

# Evaluation of skeletal muscle perfusion in a canine hind limb ischemia model using CT perfusion imaging

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## PURPOSE

We aimed to evaluate skeletal muscle perfusion in a canine hind limb ischemia model using computed tomography (CT) perfusion imaging.

## METHODS

Twelve beagles underwent embolization at the branch of the left deep femoral artery. The right hind limbs were used as controls. CT perfusion imaging was performed immediately after embolization. The perfusion parameters of the regions of interest (ROI), including blood volume (BV), blood flow (BF), mean transit time (MTT) and permeability (PMB), were obtained in both the lateral and posterior hind limb muscle groups.

## RESULTS

After embolization, the BV, BF, and PMB values in the lateral muscles of the left hind limbs were significantly lower than those in the right hind limbs ( $P > 0.05$ ), and the MTT was significantly prolonged ( $P > 0.05$ ). The values for BV, BF, MTT, and PMB in the posterior muscles of the left hind limbs were not significantly different from those in the right hind limbs ( $P > 0.05$ ). The values for BV, BF, and PMB in the lateral muscles of the left hind limbs were significantly lower than those in the posterior muscles of the left hind limbs ( $P > 0.05$ ).

## CONCLUSION

CT perfusion imaging could be used to evaluate skeletal muscle perfusion in a canine model, which may have clinical relevance in lower limb ischemia and vascular reconstruction.

Lower extremity arterial ischemic disease is a common peripheral vascular disease usually caused by arterial stenosis or occlusion, resulting in reduced arterial blood flow, decreased skeletal muscle perfusion and nerve dystrophies in the lower extremities. The clinical manifestations include pain, intermittent claudication, ulcers and, in severe cases, gangrene (1). Prior studies have shown that the ulcers do not heal, and the rate of amputation can be as high as 10% to 18% even after lower extremity revascularization with patent bypass vascular graft or endovascular angioplasty (2). However, there is no guarantee of vascular reperfusion in the ischemic areas of the affected limbs or healing of the ulcers even after a successful revascularization procedure (3, 4). Therefore, to reconstruct an effective blood supply for the ischemic regions of the lower limbs, it is necessary to conduct an objective and accurate evaluation of perfusion in the ischemic region. Commonly used clinical examination methods include Doppler ultrasound, computed tomographic angiography (CTA), magnetic resonance angiography (MRA) and digital subtraction angiography (DSA), as well as measurement of the ankle brachial index (ABI) and transcutaneous oxygen pressure (TcPO<sub>2</sub>). However, none of these methods can quantitatively and accurately evaluate the local perfusion of the skeletal muscles in the lower extremities (4–6).

With the recent development of CT perfusion imaging technology, microcirculation perfusion can be calculated and analyzed by monitoring the changes in contrast accumulation in tissues and organs after injection of intravenous contrast agent (7, 8). CT perfusion imaging is performed using an intravenous iodine-containing contrast agent to obtain a time-density curve (TDC) for each pixel in the layers by a rapid dynamic scan of the selected

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layers. Various perfusion parameters for the tissue regions of interest (ROIs) are calculated using a mathematical model, including blood volume (BV), blood flow (BF), mean transit time (MTT) and permeability (PMB). These perfusion parameters reflect the local perfusion of the tissues (1, 9–11).

CT perfusion imaging technology has been used to diagnose and treat cerebral ischemic diseases and tumors throughout the body, including those in the lung, liver, brain, head, neck, and stomach (12–17). However, there is limited information on applying this technique to evaluate skeletal muscle perfusion in the lower extremities.

Animal models of hind limb ischemia can simulate clinical peripheral arterial ischemic disease in humans and have been used in experimental research to diagnose and treat lower limb arterial ischemic disease. Most of the animal ischemic models have been produced by ligating or excising the full length of the femoral artery and its branch vessels on one of the hind limbs, causing ischemia of the targeted limb (18). This method results in trauma and damage to the limb. In addition, because it creates ischemia in the entire limb, this method does not permit selective ischemia and perfusion analysis in multiple regions of the limb. Another method for generating ischemia is high-fat diet feeding (18, 19). The pathogenesis of the diet-generated model is similar to that of humans with lower extremity arteriosclerosis, but it requires a long preparation time. In addition, neither of these methods allow the researcher to control the extent and scope of the ischemia and skeletal muscle perfusion (18–20). Therefore, new methods are needed to induce selective ischemia in animal limb models.

