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FULL PAPER

Dual-energy CT iodine maps as an alternative quantitative imaging biomarker to abdominal CT perfusion: determination of appropriate trigger delays for acquisition using bolus tracking

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Objective: Quantitative evaluation of different bolus tracking trigger delays for acquisition of dual energy (DE) CT iodine maps as an alternative to CT perfusion.

Methods: Prior to this retrospective analysis of prospectively acquired data, DECT perfusion sequences were dynamically acquired in 22 patients with pancreatic carcinoma using dual source CT at 80/140 kV_p with tin filtration. After deformable motion-correction, perfusion maps of blood flow (BF) were calculated from 80 kV_p image series of DECT, and iodine maps were calculated for each of the 34 DECT acquisitions per patient. BF and iodine concentrations were measured in healthy pancreatic tissue and carcinoma. To evaluate potential DECT acquisition triggered by bolus tracking, measured iodine concentrations from the 34 DECT acquisitions per patient corresponding to different trigger delays were assessed for correlation to BF and intergroup differences between tissue types depending on acquisition time.

Results: Average BF measured in healthy pancreatic tissue and carcinoma was 87.6 ± 28.4 and 38.6 ± 22.2 ml/100 ml min⁻¹, respectively. Correlation between iodine concentrations and BF was statistically significant for bolus tracking with trigger delay greater than 0 s ($r_{\max} = 0.89$; $p < 0.05$). Differences in iodine concentrations between healthy pancreatic tissue and carcinoma were statistically significant for DECT acquisitions corresponding to trigger delays of 15–21 s ($p < 0.05$).

Conclusion: An acquisition window between 15 and 21 s after exceeding bolus tracking threshold shows promising results for acquisition of DECT iodine maps as an alternative to CT perfusion measurements of BF.

Advances in knowledge: After clinical validation, DECT iodine maps of pancreas acquired using bolus tracking with appropriate trigger delay as determined in this study could offer an alternative quantitative imaging biomarker providing functional information for tumor assessment at reduced patient radiation exposure compared to CT perfusion measurements of BF.

INTRODUCTION

CT perfusion allows for quantitative measurement of parameters governing tissue perfusion, like blood flow (BF), local blood volume, or mean transit time. These can be used for diagnosis as well as treatment response assessment of abdominal tumors.^{1–4} However, the relatively high patient radiation exposure caused by the required dynamic acquisition still inhibits widespread clinical use of abdominal perfusion CT.⁵ While some attempts to reduce radiation exposure have been made, like a reduction of the acquired anatomical volume or the use of low-dose protocols, other limitations for abdominal CT perfusion

imaging persist: patient preparation, acquisition technique and methods for analysis of image data are complex and therefore, error-prone and impede standardization. Furthermore, use of additional contrast agent is straining for the patient and patient breathing motion has to be handled.^{3,5}

Dual energy (DE) CT uses two acquisitions performed at different mean photon energies, allowing for discrimination of different materials. In particular, three-material decomposition can be used to calculate quantitative iodine concentration maps after injection of iodinated contrast

agent, which could potentially improve diagnosis of abdominal tumors.^{6–10}

Recently, DECT iodine maps have been investigated as a dose-reduced alternative to abdominal CT perfusion measurements.^{11–14} This approach relies on the approximation of perfusion parameters by quantitative measurements of contrast agent concentrations with DECT acquisitions performed at strictly defined acquisition times to circumvent the need for a dynamic acquisition. Previous studies have elucidated the correlation between DECT iodine maps and CT perfusion maps of liver in animals and humans, and work by Stiller et al has shown an optimum acquisition time for DECT iodine maps regarding their correlation to CT perfusion measurements of BF in human pancreas.^{11–14}

With careful calibration of acquisition times, abdominal DECT iodine maps might provide a quantitative imaging biomarker tantamount to perfusion parameters such as BF, albeit at reduced patient radiation exposure compared to CT perfusion, thus overcoming important limitations of CT perfusion. DECT acquisitions can be acquired as part of routine contrast-enhanced CT without using additional contrast agent, allowing for automated post-processing and are therefore, easier to apply in clinical routine than CT perfusion. Using bolus tracking for acquisition of DECT iodine maps, results obtained by Gordic et al already show high correlation between DECT iodine maps and hepatic arterial BF.¹⁴ However, considering results of Stiller et al for the pancreas, a detailed evaluation of acquisition delays seems necessary to optimize acquisition of DECT iodine maps by bolus tracking.¹²

