Impact of dual-energy CT in detection of pancreatic adenocarcinoma

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Aims and objectives

Aims and Objective:

- To prospectively analyze the attenuation difference and conspicuity of pancreatic adenocarcinoma at two different photon energies (80 kVp and 140 kVp), acquired simultaneously by Dual Energy CT.

- The purpose of this study is to test the hypothesis that lower kVp imaging can improve detection of hypo- to iso-attenuating pancreatic malignancy.

Introduction:

1.1 Why study Pancreatic adenocarcinoma?

1.1.1 Natural history of Pancreatic adenocarcinoma:

Pancreatic adenocarcinoma accounts for 85%-95% of all pancreatic malignancies and is the fourth leading cause of cancer-related deaths.[1] Most of these malignancies are diagnosed at an advanced stage when they have already progressed to non-resectable and incurable disease [2][3] Non-resectable disease is seen at presentation in 75% of patients, with metastases (mainly to the liver and peritoneum) present in 85% of these patients.[1] Pancreatic adenocarcinoma has high mortality and morbidity with the median survival time of 6 months with metastasis and 12 months with local invasion, respectively.[2]

Thus, early detection and complete surgical resection is the only chance of improving survival.[2]

1.1.2 Contrast enhanced CT (CECT) for pancreatic imaging:

CT is the most widely available and best-validated imaging modality for diagnosing and staging patients with pancreatic cancer.[4,5] A pancreas CT protocol involves triphasic (i.e., arterial, late arterial, and venous phases) cross-sectional imaging with thin slices using multidetector CT [5,6]. One rationale for triphasic CT is that the difference in contrast enhancement between the parenchyma and adenocarcinoma is highest during the late arterial phase, thereby providing a clear distinction between a hypodense lesion in the pancreas and the rest of the organ.

1.1.3 Pitfalls of conventional contrast enhanced CT (CECT):
On imaging, pancreatic adenocarcinoma appears as low attenuation mass in pancreatic parenchymal phase. Being a fibrotic and desmoplastic tumour, post contrast enhancement is marginal.[7,8] As many as 10% of the lesions may be isoattenuating or have attenuation very close to that of normal gland and hence, can be extremely difficult to recognize.[7]

In porto-venous phase, which is routinely performed for various clinical indications, the attenuation difference between the lesion and adjacent normal parenchyma of pancreas is further reduced [7-10]

This difficulty was evidenced in a retrospective study [11] that showed that in many cases of pancreatic cancer, the diagnosis was made when previous CT data on the patient were retrospectively evaluated.

In some cases, subtle clues to the presence of pancreatic cancer were present as long as 18 months before the clinical diagnosis was made. These findings included mild pancreatic ductal dilatation with abrupt transition to normal caliber, subtle attenuation differences between tumor and gland, and morphologic changes in pancreatic gland contour.

1.2 Why Dual-energy CT (DECT)?

Dual-energy CT provides information about

- How substances behave at different energies,
- The ability to generate virtual unenhanced datasets, and
- Improved detection of iodine-containing substances on low-energy images.

Knowing how a substance behaves at two different energies can provide information about tissue composition beyond that obtainable with single-energy techniques.

1.2.1 Technical aspects of DECT:

- Acquires MDCT data at two photon energies (80 and 140 kVp) simultaneously in a single helical acquisition.[10,13,14]
- Complete pure 80-kVp, 140 kVp, virtual unenhanced and weighted-average image data sets (combination of 80 and 140 kVp data) can be generated from the raw data.
- Weighted average data can simulate the image quality of a standard 120 kVp acquisition.[10,14]