Here, we established a canine hind limb ischemia model by injecting a polyvinyl alcohol (PVA) particle embolic agent selectively into the lateral branch of the left deep

femoral artery. We then used CT perfusion imaging to evaluate the skeletal muscle perfusion in the lower limbs.

## Methods

### Animal preparation

Our study was approved by the local ethics committee for animal research, i.e., the Animal Care and Research Use Committee for Nanjing First Hospital, the Medical University. Twelve beagles (6 males and 6 females) weighing 7–10 kg were included in this study. For each beagle, the lateral branch of the left deep femoral artery was embolized, and the right hind limb was used as the control.

The beagles were anesthetized with ketamine (10 mg/kg, intramuscularly) and then anesthetized with 3% pentobarbital sodium (20–30 mg/kg, intravenously) in the forelimbs. Each beagle was immobilized on the catheter bed of an Artis angiography system (Siemens). The right inguinal region was prepared and disinfected, and a 4F vascular sheath (Terumo) and 4F pigtail catheter (Cordis) were inserted into the right femoral artery. The catheter tip was advanced into the inferior segment of the abdominal aorta, and the contrast agent (iodine Budha alcohol, 320 mg I/mL, Jiangsu Hengrui Medicine Co., Ltd.) was injected. The pigtail catheter was then replaced with a 4F H1 catheter (Cordis) by a guidewire (Terumo). The tip of the 4F H1 catheter was advanced into the left common femoral artery, where a Progreat microcatheter (Terumo) was inserted coaxially. Under the guidance of a “road map”, the microcatheter tip was moved into its final position in the lateral branch of the left deep femoral artery. The PVA (30 mg, 350–560  $\mu$ m) particle embolic agent (Hangzhou Alicon Pharm Sci & Ten Co., Ltd.) was injected through the microcatheter. The microcatheter was then withdrawn and replaced with a 4F pig tail catheter. The contrast agent was injected again for review, and the catheter and vascular sheath were removed. The following data collection protocol was used during angiography: 1) the limbs were immobilized to reduce movement artifacts before the angiography before and after embolization; 2) the head of the 4F pigtail catheter was placed 2 cm above the distal bifurcation of the abdominal aorta; 3) the contrast agent (15 mL) was injected at 4 mL/s; 4) imaging was acquired before the venous phase at 3 frames/s; 5) the target distance and the ar-

tery angiography segment were held constant (21).