Therefore, the purpose of this study was to quantitatively evaluate different acquisition delays for acquisition of DECT iodine concentration maps using bolus tracking by comparison to “conventional” CT perfusion measurements. The main goal of this evaluation was to identify an acquisition delay for bolus triggered acquisitions that results in optimal contrast between healthy tissue and tumor in calculated DECT iodine maps as well as a high correlation to CT perfusion measurements. In consequence, this study serves as an intermediate step to establish DECT iodine concentration maps as a dose-reduced alternative to pancreatic CT perfusion, focusing on the parameter BF.

METHODS AND MATERIALS

In this study, patients were imaged with a combined DECT perfusion protocol from which parameter maps of BF as well as DECT iodine concentration maps were calculated. Maps of BF and iodine concentration were compared for their ability to distinguish healthy tissue and carcinoma, and correlation between BF and iodine concentration was assessed for different acquisition delays.

Patient collective

This study was approved by the local ethics committee and conducted in accordance with the ethical standards of the World Medical Association (Declaration of Helsinki 2013). All patients

gave written informed consent for participation in this study which retrospectively analyzed prospectively acquired data.

Main inclusion criterion for prospective data acquisition was strong clinical suspicion of pancreatic adenocarcinoma as diagnosed in previous clinical examinations (ultrasound, CT, or MRI) with potentially therapeutic curative intent (*i.e.* surgical resection). The following exclusion criteria for CT perfusion acquisitions were applied: previous treatment for pancreatic carcinoma, suspicion of hypervascular tumors, manifested hyperthyroidism (thyroid-stimulating hormone below 0.1 mU l^{-1}), decreased kidney function (estimated glomerular filtration rate below 30 ml min^{-1}), known hypersensitivity to iodinated contrast-agent, inability to reproduce breathing technique, and denial of consent. A total of 22 patients were eligible for prospective data acquisition, and initial image-based diagnosis was histopathologically verified.

All prospectively acquired patients were considered for the retrospective evaluation in this study, and a total of 15 out of 22 patients could be included. Reasons for exclusion were results of histology (neuroendocrine tumor: one; pancreatitis: one), interruption of dynamic acquisition (one), excessive breathing motion during dynamic acquisition (one), and three-phase contrast-enhanced CT and DECT perfusion acquisition not performed during the same examination (three).

Image acquisition

Images were acquired with a dual source CT scanner (Somatom® Definition Flash, Siemens Medical Solutions, Forchheim, Germany).

Patients first received a three-phase contrast-enhanced abdominal CT in hydroCT technique to confirm tumor location: patients were orally administered 1.0–1.5 l of water, intravenously administered 20 mg of hyoscine butylbromide (Buscopan®; Boehringer, Ingelheim, Germany) and imaged using a 30° right anterior oblique patient position.¹⁵ 80 ml of non-ionic iodinated contrast agent (Ultravist 370; Schering, Berlin, Germany) was injected at a flow rate of 5 ml s^{-1} and reference values for automated adjustment of tube potential and current were set at 120 kV_p and 210 mAs (Table 1). Image acquisition was triggered by bolus tracking with a threshold of 120 Hounsfield Unit (HU) in the abdominal aorta at the level of the coeliac trunk.

Thereafter, a dynamic DECT perfusion acquisition was performed with a fixed delay of 13 s after start of contrast-agent injection using 80 ml contrast agent (see above) and 40 ml of saline solution as a chaser bolus, providing simultaneous acquisition of dynamic DECT data and perfusion information (Figure 1). The dynamic acquisition protocol consists of 34 axial DECT acquisitions over the course of 51 s (acquisition time 0.5 s, cycle time 1.5 s) at tube potentials of 80 and 140 kV_p using tin filtration (Table 1). The reference values for tube current modulation were set to 270 mAs (80 kV_p) and 104 mAs (140 kV_p), respectively. Each of the acquisitions covers the same craniocaudal width of 19.2 mm ($32 \times 0.6 \text{ mm}$ collimation without table feed), taking

Table 1. Acquisition protocol for the three-phase contrast-enhanced CT and the dynamic DECT perfusion sequence.

