Combined Imaging with Multi-Detector Row Computed Tomography and Diffusion-Weighted Imaging in the Detection of Pancreatic Cancer

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Pancreatic cancer is one of the most aggressive malignant tumor types. Its prognosis is extremely poor without early detection, and an accurate diagnosis with imaging techniques is vital for any chance of long-term survival after treatment. Despite the great technical advances that have been made with various kinds of imaging equipment, detection of pancreatic cancer is unsatisfactory, and new modalities are required. Diffusion-weighted imaging (DWI) on magnetic resonance imaging (MRI) has high sensitivity and specificity for the detection of pancreatic cancer; however, it does not provide anatomic information. Quite often, the necessary spatial correlation of a high-intensity area with anatomic structures is constrained. If it becomes possible to combine the imaging technique of DWI with multi-detector row computed tomography (MDCT), such as is done with positron emission tomography (PET) and computed tomography (CT), it is expected that the early diagnostic capability will improve. The objective of this study was to introduce combined imaging with DWI and CT into clinical practice to improve the diagnosis of pancreatic cancer. In the current report, we demonstrate a clinical attempt to combine DWI on MRI with the anatomical accuracy of MDCT for two patients of pancreatic adenocarcinoma. Analysis of these two patients revealed that the combined images corresponded precisely to the operative findings. Thus, the combined imaging with DWI and MDCT is useful for the detection of the pancreatic cancer.

Keywords: combination; Diffusion-weighted imaging; fusion; multi-detector row computed tomography; pancreatic cancer

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Pancreatic cancer is one of the most lethal human cancers, characterized by early systemic dissemination and extraordinary local tumor progression. Pancreatic cancer is characterized by a late presentation, and for all stages, the five-year survival rate is less than 5% (Gold and Goldin 1998). This poor prognosis relates to the uniformly advanced disease stage present at the time of diagnosis and its profound resistance to existing therapies. Thus, early detection of pancreatic cancer is required to improve this poor prognosis.

In recent years, advancements in imaging equipment have been remarkable, and the new modalities are considered indispensable for the diagnostic imaging of malignant tumors. Computed tomography (CT) is well established for the diagnosis and staging of malignant tumors. The introduction of multi-detector row computed tomography (MDCT) has allowed further refinements in detecting malignant tumors (McNulty et al. 2001; Fletcher et al. 2003). One of the most important advantages of MDCT scanners is their ability to generate multiplanar reformatted (MPR) images or 3-dimensional (3D) volume-rendered images. MPR images obtained with MDCT have high qual-

ity, providing high resolution without slice misregistration.

Diffusion-weighted imaging (DWI) is different from morphologically oriented imaging techniques in that it has the sensitivity to depict disease-associated changes of random translational molecular motion, known as diffusion or Brownian water motion (Lyng et al. 2000). In tissue characterization, the relative assessment of the magnitude of diffusion is exhibited as the apparent diffusion coefficient (ADC) (Roth et al. 2004). In DWI, the signal intensity is inhibited in tissues with high diffusion of water molecules, and high-intensity signals can be obtained in tissues with low diffusion of water molecules. In most cases, malignant tumors have increased cell density and reduced intercellular substances, resulting in inhibited diffusion of water molecules. Thus, such tumor tissues produce abnormal signals by creating contrast with normal tissues.

MDCT provides excellent analysis of anatomical structures, while MRI provides excellent diagnostic performance of density resolution and tissue characterization; as for DWI, the description of the tumor has been improved by the recent development of new software. Improvements in the diagnostic capabilities of these general purpose

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machines will be further expected from their convenience and more widespread use in the future.

Although the sensitivity and accuracy of MDCT and MRI in diagnosis of pancreatic cancer have been improved significantly, it is still difficult to diagnosis at an early stage (Bronstein et al. 2004; Kartalis et al. 2009). The sensitivities and specificities were reported as 73%-94% and 95% for CT (DelMaschio et al. 1991; Koito et al. 1997), 85% and 96% for MRI (Ichikawa et al. 2001). The difficulties in diagnosis on MDCT are thought to be due to the loss of biliary dilatation, vascular involvement and mass effect, and little attenuation difference compared with normal parenchyma. On the other hand, MRI is a little inferior in analysis of anatomical structures including the pancreas.

