INTRODUCTION

Pancreatic cancer is well-known for its high invasion and extremely poor prognosis. 1,2 Surgical resection offers the best chance of treatment. However, liver metastases are frequently found at the time of diagnosis, thus losing the opportunity of surgical intervention. In addition, operation on patient with undiagnosed liver metastases may increase the unnecessary pain and economic burden and even bring worse prognosis to the patient. Thus, the detection of liver metastases is crucial for therapeutic planning and imaging which has to provide precise diagnosis to achieve optimal medical management for each patient. 3 As a noninvasive method, conventional multislice computed tomography (CT) with dual phase imaging in arterial and portal venous phases has been widely used for diagnosing suspected pancreatic neoplasms, evaluating infiltration and lymph node metastases 4 and differentiating benign from metastatic liver lesions. 5 However, CT examination only represents the average Hounsfield value due to the partial volume effect and mixture of multiple photon energies may result in the reduction of the diagnostic value, especially for small focal lesions. 6

Recently, a new CT scan mode based on a gemstone detector and related detection system, and reconstruction or gemstone spectral imaging (GSI) was introduced to provide CT spectral imaging. This scan mode is based on the simultaneous acquisition of two data sets, high energy and low energy, which allows precisely registered data sets to create accurate material decomposition (MD) images (e.g. the water and iodine-based images) and monochromatic spectral images with energy ranging from 40 to 140 keV throughout the full 50 cm field of view. Therefore, the purpose of this study was to investigate the role of GSI in differentiation of small liver metastases from small benign lesions.

MATERIALS AND METHODS

Patients

The protocol for this study was approved by the institutional review board at our institution and informed consent for this retrospective study was acquired. From February to
December in 2010, we reviewed 43 pancreatic cancer patients with focal liver lesions. GSI examination was performed for these patients. The patients without sufficient confirmation of the nature of the lesions (n=11) were excluded. Therefore, the final study population consisted of 32 pancreatic cancer patients (21 males; 11 females; mean age: 62.56 years; age range: 45-83 years). Among these 32 cases, 18 patients had pancreatic head cancer, five patients had ampulla cancer and nine patients had distal bile duct cancer. The liver lesions with a diameter of less than 3 cm were included. The mean diameter of the liver lesion was 1.73 cm ranging from 0.5 to 2.9 cm. The maximum number of the lesions in one patient was limited to five. Liver metastasis was confirmed by surgery in 11 cases, needle aspiration biopsy in two cases and follow-up F-FDG PET/CT, ultrasound or CT/MRI scanning examination in 19 cases. Among the 11 surgery-confirmed cases, seven cases were confirmed by histological analysis and four cases were confirmed by palpation during the operation.

**Scanning Parameters**

Discovery CT750HD scanner was applied to all patients. First, unenhanced helical scans were acquired with a collimation of 5 mm, a pitch of 1.3 and a reconstruction interval of 5 mm, 120 kVp and 150 mA. Then, all patients were injected with nonionic contrast medium (Optiray 320, Montreal, Canada) through antecubital venous at a rate of 3 to 4 ml/sec for a total of 90 to 120 ml (1.5 ml/kg). Finally, dual-phase scanning was performed with GSI mode: Spectral with fast tube voltage switching between 80 and 140 kVp on adjacent views during a single rotation, 0.625 mm collimation, 0.6 second gantry rotation speed and 0.984:1 helical pitch. Images were reconstructed with a helical dynamic CT (HDCT) imaging reconstruction. From the single GSI, we can acquire the conventional polychromatic images, the iodine and water-based MD images, and a set of monochromatic images with energy ranging from 40 to 140 keV. Late arterial phase imaging was initiated within 10 seconds after enhancement of the descending aorta to 120 HU, as measured by a bolus-tracking technique (Smart Prep; GE Medical Systems). Portal venous phase images were obtained by using a 70-second delay. The images were obtained in a craniocaudal direction from the top of the diaphragm to the lower pole of the kidney during a single breath-hold.

**GSI Analyses**

Both arterial phase (AP) and portal phase (PP) were acquired from each patient (Fig. 1). Serial attenuation measurements of the liver lesions, pancreatic lesions, aorta and liver parenchyma were obtained for three times. These measurements were acquired at the midpoint of each imaging with an elliptic or circular receiver operating characteristic (ROC). The size of the ROI was determined in each individual patient by aortic and lesion dimensions. A hepatic ROC was acquired from three different levels. The average value of these three measurements in each patient was obtained.

Iodine concentration (ICL\textsubscript{AP}, ICL\textsubscript{PP}) of focal liver lesions and pancreatic lesions was obtained according to the iodine-based material decomposition images of liver and pancreatic cancer lesions, respectively (Fig. 2). The ICL value was further normalized (ICL/A) to arterial iodine concentration of aorta. Tumor-to-liver (T-to-L) contrast was calculated as ICL to liver parenchyma ratio, T-to-L was determined by the differences in attenuation measurements from ROI placed within the most enhanced portion of the neoplasm to the adjacent normal hepatic parenchyma (Fig. 2).

