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## Utility of perfusion CT in characterizing the pancreatic tumors

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### Abstract

**Purpose:** The aim of this study was to apply perfusion CT (Computed Tomography) technique to various pancreatic masses and to prospectively evaluate the perfusion parameters of pancreatic lesions and to compare these parameters with the parameters of normal pancreatic parenchyma.

**Materials and Methods:** A total of 33 subjects with pancreatic tumors underwent perfusion CT. The perfusion parameters like tBF & pBF (Tumor Blood-Flow and Pancreatic Blood-Flow), tPEI & pBF (Tumor Peak Enhancement Index and Pancreatic Peak Enhancement Index), tTTP & pTTP (Tumor Time to Peak and Pancreatic Time to peak) and tBV & pBV (Tumor Blood-Volume and Pancreatic Blood-Volume) were obtained by placing an ROI (Region of Interest) on the tumor and the normal pancreas respectively. Descriptive statistics of the perfusion values of the tumor and the normal pancreas was tabulated and statistical significance was calculated using Mann Whitney U test.

**Results:** 26 patients had adenocarcinoma, 4 had endocrine tumors, 2 had metastases and 1 had Ewing's sarcoma. Adenocarcinomas showed significantly lower BF (Blood-Flow), PEI (Peak Enhancement Index) and Blood volume (BV) but significantly higher TTP (Time to Peak) as compared to the normal pancreas ( $P<0.05$ ). Endocrine tumors showed increased BF and PEI as compared to the normal pancreas ( $P<0.05$ ). Two cases of metastases had low BF, PEI and BV but high TTP as compared to the normal pancreas. Single case of Ewing's sarcoma had reduced BF and PEI but increased TTP as compared to the normal pancreas.

**Conclusion:** Perfusion CT greatly helps in characterization of the pancreatic tumors and adds to the morphological features for a confident diagnosis.

**Keywords:** Utility, characterizing, CT, pancreatic

### Introduction

Perfusion CT is an exciting technology that allows functional evaluation of tissue vascularity. CT perfusion aims to delineate the contrast enhancement within the vessels inside a tumor and is considered to be the CT angiography for the tumor microcirculation. It measures the temporal changes in tissue density after intravenous injection of a contrast medium bolus using a series of dynamically acquired CT images. The pancreatic perfusion feasibility was first demonstrated by Miles *et al.* [1] who demonstrated the benefit of combining high spatial resolution images with functional data. The benefit of perfusion CT for differentiating pancreatitis and malignant lesions from normal pancreas has been investigated over the last few year [2, 3]. Also, the technique has the potential to be the technique of choice for the assessment of tumor response after treatment with antiangiogenic drugs [4, 5].

The aim of this study was to apply perfusion CT technique to various pancreatic masses and to prospectively evaluate the perfusion parameters of pancreatic lesions and to compare these parameters with the parameters of normal pancreatic parenchyma.

### Material and Methods

This prospective study was performed at a tertiary care center for a period of 2 years in patients with pancreatic tumors. After obtaining the Institutional ethical committee clearance, 49 contiguous patients who had pancreatic lesion on routine plain CT imaging or on an ultrasound were identified. Before the contrast CT, informed consent was obtained from these patients after explaining about the study. 33 patients gave the consent while 16 patients

refused. Inclusion criteria included patients age of 18 years and above and patients having pancreatic lesion as detected on plain CT study or on ultrasound. The exclusion criteria included > 2mg/dl of serum creatinine and/ or history of allergy to iodinated contrast media and/or patients having no histopathological confirmation.

**Imaging protocol**

Scanner used: Philips Brilliance 64 slice CT scanner.  
 Gantry rotation time: 0.75s.  
 Voltage:120 kVp  
 Current:200 mA  
 Pitch:1.5

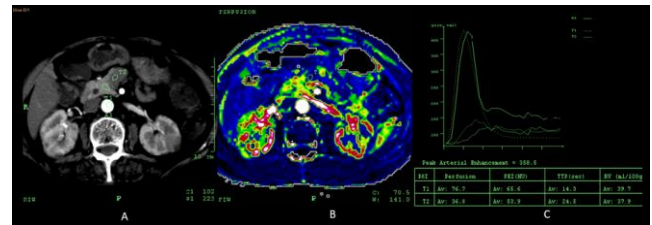
**Technique**

Plain CT scan of the abdomen was obtained in the supine position for tumor localization. A region of interest of 4-cm which included the tumor (portion of the tumor with enhancing components) and portion of normal pancreas was localized and selected for the perfusion study. Though an 18G canula inserted into a peripheral vein, intravenous bolus contrast of 50 ml was injected at a rate of 5ml/sec using a power injector. 35ml of saline flush was injected soon after the contrast bolus. 8 sec delay was given after the start of contrast injection, following which a continuous acquisition in the 8i transverse mode (8 sections per gantry rotation) was obtained. Total of 30 dynamic acquisitions with inter - cycle interval of 2.0sec.

