Computer tomography in pre-oprative staging of pancreatic cancer

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Chapter 1

Introduction and outline of the thesis
Introduction

Pancreatic carcinoma has a poor prognosis and the only chance of cure is a resection of the tumor. In 1995, shortly after introduction of spiral CT in the Academic Medical Center, the median survival of patients who had undergone a resection of a pancreatic carcinoma, was still only 14-15 months. The hospital mortality of a pancreatic resection was very high, ranging from 5-10% for a pancreatico-duodenectomy (Whipple’s procedure) up to 20% for a total pancreatectomy, although mortality was declining in specialised centers\textsuperscript{1,2,3}. The actuarial 5-years survival after a resection was approximately 10-15%, but only patients that had received a resection with microscopically tumor negative resection margins, actually had a better chance of survival\textsuperscript{4,5,6}.

For pre-operative staging no single diagnostic study appeared to be sufficient and it was advised to use a combination of diagnostic modalities as ERCP, ultrasonography, CT, angiography and laparoscopy\textsuperscript{7}. Although conventional CT was reported to predict irresectability of a pancreatic carcinoma with a high accuracy\textsuperscript{8}, this was probably largely due to patient selection. Most patients, including a large proportion of patients that had irresectable tumors, underwent a surgical exploration because surgical palliation, consisting of a double bypass (hepato-jejunostomy and gastro-jejunosotomy), was regarded as the treatment of choice for irresectable tumors. In one series for example, the resectability rate in patients that underwent a surgical exploration was only 6 percent\textsuperscript{8}. Currently insertion of biliary stents by an endoscopic procedure as a palliative treatment has become an accepted alternative for surgical palliation.

In other series in which the resectability rate was higher, probably due to a better patient selection, the accuracy of CT for staging was found to be lower, approximately 70\%\textsuperscript{9,10}. It was concluded that CT predicton of irresectability of a tumor was relatively good, while CT prediction of a tumor to be resectable was more difficult and only correct in approximately 50\% of the patients\textsuperscript{10}. Besides the presence of small metastases, that were often missed by CT, an important cause for tumor irresectability was invasion by tumor in the peripancreatic vessels, like the portal vein and the superior mesenteric veins and arteries. This invasion was often discovered at a late stage during surgical exploration, meaning that a lot of surgical dissection already had been made. Therefore a more adequate detection of vascular invasion was an important goal of pre-operative imaging. To improve pre-operative staging several modalities were being used. Pulsed Doppler was added to sonography (duplex sonography), which enabled measurement of increased velocity of flow in vessels, which signified narrowing of a vessel, followed
by Color Doppler sonography, which enabled color coding of flow velocities\textsuperscript{11}. Double catheter angiography was performed, with simultaneous injections in the superior mesenteric artery and celiac trunc, in order to enhance portal, splenic, and superior mesenteric veins. These modalities were the standard pre-operative examinations to determine vascular invasion until spiral CT was introduced.

In spiral CT the X-ray tube continuously rotates around the patient, who is moved at a fixed speed through the CT opening (gantry). Large datasets are thus collected in a spiral fashion, instead of the discontinuous slice by slice mode, that had been used previously\textsuperscript{12}. This spiral or helical technique allowed rapid acquisition of data and enabled a more effective use of intravenously administered contrast material, to enhance the liver, the pancreatic parenchyma, and the surrounding vessels. Further developments of CT has led to the use of multiple detector rings instead of only one ring (multirow CT). At first in Dual slice CT, two parallel rings of detectors were present instead of one row, and this enabled simultaneous acquisition of the data of two slices during a single CT rotation. This technique not only allowed a shorter examination time, but also enabled the use of very thin slices, of 1 mm thickness or less, that could be reconstructed from the acquired volumetric data. These thin slices could be used for a multitude of (so-called post-process) rendering techniques, such as multiplanar reconstructions, Maximum Intensity Projection (MIP), 3D Surface rendering, and 3D Volume rendering\textsuperscript{13,14}. These rendering techniques later enabled interactive 3D renderings such as virtual endoscopy and virtual bronchoscopy. Because of the shorter scan times, multiple-phase scanning became possible, e.g. during both the arterial phase (at a delay of 20 s after contrast injection) and the portal venous phase (at a delay of 70 s). In later studies scanning during a single phase, at the optimal delay of 40-50 s after contrast injection, was shown to be sufficient for pancreatic imaging\textsuperscript{15-18}. Dual slice CT was introduced in the AMC in 1997, followed by “quadslice” CT in 1999.