In recent years, the digital image fusion procedure was developed, which enables spatially correct superposition of data from 2 or more different imaging modalities. To achieve better anatomic resolution, the combination with MDCT and DWI on MRI (DWI/CT), like the matched images with fluorodeoxyglucose positron emission tomography and CT, will improve further the anatomical localization of the tumor and the determination of the histological and the qualitative contrast.

In the current report, we demonstrate the usefulness of fusion analysis of MDCT and DWI for the diagnosis of pancreatic cancer.

Methods

MDCT imaging protocol

MDCT was performed with a commercially available MDCT scanner (Aquilion 64, Toshiba Medical Systems, Tokyo, Japan) with a gantry rotation speed of 0.5 s and a detector configuration of 32.0×1.0 mm; the moving speed of the table was 27 mm/s. The pitch was 0.84. All scans were acquired in a cephalocaudal direction. Patients underwent MDCT followed by arterial, portal, and equilibrium phases. Patients received 100 ml of iomeprol (Iomeron, 350 mg/ml, Bracco-Eisai, Otsuka, Japan) with a monophasic injection technique by means of a power injector. The contrast material was administered at a rate of 3.3 ml/s. Each phase acquisition was initiated with 35 seconds for the arterial phase, 70 seconds for the portal phase, and 150 seconds for the equilibrium phase after the injection of contrast material. MDCT examination was performed at 120 kVp and 150 mA. After MDCT examination, coronal and sagittal MPR images were also created. For reconstructed axial and MPR images, a 1.0-mm slice thickness and a 0.5-mm interval were used.

MRI protocol

All examinations were performed with a Gyroscan Intera 1.5 T containing a synergy body coil (Philips Medical Systems, Best and Heeren, The Netherlands). The apparatuses and sequences used in this study were purchased from the manufacturer as Release 12.6. All are commercially available products. The MRI protocol for localization of the tumor was as follows. T2-weighted (T2W) turbo spin echo MRI was carried out with a 37.5×37.5 -cm field of view (FOV), an echo time (TE) of 80 ms, and a repetition time (TR) of 630 ms. Eight-mm-thick slices were acquired with a 1-mm gap between slices using a 256×256 matrix. The number of slices was 20. T2W was

performed using respiratory triggering.

Diffusion-weighted single-shot echo planar imaging using a sensitivity-encoding technique (SENSE-DWI) was carried out with a 37.5×37.5 -cm FOV; a 5-mm slice thickness, a TR of 3,704 ms, a TE of 68 ms, a 256×256 matrix, and the partial Fourier factor was 0.604. The number of slices of parallel acquisition was 50. Receiver bandwidth is 1,246.9 hertz. Scan time was 5 minutes and 57 seconds. A spectral presaturation with inverse recovery (SPIR) pulse was used for fat suppression. Data were acquired with b-value settings at zero and 800 s/mm². Seven images were acquired for each slice; the first was a T2-weighted image with b = 0. The images of the next six with b = 800 were placed in each direction. DWI was performed using respiratory triggering.

Imaging analysis

Visual evaluation was performed on each of the above-mentioned images and on the fusion images, which were synthesized from T2-weighted (T2W), DWI, and MDCT. Each of the fusion images of T2W and DWI-I/800 images was synthesized on a workstation with Microsoft Windows XP (Microsoft Corporation, Redmond, WA, USA) and Philips Research Imaging Development Environment software for image registration (Philips Medical Systems, Best and Heeren, The Netherlands). The combined images with MDCT and DWI were analysed using a 3D workstation (Ziostation version 2.0.×, Ziosoft, Tokyo, Japan), which is a commercially available automated image registration software. For this, the CT and DWI data were transferred onto the workstation as DICOM (Digital Imaging and Communications in Medicine) images via the Intranet. The CT images were registered to DWI using a fully automatic voxel-based algorithm. After registration, the coregistered images were reconstructed and visualized in the coronal and axial planes. CT, MRI, and combined images were assessed by one experienced radiologist who was blinded to patient information with regard to the detection of malignancies, possible infiltration of adjacent tissue or lymph nodes, and distant metastases.

