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Intrarenal fat deposition does not interfere with the measurement of single-kidney perfusion in obese swine using multi-detector computed tomography

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Abstract

Background—Altered vascular structure or function in several diseases may impair renal perfusion. Multi-detector computed tomography (MDCT) is a non-invasive tool to assess single-kidney perfusion and function based on dynamic changes in tissue attenuation during contrast media transit. However, changes in basal tissue attenuation might hamper these assessments, despite background subtraction. Evaluation of iodine concentration using the dual-energy (DECT) MDCT mode allows excluding effects of basal values on dynamic changes in tissue attenuation. We tested whether decreased basal kidney attenuation secondary to intrarenal fat deposition in swine obesity interferes with assessment of renal perfusion using MDCT.

Methods—Domestic pigs were fed a standard (lean) or a high-cholesterol/carbohydrate (obese) diet (n=5 each) for 16 weeks, and both kidneys were then imaged using MDCT/DECT after iodinated contrast injection. DECT images were post-processed to generate iodine and virtual-non-contrast (VNC) datasets, and the MDCT kidney/aorta CT number (following background subtraction) and DECT iodine ratios calculated during the peak vascular phase as surrogates of renal perfusion. Intrarenal fat was subsequently assessed with Oil-Red-O staining.

Results—VNC maps in obese pigs revealed decreased basal cortical attenuation, and histology confirmed increased renal tissue fat deposition. Nevertheless, the kidney/aorta attenuation and iodine ratios remained similar, and unchanged compared to lean pigs.

Conclusions—Despite decreased basal attenuation secondary to renal adiposity, background subtraction allows adequate assessment of kidney perfusion in obese pigs using MDCT. These observations support the feasibility of renal perfusion assessment in obese subjects using MDCT.

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Keywords

Iodine maps; Dual-Energy Computed Tomography; Renal perfusion; Obesity; Intrarenal fat

1. Introduction

Multi-detector computed-tomography (MDCT) is a reliable and reproducible non-invasive tool for estimation of single-kidney hemodynamics and function¹. While para-aminohippurate and iothalamate clearance methods quantify renal blood flow (RBF) and glomerular filtration rate (GFR), respectively, of total renal mass (both kidneys), MDCT can quantify them in the single-kidney, which is useful in patients with unilateral or asymmetrical disease².

Thirty percent of Americans suffer from obesity³ and its implications⁴, including intrarenal fat deposition and kidney disease⁵⁻⁷. Accurate non-invasive assessments of kidney function in obese individuals is, therefore, potentially useful. Quantification of renal function using CT relies on time-attenuation curves (TAC) depicting renal transit of iodinated contrast agents. However, because the CT attenuation of fat is within a range of highly negative values, substantial fat deposition may decrease the average opacity in renal regions of interest (ROI), resulting in underestimation of parenchymal attenuation.

To avoid such interference, these background values are commonly subtracted to offset baseline values and compute the rise in CT numbers secondary to contrast media transit. However, background subtraction has several limitations, including susceptibility to imaging artifacts like motion that increase variability of CT numbers (Hounsfield Units; HU), insufficient representative background data-points to average, and subjective selection of these points. Whether background subtraction successfully accounts for a fall in renal baseline attenuation due to fat deposition is incompletely understood. We hypothesized that renal fat deposition would not interfere with assessment of single-kidney perfusion and function using MDCT.

2. Materials and Methods

The study was approved by the Institutional Animal Care and Use Committee. Domestic pigs were randomized into two groups (n=5 each): lean pigs fed a standard chow, and obese pigs a high-cholesterol/carbohydrate diet⁸.

After 16 weeks of diet, MDCT (128-slice SOMATOM Definition Flash, Siemens, Germany) scanning performed to derive standard TAC for renal function with DECT parameters: detector collimation 64×0.6mm, 0 pitch, A and B tubes at 100kV, 240mAs and 140kV(Sn), 185mAs, respectively, and D30f kernel. An iopamidol bolus (0.5mL/Kg/2sec) was injected into a catheter placed in the right atrium after a short delay. Three adjacent 5-mm slices were collected at each of the 140 successive time-points¹.

DECT images were then acquired to generate iodine and virtual-non-contrast (VNC) datasets from helical scans, using similar acquisition parameters, except for a detector

collimation 32×0.6mm and 1.2 pitch. Helical scans were acquired at the vascular phase during peak contrast enhancement following an additional injection of iopamidol (35cc; 5cc/sec) with a slice thickness of 0.6-mm and 5-mm, iodine/VNC maps and volume quantification, respectively¹.

Total cholesterol was measured by standard procedures⁹, and blood pressure as described¹⁰.

Animals were euthanized with pentobarbital (100mg/kg IV, Vortech)¹¹ and kidneys harvested. Intrarenal lipid deposition was assessed in sections stained with Oil-Red-O (Sigma-Aldrich) and analyzed using ZEN2012 (Carl ZEISS, Germany)¹².

For helical studies, the low- and high-energy images for each scan were averaged to generate mixed images using a 50% linear blend. Low and high-energy DECT image data were post-processed using a Siemens workstation with Syngo.via using ‘Liver-VNC’ application (Siemens Healthcare), with subsequent output including both VNC and iodine maps. For iodine maps, the value for each pixel corresponded to the concentration of iodine (mg/ml). VNC maps were used to measure and compare the baseline CT number between groups.