1.2.2 Potential clinical implications of DECT for Pancreatic imaging:
• Greater attenuation of contrast material is achieved with 80 kVp data than at 120/140 kVps. Increased photoelectric absorption and less Compton scatter at the lower photon energies results in the phenomenon. [15]
• This scientific study was based on the hypothesis that images obtained with 80 kVp data should show greater conspicuity of a hypoenhanced pancreatic neoplasm adjacent to normal pancreatic parenchyma than images obtained with data generated at higher peak kilovoltage. This possibility may be especially relevant when data are acquired during the portal venous phase of enhancement, when the attenuation differences of malignant pancreatic tumors and adjacent normal parenchyma are decreased.
Methods and materials

2.1 Subjects:

From January 2011 to February 2012, 50 patients of pancreatic focal lesions that were suspicious for adenocarcinoma were prospectively recruited for DECT evaluation. Of which, 21 patients (age 42-75 years) were confirmed as pancreatic adenocarcinomas on histology. All lesions were less than 4cm in their greatest dimension.

Biophysical characteristics of none of our subjects resulted in poor diagnostic quality images. There were no exclusion from the preliminary data set of 21 subjects.

Further sub-categorization and analysis with respect to age, gender and other comorbidities, pancreatic ductal dilatation, calcification or stage of the disease were not studied.

2.2 Image acquisition:

Multiphasic CT was performed with a dual-energy, 64-section multi-detector row CT scanner of one of the leading vendors. Dual-energy acquisition was performed by rapid switching of both tube voltage and tube current settings by using a single-source CT system. Two axial CT acquisitions at fixed-energy spectra-140 kVp and 80 kVp were obtained sequentially at the same anatomic level in a single rotation.

CT parameters:

Contrast media: Non-ionic Iopromide 300mg/ml
Dose: 90-120 ml (1.5ml/Kg ml)
Rate: 4-5 ml/s with power injector through antecubital vein
Delay of 80 seconds post injection (portovenous phase)
Detector configuration (mm) 64 x 0.625
Peak kilovoltage (kVp) 140- Tube current (mA) 385
Peak kilovoltage (kVp) 80- Tube current (mA) 675
Gantry revolution time (sec) 0.8
Scan coverage (mm) 280
Reconstructed section thickness (mm) 2.5, interval (mm) 2.5
Display field of view (cm) 22-25

2.3 Data interpretation:
Region of interest for HU measurement was placed in the centre of the lesion and adjacent normal pancreas in portovenous phase. The attenuation difference was calculated at both the kVp values.

2.3.1 Subjective analysis:

Representative images of all 50 patients including those with 21 adenocarcinomas were sorted in 80- and 140-kVp datasets. Two radiologists were blinded to patient identity, kVp settings and final diagnosis of the lesions. The phase of the contrast enhancement, field of view and thickness of sections were matched in each group. Observers were asked to look for possible pancreatic lesions in two data sets with different photon energies (undisclosed) and make note if one was more conspicuous than the other, or if both were equally conspicuous.

2.3.2 Statistical analysis:

Dual Energy data obtained in the porto-venous phase was reconstructed at 80 kVp and 140 kVp. Region of interest cursor was placed on the lesion and adjacent normal pancreatic parenchyma. The attenuation differences were calculated at both the kVp values.

The Mean attenuation difference, standard deviation of the attenuation differences, and their 95% confidence intervals were calculated. The means were compared using the t-test. A linear regression model was also used to evaluate the relation between the attenuation differences at 80 and 140 kVp. A p value of less than 0.05 was considered to be statistically significant.
Table 1: Attenuation values of pancreatic adenocarcinomas measured at different photon energies.

