C.D. Blanke · C. Rödel · M.S. Talamonti *Editors*

# Gastrointestinal Oncology

## A Practical Guide

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(Editors)

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Gastrointestinal Oncology

# Preface

Gastrointestinal oncology practitioners aim to establish effective prevention and treatment strategies for patients with malignancies involving the GI tract, ultimately leading to a reduction in morbidity and mortality from GI cancers. GI tumours arise from a number of distinct anatomic sites and may or may not share underlying biologic similarities; however, they differ in their required radiotherapeutic or surgical approaches for limited, curable disease, as well as their chemosensitivity and treatment patterns in the advanced or metastatic settings. The best therapeutic approach to these cancers is usually multidisciplinary, involving medical, surgical, and radiation oncologists, with strong input from pathologists, gastroenterologists, and specialists in diagnostic imaging. Making major strides in future GI cancer control will certainly involve both expert clinicians and researchers, specializing in areas including new drug development, clinical trial design, biostatistics, experimental and molecular therapeutics, and molecular pathology.

This edition of *Gastrointestinal Oncology: A Practical Guide* features chapters devoted to each of the major GI anatomic sites, as well as sections on diagnostic imaging, interventional GI oncology, practical correlative science, and non-site specific tumours such as neuroendocrine cancers and gastrointestinal stromal tumours. The emphasis of this text is to furnish useful, evidence-based clinical advice, highlighting the multidisciplinary nature of GI oncology practice. This remains an incredibly exciting time in medicine. The knowledge leaps in molecular oncology in general and characterization and treatment of GI malignancies specifically have been prodigious. We hope you find the information in this text useful, guiding your everyday practice and stimulating thought regarding potential future advances.

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# Imaging in Gastrointestinal Cancer

# 1

Minsig Choi and Anthony F. Shields

## 1.1 Introduction

Imaging has been an essential part of oncology since the discovery and use of X-rays by Roentgen. Gastrointestinal (GI) oncology has made extensive use of a number of imaging approaches which utilize X-rays, including plain films, contrast placed in the intestinal tract for barium swallows, upper gastrointestinal (UGI) series, barium enemas (BE), and in the last three decades, the extensive use of computed tomography (CT). A number of other techniques are now routinely employed including ultrasound (US), magnetic resonance imaging (MRI), and positron emission tomography (PET). Most imaging modalities provide adequate anatomic and structural images of cancer patients. Recent technological advances in functional imaging bring new insights to cancer staging and early monitoring of treatment response. This chapter concentrates on some of the new approaches to imaging and the application of older approaches where active research is being done in screening, diagnosis and staging, monitoring treatment, and surveillance in GI cancers. It also focuses on PET and PET-CT scans and novel ways of utilizing these methodologies to improve the clinical outcomes in GI cancer patients.

## 1.2 Screening

Screening of GI cancers has most commonly been done using endoscopic procedures, since one can visualize the tumors, biopsy the lesions, and even remove small lesions at the same time. This approach has been the standard of practice in the upper GI tract in populations

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and patients with high risk of esophageal and stomach cancers. In the lower GI tract, colorectal cancer screening has employed a number of techniques including fecal blood testing, stool DNA analysis, colonoscopy, X-rays with BE, and more recently, CT colonography.

### 1.2.1 Colon Cancer Screening

In recent years, colonoscopy has almost completely replaced BE for screening the entire colon, since colonoscopy has a higher sensitivity for cancer (95 and 82.9% in colonoscopy and BE, respectively) and more readily detects polyps (Rex et al. 1997; Rockey et al. 2004). Furthermore, an abnormal barium study generally requires a subsequent colonoscopy to obtain a biopsy or remove small polyps. The advent of CT colonography (also called virtual colonoscopy) may change the routine screening paradigm once again, but this remains an area of very active research. CT colonography allows one to obtain high-resolution images of the colon that include the usual cross-sectional images and, in addition, one can obtain three-dimensional endoluminal views. A number of studies have analyzed the sensitivity and specificity of CT colonography and a meta-analysis of 24 studies with 4,181 patients, published between 1994 and 2003, found a sensitivity of 93% (95% confidence interval [CI]: 73%, 98%) and specificity of 97% (95% CI: 95%, 99%) for lesions >1 cm (Halligan et al. 2005). Another meta-analysis of 30 studies, published between 1997 and 2005, found that CT colonography had a sensitivity of 82% for polyps over 10 mm (95% CI: 76–88%) (Rosman and Korsten 2007).