Patients

Among patients with suspected lesions of the pancreas, we identified two patients in whom the assessment by observers unaware of the diagnosis showed that interpretation of CT and DWI separately gave fewer correct diagnoses than reading the matched image. This study was approved by the ethical commission on research on humans of Ugo Hospital before patient enrollment. Informed consent was obtained from each patient.

Patient 1: A 72-year-old male was admitted to our hospital because of abdominal fullness. Blood tests revealed slight hepatic dysfunction. MDCT revealed a somewhat low-density area at the site of the uncinate process of the pancreas, which revealed less enhancement relative to the normal peripheral pancreatic parenchyma (Fig. 1A). Dilatation of the bile duct was revealed, but choledochal or duodenal invasion was not considered. A low-density area 3.0 cm in size was in close proximity to the portal vein and the superior mesenteric artery (SMA). Coronal multiplanar reformatted images reconstructed from axial MDCT images showed a hypoattenuating mass with a spiculated border toward the portal vein and SMA. Direct tumor-to-vessel contact with complete obliteration of the fat plane was shown, which was suspected as tumor-to-vessel contiguity. DWI on MRI clearly revealed a high-intensity area at the site of the unci-

Fig. 1. Patient 1. A 72-year-old male with cancer of the uncinus process of the pancreas. A. Multi-detector row computed tomography (MDCT) images showed less enhancement relative to the normal peripheral pancreatic parenchyma at the site of uncinus process of the pancreas (►). B. Greyscale inversion of diffusion-weighted imaging (DWI) showed a high-intensity area at the site of the uncinus process of the pancreas (►). C. Combined image with MDCT and DWI revealed both the lesser enhancement area on the MDCT and the high-intensity area of the DWI corresponded (►).

Fig. 2. Patient 2. A 76-year-old female with cancer of the head of the pancreas. A. Multi-detector row computed tomography (MDCT) images revealed a low-density area at the site of the head of the pancreas (►). B. Greyscale inversion of diffusion-weighted imaging (DWI) showed a high-intensity area at the site of the head of the pancreas (►). C. Combined image with MDCT and DWI revealed both a low-density area on the MDCT and the high-intensity area of the DWI corresponded (►).

nate process of the pancreas (Fig. 1B). The DWI and MDCT images were fused, and both the lesser enhancement area on the MDCT and the high-intensity area of the DWI corresponded (Fig. 1C). Cancer of the uncinate process of the pancreas was strongly suspected. Pancreatoduodenectomy was performed. Resected specimens revealed that the tumor was located in the uncinate process of the pancreas and was 3 cm in size, which corresponded to the imaging findings. Histological findings revealed moderately differentiated tubular adenocarcinoma.

Patient 2: A 76-year-old female was admitted to our hospital because of abdominal discomfort. Blood tests revealed elevation of transaminase. MDCT revealed a low-density area at the site of the head of the pancreas, 2 cm in size (Fig. 2A). DWI on MRI revealed a high-intensity area at the site of the head of the pancreas (Fig. 2B). The combined image with DWI and MDCT revealed that the low-density area on the MDCT and the high-intensity area of the DWI corresponded (Fig. 2C). Cancer of the head of the pancreas was strongly suspected. Pancreatoduodenectomy was performed. Resected specimens revealed that the tumor was located in the head of the pancreas and was 2 cm in size, which corresponded to the imaging findings. Histological findings revealed papillary adenocarcinoma.