At present CT scanners with 32 detector rings are operational and manufacturers are developing detectors with as many as 256 parallel rings. Other diagnostic modalities such as, endosonography, laparoscopic sonography, MRI and nuclear scintigraphy were introduced and developed rapidly, parallel to CT, and many aspects of their role for pre-operative staging are still uncertain. Because of these rapid developments further investigation of spiral CT and its value for pre-operative staging was needed.
The purpose of this thesis was therefore to establish the value of spiral CT for pre-operative staging of patients with a pancreatic and peri-ampullary tumors. Many patients suspected to have a pancreatic carcinoma are referred to a tertiary center, like the AMC, for further diagnostic evaluation and/or treatment. Among other diagnostic modalities, CT has currently an important role in staging pancreatic cancer and for treatment planning, especially in deciding whether or not to perform a surgical exploration in an attempt to perform a so-called curative resection. Because of the rapid technical development of CT, with presumed improvement of diagnostic capabilities, a re-evaluation of the use of these new CT scanners was needed.

In **chapter 2** of this thesis, the value of spiral CT to determine surgical resectability was examined. In a cohort of 56 patients with a pancreatic head carcinoma, findings on single slice spiral CT were compared with findings during surgical exploration and with findings at histo-pathological examination of resected tumors.

Vascular invasion by tumor is found in approximately half of the patients with a pancreatic carcinoma, that proves to be locally irresectable at surgical exploration. However, this invasion is often detected at a late stage of the surgical exploration, meaning that a lot of the surgical dissection already has been performed. Pre-operative detection of venous invasion is one of the goals of CT. In **chapter 3** we examined CT criteria that might determine the presence of vascular invasion by a pancreatic tumor. In 50 patients with a pancreatic carcinoma, who had undergone a surgical exploration, such CT criteria, e.g. the length of contact between a tumor and the portal vein, the amount of circumferential involvement of the vein, and the irregularity of the vessel wall, were scored on the pre-operative CT scans. Findings at CT were compared with surgical and histo-pathological findings of venous invasion, in to order to establish which CT criteria were most valuable.

Many patients, suspected to have a resectable hepato-biliary malignancy, are referred to a tertiary center for further diagnostic evaluation and/or treatment, but in most of these patients diagnostic examinations have been performed prior to referral. This raised the question, what the yield is of reviewing these studies and what the yield is of additionally performed studies. In **chapter 4** we examined the value of re-interpreting...
the radiologic examinations, that had been performed outside the AMC, in patients with suspected hepato-biliary tumors, who were referred to the AMC. A blinded panel reviewed the examinations of 87 consecutive patients. A tentative diagnosis, diagnostic plan and treatment plan were made by the panel. Also additional examinations, performed in the AMC in these patients, were reviewed and again a diagnosis and a plan were formulated. Findings of the panel were compared with the original radiological reports, the followed treatment and the surgical, histo-pathological and final clinical outcome. The value of re-interpretations and the value of additionally performed studies were assessed especially with regards to whether this had resulted in an important change in diagnosis or in a change of the treatment plan.

Detection of vascular invasion by tumor is important as this precludes a resection. For evaluation of vascular structures the transverse plane may be sub optimal, and this may be a limitation of axial CT. Spiral CT enables three dimensional rendering of vessels and this might have additional value to assess the patency of vessels. In chapter 5 we examined whether 3D rendering, compared to axial CT alone, had additional value for staging venous invasion in patients with a pancreatic head carcinoma. In 32 patients with a pancreatic head carcinoma, who underwent a surgical exploration, the findings of venous invasion at 3D CT angiography were compared with findings at the axial CT scans, and with findings of venous invasion at surgical exploration and at histo-pathological examination.

CT has limitation in determining tumor irresectability. Often a surgical exploration is performed and even a resection of the tumor (with or without positive resection margins) although CT indicates tumor irresectability or suggests a high chance for irresectability. This raised the question how patients perform after such a resection and how CT findings are correlated with survival in these patients. In chapter 6 we examined whether CT criteria, as visible on a pre-operative CT scan, could predict the survival of patients with a pancreatic carcinoma. In 72 consecutive patients with a pancreatic head carcinoma that underwent a surgical exploration, with intent to perform a resection of the tumor, the prognostic value of CT criteria, that are generally used to determine tumor irresectability, were correlated with the survival of the patients (corrected for whether or not a surgical resection had been performed).

In chapter 7 an overview is given of the diagnostic imaging modalities at present and
their relative importance for the pre-operative staging of pancreatic and peri-ampullary cancer.

In chapter 8 a summary and a conclusion of this thesis are given.

References


