# Imaging modalities for the staging of patients with colorectal cancer

#### S. Bipat<sup>1\*</sup>, M.C. Niekel<sup>1</sup>, E.F.I. Comans<sup>2</sup>, C.Y. Nio<sup>1</sup>, W.A. Bemelman<sup>3</sup>, C. Verhoef<sup>4</sup>, J. Stoker<sup>1</sup>

<sup>1</sup>Department of Radiology, Academic Medical Centre, University of Amsterdam, Amsterdam, the Netherlands, <sup>2</sup>Department of Nuclear Medicine and PET Research, VU University Medical Centre, Amsterdam, the Netherlands, <sup>3</sup>Department of Surgery, Academic Medical Centre, University of Amsterdam, Amsterdam, the Netherlands, <sup>4</sup>Department of Surgical Oncology, Erasmus University Medical Centre, Rotterdam, the Netherlands, \*corresponding author: tel.: +31 (0)20 5663102, fax: +31 (0)20-5669119, e-mail: s.bipat@amc.uva.nl

#### ABSTRACT

Dutch guidelines made the following recommendations for staging colorectal cancer (CRC). For liver metastases, computed tomography (CT) or magnetic resonance imaging (MRI) could be used. For lung metastases, imaging could be limited to chest X-ray. The primary aim of this survey was to summarise the use of imaging modalities and the variation in techniques.

Three surveys were created and sent to three groups of medical specialists, namely surgeons, radiologists and nuclear medicine physicians. The management survey included questions on the role of different modalities for evaluation of synchronous liver, lung and extrahepatic metastases. The radiological survey included questions concerning the technical aspects of ultrasound (US), CT and MRI. The nuclear medicine survey included questions concerning the technical aspects of FDG-PET and FDG-PET/CT. The management and radiological surveys were sent to abdominal surgeons and abdominal radiologists within 88 hospitals and the nuclear medicine survey to specialists within 34 hospitals.

Response rates were 75.0% (n=66/88), 77.3% (n=68/88) and 64.7% (n=22/34) for the management, radiological and nuclear medicine surveys, respectively. For liver metastases, the first modality of choice was CT in 52 (78.8%) and US in 12 hospitals (18.2%). Lung metastases were evaluated by either chest X-ray or chest CT and extrahepatic metastases mainly by CT (n=55). In the radiological and nuclear medicine surveys, some variations in techniques of US, CT, MRI, FDG-PET and FDG-PET/CT were seen.

CT is primarily used for liver and extrahepatic metastases and both chest CT and chest X-ray for lung metastases. There are discrepancies between the survey of daily practice and the present guidelines. Comparative studies on different staging strategies for colon and rectal cancer, including comparing a strategy of CT liver/abdomen versus MRI liver/abdomen for the evaluation of liver and extrahepatic disease and chest X-ray or chest CT for lung metastases would be important for well-founded adjustments of the present guidelines.

#### **KEYWORDS**

Colorectal neoplasms, diagnostic imaging, metastasis, staging

#### INTRODUCTION

Colorectal cancer (CRC) is diagnosed in the Netherlands in over 10,000 new patients per year, making colorectal cancer 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. It is expected that in 2015 the incidence of colorectal cancer will have increased to approximately 14,000 new patients per year.<sup>1</sup> A Dutch national evidence-based guideline on the diagnosis and treatment of patients with colorectal liver metastases was published in 2006.2.3 The guidelines were developed by a working group mandated by the disciplines involved in this field, including surgeons, medical oncologists, gastroenterologists, radiologists and nuclear medicine physicians. The recommendations for detection of synchronous metastases by diagnostic imaging were as follows. For synchronous liver metastases, spiral computed tomography (CT) with an intravenous contrast agent (more

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than 45 gram iodine), or magnetic resonance imaging (MRI) with a contrast agent were indicated as imaging modality. For the evaluation of lung metastases, imaging could be limited to conventional chest X-ray, based on the low prevalence of lung metastases and the occurrence of false-positives at CT. No recommendations were made for the use of <sup>18</sup>F fluorodeoxyglucose positron emission tomography (FDG-PET) and FDG-PET/CT for this patient group, since data and the use of these modalities were limited at that time.

Since the introduction of this evidence-based guideline. several improvements have been made in imaging such as the extensive use of multispiral CT, new available MRI-contrast liver agents and the more widespread use of FDG-PET and the introduction of FDG-PET/CT. 4-9 In addition, many new studies have evaluated the role of the different modalities or techniques for this patient population.10-15

At this time point it is unclear if and to what extent these improvements have led to variations in the management. To gain information on the use of imaging modalities and the variation in techniques, we performed a digital survey in all hospitals in the Netherlands. The aim of this survey was to summarise the use of imaging modalities in staging of patients with CRC and the extent of variation in techniques used by radiologists and nuclear medicine specialists.

#### METHODS

#### Survey

Three different surveys were sent to three groups of medical specialists who are mainly involved in the staging of patients with colorectal cancer, by using imaging modalities.

1) The management survey. This survey included general questions, such as information on the hospital, specialist and years of experience, and specific questions on the role of the different imaging modalities in the staging of CRC, for the evaluation of liver, lung and extrahepatic disease. The specific questions are described in *table 1*.