Phase	Tube potential [kV _p]	Tube current (effective) [mAs]	CTDI _{vol} [mGy]	Primary collimation [mm]	Slice thickness (reconstructed/increment) [mm]	Delay [s]	Gantry rotation time [s]	Number of acquisitions
1. native	120 ^a	210 ^b	14.19 ^c	2 × 64 × 0.6	3.0/2.0	4	0.5	helical
Contrast agent: 80 ml (flow 5 ml s ⁻¹); Bolus tracking ROI: abdominal aorta at the level of the coeliac trunk; trigger threshold: 120 HU; cycle time: 1.5 s; monitor delay: 10 s								
2. arterial	120 ^a	210 ^b	14.19 ^c	2 × 64 × 0.6	3.0/2.0	10	0.5	helical
3. venous	120 ^a	210 ^b	14.19 ^c	2 × 64 × 0.6	3.0/2.0	40	0.5	helical
15 min break for contrast agent clearance-patient remaining on the CT table Contrast agent: 80 with 40 ml saline solution chaser (flow 5 ml s ⁻¹)								
4. DECT perfusion	Sn140/80	104/ 270 ^b	437.31 ^c	32 × 0.6	28 × 0.6 (motion correction and evaluation) 3 × 5.0 (segmentation)	13	0.5 (full rotation) 1.5 (cycle time)	34 dynamic

The delay of the arterial and venous phase is given relative to the bolus tracking trigger, while the delay of the DECT perfusion is given relative to the start of contrast-agent injection.

^aReference values CARE kV (Siemens Medical Solutions, Forchheim, Germany).

^bReference values set for CARE Dose 4D™ (Siemens Medical Solutions, Forchheim, Germany).

^cCalculated from reference values set for tube potential and tube current.

Figure 1. Flowchart of the study progress showing an overview of the different data sets prospectively acquired as part of one comprehensive CT examination and their use for the retrospective evaluation.

care to encompass healthy pancreatic tissue and carcinoma in the scan region. Two image data sets were reconstructed per individual acquisition with a soft-tissue body kernel (B30f) and a dual-energy kernel (D30f); three consecutive image slices of 5 mm slice thickness for segmentation and 28 consecutive image

Figure 2. Example of the segmentation and the generated CT perfusion and dual energy CT iodine concentration maps (66-years-old female). The polygonal ROI was used to delineate the evaluation region (*i.e.* the whole pancreas) for the motion-correction, ROI 2 was placed in carcinoma, ROI 3 was placed in healthy tissue. Left: reference image from the dynamic 80 kV_p acquisition used to place the ROIs. Middle: CT-perfusion map of the evaluation region. Note the decreased perfusion in carcinoma (ROI 2) compared to healthy tissue (ROI 3). Right: DECT iodine concentration map of the evaluation region. Note the decreased iodine concentration in carcinoma (ROI 2) compared to healthy tissue (ROI 3). DECT; dual energy CT; ROI, region of interest.

slices of 0.6 mm slice thickness for motion correction (see below and Table 1). See Figure 1 for an overview of data sets and their use for the evaluation.

Patient radiation exposure

Patient radiation exposure was documented in terms of dose-length product (DLP), from which effective patient dose was calculated by multiplication of DLP with the appropriate conversion factor for abdominal CT examinations (0.0153 mSv/mGy·cm).¹⁶ As the dynamic DECT perfusion acquisition was performed using a dual source CT scanner (see above), radiation exposure of DECT acquisitions could additionally be separated into the individual contributions of the acquisitions at 80 and 140 kV_p.