It should be noted that these meta-analyses included older studies and the methods used for CT colonography have been evolving over time with continuous software improvement. In fact, most of the studies in these meta-analyses primarily used 2D reconstruction for the initial evaluation. Furthermore, these studies took the optical colonoscopy as the "gold standard." A study by Iannaccone et al. (2005) involved 88 patients who initially underwent CT colonography and standard colonoscopy on the same day, where the observers were unaware of the results of the other studies. The patients then underwent a repeat colonoscopy within two weeks by an endoscopist who had knowledge of the first examinations and this final evaluation served as the reference. On a per-polyp basis, for lesions ≥6 mm, the sensitivities of CT colonography and colonoscopy were 86 and 84%, respectively. On a per-patient basis the sensitivities of CT colonography and colonoscopy were 84 and 90%, respectively. While lesions less than 6 mm were difficult to detect by CT colonography, for lesions ≥6 mm the two approaches were comparable.

CT colonography is now regularly reimbursed for patients who have incomplete colonoscopies in the United States. For routine screening, payment by Medicare was denied in 2009 because of concern that most of the comparative studies were conducted in patients under the age of 65. While the cost of CT colonography is less than a colonoscopy, the fact that an abnormal CT colonography study mandates colonoscopy lessens the advantage somewhat. In the study by Johnson et al., 17 and 12% of patients had lesions ≥5 or ≥6 mm, respectively, and would require colonoscopy depending on the chosen threshold. With the CT colonography threshold set at ≥5 mm, the positive predictive value for the test

was 0.45 for adenomas ≥5 mm or cancer. Concerns about the radiation dose have also been raised, along with the cost and complications associated with the evaluation of extracolonic findings of unknown significance found on the CT scans. Overall 66% of the patients had extracolonic findings, but fortunately most were not thought to require further evaluation. The evaluation of extracolonic findings, which were needed in 16% of subjects in the study by Johnson et al. (2008), will lead to added costs and patient anxiety.

One of the continuing issues is the need for complete bowel cleansing before CT colonography, as it is done before colonoscopy. To decrease the number of false positive CT colonography studies, patients are regularly given oral contrast after purging to help differentiate retained stool from polyps (Johnson et al. 2008). Similar approaches have been studied using minimal bowel preparation and combined fecal tagging. When compared to full preparation, these methods had sensitivities of 97 and 88%, respectively, for polyps ≥6 mm (Nagata et al. 2009). Investigators are working on software filters to improve lesion detection and hence decrease the need for bowel cleansing (Oda et al. 2009). In summary, CT colonography is already finding routine use, but further testing and refinement are in order. New techniques may allow for limited bowel preparation, which is preferred by patients (Jensch et al. 2009).

### 1.2.2 Diagnosis and Staging

CT has been the standard for the diagnosis and staging of GI cancers over the last 30 years. The CT scan has a sensitivity of 75–90%, and a specificity of 80–90% (McAndrew and Saba 1999; Pasanen et al. 1992), and can elucidate important abdominal structures. CT angiography can assess the relationship of the tumor to the neighboring major vessels. MRI adds little information after conventional CT scans except for the hepatobiliary system. Its use has been defined in the individual disease chapters and is excluded from this chapter.