2) The radiological survey. This survey also included general questions, such as information on the hospital, specialist and years of experience, and the specific questions concerning the technical aspects of ultrasonography (US), CT and MRI. The specific questions are described in *table 2*.

3) The nuclear medicine survey. This survey also included general questions, such as information on the hospital, specialist and years of experience, and the specific questions concerning FDG-PET and FDG-PET/CT. The specific questions are described in the *table* 3.

Table 1. The management survey to define the role of imaging modalities

Answers

Never

US

CT

MRI

Never

Other

Never

US

CT

MRI

CCC

FDG-PET

FDG-PET/CT

Times per week

Other hospitals

4-point scale varying

4-point scale varying

from no role to major role

from no role to major role

Chest X-ray

Always (100%)

Often (50-90%)

Sometimes (<50%)

Chest CT

FDG-PET

FDG-PET/CT

Always (100%)

Often (50-90%)

Sometimes (<50%)

Always (100%),

Often (50-90%)

Sometimes (<50%)

#### Questions

Is an imaging modality used for the detection of synchronous liver metastases?

Which imaging modality is used for the detection of synchronous liver metastases? Indicate which modality is the first,

second, third choice, etc. Is imaging performed for the detection of synchronous lung metastases?

Which imaging modality is used for the detection of synchronous lung metastases?

Indicate which modality is the first, second, third choice, etc.

Is imaging used for the detection of synchronous extrahepatic abdominal metastases?

Which imaging modality is used for the detection of synchronous extrahepatic abdominal metastases? Indicate which modality is the first, second, third choice, etc.

What is the frequency of multidisciplinary meetings for colorectal cancer patients held in your institution?

Are these meetings held with consultants from the Comprehensive Cancer Centres (CCC) or with specialists from other hospitals?

To what extent are surgeons, oncologists, gastroenterologists, radiologists, nuclear medicine physicians or internists involved in the care of these patients?

To what extent do findings in the literature, availability of techniques, available expertise, associated costs, available personnel and waiting lists affect the choice for a diagnostic modality?

**Participants** 

Since surgeons are mainly involved in the management of these patients, the management survey was sent to abdominal surgeons in all 88 Dutch hospitals with the help of the 'Dutch Surgical Society' (NVvH) in November 2010. The radiological survey was sent to abdominal radiologists in all 88 Dutch hospitals with the help of the 'Radiological Society of the Netherlands' (NVvR) in November 2010. The nuclear medicine survey was sent to nuclear medicine physicians within 34 hospitals in January 2011: only hospitals with the availability and use of FDG-PET or FDG-PET/CT (based on the results of the management survey) were contacted.

**Table 2.** The radiological survey to summarise thetechnical aspect of US, CT and MRI

| Modality | Questions   | Answer   |
|----------|---|--|
| US       | What part of the abdomen<br>is imaged using US for<br>the detection of synchro-<br>nous metastases? | Solely the liver<br>Upper abdomen<br>Lower abdomen   |
|          | What type of transducer is used?  | Convex<br>Convex+Linear  |
|          | What is the frequency of the transducer?  | Mhz  |
|          | Which US technique is used?   | Grayscale imaging<br>Tissue-harmonic<br>imaging  |
|          | Is a contrast agent used for US?  | Yes (type, dose)<br>No   |
| CT       | What part of the body is<br>imaged using CT for the<br>detection of synchronous<br>metastases?      | Solely the liver<br>Upper abdomen<br>Lower abdomen<br>Thorax   |
|          | What type of CT scanner is used?  | Single-slice or multi-slice<br>Number of detectors   |
|          | Is intravenous contrast agent used?   | Yes (type, dose)<br>No   |
|          | Which phases are used<br>and what is the timing of<br>the phases?                                   | Arterial, portal or late<br>(timing)   |
| MRI      | What part of the body is<br>imaged using MRI for the<br>detection of synchronous<br>metastases?     | Liver/Upper abdomen<br>Lower abdomen   |
|          | Which MRI scanner is used?  | Strength and type of coil  |
|          | Is an intravenous contrast<br>agent used for MRI in the<br>detection of synchronous<br>metastases?  | Yes (type, dose, timing)<br>No   |
|          | What sequences are<br>used in MRI for the<br>detection of synchronous<br>metastases?                | TrW-SE, TrW-GRE,<br>TrW-FSE,<br>TrW-FATSAT, T2W-SE,<br>T2W-FSE<br>T2W-FATSAT, Dynamic<br>TrW with contrast agent,<br>HASTE, Diffusion<br>weighted sequence with<br>ADC-mapping |