Post-processing

Images were manually segmented by an abdominal radiologist (4 years of experience), selecting one reference image of 5 mm slice thickness from the dynamic perfusion acquisition for motion correction, while using three-phase contrast-enhanced abdominal CT to identify the tumor. Using software developed in-house, regions of interest (ROIs) were placed to delineate the evaluation region containing healthy pancreatic tissue and carcinoma for motion correction, and also inside the aorta, healthy pancreatic tissue and carcinoma, including only the respective tissue type (Figure 2).¹⁷ ROI placement was performed on 80 kV_p images to prevent any bias of the evaluation towards CT perfusion maps or DECT iodine maps.

Deformable motion-correction was performed for the time-resolved 80 kV_p images using software developed in-house, reconstructing a single image of 5 mm slice thickness to match the manually selected reference image.¹⁸ Results were also applied to 140 kV_p images (intrinsically co-registered by dual source acquisition). Acquisitions suffering from excessive patient breathing-motion that could not be successfully corrected were excluded from further evaluation.

CT perfusion maps of BF were calculated from motion-corrected dynamic 80 kV_p image series using the maximum-slope

model. To this end, software developed in-house was used to fit an incomplete lower gamma function to the time-density curve of each pixel in an interval manually selected by a trained radiologist, allowing to calculate BF using the maximum-slope model by Miles.^{1,12}

$$\text{Blood flow} = \frac{\text{Maximum slope of tissue curve}}{\text{Maximum of arterial input}} = \frac{\text{Maximum slope of fitted function}}{\text{Maximum of arterial input}} \quad (1)$$

DECT iodine maps were calculated for each individual acquisition of the dynamic DECT series, using three-material decomposition as implemented in software developed in-house.^{6,12}

Both maps of BF and DECT iodine maps were filtered with a median filter of size 3 × 3 pixels. An example is given in Figure 2.

Evaluation

To investigate potential acquisition delays for acquisition of DECT iodine concentration maps of the pancreas triggered by bolus tracking, iodine concentrations obtained from the 34 DECT acquisitions were evaluated with regard to their acquisition time for correlation to CT perfusion measurements of BF and differences in iodine concentrations between healthy pancreatic tissue and carcinoma. The following parameters were evaluated:

- BF (ml/100 ml min⁻¹)
- Iodine concentration (mg ml⁻¹)

CT-perfusion maps of blood flow

Mean BF was calculated for ROIs placed inside healthy pancreatic tissue and carcinoma. After testing for normality using the Kolmogorov-Smirnov test (Supplemental Material 1, Supplementary material available online.), Student's *t*-test was performed to test for intergroup differences in measured BF between healthy tissue and carcinoma, using a significance level of *p* = 0.05.

Simulating bolus tracking for acquisition of DECT iodine maps

For each of the 34 DECT acquisitions performed for each patient, an individual acquisition delay *t*_{delay} can be calculated

Figure 3. Use of a dynamic DECT series to simulate a DECT acquisition triggered using bolus tracking with different acquisition delays (t_{delay}) in a patient for whom the timing of the bolus trigger (t_{bolus}) is known from prior acquisitions. Evaluation of the acquisition “DECT m ” acquired at $t_{\text{DECT}} \approx t_{\text{bolus}}$ emulates an acquisition with $t_{\text{delay}} = 0$, while the remaining acquisitions can be used to evaluate different settings of t_{delay} . DECT, dual energy CT.

which corresponds to the necessary acquisition delay to reproduce the DECT acquisition when triggering the scan by bolus tracking. In detail, for a DECT acquisition performed at $t_{\text{DECT}} \in [13.0\text{s}, 59.5\text{s}]$, the corresponding acquisition delay t_{delay} can be calculated by subtracting the time when the trigger threshold t_{bolus} was surpassed for this patient (Figure 3), where t_{bolus} can be calculated by subtracting the acquisition delay for arterial phase imaging from the start of the arterial phase acquisition, *i.e.* $t_{\text{bolus}} = t_{\text{arterial}} - 10\text{ s}$. Furthermore, to allow comparison of calculated delays between patients, the delay is

rounded down to the nearest multiple of 1.5 s, which is the temporal spacing of the dynamic acquisition. In summary, for every DECT acquisition of each patient, the delay can be calculated as:

$$t_{\text{delay}} = \left\lfloor \frac{t_{\text{DECT}} - t_{\text{bolus}}}{1.5\text{s}} \right\rfloor \cdot 1.5\text{s} \quad (2)$$