### 1.2.3 PET Imaging: The Basics

PET scans are a noninvasive imaging modality utilizing positron emitting radioisotopes to label molecules and create different images depending on the tissue concentrations. $^{18}$F-Fluorodeoxyglucose ($^{18}$F-FDG), an analog of glucose, is the most commonly used tracer and accumulates more specifically in metabolically active cells like cancer. It capitalizes on the distinctive feature of cancer, which has a higher glycolytic index known as the Warburg (1956) phenomenon. Aside from high glucose utilization, most cancer cells have a higher expression of the glucose transporter Glut-1 than normal cells (Aloj et al. 1999; Tohma et al. 2005). Inside the cell FDG is phosphorylated by hexokinase, but further glucose metabolism is prevented by the fluorine atom. Thus, FDG preferentially accumulates in the tumor cells as illustrated in Fig. 1.1. Detectors surrounding the patient during a PET scan capture the degree of tumoral $^{18}$F-FDG. Its avidity is expressed using a standardized uptake value

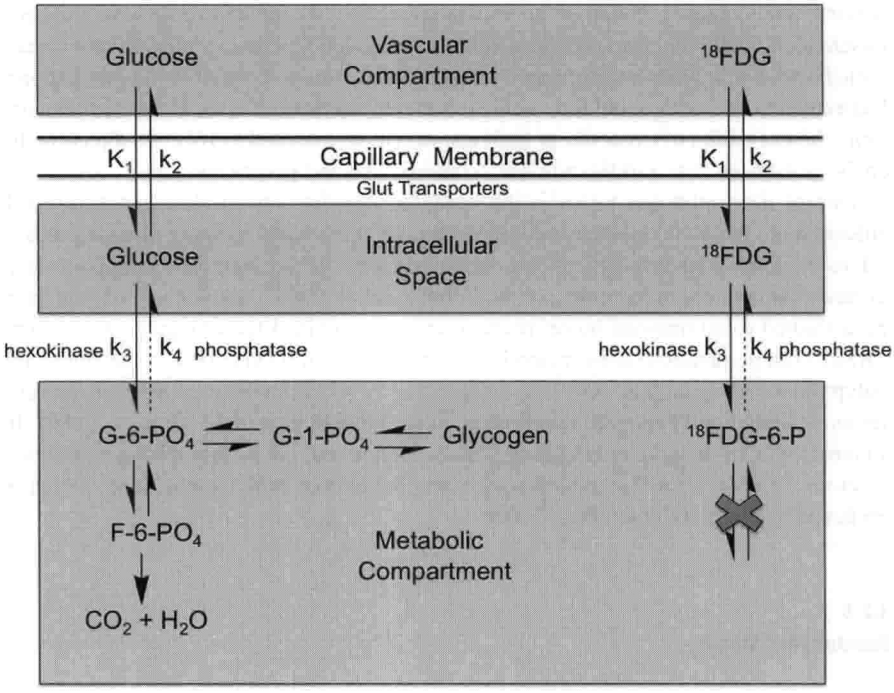


**Fig. 1.1** When glucose enters the cell, hexokinases phosphorylate glucose into glucose-6-phosphate. Glucose can undergo glycolysis producing $CO_2$, water and energy. $^{18}$F-Fluorodeoxyglucose ($^{18}$F-FDG) follows the same pathway as glucose, but, after phosphorylation, $^{18}$F-FDG is not further metabolized. Hence, FDG can preferentially accumulate in the tumor cells

(SUV). SUV is a semiquantitative measure of $^{18}$F-FDG uptake from PET images comparing it to the normal physiologic distribution. SUVs are dependent on several parameters: blood glucose level, tumor size, time after $^{18}$F-FDG injection, and spatial resolution of the images. Although kinetic parameters of $^{18}$F-FDG-PET can be expressed using Patlak and compartmental modeling, the need for prolonged imaging and the complexity of such modeling has limited most routine clinical studies to SUV quantitation to measure the activity of $^{18}$F-FDG in cancer (Gjedde and Diemer 1983; Patlak et al. 1983).