## Table 3. The nuclear medicine survey to summarise the technical aspects of PET and PET/CT

| Modality                | Questions   | Answers   |  |  |
|-------------------------|---|---|--|--|
| FDG-PET or<br>FDG-PETCT | Is NEDPAS used*   | Yes<br>No   |  |  |
| FDG-PET                 | What is the PET acquisi-<br>tion time?                                  | Minutes per bed<br>position   |  |  |
|                         | What amount of FDG is used for the detection of synchronous metastases? | MBq/kg bodyweigh  |  |  |
|                         | What are the specifica-<br>tions for the patient<br>preparation?        | Fasting time<br>Time interval<br>between FDG<br>injection and<br>scanning |  |  |
|                         | How are the images evaluated  | Quantitatively<br>Qualitatively   |  |  |
|                         | What modality is used for visually comparison?                          | CT<br>MRI<br>Other  |  |  |
| FDG-PET/CT              | What is the PET acquisi-<br>tion time?                                  | Minutes per bed<br>position   |  |  |
|                         | What amount of FDG is used for the detection of synchronous metastases? | MBq/kg bodyweigł  |  |  |
|                         | What are the specifica-<br>tions for the patient<br>preparation?        | Fasting time and<br>time interval betwee<br>FDG-injection and<br>scanning |  |  |
|                         | How is the evaluation of the images read?                               | Quantitatively<br>Qualitatively   |  |  |
|                         | Is a low dose or a<br>high dose used for CT<br>imaging?                 | Low dose (mAs, kV<br>High dose (mAs, kV                                   |  |  |
|                         | Is an intravenous<br>contrast agent used for<br>CT with FDG-PET/CT?     | Yes (type, dose,<br>phases, timing)<br>No                                 |  |  |
|                         | Is an oral contrast<br>agent used for CT with<br>FDG-PET/CT?            | Yes (type, dose)  |  |  |
|                         | Who evaluates the<br>images from the<br>FDG-PET/CT?                     | Nuclear medicine<br>physician<br>Radiologist                              |  |  |

#### Response

After two months, all non-responders were contacted, initially via email, subsequently via telephone call. We aimed to reach a response rate of at least 70%.

#### Data presentation

We used a descriptive statistical analysis to summarise the results. Continuous, normally distributed data were expressed as means, with corresponding standard deviations. Continuous, not normally distributed data, were expressed as median with ranges or as modus with ranges, depending on the type of data. Categorical data were expressed as number and percentage.

#### RESULTS

#### Response rate

The response rates were 75.0% (n=66/88), 77.3% (n=68/88) and 64.7% (n=22/34) for the management, radiological and nuclear medicine surveys, respectively. All eight academic hospitals participated in the management and radiological surveys. Based on the results of the management surveys, concerning the use of FDG-PET or FDG-PET/CT for staging of CRC, specialists within 34 hospitals were invited to complete the nuclear medicine survey. For the nuclear medicine survey five out of six (83.3%) academic medical hospitals using either FDG-PET or FDG-PET/CT participated in this survey.

#### Management survey

This survey was completed by surgeons (n=62), oncologists (n=1), internists (n=1) or this was not described (n=2). The experience of the responders ranged from one year to 29 years, with a mean of 11.3 $\pm$ 6.7 years. The availability of US, CT, MRI, FDG-PET or FDG-PET/CT was 100% (66), 100% (66), 56.1% (37) and 62.1% (41) hospitals, respectively.

*Liver metastases*: In 64 of the 66 hospitals (97.0%) imaging was always performed for the assessment of synchronous liver metastases, while in two hospitals (3.0%) imaging was often used, but not in all patients. The first modality of choice was CT in 52 hospitals (78.8%) and US in 12 hospitals (18.2%). The second choice was US in 34 hospitals (51.5%) and CT in 11 hospitals (16.7%). MRI, FDG-PET and FDG-PET/CT were not frequently used as first or second choice modality (*figure 1*).

*Lung metastases:* 53 of 68 hospitals (80.3%) always used an imaging modality for the assessment of lung metastases, in ten hospitals (15.2%) an imaging modality was often used and sometimes in three hospitals (4.5%). No imaging for lung metastases was performed in one hospital (1.5%). In all hospitals, assessment of synchronous lung metastases was done by either conventional chest X-ray or chest CT; FDG-PET or FDG-PET/CT was only used as third choice modality (*figure 2*).

*Extrahepatic abdominal metastases*: For the detection of extrahepatic abdominal metastases, imaging was used in all patients in 40 of the 66 hospitals (60.6%). Twelve hospitals (18.2%) often used an imaging modality and in 13 hospitals this was sometimes used (19.7%). One hospital

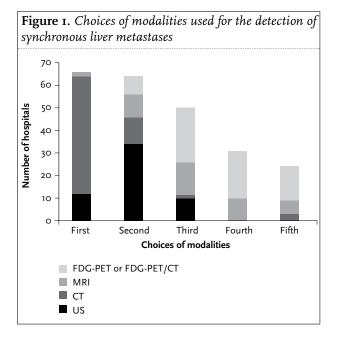


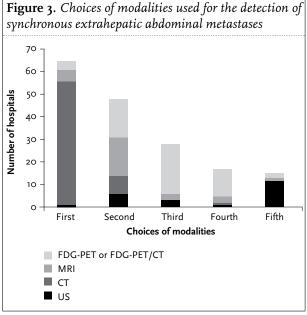
Figure 2. Choices of modalities used for the detection of synchronous lung metastases 70 60 Number of hospitals 50 40 30 20 10 o First Second Third Choices of modalities FDG-PET or FDG-PET/CT CT chest Chest X-ray

(1.5%) never used an imaging modality for the assessment of extrahepatic abdominal metastases. In most hospitals evaluating extrahepatic abdominal metastases was mainly done by CT (n=55) and to a lesser extent by US, MRI, PET and/or PET/CT (*figure 3*).