### CT perfusion imaging protocol

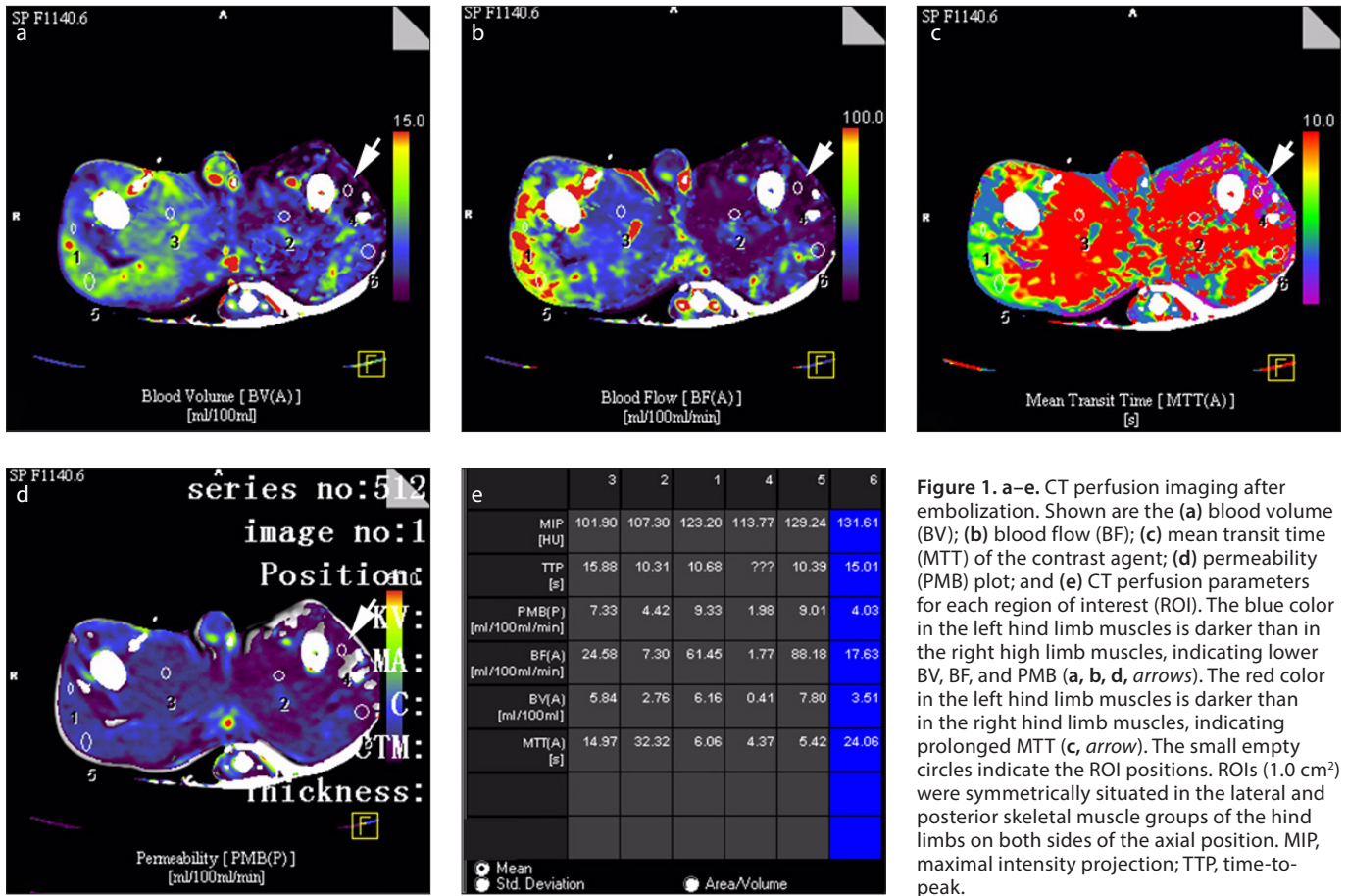
A Somatom Definition Flash second-generation dual-source CT (Siemens) was used for skeletal muscle CT perfusion imaging of the beagle hind limbs immediately after embolization. Each anesthetized beagle was secured on the CT examination bed in the supine scanning position with its limbs immobilized, and the hind limbs were positioned as straight as possible. The forelimb vein was used as an injection site and was connected to a CT-specific high-pressure syringe (Medrad). Each beagle was first positioned and scanned with a tube voltage of 100 kV and a tube current of 35 mA. Then, CT perfusion imaging was performed from the pelvis to the hind limbs. The CT “toggling table” was started after 15 s, and the contrast agent was injected through the high-pressure syringe at an injection rate of 4 mL/s. The scanning parameters were as follows: voltage, 80 kV; current, 150 mA; 4D range, 216 mm; scan time, 59.74 s; time series, 0–32 s for the first scan phase with an interval of 2 s for a total of 16 scans, then 32–59.74 s for the second scan phase with an interval 7 s for a total of 4 scans. The raw data were reconstructed into 10 mm thickness and 10 mm spacing for the perfusion analysis (22, 23).

### CT perfusion imaging reconstruction and analysis

The CT perfusion imaging data were analyzed using the Customized Tumor function of the VPCT Body software in the Siemens workstation. After correction for motion artifacts, the threshold was defined, and the target artery was selected according to a standard procedure as follows: 1) the definition threshold was -50 to 150 HU, which removed the effects of bone and air; 2) the iliac artery was used as the input artery, branch vessels were avoided, and the vessel wall was not exceeded when the target vessel was selected. The TDC of the target vessel was obtained and the deconvolution formula,  $Q(t) = FCa(t) * R(t) = Ca(t) * FR(t)$ , was used to calculate the following perfusion parameters: BV, BF, MTT and PMB. In the formula,  $Q(t)$  is the TDC of the tissue and organ,  $F$  is the blood flow,  $Ca(t)$  is the TDC of the artery,  $*$  is the convolution operator, and  $R(t)$  is the impulse residue function (1, 11). Image reconstruction and color coding were performed on the obtained param-

#### Main points

- We established a canine hind limb ischemia model to study skeletal muscle perfusion in a limb.
- This canine ischemia model could be used to achieve limb ischemia at different sites and to control the extent of embolization by selectively embolizing the targeted vessels.
- CT perfusion imaging was useful to capture the perfusion status of the multiple skeletal muscle groups with anatomical details.



