Table 1 | Results of treatment for achalasia[1]

Achalasia subtype	Number of patients	Overall success (%)	Pneumatic dilatation (% success)	Laparoscopic Heller myotomy (% success)
Type I	44	81	85	81
Type II	114	96	100	93
Type III	18	66	40	86

n=176; mean follow-up 43 months.

this report. Interestingly, for types I and II achalasia, the success rate was numerically greater after pneumatic dilatation than for LHM, although the values were so high that a statistical difference was achieved only in the type II patients (100% versus 93% success; $P<0.05$). On the other hand, the patients with type III had a dramatically higher success rate with LHM treatment (86%) than with pneumatic dilatation (40%); however, as the number in this subgroup was small (only 18 patients), these differences did not reach a level of statistical significance. One would suspect that as more patients are accumulated, a statistical effect will become apparent and no longer be masked by this type II statistical error. Interestingly, all patients with type III continued to be classified as this subtype for the entire follow-up period. This important observation speaks loudly against the tendency to consider this manometric pattern to represent early or evolving achalasia.

Just what does this report truly mean to the clinician who is actively involved in the management of patients with achalasia? And, more importantly, who should be actively involved in the management of achalasia? Let me deal with the second question first. As most practicing gastroenterologists are unlikely to see patients with achalasia very often, it is difficult for them to maintain a level of appropriate expertise with pneumatic dilatation as a treatment option and patients are thus often referred for a myotomy. Whether the inclination is for treatment of achalasia with pneumatic dilatation or LHM it is my belief that these patients should be referred to a specialist centre (centre of excellence) where an individual or a team actively treats patients with achalasia regularly. The results of the European trial strongly indicate that either pneumatic dilatation or LHM are appropriate and highly successful treatments for achalasia. This observation reinforces the suggestion that the real decision should be based on what local expertise is available; that is, whether there is an individual in the vicinity who has the experience and knowledge to treat achalasia, be it by surgical or balloon dilation.

The question of the appropriate treatment for patients with type III achalasia is a little more complex. At first glance, the results of the European trial suggest that a myotomy should be considered the treatment of choice. However, one could argue that as neither of the treatments is as successful as in patients with types I or II achalasia, it would still be reasonable to approach the patient first with the less complicated and less morbid treatment of pneumatic dilatation and to save LHM as a rescue procedure. As Spechler stated in a recent editorial "perhaps the road to Heller's myotomy should be paved with good distentions".[3] To the average practicing gastroenterologist who feels ill prepared to perform pneumatic dilatation, I would make the plea that they consider referral to a more specialized individual to accomplish treatment of their patient. I would, however, encourage the approach to include either an oesophageal specialist from among the gastroenterologists in the area for pneumatic dilatation or a surgeon for LHM, again with the concept of looking for the best local expertise available.

Interestingly, the rapidly evolving technique of high-resolution manometry has brought to light the concept of these three subtypes of achalasia. To the neophyte, this observation is often considered as new. To the experienced oesophagologist, however, subtyping of achalasia is just a new vision of a well-known concept. Interestingly, the European study was performed at a group of medical centres, none of which used high-resolution manometry to establish the diagnoses. Therefore, one could argue definitively that this old disease is well recognized and appropriately staged for therapy on the basis of good-quality manometry of any kind, and is not a new disease recently discovered by a new technology. Use of subtyping, perhaps made easier by the technique of high-resolution manometry, should continue to guide therapy decisions for patients with achalasia.

Esophageal Disorders Program, Medical University of South Carolina, 25 Courtenay Drive, Charleston, SC 29425, USA.
castell@musc.edu

Competing interests
The author declares associations with the following companies: Amenity Health, Sandhill Scientific, Takeda. See the article online for full details of the relationships.

1. Rohof, W. O. *et al.* Outcomes of treatment of achalasia depend on manometric subtype. *Gastroenterology* http://dx.doi.org/10.1053/j.gastro.2012.12.027.
2. Pandolfino, J. E. *et al.* Achalasia: a new clinically relevant classification by high-resolution manometry. *Gastroenterology* **135**, 1526–1533 (2008).
3. Spechler, S. J. Pneumatic dilation and laparoscopic Heller's myotomy equally effective for achalasia. *N. Engl. J. Med.* **364**, 1868–1870 (2011).

PANCREATIC CANCER

FDG-PET is not useful in early pancreatic cancer diagnosis

Oliver Strobel and Markus W. Büchler

Better tools for early detection and accurate staging of pancreatic cancer are needed. The role of ^{18}F-fluorodeoxyglucose (FDG)-PET in this setting is controversial. The results of a large retrospective study analyzing the value of FDG-PET in the diagnosis of pancreatic ductal adenocarcinoma are discussed here.