In summary, CT is primarily used for the evaluation for liver and extrahepatic colorectal metastases. For evaluation of lung metastases, chest CT and conventional chest X-ray are used to a comparable extent.

#### **Decision making**

Specialists involved: Specialists primarily involved in decision making were predominantly surgeons in 51 and



medical oncologists in 22 hospitals. Gastroenterologist, radiologists, nuclear medicine physicians and internists were less involved in decision making.

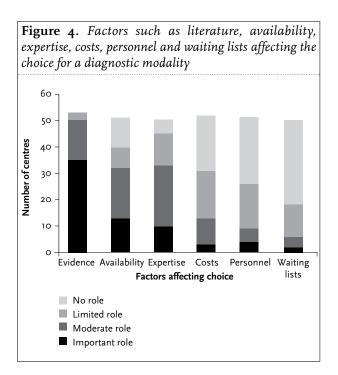
*Multidisciplinary meeting:* Multidisciplinary meetings to discuss treatment options for colorectal cancer patients were routinely held in 65 hospitals (twice a week in six hospitals, weekly in 55 hospitals and every other week in four hospitals). Meetings with other hospitals were held in 19 hospitals and consultations from the Comprehensive Cancer Centres were requested in 47 hospitals. In seven hospitals, both other hospitals as well as specialists from Comprehensive Cancer Centres were involved. Seven hospitals did not have meetings with either the Comprehensive Cancer Centres or other hospitals.

*Factors affecting choices*: The choice of imaging modality was mostly determined by evidence in the literature, followed by availability and expertise and occasionally by costs, personnel and waiting lists (*figure 4*).

#### **Radiological survey**

The radiological survey was only completed by radiologists (n=68), with experience ranging from two to 32 years, with a mean experience of 12.2±7.2 years. The radiological surveys were not completed in exactly the same 66 hospitals as the management surveys; in 50 hospitals both surveys were completed.

Ultrasonography was performed in 31 (45.6%), CT in 67 (98.5%) and MRI in 20 (22.7%) hospitals for the detection of synchronous colorectal metastases.



*Ultrasonography:* US was used for visualisation of the liver in all 31 hospitals (100%) where it was performed and for the evaluation of extrahepatic abdominal disease in 13 of these hospitals (41.9%). In all 31 hospitals (100%) a convex transducer was used and an additional linear transducer for detailed visualisation of the liver surface was used in three hospitals (9.7%). The frequency of the transducer ranges from 3 MHz to 8.5 MHz. US with harmonic imaging in combination with conventional US was performed in 22 hospitals (71.0%). One hospital (3.2%) occasionally used a contrast agent during ultrasound.

*Computed tomography*: CT was used for evaluation of liver metastases in all 67 hospitals (100%) were it was applied, for extrahepatic abdominal metastases in 63 hospitals (94.0%) and for lung metastases in 32 hospitals (47.8%). In 66 hospitals (98.5%), a multislice CT scanner was available, with the number of detectors ranging from 2 to 320 (modus 64 detectors), while one hospital (1.5%) had a single-slice CT scanner. CT was always performed with an intravenous contrast agent (100%) and the number of phases varied between hospitals. The portal phase was always used (100%), either as a single phase (52.2%) or in combination with arterial and late phases (*table 4*).

Forty-two hospitals (62.7%) used fixed timing for contrast; the arterial phase ranged from 20 to 40 seconds (modus 25 seconds), the portal phase ranged from 55 to 90 seconds (modus 70 seconds) and the late phase ranged from 120 to 360 seconds (modus 300 seconds). Twenty-three hospitals (34.3%) used bolus tracking and two hospitals (3.0%) did not report the type of timing.

The amount of iodine administrated ranged from 21 to 53 gram (mean  $35.6\pm7.2$  g). Ten hospitals (14.9%) used at least 45 gram iodine.

*Magnetic resonance imaging:* MRI was used for the evaluation of the liver disease in 12 of the 20 hospitals (60%) were it was used and for the evaluation of extrahepatic disease evaluation in nine hospitals (45.0%). The magnetic field strength of the available MRI scanners were predominantly 1.5 T (n=17), and further 3.0 T (n=2) and 1.0 T (n=2). In 15 hospitals (75.0%), an additional coil was used (14 phased array and 1 wrap around coil). Contrast agents were used in 15 hospitals (75.0%);

| <b>Table 4.</b> Phases used for the evaluation of synchronousliver lesions |                        |            |  |  |  |  |  |
|--|------------------------|------------|--|--|--|--|--|
| Phases used  | Number of<br>hospitals | Percentage |  |  |  |  |  |
| Portal phase   | 35                     | 52.2%      |  |  |  |  |  |
| Arterial + portal phases   | II                     | 16.4%      |  |  |  |  |  |
| Arterial + portal +late phases   | 18                     | 26.9%      |  |  |  |  |  |
| Portal + late phases   | 3                      | 4.5%       |  |  |  |  |  |

Gadolinium or a comparable contrast agent was used in ten hospitals and a liver specific contrast agent (Gadoxetic acid, Primovist, Bayer Schering, Berlin, Germany) was used in five hospitals. The sequences used for MRI were predominantly T2W-FSE (n=12), dynamic contrastenhanced TrW (n=12) and diffusion weighted images (n=11).