**Figure 1.** a–e. CT perfusion imaging after embolization. Shown are the (a) blood volume (BV); (b) blood flow (BF); (c) mean transit time (MTT) of the contrast agent; (d) permeability (PMB) plot; and (e) CT perfusion parameters for each region of interest (ROI). The blue color in the left hind limb muscles is darker than in the right high limb muscles, indicating lower BV, BF, and PMB (a, b, d, arrows). The red color in the left hind limb muscles is darker than in the right hind limb muscles, indicating prolonged MTT (c, arrow). The small empty circles indicate the ROI positions. ROIs (1.0 cm<sup>2</sup>) were symmetrically situated in the lateral and posterior skeletal muscle groups of the hind limbs on both sides of the axial position. MIP, maximal intensity projection; TTP, time-to-peak.

**Table 1.** Perfusion parameters for the lateral skeletal muscles in the hind limb model after embolization

	BV (mL/100 mL)	BF (mL/100 mL/min)	MTT (seconds)	PMB (mL/100 mL/min)
Lateral muscle of the left hind limb	0.790 (0.030–2.950)	4.830 (0.050–15.130)	24.900 (5.390–38.980)	2.380 (0.610–6.250)
Lateral muscle of the right hind limb	2.930 (1.550–7.360)	12.830 (3.500–55.920)	9.470 (2.590–32.320)	4.860 (2.800–17.630)
<i>P</i> <sup>a</sup>	0.002	0.008	0.005	0.005

Data are presented as median (min–max).

BV, blood volume; BF, blood flow; MTT, mean transit time; PMB, permeability.

<sup>a</sup>*P* ascertained from Wilcoxon signed-rank test comparing left hind limbs to the right hind limbs.

eters using the VPCT Body software. The chroma, saturation, and brightness values of each pixel in each map were converted into red, green, and blue. In the BV, BF and PMB maps, the red region indicates high perfusion and the blue region indicates low perfusion. In the MTT map, the red region indicates low perfusion and the pink region indicates high perfusion. The ROIs, each with an area of 1.0 cm<sup>2</sup>, were placed symmetrically on the lateral and posterior skeletal muscle groups of the hind limbs on both sides of the axial position. Large vessels, calcifications and bones were avoided. BV, BF MTT, and PMB were measured for the

ROIs in the lateral and posterior thigh muscles. (Fig. 1).

### Statistical analysis

Statistical analysis was performed using SPSS 23.0 software. The perfusion parameters were compared between the control hind limb and embolized hind limb within each muscle group. These parameters were also compared between the lateral and posterior muscles. For assessing the appropriate statistical methods, the Shapira-Wilk test was used to assess normality of our data. The Shapira-Wilk test was statistically significant (*P* < 0.05) for our measurements,

showing evidence of non-normality. Therefore, median (minimum–maximum) were calculated and Wilcoxon signed-rank test was used to test the group difference. All reported *P* values were two-sided, and *P* < 0.05 was considered statistically significant.

## Results

Hind limb ischemia models involving the left hind limb muscle were established in all 12 beagles (Fig. 2). After embolization, the BV, BF, and PMB values in the lateral muscle of the left hind limbs were significantly lower than those in the right hind limbs (*P* < 0.05), and MTT was significantly prolonged

**Table 2.** Perfusion parameters for the posterior skeletal muscles in the hind limb model after embolization

	BV (mL/100 mL)	BF (mL/100 mL/min)	MTT (seconds)	PMB (mL/100 mL/min)
Posterior muscle of the left hind limb	4.585 (2.100–7.990)	17.745 (5.100–87.220)	10.230 (1.280–33.380)	4.500 (0.000–9.330)
Posterior muscle of the right hind limb	4.000 (1.750–7.660)	14.185 (4.330–97.950)	18.090 (5.800–33.650)	3.580 (0.000–9.840)
<i>P</i> <sup>a</sup>	0.346	0.136	0.071	0.476

Data are presented as median (min–max).

BV, blood volume; BF, blood flow; MTT, mean transit time; PMB, permeability.