$^{18}$F-FDG became a useful radiotracer since it has a longer half-life of 110 min as compared to other radioisotopes. There are no pharmacologic adverse effects of the radiolabelled FDG since it uses an extremely low amount of tracer (less than a micromole). The high sensitivity and specificity of PET imaging makes it a useful tool in the diagnosis and staging of cancer patients (Bombardieri et al. 2001; Facey et al. 2007; Fletcher et al. 2008). Its reproducibility for quantitative metabolic measurements has been validated in malignant tumors using FDG-PET (Minn et al. 1995; Weber et al. 1999). PET is now approved for use in the United States for the initial staging of many cancers. Its use for restaging and assessment of treatment response has not been approved for reimbursement for GI cancers originating in the stomach, liver, pancreas, biliary tree, and small intestine, as well as neuroendocrine

cancers (http://www.cancerpetregistry.org/indications_facilities.htm) (National Oncology PET Registry (NOPR) 2009; Avril et al. 2005; Avril and Weber 2005). Although the spatial resolution for PET scans continues to improve, current resolution is approximately 0.5 cm and low-contrast dose can limit the detection of lesions two to four times larger. Hence, the ability to detect subcentimeter lesions in oncology remains a challenge. Another limitation of PET is its lack of ability to distinguish infectious or inflammatory conditions from cancer. These acute conditions attract metabolically active granulocytes and monocytes that can lead to false positive findings, particularly after surgery and radiation therapy. Additionally, physiologic $^{18}$F-FDG uptake by normal tissues can lead to false positive findings. Brain and heart tissues in particular may have avid uptake (shortly after tracer injection) while moderate uptake may be seen in the liver, spleen, and GI tract. Finally, the FDG is excreted by the urinary system. Some other areas that can have increased physiologic uptake include muscles and brown fat and lymphatic tissues. The sensitivity of these areas may often be suboptimal when the patient has recently exercised stimulating muscles, or has had an infectious or inflammatory condition leading to activity in lymphatic tissues.

The emergence of PET-CT has improved the confidence and accuracy of PET imaging because it can delineate clear anatomic relationships in areas with FDG activity. Increasingly, PET-CT is replacing dedicated PET devices in the United States and currently almost all of the new units being sold are combined PET-CT machines. Other advantages of PET-CT are its ability to perform both tests at a single convenient time point, and better-resolution images are provided as compared to fused images. Due to its recent emergence, clinical outcome using long-term survival data are not available for patients who were staged using PET-CT.

### 1.2.4 PET in Staging GI Cancers

At this point, PET is only routinely done for staging prior to surgery in GI oncology patients with esophageal cancer. For other GI cancers, PET is regularly employed as a problem-solving tool to assist in staging when other clinical or imaging studies suggest that the patient may have more widespread disease. The role for PET scans in staging esophageal cancer is derived from multiple studies demonstrating changes in the clinical decision in patients planned for surgical intervention (Flamen et al. 2000; Kato et al. 2005; van Westreenen et al. 2004). As esophagectomy has an operative mortality of 4–10%, avoiding surgical intervention in patients with distant metastasis who will not benefit from surgery is paramount (Enzinger and Mayer 2003). However, PET scans are noted to be inferior to endoscopic ultrasound (EUS) in local and regional lymph node (LN) staging with a sensitivity of 51% and specificity of 84%. Sensitivity for PET in detecting distant metastasis is 67% and specificity of 97% (van Westreenen et al. 2004). PET is regularly used in conjunction with CT scans and endoscopic US for staging esophageal cancer. PET-CT has been shown to improve sensitivity, specificity, and accuracy in staging esophageal cancer patients. Recent data show a sensitivity of 93.9%, specificity of 92%, and accuracy of 92% in patients with locally advanced squamous esophageal cancer (Yuan et al. 2006). In most of the recent clinical studies, PET can detect unsuspected metastatic

disease in 15–20% of patients, consequently changing the management approach to those patients (Flamen et al. 2000; Kato et al. 2005; van Westreenen et al. 2004).