#### Nuclear medicine survey

The nuclear medicine survey was completed by nuclear medicine physicians (n=21) and by one radiologist, with years of experience ranging from three to 28 years (mean 11.2±7.3 years). In 18 hospitals (81.8%), the Dutch protocol for standardisation of FDG (NEDPAS) was used. For evaluation of synchronous liver, lung and extrahepatic abdominal disease, FDG-PET was solely performed in two hospitals and FDG-PET/CT with either low-dose or high-dose CT in 14 hospitals.

*FDG-PET* (n=2): Patients fasted for six hours in both hospitals and were scanned 60 minutes after the injection of FDG (3 and 4.6 MBq/kg, respectively). The acquisition times were three and five minutes per bed position, respectively. Assessment was done qualitatively in both hospitals and visually compared with either CT or MRI.

*FDG-PET/CT* (*n*=14): In all hospitals, a multi-slice PET/ CT scanner was available, with the number of detectors ranging from two to 64 (modus 16 detectors). Patients fasted for either four or six hours prior to the investigation. Administration of on average 2.99 Mbq/kg FDG (min: 1.7, max: 4.6) was predominantly 60 minutes prior to the investigation. Acquisition time ranges from 1.45 to 5 minutes per bed position. A low-dose CT image was performed in 13 hospitals (92.9%) and in eight of these hospitals (61.5%) an additional high-dose CT (diagnostic CT) was performed. Only one hospital (7.1%) performed a diagnostic CT solely. For the diagnostic CT, intravenous contrast agent administration with fixed timing and portal phase CT was always performed.

Data on radiation intensity, tube voltage, amount of contrast agent and phases are presented in *table 5*. The use of oral contrast agent was limited. Evaluation of the images was done by both the radiologist and nuclear medicine physician in 12 hospitals (85.7%). In two hospitals (14.2%) only the nuclear medicine physician evaluated the PET/CT images as only low-dose CT was used.

#### DISCUSSION

This study shows that a majority of hospitals use a comparable staging strategy, with CT as the first choice for staging of liver and extrahepatic disease and either chest

CT or chest X-ray for evaluation of lung metastases. The role of US, MRI, FDG-PET and FDG-PET/CT as first choice techniques was limited.

In the radiological and nuclear medicine surveys, some variations in US, CT, MRI, PET and PET/CT techniques were seen. The majority of variation was within the accepted variation reported in the literature. In the Dutch guideline on colorectal liver metastases, recommendations were made concerning the use of a contrast agent for MRI and at least 45 grams of iodine for CT. Only a minority used at least 45 gram iodine for CT. However, this 45 gram iodine cut-off was chosen arbitrarily based on the results of a meta-analysis.<sup>16</sup> Not all hospitals used an MRI contrast agent, which could be explained by the use of recently introduced advanced MRI techniques (e.g. diffusion weighted imaging), which makes the use of contrast agent less critical.<sup>17,18</sup>

The strengths of this survey are the relatively high response rate and the participation of all types of hospitals (e.g. academic, tertiary). Therefore we believe that this survey does reflect the status of the use of imaging for the detection of synchronous colorectal metastases in the Netherlands.

This study has several limitations. First, the survey was relatively detailed and not all information requested was readily available, especially for the nuclear medicine physician dealing with the FDG-PET/CT technical features. This might explain the lower response rate for this part of the survey. Another limitation is that we did not separate the survey for colon and rectal tumours. As MRI is used for local staging of rectal cancer, there might be a difference in the utilisation of MRI for evaluation of the liver, lung and extrahepatic disease between patients with colon cancer or rectal cancer.<sup>19</sup> We chose not to perform a different survey for colon tumour and rectum tumour to enhance participation. Finally, not all management and radiology surveys were obtained from the same hospitals. However, the majority of these surveys were obtained from the same hospitals (n=50).

The Dutch guideline indicates either computed tomography (CT) or magnetic resonance imaging (MRI) as the first choice for liver staging.<sup>1,20,21</sup> This survey demonstrated that the role of MRI for staging is less prominent in daily practice as could have been expected based on the literature, where MRI has shown to have higher sensitivity rates for the detection of liver metastases than CT.<sup>17,18,22,23</sup> As the liver is the primary organ for metastatic spread (15%) of colorectal cancer, the use of the technique with the highest sensitivity seems obvious. Further, in patients with rectal cancer MRI is already part in the work-up for local staging. Presumably, lack of expertise, more limited availability and higher costs are important reasons for this rather limited use of MRI.