<sup>a</sup>*P* ascertained from Wilcoxon signed-rank test comparing left hind limbs to the right hind limbs.

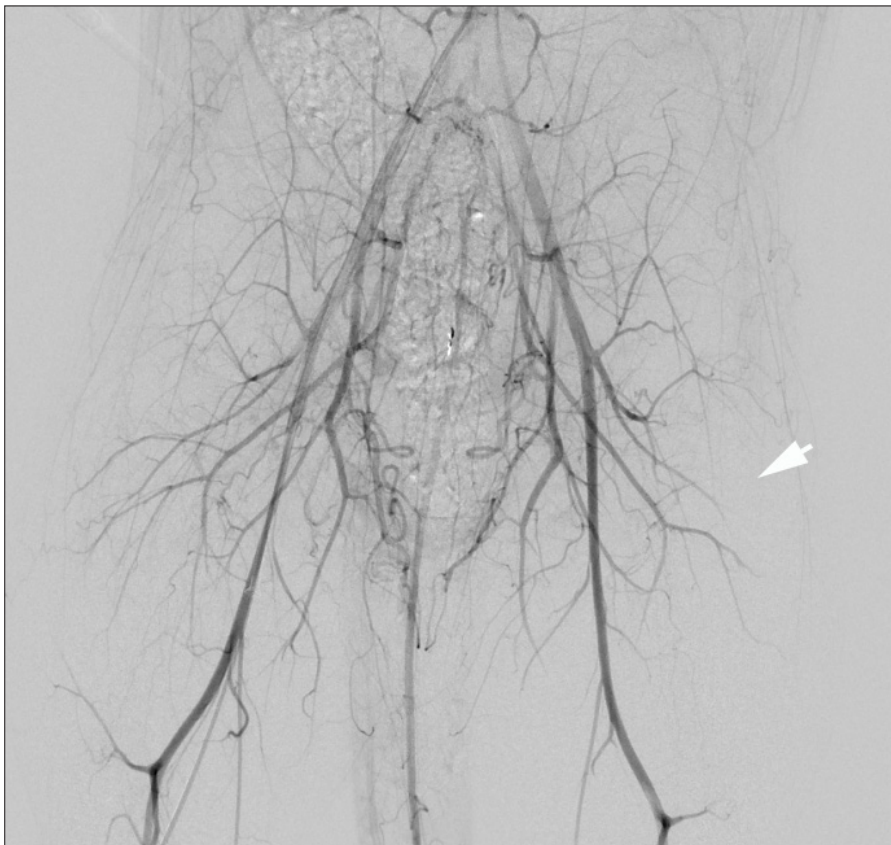
**Table 3.** Perfusion parameters for skeletal muscles in the left hind limb model after embolization

	BV (mL/100 mL)	BF (mL/100 mL/min)	MTT (seconds)	PMB (mL/100 mL/min)
Lateral muscle of the left hind limb	0.790 (0.030–2.950)	4.830 (0.050–15.130)	24.900 (5.390–38.980)	2.380 (0.610–6.250)
Posterior muscle of the left hind limb	4.585 (2.100–7.990)	17.745 (5.100–87.220)	10.230 (1.280–33.380)	4.500 (0.000–9.330)
<i>P</i> <sup>a</sup>	0.002	0.003	0.041	0.034

Data are presented as median (min–max).

BV, blood volume; BF, blood flow; MTT, mean transit time; PMB, permeability.

<sup>a</sup>*P* ascertained from Wilcoxon signed-rank test comparing the lateral muscle to the posterior muscle in the left hind limb.



**Figure 2.** Angiography of a hind limb model after embolization. The lateral vascular network of the left hind limb was significantly reduced and sparser (arrow) compared with that of the right hind limb.

( $P < 0.05$ ) (Table 1). The values for BV, BF, MTT, and PMB in the posterior muscles of the left hind limbs were not significantly different from those in the right hind limbs

( $P > 0.05$ ) (Table 2). However, the values for BV, BF, and PMB in the lateral muscle of the left hind limbs were significantly lower than those in the posterior muscles of the

left hind limbs ( $P < 0.05$ ), and MTT was significantly prolonged ( $P < 0.05$ ) (Table 3). The values for BV, BF, MTT, and PMB in the lateral muscle of the nonembolized right hind limbs were not significantly different from those in the posterior muscle of the right hind limbs ( $P > 0.05$ ) (Table 4).