Figs 1A and B: ROI for hepatic and pancreatic lesions in a patient with pancreatic cancer. A 70-year-old pancreatic cancer patient with hepatic metastases: (A) ROI for liver lesion, (B) ROI for pancreatic lesion
and that for benign cyst (p = 0.0059) (Table 1). We also
analyzed the correlation between ICL_{ap} and ICL_{pp} in the
focal hepatic lesion and ICL in the pancreatic ductal
adenocarcinoma. The results showed that ICL_{ap} in the focal
hepatic lesion was significantly correlated with ICL in the
pancreatic lesion (R = 0.8743, p = 0.0001) which suggesting
that hepatic metastasis was significantly correlated to the
pancreatic lesion. ICL_{pp} in the focal hepatic lesion was also
significantly correlated with ICL in the pancreatic lesion
(R = 0.843, p = 0.0001). In contrast, ICL in hepatic cysts
was not significantly correlated with that in the pancreatic
cancer (Table 2).

Results in Table 3 showed that T-to-L_{pp} cannot be used
for characterizing hepatic lesions (p = 0.514). ICL/A {AP},
ICL_{AP}, ICL_{PP} and T-to-L_{AP} in malignant lesions were
significantly different from those in the benign lesions which
indicating that these parameters can be used for
distinguishing benign lesions from malignant lesions.

**DISCUSSION**

The incidence of pancreatic cancer has been increasing
recently, and the overall 5-year survival rate for patients
with pancreatic adenocarcinoma was low.\(^{10}\) Recent
advances in the chemotherapy have improved the survival
of patients with pancreatic cancer. A 5-year overall survival
rate after surgical resection of pancreatic adenocarcinoma
has been reported to be 18%.\(^{11}\) Despite the poor prognosis
of patients with pancreatic cancer, surgical resection is still
the only potentially curative treatment for the disease.
However, surgical operation for the pancreatic cancer
patients with hepatic metastases often brings unnecessary
physical and economic losses. Therefore, early diagnosis
and accurate assessment of the nature of focal liver lesions
are important for diagnostic imaging.

Due to the high spatial definition, multidetector CT (MD-
CT) has been used as a key method to characterize
abdominal lesions since its emergence. With increasing
gantry speed and thinner scanner layer, the sensitivity of
MDCT for detecting lesions is increasing in recent years.
Bolus contrast material and Hounsfield value measurement
provide a valid method to characterize lesions.
Polychromatic enhanced CT images, including arterial and
portal phase, were scanned to characterize hepatic lesions.
Hepatic metastases were characterized on contrast-enhanced
MDCT as globular or peripheral enhancement, a hypotensed
lesion with circular hyperintense tissue around the lesion
or having an obscure limit from the surrounding
parenchyma.\(^{8}\) The typical feature of focal cyst on the fluid
attenuation measurements was the appearance of round oval
and no contrast-enhancement with well-defined borders.\(^{9}\)
However, MDCT incorporated polychromatic X-ray
collection technologies and its CT value was derived from the average photon energy (Fig. 3). The averaging effect from partial volume and mixture of multiple photon energies of tube voltage obscure the CT numbers, which affect the characterization of focal liver lesions, especially those with a small diameter (e.g. <1.0 cm). We have experienced the low sensitivity of MDCT in previous reports, especially when compared with MR. However, in clinical practice, patients with pancreatic cancer in most cases are undergoing MSCT as opposed to abdomen MR protocol due to both financial and logistic reasons. A new CT scanner has emerged recently. In the past 3 years, spectral imaging with gemstone detector material (GSI mode) emerges as the latest technology for CT spectral imaging. GSI is based on fast kV switching-dynamic switching between two different X-rays (80 and 140 kVp) during a single rotation. Monochromatic imaging not only improves image quality and reduces image noise but also provides discrimination of different tissue types based on material density and monochromatic image data. GSI data can be segregated among a material density pair, e.g. water and iodine. They can switch between material pairs. In radiological imaging, water and iodine-based material is commonly used because it reflects the material composition and enhancement during CT imaging. Measuring the mg/cc of iodine/water from material decomposition offers true CT number in assessment the material composition of liver lesions, which provide a means to differentiate liver metastases from benign lesions. In MDCT, liver metastases are characterized by enhancement pattern and degree. Late arterial and portal phases are the optimal phases for detecting metastatic neoplasms. The spectral imaging can provide qualitative images as the common MDCT imaging. More importantly, iodine and water scatterplot in GSI-CT provide a visualized way to assess the material composition and distribution in the areas of interests (Fig. 4). Powerful post-processing and reconstructing function of GSI spectral CT provide an extremely useful assistance to make precise radiological diagnosis.