**Table 5.** PET and PET/CT features in the hospitals using these modalities for evaluation of synchronous liver, lung andextrahepatic metastases

| PET features       |                     |   |   |                             | CT fe       | atures                      |                               |   |  |                                | PET/CT image<br>analyses   |  |
|--------------------|---------------------|---|---|-----------------------------|-------------|-----------------------------|-------------------------------|---|--|--------------------------------|--|--|
| Fasting<br>(hours) | Amount<br>FDG       | Scan<br>time                            | Time<br>after<br>FDG<br>injectic<br>(min) | PET<br>analyses<br>m        | Slice<br>CT | Low<br>dose<br>(mAs/<br>kV) | High<br>dose<br>(mAs/kV)      | IV<br>contrast<br>and<br>amount<br>Iodine | Phases<br>(sec)  | Oral<br>contrast               | Image analysis by  |  |
| 6                  | 3 MBq/kg            | 3 min/bp                                | 60  | Qualitative*†               |             |                             |                               |   |  |                                |  |  |
| 6                  | 4.6 MBq/<br>kg      | 5 min/bp                                | 60  | Qualitative*                |             |                             |                               |   |  |                                |  |  |
| 6                  | NA                  | NA                                      | 60  | Qualitative<br>Quantitative | 16          | YES<br>(50/120)             | NO                            | NO  |  | NO                             | Nuclear medicine<br>physicians <sup>‡</sup>  |  |
| 6                  | 3.45<br>MBq/kg      | 4 min/<br>bp                            | 55-65                                     | Qualitative                 | 16          | YES<br>(NA/<br>NA)          | NO                            | NO  |  | NO                             | Nuclear medicine<br>physicians   |  |
| 6                  | 2.0 - 2.2<br>MBq/kg | 3 min/bp<br>Total 7<br>positions        | 60  | Qualitative                 | 40          | YES<br>(40/120)             | NO                            | NO  |  | NO                             | Radiologists and<br>nuclear medicine<br>physicians   |  |
| 6                  | 3.0 MBq/<br>kg      | 3 min/pb<br>Total 7<br>positions        | 60  | Qualitative                 | 40          | YES<br>(20/130)             | NO                            | NO  |  | 100 ml<br>Telebrix<br>350      | Radiologists and<br>nuclear medicine<br>physicians   |  |
| 4                  | 3.2 MBq/<br>kg      | Total<br>24-32<br>min                   | 50  | Quantitative                | 16          | NO                          | YES<br>(150-<br>250/120)      | YES<br>(36 gr)                            | Portal<br>(70s)  | NO                             | Radiologists and<br>nuclear medicine<br>physicians   |  |
| 4                  | Based on<br>BMI     | 3 min/bp<br>Total 7<br>positions        | 60  | Qualitative<br>Quantitative | 16          | YES<br>(60/120)             | YES<br>150/120                | YES<br>(30 gr)                            | Portal<br>(60s)  | 25 ml<br>Telebrix              | Radiologists and<br>nuclear medicine<br>physicians   |  |
| 6                  | 3.125<br>MBq/kg     | 1.45 min/<br>bp                         | 60  | Qualitative<br>Quantitative | IO          | YES<br>(62/120)             | YES<br>(100/120)              | YES<br>(30-36<br>gr)                      |  | NA                             | Radiologists and<br>nuclear medicine<br>physicians   |  |
| 6                  | Based on<br>BMI     | 3-5 min/<br>pb<br>Total<br>24-40<br>min | 60  | Quantitative                | 6           | YES<br>(40/130)             | YES<br>(90/130)               | YES<br>(36 gr)                            | Portal<br>(70s)  | NO                             | Radiologists and<br>nuclear medicine<br>physicians   |  |
| 6                  | 3.0 MBq/<br>kg      | Total 25<br>min                         | 60  | Qualitative                 | 16          | YES<br>(25/120)             | YES<br>(350/120)              | YES<br>(31.5 gr)                          | Arterial<br>(NA)<br>Portal<br>(70s)<br>Late<br>(300s)  | 10 ml<br>Omni-<br>paque<br>350 | Radiologists and<br>nuclear medicine<br>physicians   |  |
| 6                  | 1.7 MBq/<br>kg      | 3 min/bp                                | 60-90                                     | Qualitative<br>Quantitative | 6           | YES<br>(NA/<br>NA)          | YES<br>(95/110)               | YES<br>(36 gr)                            | Portal<br>(45-50s)                                     | NA                             | Radiologists and<br>nuclear medicine<br>physicians   |  |
| 6                  | Based on<br>BMI     | Total<br>20-22<br>min                   | 60  | Qualitative                 | 16          | YES<br>(30/140)             | YES<br>(250/120)              | YES<br>(NA)                               | Arterial<br>(30s)<br>Portal<br>(90s)                   | 100 ml<br>Omni-<br>paque       | Radiologists and<br>nuclear medicine<br>physicians   |  |
| 4                  | 2.7 MBq/<br>kg      | 2.30 min/<br>bp                         | 45  | Qualitative<br>Quantitative | 64          | YES<br>20/120               | YES <sup>(</sup><br>(175/120) | YES <sup>  </sup><br>(39.6<br>gr)         | Arterial<br>(25s)<br>Portal<br>(70s)<br>Late<br>(360s) | 50 ml<br>Telebrix<br>350       | Low dose: nuclear<br>medicine physicians<br>High dose:<br>Radiologists and<br>nuclear medicine<br>physicians |  |
| 4                  | 3.0 MBq/<br>kg      | 4 min/bp                                | 60  | Qualitative                 | 64          | YES<br>(NA/<br>NA)          | YES§<br>(NA/NA)               | YES∥<br>(NA)                              | Portal<br>(NA)   | NO                             | Radiologists and<br>nuclear medicine<br>physicians   |  |
| 4                  | Based on<br>BMI     | 4 min/bp<br>Total 5 -6<br>positions     | 60  | Qualitative<br>Quantitative | 40          | YES<br>(30/120)             | NO                            | NO  |  | NO                             | Radiologists and<br>nuclear medicine<br>physicians   |  |

bp = bed position; \* FDG-PET data were visually compared with either CT or MRI; mAs = radiation intensity; NA = not available; \* FDG-PET data were used for fusion with CT using software; \* 80% is always performed with low-dose CT and therefore read by nuclear medicine physicians; <sup>1</sup> high-dose CT is not always performed; <sup>II</sup> contrast agent is only administrated for high-dose CT scans.