## Discussion

We established a canine hind limb ischemia model for skeletal muscle perfusion analysis by selectively injecting embolic material into the lateral branch of the left deep femoral artery. Unlike the other animal models where the entire femoral artery is ligated or high-fat diet is used to create lower extremity arteriosclerosis, our method is minimally invasive, relatively easy and fast to perform, and readily reproducible. In addition, unlike other models, our method can establish focused ischemia in different regions of the limb by selectively embolizing branches of the limb vessels. Our study was unique in that we combined CT perfusion imaging with percutaneous selective embolization of the limb vessel to evaluate skeletal muscle perfusion. Our study approach enabled us to quantify the perfusion status of the skeletal muscles with cross-sectional anatomical details using CT scanning. Furthermore, we took advantage of the linear relationship between contrast concentration and CT attenuation, which facilitated accurate quantification (9–11). On the other hand, there was a nonlinear



**Table 4.** Perfusion parameters for skeletal muscles in the right hind limb model after embolization

	BV (mL/100 mL)	BF (mL/100 mL/min)	MTT (seconds)	PMB (mL/100 mL/min)
Lateral muscle of the right hind limb	2.930 (1.550–7.360)	12.830 (3.500–55.920)	9.470 (2.590–32.320)	4.860 (2.800–17.630)
Posterior muscle of the right hind limb	4.000 (1.750–7.660)	14.185 (4.330–97.950)	18.090 (5.800–33.650)	3.580 (0.000–9.840)
<i>P</i> <sup>a</sup>	0.099	0.530	0.308	0.433

Data are presented as median (min–max).

BV, blood volume; BF, blood flow; MTT, mean transit time; PMB, permeability.

<sup>a</sup>*P* ascertained from Wilcoxon signed-rank test comparing the lateral muscle to the posterior muscle in the right hind limb.

relationship between the signal intensity and concentration of paramagnetic contrast medium in magnetic resonance perfusion imaging. The magnetic resonance perfusion method may be limited by its poor reproducibility caused by differences in pulse sequences and the magnetic resonance hardware, as well as its greater susceptibility to artifacts caused by metal or air-bone interfaces (7).

Our study is consistent with the literature indicating that animal hind limb ischemia models established by percutaneous interventional embolization have lower mortality and cause less inflammatory response than those established using surgical approaches (10). We used PVA particles as the embolic material because the particle size was uniform, the dosage adjustment was simple, and the cost was reasonable. Prior studies have used various types of embolic materials, such as autologous thrombus, micro-coils, and N-butyl cyanoacrylate. However, the efficacy of each embolic material remains unclear and there is no standard recommendation for selection of embolization material for creating a limb ischemia model (18–20). Although this work establishes that PVA particles can induce limb ischemia, future work is needed to directly compare the efficacy of each model.

At present, clinical evaluation of the severity of lower extremity arterial disease and treatment response are accomplished mainly by clinical examination (symptom improvement, the arterial pulse of the lower extremity, and flat walking distance), ABI, TcP02, Doppler ultrasound, CTA, MRA or DSA. However, these approaches have limitations (1, 11). For example, clinical examination might be subjective. The measurement of ABI is specific, but the sensitivity is low. The measurement of TcP02 can be influenced by many factors, including blood oxygen concentration, skin thickness at the measurement site, edema, and

inflammation. Doppler ultrasound, CTA, MRA and DSA can evaluate of the morphology of the lower extremity arterial lumen, which may not reflect the changes in perfusion between skeletal muscles (5, 6, 24). New methods for evaluating limb perfusion are needed. Our animal model of hind limb ischemia, which is presented in this study, may be useful for testing different methods in perfusion and vascular reconstruction research.

The perfusion analysis of our canine hind limb ischemia model confirmed that it causes selective embolization of the limb skeletal muscles. The BV, BF, and PMB values in the lateral muscles of the left hind limbs were significantly lower than those in the nonembolized contralateral side, and MTT was significantly prolonged. MTT was defined as the average time taken by blood elements to traverse the vasculature, from the arterial to venous ends, as presented in the formula  $MTT = BV/BF$ . It was used as a surrogate marker for perfusion pressure. In our study, MTT was significantly prolonged because the blood volume was decreased and the perfusion pressure was increased from the arterial end to the venous end after the artery was embolized. These results indicate that embolism decreases the skeletal muscle perfusion of the hind limb lateral muscles. However, the perfusion parameter values for the posterior muscles in the embolized left side were not significantly lower than those for the posterior muscles of the nonembolized right side. Our selective embolization model targeted the lateral branch of the left deep femoral artery, which mainly perfused the lateral skeletal muscles of the left hind limb. Thus, it was expected that the lateral muscles, but not the posterior muscles, would show hypoperfusion.

