**FULL PAPER** *Internal Medicine*

# Establishment of optimal scan delay for multi-phase computed tomography using bolus-tracking technique in canine pancreas

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ABSTRACT. To establish a protocol for a multi-phase computed tomography (CT) of the canine pancreas using the bolus-tracking technique, dynamic scan and multi-phase CT were performed in six normal beagle dogs. The dynamic scan was performed for 60 sec at 1-sec intervals after the injection (4 ml/sec) of a contrast medium, and intervals from aortic enhancement appearance to aortic, pancreatic parenchymal and portal vein peaks were measured. The multi-phase CT with 3 phases was performed three times using a bolus-tracking technique. Scan delays were 0, 15 and 30 in first multi-phase scan; 5, 20 and 35 in second multi-phase scan; and 10, 25 and 40 sec in third multi-phase scan, respectively. Attenuation values and contrast enhancement pattern were analyzed from the aorta, pancreas and portal vein. The intervals from aortic enhancement appearance to aortic, pancreatic parenchymal and portal vein peaks were 3.8 ± 0.7, 8.7 ± 0.9 and 13.3 ± 1.5 sec, respectively. The maximum attenuation values of the aorta, pancreatic parenchyma and portal vein were present at scan sections with no scan delay, a 5-sec delay and a 10-sec delay, respectively. When a multi-phase CT of the canine pancreas is triggered at aortic enhancement appearance using a bolus-tracking technique, the recommended optimal delay times of the arterial and pancreatic parenchymal phases are no scan delay and 5 sec, respectively.

KEY WORDS: bolus-tracking technique, canine, multi-phase CT, pancreas

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The canine pancreas is a thin, V-shaped organ, located caudal to the liver and stomach [8]. Pancreatitis and pancreatic tumor including insulinoma or adenocarcinoma are the most important pancreatic diseases in dogs. Several imaging techniques, including ultrasonography, computed tomography (CT) and single-photon emission computed tomography, have been used to evaluate canine pancreatic diseases [12, 13, 19, 22]. Of these methods, ultrasonography has been considered as noninvasive and effective modalities for visualizing pancreas, but also has disadvantages. Gas filled stomach may hinder imaging of entire pancreas, especially left limb [17], and patient may feel pain due to transducer pressure during ultrasonographic examination. Because of these difficulties, the evaluation of pancreas by US depends on the sonographer's skill [22]. Therefore, to overcome these challenges for imaging pancreas, CT has been used to evaluate pancreas in dogs.

Conventional CT can be a valuable imaging technique for evaluation of acute pancreatitis and insulinoma in the dog [13, 22], and a study described that the use of a previously established dual-phase CT protocol for the presurgical diagnosis and staging of pancreatic inulinoma has been applied in dogs [6, 20]. The recent study reported that CT findings of suspected pancreatitis included enlarged, homogeneously to heterogeneously attenuating and contrast-enhancing pancreas with ill-defined borders in dogs [2]. Although single or dual-phase scan is considered to be enough for evaluating pancreas in veterinary medicine, CT examinations of the pancreas in human medicine have been performed at different phases of contrast enhancement; arterial, pancreatic parenchymal, portal and venous phases [18, 21].

Contrast-enhanced CT techniques, such as fixed scan delay, test bolus and bolus tracking, have been described for multi-phase pancreatic imaging in humans [1, 5, 10, 11]. CT scan using fixed scan delay is a method without consideration of individual variations like cardiac output. To acquire images at each precisely determined enhancement phase, it is essential to first use a dynamic scan (test bolus method) or bolus-tracking technique to measure contrast arrival time. In veterinary medicine, a dual-phase scan using previous dynamic scans as the test bolus method for the pancreas has been described [6, 20]. To overcome the disadvantages of the test bolus method, which is a time-consuming and labor-intensive method, commercial software mentioned to bolus-tracking technique is available that automates the process of triggering the dual-phase scan as the vessel contrast medium reaches attenuation adequate for scanning. While the scanning delay for CT imaging with a bolus-tracking technique for arterial, pancreatic parenchymal, portal venous and hepatic parenchymal contrast enhancement has been determined in humans [18], pancreatic parenchymal phase has been reported in a veterinary literature using dynamic CT scan [12].