ROIs were drawn on mixed images (iodine contrast, soft tissue, fat), iodine alone maps (isolated iodine concentrations), and VNC maps (soft tissue, fat) in the cortex, medulla, and aorta at the same tomographic levels as perfusion slices, close to the kidney hilum. Iodine concentrations (mg/ml) and CT numbers (HU) were recorded in each ROI in 3-4 images of the kidney showing clear delineation between the medulla and cortex, and then subsequently averaged. Because iodine maps (and, hence, concentration) cannot be easily derived from perfusion images for generation of iodine TAC, we used the ratio (kidney tissue/aorta) of the CT numbers and iodine concentrations to assess functional changes of either iodine concentrations (ml/mg) or CT numbers (iodine contrast, soft tissue, and fat). Previous studies have used the ratio between the peak-height of the tissue TAC to the area under the input-function (e.g., aorta) TAC to calculate single-kidney perfusion¹³. Comparably, we used the ratio between the cortical or medullary and aorta CT number and iodine concentration as a rough index of renal perfusion. The ratios in helical mixed images are quantified from CT_{ROI} and CT_{Aorta} , the CT number in the kidney and aorta, respectively, CT_{Ratio} represents their ratio.

$$CT_{ROI}/CT_{Aorta}=CT_{Ratio}$$

Similarly in helical iodine maps, I_{ROI} and I_{Aorta} are iodine concentration (ml/mg) in the kidney and the aorta, respectively, and I_{Ratio} represents the iodine ratio between them.

$$I_{ROI}/I_{Aorta}=I_{Ratio}$$

Kidney volumes were evaluate using Analyze™ software (Biomedical Imaging Resource; Mayo Clinic)² and renal function from CT-generated TACs fitted with a Γ -variate model (Matlab, MathWorks, R2013B)^{1, 10}. For background subtraction, tissue attenuation observed

on three images immediately preceding the contrast bolus arrival was averaged and set to zero (Figure 1). Then renal function was assessed from TAC using the rise in CT numbers (HU) from the zeroed baseline^{2, 14}.

Mean values and standard deviations express results, and two-tailed unpaired t-tests (JMP-10.0, SAS) compare between lean and obese pigs. $P = 0.05$ was considered statistically significant.

3. Results

Sixteen weeks after initiation of diet, body weight, mean blood pressure, and lipid levels were higher in obese compared to lean pigs (Table 1), as were CT_{Ratio} and I_{Ratio} , consistent with cortical hyper-filtration that characterizes obesity. There was no difference between cortical or medullary I_{Ratio} and CT_{Ratio} within either group ($p > 0.05$, Figure 3A). In VNC maps, we observed significantly lower cortical CT numbers in the obese group (Figure 3B), but not in the medulla.

Single-kidney volumes were increased in obese pigs, whereas their perfusion measured from TAC did not differ between the groups. Both GFR and RBF were higher in obese pigs, suggesting hyper-filtration (Table 1).

Finally, Oil-Red-O values confirmed higher fat deposition in obese pig-kidneys (Figure 2C).

In summary, we found that changes in CT_{Ratio} (after background subtraction) and I_{Ratio} (excluding basal attenuation) were comparable in lean and obese swine, suggesting that intrarenal adiposity does not interfere with quantification of single-kidney perfusion and function using MDCT-derived TAC. Therefore, background subtraction used for CT renal function assessment is adequate for eliminating the potentially confounding attenuation of fat. These observations may be relevant for the use of TAC for MDCT perfusion assessments in other organs as well.

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Figure 1.

TAC of aorta showing the background data-points collected, averaged, and zeroed in order to assess a rise in CT number over baseline. Raw data: black; Γ -variate model fitting: red.

Figure 2.

A: Iodine map depicting ROI in the aorta (white), cortex (yellow), and medulla (blue). B: Oil-Red-O staining indicating deposited fat (red) in obese pig kidneys.

Figure 3.

A. CT number (HU, light dotted) and iodine (mg/ml, dark dotted) kidney/aorta ratios were similarly elevated in the renal cortex and medulla of obese pigs. B. CT number (HU) values in VNC show lower cortical attenuation in obese.

Table 1

Systemic characteristics and renal function at 16 weeks.

Parameter	Lean	Obese
N(kidneys)	5(10)	5(10)
Body weight(Kg)	72.8±10.8	92.1 ±2.2 *
Mean blood pressure(mmHg)	100.4±10.7	126.7±7.8 *
Total cholesterol(mg/dl)	83.7±6.8	434.6±79.1 *
Total Renal Volume(cc)	137.8±18.6	222.2±20.8 *
Cortical Volume(cc)	108.1±17.9	181.2±22.9 *
Medullary Volume(cc)	29.6±2.5	41.0±4.2 *
Cortical Perfusion(ml/min/cc)	4.0±0.7	4.1 ±0.5
Medullary Perfusion(ml/min/cc)	2.9±0.9	2.6±1.5
RBF(ml/min)	495.2±50.3	746.9±65.3 *
MDCT-GFR(ml/min)	75.8±11.1	144.5±17.0 *

* p 0.05 vs. Lean.

RBF: renal blood flow, GFR: glomerular filtration rate, MDCT: Multi-detector computed-tomography