For evaluating lung metastases, the Dutch guidelines recommend the use of conventional chest X-ray<sup>I,20,2I</sup> as different studies, including a recent Dutch study, have shown the limited role of chest CT (chest CT has many false-positives).12 However the UK guideline prefers chest CT<sup>24</sup> and USA guidelines recommend conventional chest X-ray for colon cancer,<sup>25</sup> and in case of resectable rectal cancer an additional chest CT.<sup>26</sup> From a practical point of view, a chest CT is a simple addition to the - widespread utilised - CT for detection of liver and extrahepatic diseases and this presumably explains this inconsistency between evidence and daily practice/guidelines. This difference in viewpoints is reflected in the results of this survey where both chest CT as well as conventional chest X-ray are used to a comparable extent. In addition, some responders noted that chest CT was predominantly used for staging of rectal cancer which is in line with the USA guideline. As the prevalence of lung metastases is higher in rectal cancer compared with colon cancer,27 the role of chest CT should be more clearly defined in the Dutch guidelines and differentiating between patients with colon cancer and rectal cancer might be a sensible approach.

For the evaluation of extrahepatic abdominal disease, no recommendations were made in the Dutch guidelines.<sup>1,20,21</sup> In international guidelines CT is preferred as is also seen in our survey. This may be different between patients with rectal and colon cancer, where in the former MRI is used for local staging and might be extended as an abdominal MRI.<sup>24/26</sup>

The Dutch guidelines lag behind in following current insights into the role of FDG-PET and FDG-PET/CT.<sup>28,29</sup> In USA guidelines these modalities are already playing a major role<sup>24</sup> and this is also seen in clinical practice to some extent. However, the role of FDG-PET and FDG-PET/ CT as routine investigation in staging CRC is not well established and is primarily used in specific groups of patients.<sup>30</sup>

In summary, the present Dutch guidelines on staging of patients with colorectal cancer are only partly in line with recent international guidelines and on some aspects there is considerable discrepancy between the guideline and the findings of the survey. A potentially important reason for this discrepancy between guideline and daily practice – as well as between guidelines – is the lack of cost-effectiveness studies comparing different strategies. Hospitals will therefore either use a commonly used established strategy or develop a different strategy based on variable weighting of different issues, including evidence, availability and costs. This leads to variation in work-up with either over- or under-utilisation of imaging techniques. Research into the optimal strategy of staging of patients with CRC is therefore mandatory. There is only one German study comparing the costs of whole body MRI with the costs of a conventional diagnostic algorithm for the staging of rectal cancer, consisting of abdominal ultrasound and chest X-ray (chest/abdominal CT in the case of positive findings at abdominal ultrasound or chest X-ray).<sup>19</sup> They reported substantial savings when whole-body MRI was used for the preoperative TNM staging of patients with rectal cancer; however, no data on the effectiveness in terms of diagnostic accuracy have been reported.

We therefore propose to perform cost-effectiveness studies for the comparisons of different staging strategies for colon and rectal cancer separately, including comparing a strategy of CT liver/abdomen versus MRI liver/abdomen for the evaluation of liver and extrahepatic disease and chest X-ray or chest CT for lung metastases and studying the additional role of FDG-PET and FDG-PET/CT. Based on these data well-founded adjustments can be made to the present guidelines