### Table 1: Iodine concentration for different parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ICL/AAP</th>
<th>ICL AP</th>
<th>ICL PP</th>
<th>T-to-L AAP</th>
<th>T-to-L PP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastases</td>
<td>0.20 ± 0.31</td>
<td>1.56 ± 1.13</td>
<td>2.16 ± 1.21</td>
<td>1.42 ± 0.82</td>
<td>0.66 ± 0.19</td>
</tr>
<tr>
<td>Cysts</td>
<td>0.04 ± 0.03</td>
<td>0.51 ± 0.31</td>
<td>0.84 ± 0.63</td>
<td>0.63 ± 0.33</td>
<td>0.28 ± 0.21</td>
</tr>
<tr>
<td>p-value (p &lt; 0.05)</td>
<td>0.004</td>
<td>0.001</td>
<td>0.0456</td>
<td>0.0059</td>
<td>0.6536</td>
</tr>
</tbody>
</table>

Iodine concentration and p-value for the parameter of ICL/AAP, ICL PP, ICL AP, T-to-L AAP and T-to-L PP, p < 0.05

### Table 2: Correlation analysis between hepatic focal lesions and pancreatic lesions in arterial and portal phase

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Correlation coefficient</th>
<th>p-value (0.01)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastases (pancreatic cancer)</td>
<td>AP 0.8754</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>PP 0.843</td>
<td>0.0001</td>
</tr>
<tr>
<td>Cysts (pancreatic cancer)</td>
<td>AP 0.35428</td>
<td>0.3152</td>
</tr>
<tr>
<td></td>
<td>PP 0.50242</td>
<td>0.1389</td>
</tr>
</tbody>
</table>

### Table 3: ROC curve analyzing, including sensitivity, specificity, area under curve

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>AUC (95%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICL AP</td>
<td>80</td>
<td>94.7</td>
<td>0.898 (0.815-0.982)</td>
<td>0.000</td>
</tr>
<tr>
<td>ICL/AAP</td>
<td>82.1</td>
<td>95.2</td>
<td>0.898 (0.815-0.980)</td>
<td>0.000</td>
</tr>
<tr>
<td>ICL PP</td>
<td>80</td>
<td>68.4</td>
<td>0.55 (0.389-0.720)</td>
<td>0.514</td>
</tr>
<tr>
<td>T-to-L AP</td>
<td>85.7</td>
<td>83.3</td>
<td>0.89 (0.799-0.993)</td>
<td>0.000</td>
</tr>
<tr>
<td>T-to-L PP</td>
<td>91.4</td>
<td>84.2</td>
<td>0.902 (0.805-0.998)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Fig. 3: Assessment of hepatic cyst. A 72-year-old man with hepatic cyst, small lesion difficult to characterize by MDCT
Compared with conventional CT imaging in which the diagnosis is affected by the experience of the readers, the spectral imaging provides more objective and quantitative parameters that are less affected by the experience of the readers. To our knowledge, MDCT estimates enhancement based on the arterial and portal phases. We normalized the parameters ICL/A and compared these parameters with statistical analysis. In our study, three parameters ICL_{AP}, ICL_{PP} and T-to-L_{AP} (after normalization) had significant difference between liver lesions and benign cysts. Therefore, these parameters can be used alone for differentiation diagnosis. We also discovered the close correlation of material composition between hepatic metastases and pancreatic cancer. ICL in hepatic metastasis was significantly correlated to that in the pancreatic lesions. In contrast, ICL of hepatic cysts was not significantly correlated to that in the pancreatic lesions. This correlation analysis indicated that the hepatic metastases lesions had similar material composition to pancreatic cancers. The gemstone spectral monochromatic CT imaging can assist the radiologists to characterize focal liver lesions from both the qualitative and quantitative angles.

In addition to these advantages, our study still has some limitations. First, histopathologic confirmation and/or intraoperative surgery were only available in 18 of the 55 lesions (13 of 32 patients). Obtaining histopathological diagnosis in all patients would be desirable, but this is difficult due to both practical and particularly ethical reasons in many cases. Nevertheless, we obtained PET-CT, ultrasound and other imaging follow-up examinations to verify these results. Second, we excluded the benign liver lesions: Hemangioma, focal fatty infiltration and ignored the original liver tumors from our sample which might affect the results.

CONCLUSION

Gemstone spectral imaging not only provides material decomposition and monochromatic spectral imaging but also gives us several quantitative parameters in characterizing focal liver lesions. GSI scanner was superior in the detection and classification of focal liver lesions in patients with pancreatic cancer.

ACKNOWLEDGMENT

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REFERENCES