

## Barium Angiography in Small Animals

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Angiography is defined as the imaging of the vascular system. X-ray is the most common imaging modality used for this application. Iodinated agents are typically used to absorb X-rays and provide contrast during clinical and preclinical imaging. Unfortunately, many of the clinical agents may not work effectively or provide sufficient contrast in small animals. Moreover, expensive instrumentation, such as X-ray computed tomography (CT) or magnetic resonance imaging (MRI), may be unavailable to the preclinical researcher. In this study, we present a method of using less-expensive barium sulfate to achieve high-resolution angiograms in small animals using planar X-ray, and we subsequently compare the vascular structural anatomy in various transgenic mice.

Barium sulfate is a white crystalline solid that is insoluble in water and has well-known X-ray contrast. Barium sulfate has been widely used in "barium meal," "barium swallow," and "barium enema" preparations for the visualization of the structural and motility abnormalities of the gastrointestinal tract, and it is used mostly in pediatric populations. Barium sulfate in vascular circulation is usually lethal as a result of the obstruction of blood flow, and thus its application to angiography is limited to post-mortem studies. Although iodinated contrast agents are generally used for intravascular imaging, we found barium gives better contrast than iodine compounds in small animals such mice.

### Methods

**Animal Preparation:** Mice were 10-12 weeks old with approximate weights of 25-30 g, and all animal procedures were performed in accordance with the National Institute of Health Guidelines for Animal Research. Mice were anesthetized with sodium pentobarbital according to body weight (70 mg/kg). The right carotid artery was dissected out and cannulated with PE-10 tubing for heart and kidney angiograms. The jugular vein was cannulated for pulmonary angiogram. All mice were heparinized with heparin saline (10 units/mL) and euthanized by supersaturated KCl solution. The KCl solution is used to stop the heart in diastole with the coronary arteries opened.

**X-ray Angiography:** The size of barium particles range from 1-100  $\mu\text{m}^3$ . We suspended barium sulfate (0.1 g/mL) in 50 mM Tris-buffer (pH 5.0) and infused 1 mL volume at constant pressure and flow with a syringe pump (rate of 200  $\mu\text{L}/\text{min}$ ) through a given intravascular route. All images were taken with the In-Vivo MS FX PRO Imaging System. Dissected animals were placed in the X-ray chamber and angiograms were captured with a Radiographic Phosphor Screen. Three min X-ray images were taken at 35 Kvp. Available aluminum filters were not used to harden the beam. Aperture settings included an F-stop = 4 and a field of view between 40 and 120 mm to capture different organs.

## Results

X-ray imaging with barium sulfate contrast enhancement produced angiograms of different soft tissue structures. First, the top frame of Fig. 1 displays vasculature in the heart when barium was administered via the carotid artery. Under identical conditions, vasculature can be seen extending down the aorta and branching into the kidneys and femoral arteries (Fig. 1A). When the barium contrast media was administered via the jugular vein, the vasculature in the lungs was visualized with stunning resolution.

Using these techniques, we recently reported a study of vascular heterogeneity in vascular beds of transgenic mice compared with wild-type black mice. The vascular density in CBS-/+ and Akita hearts decreased, while it was increased in lungs of CBS-/+ and MMP-9-/. There was decreased vascular density in liver and kidney of Akita mice. Vascular density in brain, kidney, and mesentery was decreased in CBS-/+ mice.

## Conclusion

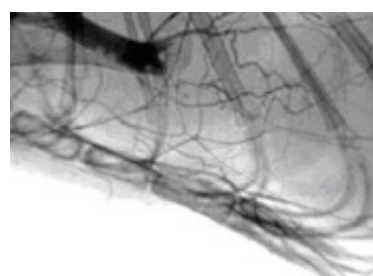
Barium sulfate angiography provides a highly cost-effective method to produce high-contrast images using basic X-ray imaging, which would otherwise be obtained by expensive CT angiograms. This technique can be applied to study various structural abnormalities in the vascular system of small animals such as in aortic dissection, atherosclerotic coronary arteries, etc. It also has the potential to be widely used in various cancer studies as well.

## References

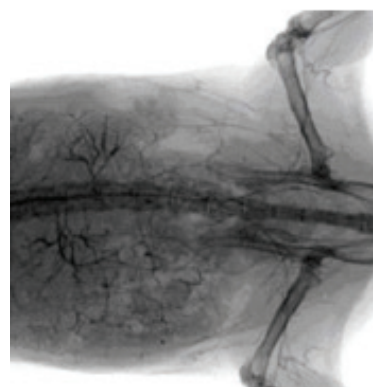
1. Zalev A. H. "Venous barium embolization, a rare, potentially fatal complication of barium enema: 2 case reports." *Can. Assoc. Radiol. J.* 1997, 48(5-6), 323-6.
2. Givvimani S., Sen U., Tyagi N., Munjal C, Tyagi S. C. "X-ray imaging of differential vascular density in MMP-9-/-, PAR-1-/-, hyperhomocysteinemic (CBS-/+ ) and diabetic (Ins2-/+ ) mice." *Arch. Physiol. Biochem.* 2011, 117(1), 1-7.
3. Myojin, K., Taguchi, A., Umetani, K., Fukushima, K., Nishiura, N., Matsuyama, T., Kimura, H., Stern, D. M., Imai, Y. Mori, H. "Visualization of intracerebral arteries by synchrotron radiation microangiography." *Am. J. Neuroradiol.* 2007, 28, 953-957.

(A) Mouse coronary angiogram showing right and left coronary arteries along with the arch of the aorta. (B) Mouse renal angiogram showing right and left renal arteries arising from the descending aorta. (C) Mouse pulmonary angiogram showing vasculature in the lungs.

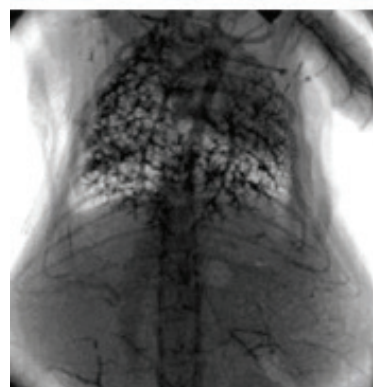
Figure 1



(A)



(B)



(C)