

[64] Fenlon H, Nunes D, Schroy P, et al. A Comparison of Virtual and Conventional Colonoscopy for the Detection of Colorectal Polyps. The New England Journal of Medicine 1999;341(11):1496–1503. [PubMed: 10559450]

[65] Fletcher J, Johnson C, Welch T, et al. Optimization of CTC Technique: Prospective trial in 180 patients. Radiology 2000;216(4):704–711. [PubMed: 10966698]

[66] Yee J, Akerkar G, Hung R, et al. Colorectal Neoplasia: Performance characteristics of CTC for detection in 300 patients. Radiology 2001;219(4):685–692. [PubMed: 11376255]

[67] Johnson D, Harmsen W, Wilson L, et al. Prospective Blinded Evaluation of CTC for Screen Detection of Colorectal Polyps. Gastroenterology 2003;125(2):311–319. [PubMed: 12891530]

[68] Pickhardt P, Choi R, Hwang I, et al. Computed Tomographic VC to Screen for Colorectal Neoplasia in Asymptomatic Adults. The New England Journal of Medicine 2003;349(12):2191–2200. [PubMed: 14657426]

[69] Johnson C, Chen MH, Toledano A, et al. Accuracy of CTC for Detection of Large Adenomas and Cancers. The New England Journal of Medicine 2008;359(12):1207–1217. [PubMed: 18799557]

[70] Regge D, Laudi C, Galatola G, et al. Diagnostic Accuracy of Computed Tomographic Colonography for the Detection of Advanced Neoplasia in Individuals at Increased Risk of Colorectal Cancer. The Journal of the American Medical Association 2009;301(23):2453–2461.

[71] Brenner D, Georgsson M. Mass Screening with CTC: Should the radiation exposure be of concern? Gastroenterology 2005;129(2):328–337. [PubMed: 16012958]

[72] Neri, E.; Faggioni, L.; Cerri, F., et al. CTC versus Double-Contrast Barium Enema for Screening of Colorectal Cancer: Comparison of radiation burden. 2009. Published online by September 24:

[73] Brenner DJ, Hall EJ. Computed Tomography – An increasing source of radiation exposure. The New England Journal of Medicine 2007;357(11):2277–2284. [PubMed: 18046031]

[74] Lu H, Li X, Li L, Chen D, Xing Y, Wax M, Hsieh J, Liang Z. Adaptive Noise Reduction toward Low-Dose CT. Proc SPIE Medical Imaging 2003;5030:759–766.

[75] Wang J, Li T, Lu H, Liang Z. Penalized Weighted Least-Squares Approach to Sinogram Noise Reduction and Image Reconstruction for Low-Dose X-ray CT. IEEE Transactions on Medical Imaging (TMI) 2006;25:1272–1283.

[76] Wang J, Wang S, Li L, Lu H, Liang Z. VC Screening with Ultra Low-Dose CT & Less-Stressful Bowel Preparation: A computer simulation study. IEEE Transactions on Nuclear Science 2008;55 (5):2566–2575. [PubMed: 19169383]

[77] Rust G, Aurich V, Reiser M. Noise/Dose Reduction and Image Improvements in Screening VC with Tube Currents of 20 mAs with Nonlinear Gaussian Filter Chains. Proc SPIE Medical Imaging 2002;4683:186–197.

[78] Purkayastha S, Tekkis P, Athanasiou T, et al. Magnetic Resonance Colonography versus Colonoscopy as a Diagnostic Investigation for Colorectal Cancer: A meta-analysis. Clinical Radiology 2005;60 (6):980–989. [PubMed: 16124980]

[79] Laks S, Macari M, Bini E. Positional Change in Colon Polyps at CTC. Radiology 2004;231(4):761–766. [PubMed: 15163817]

[80] Liang, Z.; Yang, F.; Wax, M., et al. Inclusion of A Priori Information in Segmentation of Colon Lumen for 3D VC. Conf Record IEEE NSS-MIC, in CD-ROM; 1997.

[81] Liang, Z. Electronic Colon Cleansing Techniques: Past, present, and future. The 11th International Conference on Medical Image Computing and Computer Assisted In-

tervention (MICCAI) Workshop – "New Era of Virtual Colonoscopy"; New York City, NY. September 6; 2008. p. 26-32.

[82] Liang Z, MacFall J, Harrington D. Parameter Estimation and Tissue Segmentation from Multispectral MR Images. IEEE Transactions on Medical Imaging 1994;13(3): 441–449. [PubMed: 18218519]

[83] Summers R, Johnson C, Pusanik L, et al. Automated Polyp Detection at CTC: Feasibility assessment in a human population. Radiology 2001;219(1):51–59. [PubMed: 11274534]

[84] Yoshida H, Nappi J. Three-Dimensional Computer-Aided Diagnosis Scheme for Detection of Colonic Polyps. IEEE Transactions on Medical Imaging 2001;20(8):1261–1274. [PubMed: 11811826]

[85] Wang Z, Liang Z, Li L, et al. Reduction of False Positives by Internal Features for Polyp Detection in CT-Based VC. Medical Physics 2005;32(12):3602–3616. [PubMed: 16475759]

[86] Zhu H, Liang Z, Barish M, Pickhardt P, et al. Increasing Computer-aided Detection Specificity by Projection Features for CTC. Medical Physics, to appear. 2010

[87] Liang Z, Lakare S, Wax M, et al. A Pilot Study on Less-Stressful Bowel Preparation for VC Screening with Follow-up Biopsy by OC. Proc SPIE Medical Imaging 2005;5746:810–816.

[88] Pickhardt, P.; Kim, D. CTC: Principles and practice of virtual colonoscopy. Saunders, Elsevier; Philadelphia, PA, USA: 2009.

[89] Park S, Lee S, Choi E, et al. Flat Colorectal Neoplasma Definition, Importance, and Visualization on CTC. American Journal of Roentgenology 2007;188(5):953–959. [PubMed: 17377029]

[90] Liang Z, Wang S. An EM Approach to MAP Solution of Segmenting Tissue Mixtures: A numerical analysis. IEEE Transactions on Medical Imaging 2009;28(2):297–310. [PubMed: 19188116]

[91] Wang S, Li L, Cohen H, Mankes S, Chen J, Liang Z. An EM Approach to MAP Solution of Segmenting Tissue Mixture Percentages with Application to CT-based VC. Medical Physics 2008;35(12):5787–5798. [PubMed: 19175136]

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