Staging of gastric carcinoma using PET is complicated by the high physiologic uptake of FDG in normal gastric mucosa. Sensitivity of primary tumors varies from 58 to 94% with specificity of 78–100% (Dassen et al. 2009). The wide ranges of sensitivity and specificity may be related to the location and tumor histology. Proximal gastric cancers behave like esophageal cancer and are easily detected with PET while tumors in the distal stomach have a low sensitivity. Tumor histology can also affect the PET sensitivity; tumors with diffuse subtype and mucinous adenocarcinoma have a low sensitivity due to the small concentration of active cancer cells compared to its background. Up to 30% of gastric cancers may not be assessed with PET (Ott et al. 2008; Stahl et al. 2003). Overall, locoregional staging using PET is poor with a sensitivity of 28% as compared to CT scan with a sensitivity of 68%, but with a higher specificity of 96% (Dassen et al. 2009). Limited studies done on PET for gastric cancer distant staging shows a sensitivity of 67–85% and specificity of 74–88% (Yoshioka et al. 2003).

PET has a limited role in the initial staging of patients with colorectal cancer and currently is not routinely used if metastatic disease is not suspected based on CT or other studies. The benefit and risk ratio for surgical intervention in colorectal cancer is high and the morbidity is low. Additionally, precancerous adenomatous polyps also demonstrate higher FDG uptake and PET is not sensitive for locoregional staging. It is a useful test for patients with potentially resectable hepatic metastasis and in those with recurrent disease. PET can detect additional systemic metastasis and can be helpful in preventing futile laparotomies. Figure 1.2 illustrates

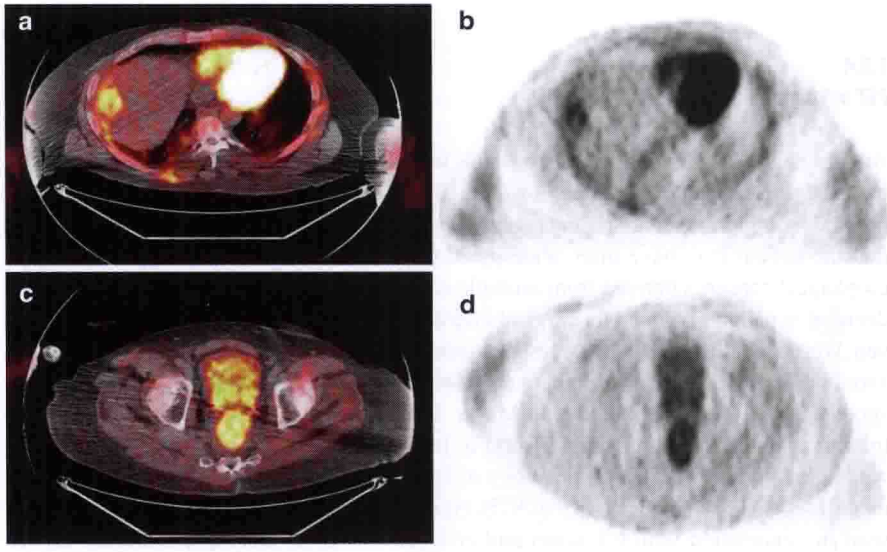


**Fig. 1.2** Fused positron emission tomography/computed tomography (PET/CT) scans (**a**, **c**) and PET alone (**b**, **d**) of a patient with a lesion seen in the rectum (images **c**, **d**) and in the liver (images **a**, **b**). Because of an elevated creatinine the routine CT scan was done without contrast and did not show this liver lesion, although a larger lesion in the dome was visualized (not shown)