#### References

- 1. www.vikc.nl.
- Bipat S, van Leeuwen MS, IJzermans JN et al. Evidence-based guideline on management of colorectal liver metastases in the Netherlands. Neth J Med. 2007;65:5-14.
- 3. www.oncoline.nl.
- Coenegrachts K. Magnetic resonance imaging of the liver: New imaging strategies for evaluating focal liver lesions. World J Radiol. 2009;1:72-85.
- Coenegrachts K, Matos C, ter Beek L, et al. Focal liver lesion detection and characterization: comparison of non-contrast enhanced and SPIO-enhanced diffusion-weighted single-shot spin echo echo planar and turbo spin echo T2-weighted imaging. Eur J Radiol. 2009;72:432-9.
- Yasui O, Sato M, Kamada A. Diffusion-weighted imaging in the detection of lymph node metastasis in colorectal cancer. Tohoku J Exp Med. 2009;218:177-83.
- Muhi A, Ichikawa T, Motosugi U, et al. Diagnosis of colorectal hepatic metastases: Contrast-enhanced ultrasonography versus contrastenhanced computed tomography versus superparamagnetic iron oxide-enhanced magnetic resonance imaging with diffusion-weighted imaging. J Magn Reson Imaging. 2010;32:1132-40.
- Meijerink MR, van Waesberghe JH, Golding RP, et al. Subtractionmultiphase-CT unbeneficial for early detection of colorectal liver metastases. Eur J Radiol. 2010;74:e132-7.
- Wiering B, Vogel WV, Ruers TJ, Oyen WJ. Controversies in the management of colorectal liver metastases: role of PET and PET/CT. Dig Surg. 2008;25:413-20.
- Wiering B, Adang EM, van der Sijp JR, et al. Added value of positron emission tomography imaging in the surgical treatment of colorectal liver metastases. Nucl Med Commun. 2010;31:938-44.
- Maas M, Rutten IJ, Nelemans PJ, et al. What is the most accurate whole-body imaging modality for assessment of local and distant recurrent disease in colorectal cancer? A meta-analysis: Imaging for recurrent colorectal cancer. Eur J Nucl Med Mol. Imaging 2011 [Epub ahead of print].
- Grossmann I, Avenarius JK, Mastboom WJ, Klaase JM. Preoperative staging with chest CT in patients with colorectal carcinoma: not as a routine procedure. Ann Surg Oncol. 2010;17:2045-50.
- Manfredi S, Lepage C, Hatem C, Coatmeur O, Faivre J, Bouvier AM. Epidemiology and management of liver metastases from colorectal cancer. Ann Surg. 2006;244:254-9.
- McIntosh J, Sylvester PA, Virjee J, Callaway M, Thomas MG. Pulmonary staging in colorectal cancer--is computerised tomography the answer? Ann R Coll Surg Engl. 2005;87:331-3.

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- 15. Delbeke D, Martin WH. FDG PET and PET/CT for colorectal cancer. Methods Mol Biol. 2011;727:77-103.
- Bipat S, van Leeuwen MS, Comans EF, et al. Colorectal liver metastases: CT, MR imaging, and PET for diagnosis--meta-analysis. Radiology. 2005;237:123-31.
- Coenegrachts K, De Geeter F, ter Beek L, et al. Comparison of MRI (including SS SE-EPI and SPIO-enhanced MRI) and FDG-PET/CT for the detection of colorectal liver metastases. Eur Radiol. 2009;19:370-9.
- Coenegrachts K, Orlent H, ter Beek L, et al. Improved focal liver lesion detection: comparison of single-shot spin-echo echo-planar and superparamagnetic iron oxide (SPIO)-enhanced MRI. J Magn Reson Imaging. 2008;27:117-24.
- Huppertz A. Schmidt M, Wagner M, et al. Whole-Body MR Imaging versus Sequential Multimodal Diagnostic Algorithm for Staging Patients with Rectal Cancer: Cost Analysis Fortschr Röntgenstr. 2010;182:793-802.
- National Working Group on Gastrointestinal Cancers. Colon cancer. Amsterdam, The Netherlands: Association of Comprehensive Cancer Centres (ACCC); 2008 Sep 23. p70.
- National Working Group on Gastrointestinal Cancers. Rectal cancer. Amsterdam, The Netherlands: Association of Comprehensive Cancer Centres (ACCC); 2008 Oct 14. p82.
- 22. Niekel MC, Bipat S, Stoker J. Diagnostic imaging of colorectal liver metastases with CT, MR imaging, FDG PET, and/or FDG PET/CT: a meta-analysis of prospective studies including patients who have not previously undergone treatment. Radiology 2010; 257:674-84.

- Kim HJ, Kim KW, Byun JH, et al. Comparison of mangafodipir trisodiumand ferucarbotran-enhanced MRI for detection and characterization of hepatic metastases in colorectal cancer patients. JR Am J Roentgenol. 2006;186:1059-66.
- 24. Association of Coloproctology of Great Britain and Ireland. Guidelines for the management of colorectal cancer. London (UK): Association of Coloproctology of Great Britain and Ireland; 2007. p11721.
- Rosen MP, Bree RL, Foley WD, Gay SB, Grant TH, Heiken JP, et al. ACR Appropriateness Criteria
   Pretreatment Staging Colorectal Cancer 2008.
- 26. Suh WW, Johnstone PA, Blackstock AW, et al. Expert Panel on Radiation Oncology-Rectal/Anal Cancer. ACR Appropriateness Criteria® resectable rectal cancer 2007
- Mitry E, Guiu B, Cosconea S, Jooste V, Faivre J, Bouvier AM. Epidemiology, management and prognosis of colorectal cancer with lung metastases: a 30-year population-based study. Gut 2010;59:1383-88.
- 28. Lambregts DM, Maas M, Cappendijk VC, et al. Whole-body diffusionweighted magnetic resonance imaging: Current evidence in oncology and potential role in colorectal cancer staging.Eur J Cancer. 2011 Epub ahead of print
- Chowdhury FU, Shah N, Scarsbrook AF, Bradley KM. [18F]FDG PET/ CT imaging of colorectal cancer: a pictorial review. Postgrad Med J. 2010;86:174-82.
- Van Cutsem E, Oliveira J. Primary colon cancer: ESMO clinical recommendations for diagnosis, adjuvant treatment and follow-up. Ann Oncol. 2009;20:49-50.