Compromised perfusion in femoral head of normal Wistar rats: distinctive perfusion MRI evidence of contrast wash-out delay

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Introduction: Clinical studies have shown that femoral head has a poorer blood supply compared to femoral neck and femoral shaft (1, 2). Because of the absence of an effective collateral circulation, the femoral head is at an especially high risk of ischemic injury. Relatively mild haemodynamic impairment which may not necessarily compromise other sites has the potential to cause osteonecrosis of the femoral head. In animals, avascular necrosis of the femoral head is sporadically encountered in dogs (3). Perthes disease–like necrosis of the femoral head and neck occurs in some breeds of small dogs (3). Osteonecrosis of femoral head is seen in spontaneously hypertensive rats (4,5). Recently it was reported that delayed wash-out in dynamic contrast enhanced (DCE) MRI suggest blood stasis or outflow obstruction in the tissue (6). Delayed wash-out was seen in sites of bone marrow edema, osteoarthritis, and avascular osteonecrosis (6). In this study, the DCE MRI wash-out characteristics of femoral head in normal rats were investigated, and comparison was made to those of proximal and distal femoral diaphysis, distal femoral epiphysis, proximal tibial epiphysis, and proximal tibial diaphysis.

Materials and Methods: The experimental protocol was approved by the local animal experiment ethics committee. Matured Wistar rats of 7 months old were used in this study. Right hip (n=18) DCE MRI studies were performed on a 1.5T (Intera NT) clinical whole-body imaging system (Philips Healthcare), and right knee (n=12) DCE MRI studies were performed on a 3 T (Achieva) clinical whole-body imaging system (Philips Healthcare). Before the MR imaging, rat tail vein was cannulated with a 24G heparinised catheter. For hip MRI, rat was positioned supinely in a custom-made cradle. A surface coil with a diameter of 4.7 cm was placed just under the hip as the radiofrequency (RF) receiver and the body volume coil was used as the RF transmitter. After the positioning scan, a plane through the femoral head, femoral neck, and femoral shaft of the right side femur was prescribed by the three-point planscan tool. For knee MRI, a single loop coil with diameter of 2.3 cm (finger coil) was used as the RF receiver and the body volume coil was used as the RF transmitter. A custom made perspex platform was used to hold the finger coil and rats. Animals were placed on a perspex platform with one hind leg extending through the RF coil, with the knee centred in it. To prevent motion, the animal's right paw was secured to a secondary lower platform. After the scout scan, a central sagittal plane of knee was prescribed. The dynamic MR scan series was obtained with a short T1-weighted gradient echo sequence. The temporal resolution was approximately 0.6 second. MRI contrast agent was Gd-DOTA. A dose of 0.3mmol/kg (0.15 ml for a 250gram rat) was hand-injected after initial baseline 60 image acquisitions as quick bolus and followed by a flush of 0.5 ml normal saline. The total dynamic MRI duration was approximately 8 min for hip and 4.5 min for knee. For quantification, the MR data of initial 4.5 min acquisition of both joints were used. Dynamic MRI images were processed in a radiologic workstation (Workspace, Philips Healthcare). Region of interest (ROI) was drawn over the cancellous part of 1) femoral head (FH) 2) proximal femoral diaphysis (PFD), 3) distal femoral diaphysis (DFD), 4) distal femoral epiphysis (DFE), 5) proximal tibial epiphysis (PTE), 6) proximal tibial diaphysis (PTD). The signal enhancement over time was recorded, and maximum wash-out and wash out rate were computed. Maximum wash-out was defined as the MR signal change post the initial fast phase peak enhancement to the time point of 4.5 min post contrast injection. Wash-out rate is derived from the maximum wash-out divided by the duration of the maximum wash-out phase (in second) in the study.

Results: After the initial fast wash-in phase, for FH a continuous further slow wash-in was observed (Fig 1), while all PFD, DFD, DFE, PTE, and PTD had MR signal decrease post peak enhancement (Fig 1, Fig 2). The quantitiave data of maximum wash-out and wash-out rate are shown in table 1.