As t_{bolus} differs between patients, extreme values of t_{delay} need not possess a corresponding DECT acquisition for all patients. In consequence, values of t_{delay} where data from at least one patient was missing were excluded from the evaluation (Figure 4). Therefore, the number of evaluated acquisitions, and the number of evaluated t_{delay} , was limited by the longest common subsequence of available DECT acquisitions, n_{eval} , which can be determined from the highest (t_{high}) and lowest (t_{low}) values of t_{bolus} as:

$$n_{\text{eval}} = \left\lfloor \frac{51\text{s} - (t_{\text{high}} - t_{\text{low}})}{1.5\text{s}} \right\rfloor \quad (3)$$

Evaluation of iodine concentration with respect to simulated acquisition delay

Mean iodine concentrations were calculated for ROIs inside healthy tissue and carcinoma (Figure 2) for all n_{eval} iodine maps corresponding to respective t_{delay} . Descriptive statistics of mean iodine concentrations were evaluated at each t_{delay} to estimate separation between tissue types. After testing for normality using the Kolmogorov–Smirnov test (Supplemental Material 1), Student's *t*-test was performed to test for intergroup differences in mean iodine concentration between healthy tissue and carcinoma for all t_{delay} , adjusting the significance level ($p < 0.05$) using the Holm–Bonferroni correction for multiple testing because of the high number of tests. To compare CT perfusion measurements

Figure 4. Use of multiple dynamic DECT series to simulate DECT acquisitions using bolus tracking with different acquisition delays (t_{delay}). The number of evaluated values for t_{delay} , n_{eval} , is limited by the longest common subsequence of available DECT acquisitions, which is determined by the earliest (t_{low}) and latest (t_{high}) bolus trigger timings (cf. equation 3). Only values of t_{delay} where DECT acquisitions exist for all patients can be evaluated. DECT, dual energy CT.

Figure 5. Boxplot of blood flow determined using the maximum-slope model measured inside healthy pancreatic tissue and carcinoma. *difference is statistically significant ($p < 0.05$).

and DECT iodine measurements, correlation between mean BF (as determined from CT perfusion) and mean iodine concentrations (as determined from DECT) was calculated for each t_{delay} using Pearson's formula with the Holm–Bonferroni correction ($p < 0.05$).

Deformable motion-correction could be successfully completed for included patients, and CT perfusion maps of BF and DECT iodine maps could be calculated as described above.

Statistical testing was performed using EXCEL® 2010 (Microsoft Corporation; Redmond, WA) and SAS 9.4 (SAS Institute; Cary, NC).

RESULTS

Average BF measured in ROIs placed in healthy pancreatic tissue and carcinoma was 87.6 ± 28.4 and 38.6 ± 22.2 ml/100 ml min⁻¹, respectively (Figure 5). Differences in measured BF were statistically significant ($p < 0.05$).

Evaluation of iodine concentration with respect to simulated acquisition delay

Average delay between start of contrast agent injection and start of arterial phase acquisition of the three-phase abdominal contrast-enhanced CT was 32.9 ± 3.1 s, resulting in average $t_{\text{bolus}} = 22.9 \pm 3.1$ s. Minimum bolus tracking timing was $t_{\text{low}} = 19.0$ s, and maximum bolus tracking timing was $t_{\text{high}} = 30.7$ s, resulting in a sample size of 27 DECT acquisitions with $t_{\text{delay}} \in [-6 \text{ s}, 33 \text{ s}]$ that could be used for evaluation (equation 3).

Averages and quartiles of iodine concentrations in healthy pancreatic tissue and carcinoma are shown in Figure 6 for different t_{delay} . A high degree of separation in measured iodine concentrations between healthy tissue and carcinoma can be observed for a delay between 15 and 21 s.