References: "Department of Radiology, Jaslok Hospital and Research Centre, Mumbai/IN. 2012"

<table>
<thead>
<tr>
<th>No.</th>
<th>Attenuation at 80kVp</th>
<th>Attenuation at 140 kVp</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Malignant lesion</td>
<td>Normal parenchyma</td>
</tr>
<tr>
<td>1</td>
<td>45</td>
<td>130</td>
</tr>
<tr>
<td>2</td>
<td>72</td>
<td>151</td>
</tr>
<tr>
<td>3</td>
<td>51</td>
<td>132</td>
</tr>
<tr>
<td>4</td>
<td>38</td>
<td>128</td>
</tr>
<tr>
<td>5</td>
<td>42</td>
<td>140</td>
</tr>
<tr>
<td>6</td>
<td>68</td>
<td>153</td>
</tr>
<tr>
<td>7</td>
<td>33</td>
<td>78</td>
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<tr>
<td>8</td>
<td>76</td>
<td>134</td>
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<tr>
<td>9</td>
<td>59</td>
<td>148</td>
</tr>
<tr>
<td>10</td>
<td>46</td>
<td>116</td>
</tr>
<tr>
<td>11</td>
<td>61</td>
<td>155</td>
</tr>
<tr>
<td>12</td>
<td>56</td>
<td>108</td>
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<td>144</td>
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<td>15</td>
<td>49</td>
<td>135</td>
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<td>16</td>
<td>34</td>
<td>97</td>
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<td>17</td>
<td>67</td>
<td>150</td>
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<td>18</td>
<td>78</td>
<td>166</td>
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<td>19</td>
<td>42</td>
<td>132</td>
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<td>20</td>
<td>54</td>
<td>117</td>
</tr>
<tr>
<td>21</td>
<td>31</td>
<td>101</td>
</tr>
</tbody>
</table>
Table 1: Attenuation values of pancreatic adenocarcinomas measured at different photon energies.

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Results

3.1 Subjective analysis:

Both observers detected all 21 cases of pancreatic adenocarcinoma and noted better subjective lesion conspicuity at 80kVp in majority of the cases.

<table>
<thead>
<tr>
<th>Observer 1</th>
<th>No difference</th>
<th>80 kVp was better</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>Observer 2</td>
<td>No difference</td>
<td>80 kVp was better</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>14</td>
</tr>
</tbody>
</table>

Table 2: Subjective analysis for conspicuity of lesions by two observers.

References: "Department of Radiology, Jaslok Hospital and Research Centre, Mumbai, IN, 2012"
Fig. 1: MDCT Abdomen with oral and IV contrast of 56 year old man with abdominal pain and weight loss. (a, b) 140 kVp axial sections show subtle area of decreased attenuation (arrow) in the head of pancreas. Attenuation difference between the lesion and normal parenchyma was 28 HU. (c, d) 80 kVp axial sections show better conspicuity of the hypodense pancreatic lesion. Attenuation difference between lesion and normal pancreas was 58 HU.

References: "Department of Radiology, Jaslok Hospital and Research Centre, Mumbai/IN. 2012"
Fig. 2: MDCT Abdomen with oral and IV contrast of 68 year old woman with recurrent abdominal pain. (a, b, c) 140 kVp axial sections show subtle area of decreased attenuation (arrow) in the head of pancreas. Attenuation difference between the lesion and normal parenchyma was 43 HU. (d, e, f) 80 kVp axial sections show better conspicuity of the hypodense pancreatic lesion. Attenuation difference between lesion and normal pancreas was 70 HU.

References: "Department of Radiology, Jaslok Hospital and Research Centre, Mumbai/IN. 2012"

3.2 Statistical analysis:
• At 80 kVp the mean difference (standard deviation of 15.32) in attenuation between the lesion and adjacent parenchyma was 77 (45-98). The 95% C.I. were 70.03- 83.97.
• The mean difference (standard deviation of 15.45) at 140 kVp was 41.62 (17-74). The 95% C.I. were 34.58-48.65.