Strobel, O. & Büchler M. W. *Nat. Rev. Gastroenterol. Hepatol.* **10**, 203–205 (2013); published online 12 March 2013; doi:10.1038/nrgastro.2013.42

Pancreatic ductal adenocarcinoma is one of the leading causes of cancer-related deaths. The combination of surgical resection and chemotherapy is the only treatment approach that provides a potential cure. However, the majority of patients have advanced tumours with metastases at the time of diagnosis and are not suitable candidates for surgical

Box 1 | Potential uses of FDG-PET*

- To aid decision-making in patients with large primary tumours or high serum levels of carbohydrate-antigen 19-9[7]
- To act as a noninvasive tool to confirm metastases in patients with liver and lung lesions that remain unclear after conventional imaging
- To aid in monitoring the response of patients who are receiving chemotherapy or chemoradiation in a neoadjuvant or palliative setting
- To monitor recurrence in patients with increased tumour markers but no evidence of disease by conventional imaging

*In advanced pancreatic cancer.

resection. Multi-detector CT and MRI are accepted as the diagnostic imaging modalities of choice in the current guidelines,[1] but these modalities are of limited value in the detection of small primary tumours (<2 cm) and small metastases. Improvements in the diagnostic tools used for the early detection and accurate staging of pancreatic cancer are therefore urgently needed.

In other solid tumours, such as melanoma, ^{18}F-fluorodeoxyglucose (FDG)-PET is successfully used to visualize enhanced tumour metabolism and can detect early stage primary tumours and small metastases. By contrast, the value of FDG-PET in the diagnosis and staging of pancreatic cancer is still controversial. Pioneering studies during the 1990s reported a high sensitivity and specificity of FDG-PET in the diagnosis of pancreatic cancer.[2] With technological advances, the metabolic data produced by FDG-PET is today interpreted together with anatomical information in combined PET–CT scans. In 2011, a meta-analysis of 51 studies found that combined PET–CT was the most sensitive tool in diagnosing pancreatic cancer (sensitivity 90.1%, specificity 80.1%), whereas endoscopic ultrasonography (EUS) was the most specific (sensitivity 81.2%, specificity 93.2%).[3] However, in most patients with suspected pancreatic cancer, CT or MRI together with clinical data are sufficient to establish a diagnosis and for staging; an additional FDG-PET procedure is therefore unnecessary.

The important question for the clinician remains: is FDG-PET able to provide additional information that, when combined with data derived from CT, MRI and EUS, alters clinical decision-making in patients with suspected pancreatic cancer? Matsumoto *et al.*[4] sought to answer this question in a large retrospective study. In contrast to previous studies, they focused on lesions that are frequently missed or misdiagnosed by conventional imaging on small primary pancreatic cancers and metastatic lesions, and on the distinction between cancer and focal mass-forming pancreatitis. Importantly, FDG-PET was not effective in detecting small and early stage pancreatic cancer; FDG-PET identified only 11 (68.8%) of the 16 tumours ≤20 mm, and only half of the International Union Against Cancer stage 0 and stage 1 tumours. FDG-PET alone was inferior to both CT and MRI in the detection of liver metastases (detection rates: FDG-PET 38%, CT 60% and MRI 60%), and also tended to be inferior to CT in the detection of both peritoneal and lung metastases. FDG-PET was superior to CT and MRI in the detection of bone metastases, but this finding is of limited clinical significance, as bone metastases appear at a late stage in pancreatic cancer, when other metastases are also normally evident. Furthermore, in this study, FDG-PET did not help in the distinction of pancreatic cancer from focal mass-forming pancreatitis, which was FDG-PET-positive in 79% of cases.[4]

> “...the value of FDG-PET in the diagnosis and staging of pancreatic cancer is still controversial...”

In spite of the good overall diagnostic values of combined PET–CT,[3,5] these results challenge the usefulness of additional metabolic data from FDG-PET in the standard diagnostic work-up of patients with pancreatic cancer. The data presented by Matsumoto *et al.*[4] clearly demonstrate that FDG-PET is not useful for the detection of early pancreatic ductal adenocarcinoma. This main finding does not come as a surprise. A correlation between FDG accumulation and tumour size and the resulting limitation of FDG-PET in the detection of small, early stage cancers has already been noted in previous work.[2] By contrast, the finding of Matsumoto *et al.*[4] that focal mass-forming pancreatitis was frequently FDG-PET positive is inconsistent with previous data, which reported that head masses in chronic pancreatitis rarely exhibited enhanced FDG uptake.[2] Possible explanations for this discrepancy are alterations of FDG uptake by previous surgical or endoscopic interventions[2] and the inclusion of patients with autoimmune pancreatitis (6 of 14 cases with pancreatitis in this study[4]), which has enhanced FDG uptake owing to high inflammatory activity.[6]