Therefore, the aim of this study is to determine the optimal

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scanning delay for a multi-phase CT scan of the pancreas using the bolus-tracking technique in normal beagle dogs.

## MATERIALS AND METHODS

*Experimental animals*: This study was performed under the guidance of the Chungnam National University Animal Care and Use Committee. Six normal beagle dogs (4 intact males and 2 intact females) with a mean age of 2 years and body weights between 7 and 13 kg (mean 9 kg) were used for the study. Physical examinations, complete blood cell counts, serum chemistry analyses and radiography of the thorax and abdomen were performed to determine that the dogs were clinically healthy.

### *CT scan technique and image analyses*

*Anesthesia*: Prior to the CT scan, the dogs were fasted for 12 hr. The dogs were premedicated with 0.3 mg/kg midazolam (Midacum® inj., Myungmoon Pharm. Co., Ltd., Seoul, Korea) intravenously, and anesthesia was induced with 5.0 mg/kg of propofol (Provive® inj., Myungmoon Pharm. Co., Ltd.) intravenously. After endotracheal intubation, anesthesia was maintained with isoflurane (Ifran®, Hana Pharm. Co., Ltd., Seoul, Korea) and oxygen.

The anesthetized dogs were placed in sternal recumbency on the CT table, and a 20-gauge over-the-needle catheter in the cephalic vein was connected to an angiographic power injector (Salient™, Imaxeon Pty. Ltd., Sydney, Australia). To avoid motion artifact due to respiration, each dog was hyperventilated before the CT scan, and intermittent positive pressure ventilation (15–20 cm $H_2O$) was administered during the scan.

*Survey scan*: A survey scan was obtained using a helical CT scanner (Alexion™, Toshiba, Otawara, Japan) and the following parameters: 120 kVp, 150 mA, 2-mm slice thickness, 0.75-sec rotation time and 0.938 collimation beam pitch. The images were reconstructed using 2-mm thick slices and reconstruction intervals of 1 mm. Prior to the dynamic scan, a survey scan of the entire abdomen extending from the diaphragm to coxofemoral joint level was performed to identify the scan level location of the pancreatic body.

*Dynamic scan*: A contrast medium (Omnipaque®, GE healthcare Ireland, Cork, Ireland) with an iodine concentration of 300 mg iodine/m*l* was administered at a dosage of 600 mg iodine/kg using an angiographic power injector at a rate of 4 m*l*/s and an injection pressure ≤200 psi. The dynamic scan was initiated at the time of injection of the contrast medium and continued for 60 sec at 1-sec intervals. The scan parameters were 120 kVp, 120 mA, 2-mm thick slices and a 1-sec rotation time. Images were reconstructed with an interval of 1 sec. All images were reconstructed using standard kernel frequency.

*Multi-phase scan*: A multi-phase scan was performed using a crossover design with the same 6 beagle dogs. The multi-phase CT scan was performed using a bolus-tracking technique 3 times at intervals of 3 days, and 3 phase series were obtained in each multi-phase CT scan. Scan delays were 0, 15 and 30; 5, 20 and 35; and 10, 25 and 40 sec in the first, second and third CT scans, respectively. This procedure was modified from methods described in human studies [18].

The scan range was determined from the survey CT images. The range of the first phase was from the cranial margin of the diaphragm to the caudal level, covering the entire pancreas in a caudocranial direction. The CT scan of the second and third phases was in a craniocaudal direction equal to the range of the first phase.