	Hip		Knee			
	FH (n=18)	PFD (n=18)	DFD (n=11)	DFE (n=12)	PTE (n=11)	PTD (n=7)
Mean MaxOut	0.175	***-0.511***	***-0.208***	***-0.185***	***-0.217***	***-0.104***
SD MaxOut	0.129	0.192	0.067	0.095	0.096	0.066
Mean Rout	0.053	-0.142	-0.056	-0.049	-0.054	-0.03
SD Rout	0.038	0.051	0.024	0.026	0.022	0.021

Table 1. MaxOut: Maxumum wash-out; Rout: Washout rate; n: number of joints used for analysis. Positive value of FH indicates MR signal increase. Negative values of PFD, DFD. DFE, PTE, and PTD indicate MR signal decrease.

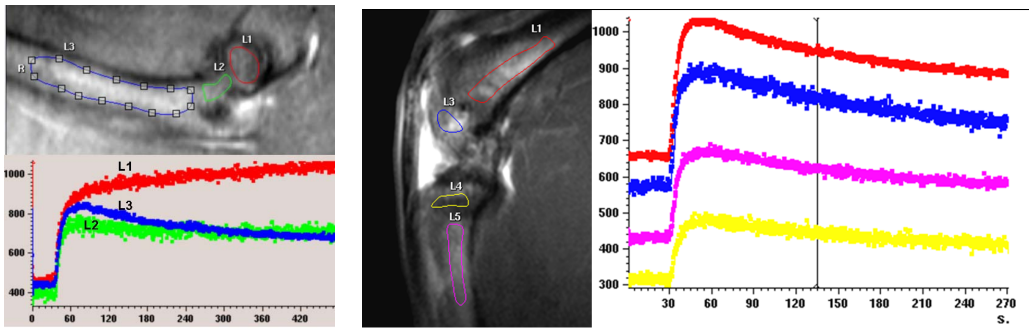

Fig 1. A: T1W anatomical image depicting femoral head (L1), femoral neck (L2), and femoral shaft (L3). B: time-signal intensity curve of DCE MRI data; Y-axis: signal intensity in arbitrary unit, X-axis: time in second. After a rapidly rising slope during the early phase, the time-signal intensity curve drops quickly after peak enhancement in proximal femoral shaft (L3, blue line). In contrast, after a rapidly rising phase, in femoral head the time-signal intensity curve continues to increase slowly, no wash-out is observed after 440 seconds post contrast injection (L1, red line). That of femoral neck is close to femoral shaft thought the wash-out is slightly slower than the shaft. Fig 2, MRI sagittal view of right knee of a rat. A: T1W anatomical image depicting lower femoral shaft (L1), femoral epiphysis of the knee (L3), and tibial epiphysis of the knee (L4), upper tibial shaft (L5). B: time-signal intensity curve of DCE MRI data. After bolus injection of Gd-DOTA, all four regions have a rapid rising phase, then the time-signal intensity curve decrease after peak enhancement.

Discussion and Conclusion: Our in vivo MRI observation suggested that even in normal matured Wistar rats the perfusion of femoral head is compromised compared with other bone sites, possibly being due to blood stasis or outflow obstruction. Femoral shaft, femoral and tibial epiphysis of the knee, and proximal tibial diaphysis showed a wash-in phase followed by a wash-out phase. To our knowledge, that normal rats have compromised perfusion in femoral head has not been reported. This information will be relevant for understanding the physiology and pathphysiology of hip joint diseases in animal models.

References: ***1.*** Wang YX et al. *Bone*. 2009;45:711-5. ***2.*** Kubo T, et al. *Ann Nucl Med*. 2001;15: 231–235. ***3.*** Boss JH, Misselevich I. *Vet Pathol* 2003; 40:345–354. ***4.*** Hirano T, et al. *Acta Orthop Scand*. 1989;60:407-410. ***5.*** Iwasaki K, et al *Clinical Orthopaedics and Related Research* 1992; 277: 31-40. ***6.*** Lee JH, et al. *Orthop Clin North Am*. 2009;40:249-257.