**Image analysis and interpretation**

A total of 240 perfusion images were obtained in each patient which were transferred to the CT perfusion analysis software. Free hand ROI's were then placed in aorta, normal pancreas and the pancreatic tumor to obtain the respective time-density curves, taking care to not to include calcification, necrosis and blood vessels within the ROI. Quantitative assessment and calculation of perfusion parameters were performed. The resulting perfusion values could be visualised on colour maps. (Figure 1)  
 Perfusion Parameters recorded were BF (Perfusion - ml/100gm/min), BV (ml/100gm), PEI (HU) and TTP (s)  
 Images were interpreted by a radiologist who is blinded to the histopathological diagnosis. Findings were then

correlated with the histopathological diagnosis and tabulated at the end of the study.



**Fig 1:** Perfusion CT image (A) shows a hypoattenuating mass (T2) in the head of pancreas CT perfusion color map of blood flow (B) shows mass in pancreatic head has a distinct range of colors compared with the background normal pancreatic parenchyma (T1). Time density curves (C) shows Blood flow in ROI (T2) drawn for the adenocarcinoma was low (36.8 ml/100 g/min) as compared to ROI (T1) in normal pancreatic parenchyma (76.7 ml/100 g/min).

**Observation and Results**

Pancreatic adenocarcinoma was the most common pancreatic mass constituting to 79% of the tumors, while all the other masses, i.e. Endocrine tumours and metastases were less common in our study. One case of Ewing's sarcoma of the pancreas was diagnosed on histopathology (Table 1).

**Table 1:** shows different pancreatic tumors and their total numbers.

|                  | No. | Percentage |
|------------------|-----|------------|
| Adenocarcinoma   | 26  | 79         |
| Endocrine tumors | 4   | 12         |
| Metastases       | 2   | 6          |
| Ewing's sarcoma  | 1   | 3          |
| Total            | 33  | 100        |

Most of the patients in the study were in the age range of 40 to 60 years. Minimum age was 25 years, Maximum age was 78 years, Mean age was 51.5 years.

**Comparison of Perfusion values from the 26 pancreatic adenocarcinomas and the normal pancreatic tissue.**

**Table 2:** Perfusion values in adenocarcinomas and normal pancreatic tissue

| Statistics | tBF   | tPEI  | tTTP  | tBV   | pBF   | pPEI  | pTTP  | pBV   |
|------------|-------|-------|-------|-------|-------|-------|-------|-------|
| Min.       | 2.90  | 5.7   | 13.7  | 2.90  | 11.0  | 23.70 | 8.00  | 7.80  |
| Max.       | 78.80 | 76.9  | 59.30 | 91.70 | 161.2 | 165.0 | 58.30 | 321.5 |
| Mean       | 15.60 | 23.09 | 41.17 | 19.96 | 69.86 | 52.18 | 20.16 | 52.31 |
| S.D        | 14.87 | 15.44 | 14.57 | 20.02 | 37.96 | 26.51 | 9.08  | 54.97 |

Perfusion (BF) ranged from 2.9 to 78.8 ml100gm<sup>-1</sup>min<sup>-1</sup> (Mean + SD =15.6 + 14.87), PEI ranged from 5.7 to 76.9 HU (Mean + SD =23.1 + 15.4), Blood volume ranged from 2.9 to 91.7 ml100gm<sup>-1</sup> (Mean + SD= 41.2 + 14.6) and TTP ranged from 13.7 to 59.3s (Mean + SD =41.7 + 14.6) in adenocarcinomas.

In all 26 patients with adenocarcinoma, Perfusion, PEI and the blood volume of the pancreatic adenocarcinoma was

lower than that of the pancreatic parenchyma (P<0.05). The TTP of the pancreatic adenocarcinoma was greater than that of the pancreatic parenchyma (P>0.05).