For the clinician, accurate staging of pancreatic cancer, especially identification of small metastases, is even more important than the detection of small primary tumours. If pancreatic cancer is suspected but not identified by preoperative imaging, the best ‘diagnostic’ option remains surgical exploration and resection. Given the high mortality rate in patients with pancreatic cancer compared with the low morbidity and mortality rates in patients after pancreatic resections, surgery for a benign lesion has to be preferred over missing a potentially curable pancreatic cancer. By contrast, surgical exploration in seemingly resectable tumours frequently reveals small (3–5 mm) liver or peritoneal metastases that were not identified by state-of-the-art preoperative diagnostic workup.[1] Here, better preoperative staging is mandatory to avoid unnecessary surgical explorations. In contrast to the data presented by Matsumoto *et al.*[4] for FDG-PET alone, meta-analyses of previous studies have demonstrated an increased sensitivity of PET–CT in the identification[3] and staging[5] of advanced pancreatic cancer.

Although FDG-PET is not useful in the diagnosis of early pancreatic cancer, it can be helpful for decision-making in difficult cases of advanced pancreatic cancer (Box 1). Patients with large primary tumours or high serum levels of carbohydrate-antigen 19-9[7] are considered at increased risk of metastatic disease and might benefit from an intensified diagnostic work-up, potentially including staging laparoscopy and PET–CT. FDG-PET can also help as a noninvasive tool to confirm metastases in patients with liver and lung lesions that remain unclear after conventional imaging. The combined metabolic and anatomical information by PET–CT can also help to monitor the therapeutic response of patients receiving chemotherapy or chemoradiation in a neoadjuvant or palliative setting.[8] PET–CT might be useful in diagnosing and monitoring disease recurrence, especially in patients that present with increasing tumour markers, but without evidence of disease by conventional imaging.[9] However, data on the value of FDG-PET in these settings are limited and further studies are needed.

Overall, although FDG-PET is not useful in the diagnosis of early pancreatic cancer, it might be helpful for specific questions in patients with advanced pancreatic cancer. In other tumour entities, PET with alternative

tracers to FDG has become a standard diagnostic tool. One promising example is PET with somatostatin receptor-based tracers, which has been successfully introduced in the diagnostic work-up of gastroenteropancreatic neuroendocrine tumours.[10] One focus of future research should definitely be the development of more specific PET tracers for pancreatic ductal adenocarcinoma.

*Department of General, Visceral, and Transplantation Surgery, University Hospital Heidelberg, Im Neuenheimer Feld 110, 69120 Heidelberg, Germany (**O. Strobel, M. W. Büchler**).*
Correspondence to: M. W. Büchler
markus.buechler@med.uni-heidelberg.de

Competing interests
The authors declare no competing interests.

1. Tempero, M. A. *et al.* Pancreatic adenocarcinoma, version 2.2012: featured updates to the NCCN Guidelines. *J. Natl Compr. Canc. Netw.* **10**, 703–713 (2012).
2. Friess, H. *et al.* Diagnosis of pancreatic cancer by 2-^{18}F-fluoro-2-deoxy-D-glucose positron emission tomography. *Gut* **36**, 771–777 (1995).
3. Tang, S. *et al.* Usefulness of ^{18}F-FDG PET, combined FDG-PET/CT and EUS in diagnosing primary pancreatic carcinoma: a meta-analysis. *Eur. J. Radiol.* **78**, 142–150 (2011).
4. Matsumoto, I. *et al.* 18-Fluorodeoxyglucose positron emission tomography does not aide in diagnosis of pancreatic ductal adenocarcinoma. *Clin. Gastroenterol. Hepatol.* http://dx.doi.org/10.1016/j.cgh.2012.12.033.
5. Dibble, E. H. *et al.* PET/CT of cancer patients: part 1, pancreatic neoplasms. *AJR Am. J. Roentgenol.* **199**, 952–967 (2012).
6. Kamisawa, T. *et al.* FDG-PET/CT findings of autoimmune pancreatitis. *Hepatogastroenterology* **57**, 447–450 (2010).
7. Hartwig, W. *et al.* CA19–9 in potentially resectable pancreatic cancer: perspective to adjust surgical and perioperative therapy. *Ann. Surg. Oncol.* http://dx.doi.org/10.1245/s10434-012-2809–1.
8. Kittaka, H. *et al.* Role of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography in predicting the pathologic response to preoperative chemoradiation therapy in patients with resectable T3 pancreatic cancer. *World J. Surg.* **37**, 169–178 (2013).
9. Cameron, K. *et al.* Recurrent pancreatic carcinoma and cholangiocarcinoma: ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT). *Abdom. Imaging* **36**, 463–471 (2011).
10. Treglia, G., Castaldi, P., Rindi, G., Giordano, A. & Rufini, V. Diagnostic performance of Gallium-68 somatostatin receptor PET and PET/CT in patients with thoracic and gastroenteropancreatic neuroendocrine tumours: a meta-analysis. *Endocrine* **42**, 80–87 (2012).