Results of Student's t -test for intergroup differences between iodine concentrations in healthy pancreatic tissue and carcinoma

Figure 6. Evaluation of iodine concentration measurements for different acquisition delays (t_{delay}). Top: mean values (continuous lines), upper and lower quartiles (shaded areas) of iodine concentrations measured in healthy pancreatic tissue (blue) and carcinoma (red). Middle: Student's t -test for intergroup differences in measured iodine concentration between healthy pancreatic tissue and carcinoma. Bottom: correlation between iodine concentration and blood flow, and statistical significance of the correlation.

for different t_{delay} are depicted in Figure 6. The resulting p -value is below the corrected significance threshold of $p \approx 0.0056$ for all $t_{\text{delay}} > 9$ s.

Correlation between BF and measured iodine concentrations was low to high, depending on t_{delay} (Figure 6).¹⁹ The maximum correlation between iodine concentrations and BF was high ($r_{\text{max}} = 0.89$) and occurred at $t_{\text{delay}} = 19.5$ s. Overall correlation is high ($r > 0.8$) for all t_{delay} between 16.5 and 21 s. Correlation was statistically significant for all $t_{\text{delay}} > 0$ s according to the corrected significance threshold of $p = 0.01$.

Patient radiation exposure

The average DLP for a conventional CT perfusion acquisition at a tube potential of 80 kV_p was 260 ± 67 mGy·cm, compared to 13 ± 3 mGy·cm for an individual DECT acquisition providing the same anatomical coverage of 19.2 mm, corresponding to an effective dose of 3.90 ± 1.01 and 0.20 ± 0.04 mSv, for 80 kV_p perfusion series and individual DECT acquisitions, respectively.

DISCUSSION

CT perfusion shows promising results for diagnosis and treatment response assessment of abdominal tumors, but its clinical use was long hindered by the relatively high patient radiation exposure caused by the dynamic acquisition. While technical advances have helped to reduce radiation exposure resulting in the development of “low-dose CT-perfusion protocols”, the use of DECT iodine maps as an alternative to CT perfusion measurements offers a comprehensive approach to reduce patient radiation exposure and overcome important limitations of CT perfusion.^{5,11–14} DECT iodine maps could provide a quantitative imaging biomarker for abdominal tumor assessment tantamount to CT perfusion measurements and acquisition of DECT iodine maps by bolus tracking could easily be integrated into current clinical imaging protocols for the abdomen.

In this study, suitable acquisition delays for acquisition of DECT iodine concentration maps using bolus tracking were determined by evaluating iodine maps at different acquisition times for their correlation to CT perfusion measurements of BF and ability to differentiate healthy pancreatic tissue and carcinoma. The results show that bolus tracking can be used to obtain quantitative single-acquisition DECT iodine maps with high correlation to conventional abdominal CT perfusion measurements of BF. The evaluation reveals a window for DECT acquisitions using bolus tracking with an acquisition delay between 15 and 21 s relative to surpassing the threshold of 120 HU measured in the abdominal aorta at the coeliac trunk. An example for a DECT iodine map acquired with a delay of 16.5 s and comparison to iodine maps acquired with different acquisition delays can be seen in Figure 7. Iodine maps acquired within this window not only demonstrate high correlation to BF but also a high degree of separation in iodine concentrations between healthy pancreatic tissue and carcinoma leading to a statistically significant intergroup difference in measured iodine concentrations (Figure 6). The suggested acquisition window is right after currently performed arterial phase acquisitions (Table 1) and in line with earlier results, which suggested an acquisition between arterial and pancreatic

phases.^{12,20} Performing a single DECT acquisition instead of a dynamic 80 kV_p series is associated with a potential reduction in patient radiation exposure of up to 95%.