Discussion

The development of various kinds of diagnostic equipment, such as sonography, CT, and MRI, has contributed to improved diagnosis and staging of pancreatic cancer; however many pancreatic cancer cases are detected at advanced stages. Because of early lymphatic and hematogenous spread and a propensity for invasive growth, only 3–22% of pancreatic cancers are resectable at the time of diagnosis (Roche et al. 2003). Several years ago, functional imaging was introduced as a new diagnostic modality in addition to conventional morphologic imaging. Functional FDG-PET has higher sensitivity and specificity than CT for tumor detection (Kantorová et al. 2003; Antoch et al. 2004). Zimny et al. (1997) reported that PET showed an overall sensitivity of 85%, a specificity of 84%, a negative predictive value of 71%, and a positive predictive value of 93%. In a subgroup of patients with normal serum glucose levels, the results were 98%, 84%, 96% and 93%, respectively. Delbeke et al. (1999) demonstrated that FDG-PET had a higher sensitivity, specificity and accuracy than CT in diagnosing pancreatic cancer (92%, 85% and 91% for FDG-PET versus 65%, 61% and 65% for CT, respectively). Potential roles of FDG-PET in pancreatic cancer imaging have been demonstrated, but functional imaging does not have the same resolution and landmarks as anatomic imaging. This limitation has been overcome by using co-registered functional PET and anatomic CT images (PET/CT), which has been used more commonly (Hosten et al. 2000). Lemke et al. (2004) compared the diagnostic value of CT, PET, and PET-CT fusion in 104 patients with suspected pancreatic lesions. They reported that image fusion improved the sensitivity of malignancy detection from 76.6% (CT) and 84.4% (PET) to 89.1% (image fusion).

Compared to CT alone, image fusion increased the sensitivity of detecting infiltration of adjacent tissue from 47.7% to 68.2%. Furthermore, in unresectable, locally advanced pancreatic cancer (LAPC), Topkan et al. (2008) compared CT with co-registered PET as the basis for delineating the gross tumor volume for planning of radiation therapy. They revealed the usefulness of PET/CT-based target volume delineation in patients with LAPC, and they suggested that the potential benefit of incorporating PET into radiation therapy might be the reduction in geographic misses associated with CT-based planning.

As another imaging approach, DWI on MRI has been applied to the evaluation of pancreatic cancer. The sensitivity and specificity for the detection of pancreatic adenocarcinoma were reported as 96.2% and 98.6%, respectively (Ichikawa et al. 2007). Regarding its high sensitivity and specificity, DWI has also become another imaging method for pancreatic cancer. MRI generally provides better tissue contrast than other diagnostic imaging methods, and it enables simultaneous observations of parenchymatous organs, vessels, and soft tissues. CT is considered better for the depiction of morphology, because it has superior spatial and temporal resolution. MRI is considered better for the depiction of tissue characterization, because it has superior contrast resolution. MRI is considered useful for the examination of lesions, including malignant lesions, and there are high expectations for DWI to be effective in the body trunk region. However, DWI cannot evaluate local extension of the tumor and the relationship of the tumor with the surrounding vessels. Therefore, DWI is always additional and complementary to anatomic imaging in patients considered for some treatments. Consequently, evaluations of the size and morphology of the tumor and lymph node and their internal characteristics must be performed by such combinations of methods. If fusion imaging of MDCT and DWI can be performed, it can be a useful diagnostic modality. In the present study, we used new equipment for image analysis to diagnose pancreatic cancer. The disadvantage of DWI/CT is that it cannot be performed simultaneously with the patient in the same body posture, unlike PET/CT. As a result, it will be necessary to develop a fusion method for organs affected by peristalsis, such as the intestines. Fusion of PET and CT images is an ideal combination, but PET/CT is available only at a limited number of facilities at the present time. Other issues include exposure to radioactive isotopes and high cost. Fusion of DW and CT images can be performed at any facility with MRI and CT, which are more common.

DWI/CT might become a useful modality for diagnosis and treatment if the resolution and image quality of DWI can be improved, the detectability of lesions can be improved, findings can be accumulated, and the development of image analysis software can be advanced.

Conflict of Interest

The authors have no conflict of interest.

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