**Comparison of Perfusion values from the four pancreatic endocrine tumours and the normal pancreatic tissue.**

**Table 3:** Perfusion values in endocrine tumors and normal pancreatic tissue

| Statistics | tBF   | tPEI  | tTTP  | tBV   | pBF   | pPEI  | pTTP  | pBV   |
|------------|-------|-------|-------|-------|-------|-------|-------|-------|
| Min.       | 98.80 | 43.20 | 12.30 | 31.60 | 11.0  | 23.70 | 8.00  | 7.80  |
| Max.       | 123.2 | 104.1 | 16.40 | 69.80 | 161.2 | 165.0 | 58.30 | 321.5 |
| Mean       | 110.1 | 67.78 | 14.18 | 50.35 | 69.86 | 52.18 | 20.16 | 52.31 |
| S.D        | 11.65 | 26.07 | 1.70  | 15.61 | 37.96 | 26.51 | 9.08  | 54.97 |

Perfusion ranged from 98.8 to 123.2 ml100gm<sup>-1</sup>min<sup>-1</sup> (Mean + SD= 110.1+ 11.65), PEI ranged from 43.2 to 104.1HU (Mean + SD= 67.8 + 26.7), Blood volume ranged from 31.6 to 69.8 ml100gm<sup>-1</sup> (Mean + SD= 50.4 + 15.61) and TTP ranged from 12.3 to 16.4 s (Mean + SD= 14.2 + 1.70) in endocrine tumours.

Endocrine tumours had perfusion characteristics of increased perfusion and PEI as compared to the normal pancreas (P<0.05), but their blood volume TTP was similar to that of the normal pancreatic parenchyma (P<0.05).

**Comparison of Perfusion values from the two pancreatic metastases and the normal pancreatic tissue**

**Table 4:** Perfusion values in pancreatic metastases and normal pancreatic tissue

| Statistics | tBF  | tPEI  | tTTP  | tBV  | pBF   | pPEI  | pTTP  | pBV   |
|------------|------|-------|-------|------|-------|-------|-------|-------|
| Min.       | 8.10 | 16.10 | 38.80 | 3.80 | 11.0  | 23.70 | 8.00  | 7.80  |
| Max.       | 8.40 | 21.90 | 59.30 | 5.90 | 161.2 | 165.0 | 58.30 | 321.5 |
| Mean       | 8.25 | 19.00 | 49.05 | 4.85 | 69.86 | 52.18 | 20.16 | 52.31 |
| S.D        | 0.21 | 4.10  | 14.50 | 1.48 | 37.96 | 26.51 | 9.08  | 54.97 |

Perfusion ranged from 8.1 to 8.4 ml100gm<sup>-1</sup>min<sup>-1</sup> (Mean + SD =8.25 + 0.212), PEI ranged from 16.1 to 21.9HU (Mean + SD =19.0 + 4.1), Blood volume ranged from 3.8 to 5.9 ml100gm<sup>-1</sup> (Mean + SD =4.85 + 1.48) and TTP ranged from 38.8 to 59.3s (Mean + SD =49.05 + 14.5) in metastatic lesions to the pancreas.

Pancreatic metastases had perfusion characteristics of decreased perfusion, PEI and blood volume as compared to the normal pancreas, but their TTP was greater than that of the normal pancreatic parenchyma.

**Comparison of Perfusion values from one case of Ewing’s sarcoma of the pancreas and the normal pancreatic tissue**

**Table 5:** Perfusion values in Ewing’s sarcoma and normal pancreatic tissue

|      | tBF  | tPEI | tTTP | tBV  | pBF   | pPEI  | pTTP  | pBV   |
|------|------|------|------|------|-------|-------|-------|-------|
| Mean | 10.2 | 12.2 | 49.1 | 47.2 | 69.86 | 52.18 | 20.16 | 52.31 |

Ewing’s sarcoma of the pancreas had perfusion characteristics of decreased perfusion and PEI; and increased TTP as compared with that of the normal pancreatic parenchyma. The blood volume however was almost similar to that of normal pancreatic parenchyma.

**Discussion**

**Pancreatic adenocarcinomas and the normal pancreatic tissue**

Sonja Kandel *et al.* [6] evaluated perfusion differences between normal and diseased pancreatic tissue. Perfusion ranged from 0.20 to 1.81 min-1 with an average value of 0.80. The perfusion of pancreatic adenocarcinomas was significantly lower than all three normal pancreatic regions

(head vs. tumour: P<0.01, body vs. tumour: P<0.001, and tail vs. tumour: P<0.001).

Jin Xu *et al.* [7] recorded the BF, BV and the permeability surface area product (PS) of normal pancreas as 135.24 + 48.36 ml min<sup>-1</sup> 100g<sup>-1</sup>, 200.55 + 54.96 ml 100 g<sup>-1</sup>, and 49.75 + 24.27 ml min<sup>-1</sup> 100 g<sup>-1</sup>, respectively. BF, BV, and PS values of the tumor tissue of pancreatic adenocarcinoma decreased significantly as compared to normal pancreas (P < 0.05). Hence, they concluded that a significant decrease of BF, BV, and PS was observed in pancreatic adenocarcinoma compared to normal pancreatic parenchyma.