A bolus-tracking program (SureStart™, Toshiba) was used to monitor contrast enhancement after injection of the contrast medium. The region of interest (ROI) for the bolus tracking was placed in the aorta at the level of the scan starting position. Scan monitoring for the aorta was started concurrently with the administration of the contrast medium. Injection parameters were the same with those in dynamic scan. The first phase scanning was triggered at 50 Housfield Units (HU) of aortic enhancement by bolus tracking. The multi-phase scan parameters were 120 kVp, 150 mA, 2-mm slice thickness, 0.75-sec rotation time and 1.438 collimation beam pitch. Acquired images were reconstructed using 2-mm thick slices and reconstruction intervals of 1 mm. All images were reconstructed using the standard kernel frequency.

*Image analyses*: The CT images of dynamic scan were evaluated using a commercial software program (Rapidia®, Infinitt Healthcare Co., Ltd., Seoul, Korea). ROI with a circle of 10 pixels in diameter was placed at the aorta, pancreatic body and portal vein, and a time attenuation curve was generated. Pancreatic attenuation values and time to aortic enhancement appearance, aortic peak, pancreatic parenchymal peak and portal vein peak were measured, and intervals from aortic enhancement appearance to aortic, pancreatic parenchymal and portal vein peaks were calculated. Multi-phase CT images of nine series were analyzed using a software program (Infinitt PACS, Infinitt Healthcare Co., Ltd.). ROI were placed at the aorta, pancreatic body and portal vein. Attenuation values were measured from the ROI on the images at the same level in the 3 phase series. The mean attenuation values were calculated, and maximum mean values for aorta, pancreatic parenchyma and portal vein were identified.

*Data analyses*: All data were expressed as the mean and standard deviation. Statistical analysis was performed using the SPSS statistical software program (IBM SPSS Statistics 21.0, IBM Corp., Armonk, NY, U.S.A.). Mean aorta, pancreatic parenchyma and portal vein values at each scan delay were evaluated statistically using the Mann-Whitney and Kruskal-Wallis tests in SPSS. Values of $P<0.05$ were considered statistically significant.

## RESULTS

The time attenuation curve of the aorta, pancreas and portal vein was acquired from the dynamic CT images. Attenuation parameters of the aorta, pancreas and portal vein are shown in Table 1.

The time to aortic enhancement appearance after contrast injection was 4.7 ± 0.7 sec, and times to aortic, pancreatic parenchymal and portal vein peaks were 8.5 ± 0.8, 13.3 ±

Table 1. Attenuation parameters for the aorta, pancreas and portal vein in normal beagle dogs

| Measurement | Aortic Enhancement Appearance | Aortic Peak | Pancreatic Parenchymal Peak | Portal Vein Peak |
|---|---|---|---|---|
| Arrival Time after Contrast Injection (sec) | 4.7 ± 0.7 | 8.5 ± 0.8 | 13.3 ± 0.7 | 18.0 ± 1.2 |
| Interval from Aortic Enhancement Appearance (sec) | - | 3.8 ± 0.7 | 8.7 ± 0.9 | 13.3 ± 1.5 |
| Pancreatic Attenuation Value (HU) | 50.7 ± 7.6 | 83.7 ± 12.1[a)] | 133.4 ± 19.9[a), b)] | 109.8 ± 13.7[a), b)] |

Data are expressed as mean ± SD. a) The pancreatic attenuation and aortic enhancement appearance values differed significantly with that at aortic enhancement appearance. b) The pancreatic attenuation and aortic peak values differed significantly with that at aortic peak.

Table 2. Attenuation values for aorta, pancreatic parenchyma and portal vein on nine series of multi-phase CT images with 5 sec intervals

| Scan Delay (sec) | Region of Interest (HU) | | |
|---|---|---|---|
| | Aorta | Pancreatic Parenchyma | Portal Vein |
| 0 | 575.5 ± 219.5 [a)] | 124.8 ± 14.9 [b)] | 79.3 ± 40.6 [e)] |
| 5 | 214.8 ± 47.8 [a)] | 151.0 ± 14.5 [b),c)] | 122.3 ± 45.1 [e),f)] |
| 10 | 148.5 ± 25.0 | 129.5 ± 10.6 [c),d)] | 215.8 ± 44.8 [f)] |
| 15 | 203.7 ± 21.7 | 108.2 ± 7.5 [d)] | 213.2 ± 13.3 |
| 20 | 194.8 ± 28.4 | 111.5 ± 10.0 | 206.2 ± 13.8 |
| 25 | 186.7 ± 13.3 | 109.2 ± 5.0 | 207.2 ± 13.7 |
| 30 | 176.5 ± 8.7 | 101.0 ± 9.7 | 190.3 ± 17.5 |
| 35 | 173.5 ± 13.7 | 101.7 ± 10.0 | 189.7 ± 13.1 |
| 40 | 175.3 ± 19.9 | 99.0 ± 4.5 | 186.2 ± 14.0 |