Even though earlier studies have already shown a high correlation between DECT iodine maps and CT perfusion maps of liver and pancreas, previous studies were limited in their evaluation of potential acquisition times. While Zhang et al used fixed acquisition times for arterial and venous phase iodine maps obtained in an animal model, Thaïss et al relied on manual identification of peak aortic enhancement.^{11,13} Gordic et al investigated bolus tracking for DECT acquisitions of the liver, but the fixed acquisition delay was based on information from prior single-energy acquisitions.¹⁴ Although Stiller et al suggested an optimum acquisition time defined by peak tissue-enhancement, our results demonstrate that with bolus tracking a reliable acquisition of DECT iodine concentration measurements is possible in an acquisition window of about 6 s to assess BF in pancreatic tumors.¹²

Correlation between CT perfusion measurements of BF and DECT iodine concentration measurements in the human pancreas shown here exceeds results from earlier studies.¹² Even though no direct comparison to the hepatic acquisition protocol used by Gordic et al is possible, the investigation of different acquisition delays for DECT acquisitions triggered using bolus tracking might also yield improved correlation between measured iodine concentrations and CT perfusion measurements of the liver.¹⁴

Study limitations

The evaluation in this study was focused on the pancreas as an example for the abdominal organs, as the vascular system of the pancreas is less complex than that of the liver. It is to be expected that the same sort of evaluation presented here is necessary to translate the results to other abdominal organs and additional adjustments may be necessary to account for the dual vascular supply of the liver.

The DECT perfusion protocol used in this study allows for simultaneous acquisition of dynamic DECT data and perfusion information, but technical limitations prohibit any movement of the patient table, limiting the z-coverage to 19.2 mm. The reduced z-coverage provides some limitations to the evaluation, e.g. reduced efficiency of motion-correction, and results in comparatively low effective dose values that would increase with increased scan coverage.

Time for contrast agent washout between three-phase contrast-enhanced CT acquisition and DECT perfusion acquisition was 15 min, which is comparable to other studies using multiple contrast-enhanced acquisitions.^{3,5} This can be considered a reasonable compromise allowing for sufficient washout of contrast agent, while still assuming the individual circulatory function to be sufficiently constant between acquisitions to use information on bolus tracking. Furthermore, comparability of DECT iodine concentration measurements and CT-perfusion measurements should be unaffected as data for both measurements was simultaneously acquired using the DECT perfusion protocol.

Although different CT-perfusion models offer a multitude of parameters, this study was focused on the evaluation of BF calculated with the maximum-slope model. Compared to other models, the maximum-slope model is computationally simple and robust, and BF can be considered the most wide-spread perfusion parameter for evaluation of pancreatic carcinoma which has seen the longest use.^{1,21,22} However, in the future, the methodology presented in this study could be transferred to the evaluation of further perfusion parameters and models.

While the small sample size of only 15 evaluated patients can be considered a limitation of this study, statistically significant

results could be observed despite the small number of subjects. Since the main goal of this study was the quantitative evaluation of acquisition delays for the use of bolus tracking as a means to trigger acquisition of DECT iodine concentration maps, the sample size can be considered sufficient with respect to the results. However, to establish DECT iodine concentration maps as an alternative quantitative imaging biomarker to abdominal CT perfusion, further evaluation is still necessary. A prospective study is necessary to confirm the accuracy of the determined acquisition window for individual patients, as circulatory function and enhancement patterns of tumors are highly individual. Furthermore, future studies will have to evaluate diagnostic image quality and clinical benefit for diagnosis and treatment response assessment of abdominal tumors, as the evaluation of the potential to differentiate pancreatic carcinoma from healthy tissue performed in this study only provides an initial, indirect assessment of the diagnostic value of DECT iodine maps.

CONCLUSION

For the pancreas, a DECT acquisition with an acquisition delay of 15 to 21 s after reaching a threshold of 120 HU in the abdominal aorta at the coeliac trunk provides high correlation to conventional CT perfusion measurements of BF and a statistically significant separation in measured iodine concentrations between healthy pancreatic tissue and carcinoma. After clinical validation, DECT iodine maps acquired using bolus tracking with appropriate acquisition delay could provide a quantitative imaging biomarker for diagnosis and treatment response assessment of abdominal tumors that might provide an alternative to certain parameters of conventional CT-perfusion measurements (e.g. BF) at severely reduced patient-radiation exposure.

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DISCLOSURE

Gregor Pahn joined Philips GmbH Market DACH (Hamburg, Germany) after completion of his work on this study.

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