a patient with recurrent rectal cancer with three liver lesions. The sensitivity of PET for hepatic lesions is 92% and specificity is high at 96% while CT has a sensitivity of 83% and specificity of 84% (Wiering et al. 2005). PET also has a sensitivity of 91% and specificity of 98% in detecting extrahepatic lesions as compared to 61 and 91% for CT. In a number of clinical studies, PET has been shown to alter therapeutic management in 20–32% of patients with potentially resectable metastatic disease. These changes include avoidance of surgery, initiation of palliative chemotherapy, or change in the extent of surgical interventions. PET is not helpful in detecting lesions less than 1 cm and in patients with peritoneal carcinomatosis. A recent randomized trial was done to compare the outcome in patients with potentially resectable liver metastases. Patients underwent routine staging with or without PET prior to planned surgery. Overall PET was found to decrease the number of futile surgeries by 38%. With routine CT evaluation of 75 patients who went to surgery, 34 (45%) were found to have unresectable disease or recurred within 6 months. When PET was included 21 of 75 (28%) patients had unnecessary surgery (Wiering et al. 2005; Ruers et al. 2009). Compared to the use of dedicated PET devices, data on the utilization of PET-CT are evolving; PET-CT in most clinical scenarios leads to a change in patient management in 11–21% (Lubezky et al. 2007; Rappeport et al. 2007; Selzner et al. 2004).

In pancreatic cancer, even pancreaticoduodenectomy (Whipple procedure) cures only a tiny fraction of patients. This procedure has a high surgical and postoperative mortality of up to about 5%. Overall evidence shows that PET can be beneficial, mostly by avoiding futile surgeries. PET's sensitivity is 91% and its specificity is 86% (BCBS 2000). PET is also a useful tool in the initial work-up of pancreatic masses of unknown origin (Heinrich et al. 2005; Sperti et al. 2007). Masses with increased FDG retention are more likely to be cancer, but inflammatory conditions can also be visualized with PET. On the other hand, PET can miss some mucinous tumors and those with extensive fibrosis. Table 1.1 summarizes the sensitivity and specificity of PET scan in staging for different GI cancers.

In liver and hepatobiliary cancers, FDG-PET is not helpful in staging and surveillance. Hepatocellular cancer (HCC) shows poor uptake of FDG due to a high level of glucose-6-phosphatase, which is responsible for dephosphorylating $^{18}$F-FDG (Garcea et al. 2009). Only 30–60% of primary HCC have avid FDG uptake (Okazumi et al. 1992). PET still

**Table 1.1** Sensitivity and specificity of positron emission tomography (PET) scan in gastrointestinal cancers

| Site | Staging | Sensitivity | Specificity | References |
|---|---|---|---|---|
| Esophagus | Locoregional<br>Distant | 51% (34–69)<br>67% (58–76) | 84% (76–91)<br>97% (90–100) | van Westreenen et al. (2004) |
| Stomach | Locoregional<br>Distant | 27.5% (18–46)<br>67–85% | 96% (91–100)<br>74–88% | Dassen et al. (2009) |
| Liver | Whole body | 61% | NA | Park et al. (2008) |
| Colorectum | Hepatic lesion<br>Extrahepatic | 88% (85–95)<br>92% | 96%<br>95% | Wiering et al. (2005) |
| Colon | Whole body | 85% | 90% | Wiering et al. (2005) |
| Pancreas | Whole body | 91% | 86% | BCBS (2000) |

may be useful in patients at risk for HCCs who have a rising alpha-fetoprotein. In such patients liver scarring and regeneration may hide a growing tumor on routine CT and MRI. A positive PET scan may help direct biopsies, but a negative scan does not rule out cancer. A recent Korean study shows that FDG-PET has a sensitivity of 61%, which could be improved to 83% using dual tracer imaging using $^{11}$C-acetate (Park et al. 2008). However, performance of PET remained poor in small and well-differentiated tumors. Future studies with dual tracer imaging may prove to be valuable in PET for primary hepatobiliary tumors.