We have shown that our interventional embolization method could be used to achieve ischemia at different sites by direct-

ing the catheter to different branch vessels. Moreover, this method could be used to control the extent of embolization by embolizing multiple vessels during the same session. With this approach, CT perfusion imaging could be used to quantitatively evaluate the perfusion status of various limb skeletal muscle groups.

There are several limitations in this study. First, our study was limited by a small sample size, which generated a limited number of perfusion data sets. Second, this animal model preparation needed skillful work from an interventional radiologist and an angiographer or a researcher with similar expertise, which may limit its general application in animal research on limb ischemia. Third, CT perfusion imaging was obtained after percutaneous angiography and embolization. The operator-dependent nature of the angiographic procedure may have caused some variation. For example, the positioning of the angiographic catheter and the exact amount of embolic material used during the angiographic procedure might be slightly different among the angiographers. However, we followed a standardized protocol for angiography and data collection to minimize these potential sources of variation. Lastly, the animal hind limb ischemia model represented acute ischemia, which may be similar to some forms of limb ischemia in humans. However, chronic rather than acute ischemia is more commonly seen in clinical practice. Therefore, the information generated from our animal model may not be readily applicable to clinical scenarios. Future studies should be done in a larger sample size with a revised animal model relevant to chronic ischemia. Despite the limitations, there are strengths in this study. We established a promising animal model to selectively study skeletal muscle perfusion in a limb. Also, we used CT perfusion imaging to capture the perfusion status of the multiple

skeletal muscle groups. Our combination of percutaneous angiography and CT scanning enabled both precise embolization with catheter-directed angiography and detailed anatomical confirmation with CT perfusion imaging.

In conclusion, we have shown that CT perfusion imaging can be used to evaluate skeletal muscle perfusion in a canine hind limb ischemia model. Compared with other models, this method caused less trauma, was relatively easy to perform, and had higher reproducibility. Our method may provide a tool to study lower limb revascularization in ischemia and perfusion research.

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#### Conflict of interest disclosure

The authors declared no conflicts of interest.