Abe *et al.* [2] compared the quantitative tissue blood flow in pancreatic tumours measured by xenon CT and perfusion CT and found, in addition to the good linear correlation between the two imaging techniques, that adenocarcinomas display values ranging between 22.1 to 50.0 ml min-1 100gm-1 on perfusion CT.

In the current study, the pancreatic adenocarcinomas revealed a significant decrease of BF, BV, and PEI and an increase in TTP, in pancreatic adenocarcinomas as compared to normal pancreatic parenchyma.

The perfusion values of adenocarcinomas in our study matched the results in other studies. The results correspond to the clinical experience that conspicuity of pancreatic cancers in best during peak enhancement of the pancreas on spiral and multislice CT examinations.

**Pancreatic endocrine tumours with normal pancreatic parenchyma**

Gaspard d’Assignies *et al.* [8] observed a high correlation (r = 0.620, P< .001) between tumor blood flow and intratumoral microvascular density (MVD) in pancreatic endocrine tumours. Blood flow was significantly higher (P =0.02) in the group of benign endocrine tumours (WHO 1) than in the groups of tumours of indeterminate prognosis (WHO 2) or well-differentiated carcinomas (WHO 3). There was no significant difference in the BF, BV, MTT and PS between tumours and normal parenchyma in this study probably due to the large variety of tumours in this study which ranged from benign to highly malignant.

Xue HD *et al.* [9] measured perfusion parameters of normal pancreatic parenchyma in 9 subjects as follows: BF = 104. 9 +/- 28.9 ml min<sup>-1</sup> 100g<sup>-1</sup>, BV = 166.4 +/- 41.8 ml 100 g<sup>-1</sup>, TTP = 133.3 +/- 24.4 seconds, Permeability = 81.3 +/- 24.4 ml 100gm-1 min-1 and PEI = 121.3 +/- 31.1 HU, and in 12 subjects with insulinoma as follows: BF = 206.5 +/- 42.2 ml min<sup>-1</sup> 100 g<sup>-1</sup>, BV = 315.9 +/- 79.0 ml 100 g<sup>-1</sup>, TTP = 123.2 +/- 18.8 seconds, Permeability = 102.5 +/- 54. 8 ml 100gm<sup>-1</sup> min<sup>-1</sup>, and PEI = 221.3 +/- 48.5 HU. Results of BF, BV and PEI in these two kinds of tissue showed significant differences (P< 0.01), while there were no significant difference (P > 0.05) in TTP and permeability between normal pancreatic parenchyma and insulinoma. They inferred that benign insulinoma therefore have perfusion characteristics of increased blood flow and blood volume, but their TTP is consistent with normal pancreas and that they have normal permeability.

Abe *et al.* [2] found a blood flow value of 196.2 ml 100 g<sup>-1</sup> min<sup>-1</sup> in one gastrinoma.

The pancreatic endocrine tumours in our study demonstrated increased perfusion (BF) values and PEI as compared to normal pancreatic parenchyma, while their BV and TTP was similar to that of normal pancreatic parenchyma. This is probably due to the low number of subjects with different grades of tumour in the current study.

#### **Pancreatic metastases with normal pancreatic parenchyma**

In the current study, there were two subjects with pancreatic metastases. Both lesions were metastases from squamous cell carcinomas, one from carcinoma of the buccal mucosa and the other from bronchogenic carcinoma.

Pancreatic metastases showed a significant decrease of BF, BV, and PEI and an increase in TTP, as compared to normal pancreatic parenchyma. This indicates that these metastatic lesions from squamous cell carcinomas are hypovascular as compared to the normal pancreas. However, since there were only two subjects with pancreatic metastases, it is difficult to evaluate the relationship of their perfusion values with normal pancreatic parenchyma.

#### **Ewing's sarcoma of the pancreas with normal pancreatic parenchyma**

There was one case of histologically proven Ewing's sarcoma of the pancreas in our study whose BF, BV and PEI were lower while the TTP was higher than normal pancreatic tissue.

The restricted slice number was one of the limitations in the study. 64 slice CT scanner can only perfuse 4cm of the tissue of interest per cycle. So, the entire pancreatic gland perfusion was not possible. So neither the entire pancreatic gland nor the whole tumour volume in case of larger tumours can be imaged in full without table motion during imaging. Thus, our limited region of interest might have been "nonrepresentative" of whole tumour perfusion, especially in large and heterogeneous lesions.

#### **Conclusion**

Perfusion CT greatly helps in functional characterization of the pancreatic tumors, especially the adenocarcinomas which has shown consistent results across different studies and acts as a surrogate marker for a confident diagnosis.

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