## 1.3 Monitoring Response to Treatment

The recent advances in targeted therapy for cancer have led to individualized therapy for cancer patients based on molecular and other biomarkers. Monitoring such therapies itself may affect the clinical outcome. Normal CT and MRI scans measure anatomic changes to current treatment and such changes have been monitored through either the World Health Organization (WHO) classification or response evaluation criteria in solid tumors (RECIST) (Miller et al. 1981; Therasse et al. 2000). WHO classification defines tumor measurement by utilizing the product of two perpendicular diameters (bidimensional) as criteria for measurement. It groups response into four different categories: complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD). Complete radiologic disappearance without any new lesions was considered CR. A 50% decrease in size is considered PR while a 30% increase in size was deemed progression of disease. Anything that does not meet the above criteria is considered SD (Miller et al. 1981). RECIST uses unidimensional measurement to simplify the monitoring and has been validated in recent clinical studies (Therasse et al. 2006). When multiple measurable tumors are noted, each measurement is added. Response is reported as PR if there is more than a 30% decrease in unidimensional diameter and PD if more than 20% growth is noted (Therasse et al. 2000). The RECIST working group reviewed 6,500 patients and more than 18,000 lesions to find out how the criteria affect patients and overall outcome. In 2009, the group came up with RECIST 1.1, decreasing the number of maximum target lesions from 10 to 5 (five to two per organ) and defined criteria for measuring LNs using the short axis. RECIST 1.1 also adds new lesions on FDG-PET as PD, incorporating new technology to the RECIST (Eisenhauer et al. 2009).

Both WHO criteria and RECIST offer simple approaches to determine anatomic size and tumor changes during a therapeutic treatment as an indicator of response. Although RECIST has been validated to correlate with clinical outcome, these responses have been correlated to neither pathologic response nor survival outcome in certain GI cancers. In pancreatic cancer, for example, use of doublet therapy produces a higher response rate than does the use of gemcitabine alone, but no difference in overall survival is noted in multiple phase III trials (Oettle et al. 2005; Rocha Lima et al. 2004). Most trials in pancreatic cancer continue to use survival as the primary endpoint. Similarly, studies demonstrate that RECIST cannot accurately demonstrate clinical

benefit in patients with GI stromal tumors (GIST) treated with imatinib (Benjamin et al. 2007; Choi et al. 2007).

Cellular degradation and reconstruction of tumor tissue is the final step in treatment, making early monitoring difficult using anatomic images. The recent use of targeted therapies has led to other cutoffs to evaluating response, since tumor shrinkage may not be seen and disease stabilization is more common. Studies of drug development now include waterfall plots where the change in tumor size at a specified time or greatest change in size may be plotted (Arnold et al. 2008; Ratain et al. 2006). Instead of categorizing tumor response to arbitrary categories, waterfall plots measure change in tumor size as a continuous variable. Patients with limited tumor growth are considered to benefit from such a treatment even in the absence of major tumor shrinkage. Further improvements in both morphologic and functional imaging are clearly needed for better monitoring of patients with GI cancers.

Early treatment monitoring is crucial to avoid toxicity and the costs associated with ineffective therapy. Furthermore, improved measurements may provide for the earlier use of alternate therapies to impact clinical outcome. PET data suggest the amount of FDG uptake in tumor cells is correlated with the number of viable cancer cells. Hence, decline in FDG-PET avidity is hypothesized to represent a decrease in the number of viable cancer cells, though it might also represent a transport phenomenon. This concept has been tested for PET in early assessment of cancer treatment in esophageal, breast, and head and neck cancers (Juweid and Cheson 2006). Wahl et al. recently reported new response criteria incorporating PET for monitoring cancer treatment, naming the system PET evaluation criteria in solid tumors (PERCIST) (Wahl et al. 2009). Actual usage of PERCIST will require validation studies in GI cancer and its treatments. If further studies could refine the use of PET in monitoring and correlate its results to clinical outcome, such progress will improve the current concept of individualizing therapy.