#### References

1. Cooper KJ, Peña C, Benenati J. Determining end points for critical limb ischemia interventions. *Tech Vasc Interv Radiol* 2016; 19:104–112. [\[CrossRef\]](#)
2. Varela C, Acín F, de Haro J, et al. The role of foot collateral vessels on ulcer healing and limb salvage after successful endovascular and surgical distal procedures according to an angiosome model. *Vasc Endovascular Surg* 2010; 44:654–660. [\[CrossRef\]](#)
3. Iida O, Nanto S, Uematsu M, et al. Importance of the angiosome concept for endovascular therapy in patients with critical limb ischemia. *Catheter Cardiovasc Interv* 2010; 75:830–836. [\[CrossRef\]](#)
4. N, Mukherjee. Critical and acute limb ischemia: an overview. *Angiology* 2014; 65:137–146. [\[CrossRef\]](#)
5. Su H, Lou W, Gu J. Clinical values of hemodynamics assessment by parametric color coding of digital subtraction angiography before and after endovascular therapy for critical limb ischaemia. *Zhonghua Yi Xue Za Zhi* 2015; 95:3036–3040.
6. Göllitz P, Struffert T, Lücking H, et al. Parametric color coding of digital subtraction angiography in the evaluation of carotid cavernous fistulas. *Clin Neuroradiol* 2013; 23:113–120. [\[CrossRef\]](#)
7. Razeq AA, Tawfik AM, Elsorogy LG, Soliman NY. Perfusion CT of head and neck cancer. *Eur J Radiol* 2014; 83:537–544. [\[CrossRef\]](#)
8. Tawfik AM, Razeq AA, Elhawary G, Batouty NM. Effect of increasing the sampling interval to 2 seconds on the radiation dose and accuracy of CT perfusion of the head and neck. *J Comput Assist Tomogr* 2014; 38:469–473. [\[CrossRef\]](#)
9. Benitez E, Sumpio BJ, Chin J, Sumpio BE. Contemporary assessment of foot perfusion in patients with critical limb ischemia. *Semin Vasc Surg* 2014; 27:3–15. [\[CrossRef\]](#)
10. Zhuang ZW, Shi J, Rhodes JM, Tsapakos MJ, Simons M. Challenging the surgical rodent hindlimb ischemia model with the miniinterventional technique. *J Vasc Interv Radiol* 2011; 22:1437–1446. [\[CrossRef\]](#)
11. Alexandrescu V, Hubermont G. The challenging topic of diabetic foot revascularization: does the angiosome-guided angioplasty may improve outcome. *J Cardiovasc Surg (Torino)* 2012; 53:3–12.
12. Afat S, Brockmann C, Nikoubashman O, et al. Diagnostic accuracy of simulated low-dose perfusion CT to detect cerebral perfusion impairment after aneurysmal subarachnoid hemorrhage: a retrospective analysis. *Radiology* 2018; 287:643–650. [\[CrossRef\]](#)
13. Wang Y, Hobbs BP, Ng CS. CT perfusion characteristics identify metastatic sites in liver. *Biomed Res Int* 2015; 2015:120749. [\[CrossRef\]](#)
14. Chen X, Xu Y, Duan J, Li C, Sun H, Wang W. Correlation of iodine uptake and perfusion parameters between dual-energy CT imaging and first-pass dual-input perfusion CT in lung cancer. *Medicine (Baltimore)* 2017; 96:e7479. [\[CrossRef\]](#)
15. Tawfik AM, Nour-Eldin NE, Naguib NN, et al. CT perfusion measurements of head and neck carcinoma from single section with largest tumor dimensions or average of multiple sections: agreement between the two methods and effect on intra- and inter-observer agreement. *Eur J Radiol* 2012; 81:2692–2696. [\[CrossRef\]](#)
16. Tawfik AM, Razeq AA, Elsorogy LG, et al. Perfusion CT of head and neck cancer: effect of arterial input selection. *AJR Am J Roentgenol* 2011; 196:1374–1380. [\[CrossRef\]](#)
17. Sun Z, Cheng X, Ge Y, et al. An application study of low-dose computed tomography perfusion imaging for evaluation of the efficacy of neo-adjuvant chemotherapy for advanced gastric adenocarcinoma. *Gastric Cancer* 2018; 21:413–420. [\[CrossRef\]](#)
18. Del Giudice C, Ifergan G, Goudot G, et al. Evaluation of a new model of hind limb ischemia in rabbit. *J Vasc Surg* 2018; 68:849–857. [\[CrossRef\]](#)
19. Liddell RP, Patel TH, Weiss CR, et al. Endovascular model of rabbit hindlimb ischemia: a platform to evaluate therapeutic angiogenesis. *J Vasc Interv Radiol* 2005; 16:991–998. [\[CrossRef\]](#)
20. Shin CI, Kim HC, Song YS, et al. Rat model of hindlimb ischemia induced via embolization with polyvinyl alcohol and N-butyl cyanoacrylate. *Korean J Radiol* 2013; 14:923–930. [\[CrossRef\]](#)
21. Lou WS, Su HB, Huang KY, et al. Evaluation of distal hemodynamic changes of lower extremity after endovascular treatment: correlation between measurements of color-coded quantitative digital subtraction angiography and ankle-brachial index. *J Vasc Interv Radiol* 2016; 27:852–858. [\[CrossRef\]](#)
22. Iezzi R1, Santoro M, Dattesi R, et al. Foot CT perfusion in patients with peripheral arterial occlusive disease (PAOD): a feasibility study. *Eur J Radiol* 2013; 82:e455–464. [\[CrossRef\]](#)
23. Hur S, Jae HJ, Jang Y, et al. Quantitative assessment of foot blood flow by using dynamic volume perfusion CT technique: a feasibility study. *Radiology* 2016; 279:195–206. [\[CrossRef\]](#)
24. Barfett J, Velauthapillai N, Kloeters C, Mikulis DJ, Jaskolka JD. An en bloc approach to CT perfusion for the evaluation of limb ischemia. *Int J Cardiovasc Imaging* 2012; 28:2073–2083. [\[CrossRef\]](#)