Data are expressed as mean ± SD. a–f) The values sharing the same superscript letter differ significantly from each other ($P<0.05$).

0.7 and 18.0 ± 1.2 sec, respectively. The intervals from aortic enhancement appearance to aortic, pancreatic parenchymal and portal vein peaks were 3.8 ± 0.7, 8.7 ± 0.9 and 13.3 ± 1.5 sec, respectively.

The pancreatic attenuation values at aortic enhancement appearance, aortic, pancreatic parenchymal and portal vein peaks were 50.7 ± 7.6, 83.7 ± 12.1, 133.4 ± 19.9 and 109.8 ± 13.7 HU, respectively. The pancreatic attenuation value was significantly higher at the pancreatic parenchymal peak than at the aortic peak, and significantly higher at the aortic peak than at aortic enhancement appearance.

The mean attenuation values of the aorta, pancreatic parenchyma and portal vein of multi-phase CT images of total nine series are summarized in Table 2. The maximum mean attenuation values of the aorta, pancreatic parenchyma and portal vein were present at scan sections with no scan delay, a 5-sec delay and a 10-sec delay, respectively (Fig. 1).

The mean attenuation value of the aorta was highest at no delay. The maximum mean attenuation value at no delay was significantly higher than at the 5-sec delay. After a 15-sec delay, the change in the mean attenuation value of the aorta decreased gradually without significant differences. The maximum mean attenuation value of the pancreatic parenchyma at the 5-sec delay was significantly higher than that at no scan delay and 10-sec delay, and mean attenuation at 10-sec delay was significantly higher than that at 15-sec delay. The change in mean attenuation value decreased gradually after the 15-sec delay without significant differences. The maximum mean attenuation value of the portal vein increased significantly between the 0 to 10-sec delays and decreased gradually between the 10 to 35-sec delay with no significant difference.

## DISCUSSION

Dynamic CT scanning has been recommended to determine scan delays in dual-phase CT scans of the liver and pancreas in veterinary medicine [6, 25]. According to these studies, analysis of the contrast enhancement pattern using dynamic CT shows the time to aortic enhancement appearance, and the aortic and portal vein peaks that are applied to the multi-phase CT scan. Times to aortic enhancement appearance, aortic peak and portal vein peak were 8.6, 12.0 and 33.0 sec in a previous study [25], and 6.3, 10.5 and 32.0 sec in another study [6]. The intervals from aortic enhancement appearance to aortic peak were 3.4 and 4.2 sec in the previous studies, respectively [6, 25]. These results showed slower values than this study. This difference was probably caused by iodine delivery rate of flow rate, duration and volume as injection-related factors and cardiac output as patient-related factor [3, 4, 15]. Although the time to aortic peak in this study was faster than in previous studies, the interval to aortic enhancement appearance was similar. Thus, the difference of time to aortic peak probably resulted from differences in aortic enhancement appearance. Therefore, it may be difficult to obtain an optimal aortic phase in every