The mean attenuation difference was significantly higher in the 80kVp compared with the 140 kVp (p<0.001).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Obs</th>
<th>Mean</th>
<th>Std. Err.</th>
<th>Std. Dev.</th>
<th>95% Conf. Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>diff 80</td>
<td>21</td>
<td>77</td>
<td>3.343081</td>
<td>15.31992</td>
<td>70.02564- 83.97354</td>
</tr>
<tr>
<td>diff 140</td>
<td>21</td>
<td>41.61905</td>
<td>3.371785</td>
<td>15.45146</td>
<td>34.58563- 48.65247</td>
</tr>
<tr>
<td>diff</td>
<td>21</td>
<td>35.38095</td>
<td>2.381952</td>
<td>10.91548</td>
<td>30.41229- 40.34962</td>
</tr>
</tbody>
</table>

Table 3: t-test

References: "Department of Radiology, Jaslok Hospital and Research Centre, Mumbai/IN. 2012"
Table 4: Wilcoxon signed-rank test

References: "Department of Radiology, Jaslok Hospital and Research Centre, Mumbai/IN. 2012"

In linear regression model, the equation was as follows:

\[
\text{Attenuation difference at 80kVP} = 46.12 + 0.74 \times \text{Attenuation difference at 140 kVp}
\]

For example, at 140 kVp when the observed difference in attenuation for the lesion and normal parenchyma was none, the attenuation difference of 46.12 will be expected at 80 kVp. Furthermore, each unit increase in the attenuation difference at 140 kVp was
associated with 0.74 (95% CI: 0.43 to 1.06) unit increase in the attenuation difference at 80 kVp.

Hence, the visibility and detection of pancreatic adenocarcinomas at 80 kVp is expected to significantly improve regardless of the absolute attenuation difference at 140 kVp.
Table 2: Subjective Analysis for conspicuity of lesion by two observers.

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Table 3: t-test

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### Wilcoxon signed-rank test

<table>
<thead>
<tr>
<th>Sign</th>
<th>Obs</th>
<th>Sum ranks</th>
<th>Expected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>21</td>
<td>231</td>
<td>115.5</td>
</tr>
<tr>
<td>Negative</td>
<td>0</td>
<td>0</td>
<td>115.5</td>
</tr>
<tr>
<td>Zero</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>All</td>
<td>21</td>
<td>231</td>
<td>231</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Unadjusted variance</th>
<th>827.75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjustment for ties</td>
<td>(−)1.75</td>
</tr>
<tr>
<td>Adjustment for zeros</td>
<td>0</td>
</tr>
<tr>
<td>Adjusted variance</td>
<td>826</td>
</tr>
</tbody>
</table>

\[ Ho: \text{diff 80} = \text{diff 140} \]
\[ z = 4.019 \]
\[ \text{Prob} > |z| = 0.0001 \]

**Table 4:** Wilcoxon signed-rank test

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**Fig. 1:** MDCT Abdomen with oral and IV contrast of 56 year old man with abdominal pain and weight loss. (a, b) 140 kVp axial sections show subtle area of decreased attenuation (arrow) in the head of pancreas. Attenuation difference between the lesion and normal parenchyma was 28 HU. (c, d) 80 kVp axial sections show better conspicuity of the hypodense pancreatic lesion. Attenuation difference between lesion and normal pancreas was 58 HU.

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Conclusion

- **Detection and visibility** of pancreatic tumours improved at 80 kVp as compared to 140 kVp, as per both, subjective and objective analysis.
- This difference was **statistically significant** when tested with two independent tests, namely, t-test and Wilcoxon signed-rank test. (p<0.001)
- The conspicuity of pancreatic adenocarcinomas at 80 kVp is expected to significantly improve regardless of the absolute attenuation difference at 140 kVp.
- Improved detection of pancreatic adenocarcinoma in portovenous phase of 80 kVp has a potential to reduce false negative results on contrast enhanced CT. This in turn is likely to result in better prognosis of this rapidly fatal malignancy.
- The attenuation differences at 120 kVp, contrast to noise ratio and other imaging parameters were not studied. Small sample size is a **limitation** of this study.
References

1. Ros PR, Mortelé KJ. Imaging features of pancreatic neoplasms. JBR-BTR 2001;84(6):239-249