### 1.3.1 Use of FDG-PET in Monitoring Early Response to Treatment

#### 1.3.1.1 Esophageal Cancer

Recent clinical trials have shown that the use of neoadjuvant chemotherapy and chemoradiotherapy for locally advanced gastroesophageal cancer improves overall survival. Monitoring early response to therapy is important in this disease since patients responding to neoadjuvant therapy have better clinical outcomes than nonresponding patients. Weber et al. studied 37 patients with locally advanced gastroesophageal cancer who received neoadjuvant chemotherapy. FDG-PET was done at baseline and on day 14 of the first cycle of chemotherapy. The percentage change in SUV was more prognostic than the absolute value of SUV. Patients with more than a 35% decrease in SUV were considered PET responders while those who had less were considered nonresponders. The two-year survival and overall survival rates of PET responders were 49% and >48 months, respectively, as compared to 9% and 20 months, respectively, for nonresponders ($p=0.04$).

The same group assessed 44 patients with locally advanced gastric cancer. A similar outcome was noted; PET responders had survival of >48 months while nonresponders had 17 months ($p=0.001$) (Weber et al. 2001). Nine patients did not have PET activity in the baseline and were excluded from further analysis. Wieder et al. evaluated 27 patients with neoadjuvant chemoradiotherapy and used 30% SUV changes as criteria for PET response. PET responders had median overall survival of >38 months as compared to 18 months for nonresponders (Wieder et al. 2004). Other similar studies assessing treatment response using PET for gastroesophageal cancer are listed in Table 1.2.

A multi-institutional study testing the feasibility of PET-guided therapy in gastroesophageal cancer was conducted by Lordick et al. This study enrolled 110 patients with gastroesophageal cancer and the PET scan was done at 2 weeks after induction chemotherapy was used to identify patients with metabolic response. Metabolic responders were predefined as patients with SUV decrease of more than 35% from baseline. Patients who were metabolic responders continued to receive chemotherapy for 12 weeks while nonresponders discontinued chemotherapy and immediately had surgical resection. The median overall survival for metabolic responders was not reached, whereas median overall survival for nonresponders was 25.8 months ($p=0.015$) (Lordick et al. 2007). The study also demonstrated a correlation of metabolic responders and pathologic response. Major histopathologic regression (Ia or Ib) was seen in 59% of patients who were metabolic responders but no histopathologic regression was seen in PET nonresponders. These findings may enable future clinical trials to utilize PET scans to tailor multimodality therapy for gastroesophageal cancers.

#### 1.3.1.2 Colorectal Cancer

There have been several small studies assessing PET in monitoring patients with colorectal cancers. Findlay et al. monitored 18 patients with colon cancer and liver metastasis who were treated with infusional 5FU and interferon. Although the tumor–liver ratio and SUV did not correlate with treatment response at 1–2 weeks, more than 15% decrease in tumor–liver ratio at 4–5 weeks was able to predict the ultimate response as measured by CT (done later in treatment) with a sensitivity of 100% and specificity of 90% (Findlay et al. 1996). No survival data were available for responders vs. nonresponders. Most of the other small studies investigated 20–30 patients who received chemoradiotherapy for rectal cancer and investigated different PET parameters and pathologic response. Guillem et al. reported a long-term outcome of 15 patients with locally advanced rectal cancer treated with 5FU-based chemoradiotherapy and usage of PET monitoring. An SUV change from baseline and at 5 weeks after chemoradiotherapy of less than 62.5% was predictive of disease recurrence (Guillem et al. 2004). Capirci et al. conducted the largest study, which investigated 81 patients with stage II and III rectal cancer who received neoadjuvant chemoradiotherapy. PET done at 1 month after completion of CRT had a sensitivity of 45% in detecting patients with complete pathologic response and specificity of 78% (Capirci et al. 2004). PET accuracy was only 56% and there were no survival data for comparison. Table 1.3 lists recent investigations using PET for response in colorectal cancer. Overall, utilization of PET for colorectal cancer treatment is still in the preliminary stage and further experimental trials are needed to further elucidate its usage.