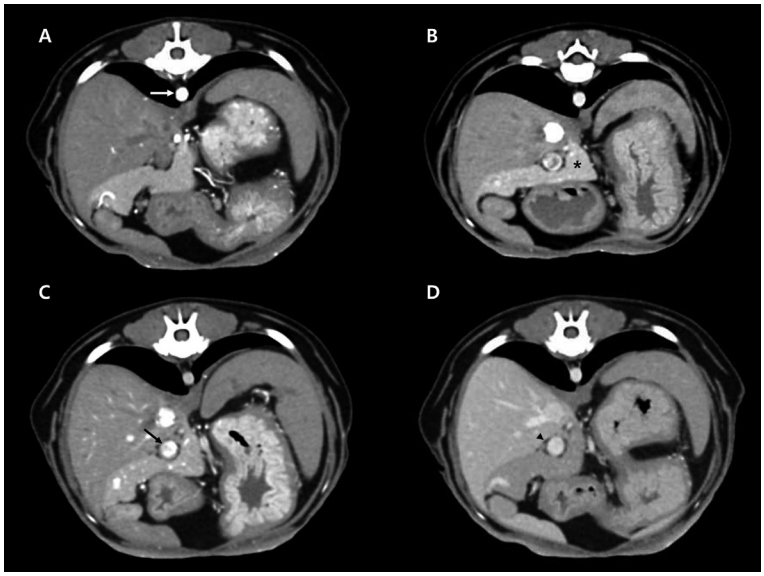


Fig. 1. Transverse CT images with no scan delay (A), 5-sec scan delay (B), 10-sec scan delay (C) and 30-sec scan delay (D) at the level of pancreatic body. (A) Arterial phase shows the maximal aortic contrast enhancement (white arrow). (B) Pancreatic parenchymal phase shows the maximal contrast enhancement of pancreas (asterisk). (C) Portal phase has the heterogeneous maximal contrast enhancement of portal vein (black arrow). (D) Delayed phase shows the homogenous venous contrast enhancement (black arrowhead) and hepatic enhancement.

CT examination, if a fixed scan delay is used for the multiphase CT scan.

Studies in humans have described the usefulness of differentiating pancreatic parenchymal and arterial phases [9, 21, 23]. Human pancreatic adenocarcinomas have a maximum tumor-to-pancreas attenuation difference in the pancreatic parenchymal phase because of hypovascularization of the mass [7, 9], and detection of pancreatic insulinomas is valuable in the arterial phase because of hypervascularization of the mass [16]. In veterinary medicine, the difference between the CT values of the pancreatic mass and normal pancreatic parenchyma was reported to be highest at the arterial phase in a pug with an insulinoma [12]. CT images for pancreatic adenocarcinoma have not been described. However, in a recent contrast-enhanced ultrasonography study of canine pancreatic tumors, canine pancreatic adenocarcinoma was observed as hypovascular lesions [24]. The mean of normal pancreatic attenuation values at pancreatic parenchyma peak was significantly higher than at the aortic peak in this study. This means that optimal pancreatic enhancement can be shown at the pancreatic parenchymal phase, which needs to be distinguished from the arterial phase to evaluate hypovascularized pancreatic lesions in dogs. In a veterinary literature, pancreatic parenchymal peak was 28 sec after the injection and slower than in this study [12]. As aortic enhancement appearance, it was thought that the difference was caused by individual patient or injection-related factors.

In the recent veterinary study, three-phase CT of arterial, venous and delayed phases was used to evaluate the pancreatitis, where they reported that CT findings of pancreatitis were enlarged, homogeneously to heterogeneously attenuating and contrast-enhancing pancreas with ill-defined borders reflecting the beneficial information for the prognostic factors [2]. It is expected that the pancreatic parenchymal phase will make CT findings more accurate for measuring the size of pancreas and identifying contrast enhancing pattern than the other phase in dogs with pancreatitis. However, a further study was required for a clinical application, because pancreatic parenchyma in chronic pancreatitis causing a dilatation or stricture of the pancreatic duct may be insufficiently enhanced in the pancreatic parenchymal phase [14].

Optimal phase images have to provide maximum peripancreatic vascular enhancement, because pancreatic vessels are small. In comparison to the arterial and pancreatic parenchymal phases, the portal phase series reveals information about the pancreatic venous system [21]. The portal phase should be started before the portal vein peak. Contrast enhancement pattern of portal vein in this study is faster than in previous studies [6, 25]. The bolus-tracking technique cannot identify the optimal start time for the second phase. This is a disadvantage of the bolus-tracking technique. Fortunately, although the start of the portal phase cannot always be set at the portal vein peak by the inter-scan reset, the variation does not affect the scan quality [25]. In human, scan delay of the portal vein peak may not be optimal for evaluating venous invasion, because of the frequent presence of heterogeneous enhancement caused by incompletely mixed contrast material returning from organs through the portal

veins, and images obtained with a more delayed time in the portal vein [9]. The scan start of the portal phase can be determined from a relatively wider range than that of the arterial or pancreatic parenchymal phases.

The maximum mean attenuation value of the aorta was obtained at a scan section of 0–5 sec as no scan delay was triggered. This result means that the scan starting with no scan delay after triggering by the bolus-tracking technique is the start of the arterial phase. A scan with no scan delay is similar to the arterial phase of a dual-phase scan in veterinary medicine and is initiated at the aortic enhancement appearance [6]. Because mean attenuation values decrease rapidly in the 5-sec scan section after the aortic peak point, the pure arterial phase allows a short scan duration of about 5 sec. The maximum mean attenuation value of the pancreatic parenchyma shown in this study was at the 5-sec scan delay. Therefore, a scan section with a 5-sec delayed time using a bolus-tracking technique is the pancreatic parenchymal phase. Similar to the aorta, the mean attenuation value of the pancreatic parenchyma changes rapidly before and after the pancreatic parenchymal peak. Therefore, the CT scan duration should be short enough to obtain the optimal pancreatic parenchymal phase. The delayed time for the mean attenuation value peak of the portal vein correlates with the scan section at 10 to 15 sec. After the mean attenuation value peak, the mean attenuation value of the portal vein tended to maintain until the 25-sec scan delay, and the pancreas decreased steadily with no significant differences. It appears that a wide range of scan delays or long scan duration can be used for the portal phase in a multi-phase scan of the pancreas.

The maximum mean attenuation value of the aorta was obtained at the 0–5 sec scan section. The no scan delay involved an interval of 3.8 sec from the aortic enhancement appearance to the aortic peak. The pancreatic parenchymal peak interval from the aortic enhancement appearance was 8.7 sec, and the maximum mean attenuation value of the pancreatic parenchyma was shown at the 5–10 sec scan section. The time to portal vein peak from aortic enhancement appearance was 13.3 sec, and the mean attenuation value peak was represented at the 10–15 sec scan section. The peak time should occur within the scan duration for optimal contrast enhancement of the target organ. In this study, a multi-phase CT scan using a bolus-tracking technique included the peak time of maximal contrast enhancement for the aorta, pancreas and portal vein.

Based on the results of this study, the arterial and pancreatic parenchymal phases have to be performed within 10 sec after contrast injection. To acquire 2 phases, a fast table movement through thicker scan slices, higher pitch and a shorter rotation time are required. Increasing the number of detector rows reduces scanning time and enables scanning of the entire pancreas during the most intense period of pancreatic enhancement [21]. A multi-phase scan to assess detailed arterial and pancreatic parenchymal phases could be performed by using a high performance CT scanner.

This study had some limitations. First, selected dogs had the normal pancreas clinically, but were not confirmed by histopathologic examination. Second, considering the scan duration, fast wash-out of contrast medium for pancreas and anatomic difference of pancreatic lobes, the optimal scan delay for right pancreatic lobe could be different with the results of this study. Third, an inter-scan section of 1–2 sec in CT scan with no scan delay after trigger using bolus-tracking technique was not considered. Finally, a further study with bolus geometry to look at variables, such as flow rate, volume, concentration and injection duration, should be considered.

In conclusion, the bolus-tracking technique is considered as a useful method for multi-phase CT scanning of the canine pancreas. When a multi-phase CT scan of the canine pancreas is triggered at 50 HU of aortic contrast appearance using a bolus-tracking technique, the recommended optimal delay times of the arterial and pancreatic parenchymal phases are no scan delay and 5 sec, respectively.

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