In Vivo Synchrotron Radiation Coronary Micro-angiography in the Rat

Previously in our laboratory, synchrotron radiation coronary micro-angiography (SRCA) using Langendorff-perfused rat hearts succeeded in visualizing a coronary artery of 50 μm in diameter. However, in vivo rat SRCA poses the problem of compromised temporal resolution due to the rapid heart rate. As a countermeasure, we have established a simple method of in vivo rat SRCA with induced bradycardia. A catheter for angiography was inserted into the carotid artery. SRCA was performed after the bradycardic agent was given intravenously. As a result, our SRCA system could detect a coronary artery of 45 μm in diameter in the in vivo rat.

Clinical X-ray angiography can provide images of coronary arteries having a minimum diameter of 300 μm. However, the proliferation of collateral arteries in ischemic heart disease and of new blood vessels in regenerative medicine occurs at smaller arteriole sizes. Previously, we reported that the application of synchrotron radiation in coronary micro-angiography using Langendorff-perfused rat hearts could visualize a coronary artery of 50 μm in diameter [1]. However, in vivo rat SRCA had the problem that the rapid heart rate of rats degraded the temporal resolution. Therefore, the purpose of this study was to establish a simple method of in vivo rat SRCA with high temporal resolution.

SRCA was performed at AR-NE7A. Synchrotron radiation consists of a wide range of wavelengths emitted by charged particles with speeds close to that of light when their orbits are bent by a magnetic field. Synchrotron radiation was obtained from a 6.5-GeV electron beam and converted to 33.3-KeV monochromatic X-rays by 13-degree reflection from a silicon crystal. Images were taken using a two-dimensional recording system consisting of a high-sensitivity CCD camera. This SRCA system has the high resolution of 9 μm per pixel, and its visual field is 36 mm × 24 mm. The high temporal resolution allows the setting of arbitrary SRCA exposure times, and the high-density resolution can differentiate slight variations in density. The exposure time used in this study was 30 milliseconds, and the maximum acquisition rate was 3 images per second.

Wistar rats were anesthetized. A micro polyethylene catheter for angiography was inserted into the carotid artery. Temporary bradycardia was induced with an intravenous bolus injection of 5 mg of ATP. SRCA was performed after ATP injection [2].

Figure 1 shows an image obtained by in vivo SRCA in a rat with a normal heart rate (300 beats per minute). The image is blurred due to the movement caused by the rapid heart rate. As a solution to this, we induced temporary bradycardia with ATP. This simple technique involves just lowering the heart rate and maintaining bradycardia for a few minutes. An electrocardiogram was recorded during SRCA. After ATP administration, the average heart rate decreased from about 380 to about 70 beats per minute. As a result, our SRCA system could visualize a coronary artery as small as 45 μm in diameter in an in vivo rat (**Fig. 2**).

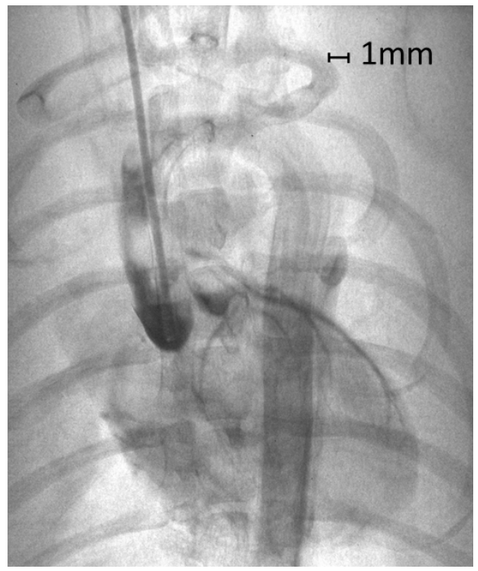

Figure 1: In vivo rat SRCA obtained in a preliminary experiment.

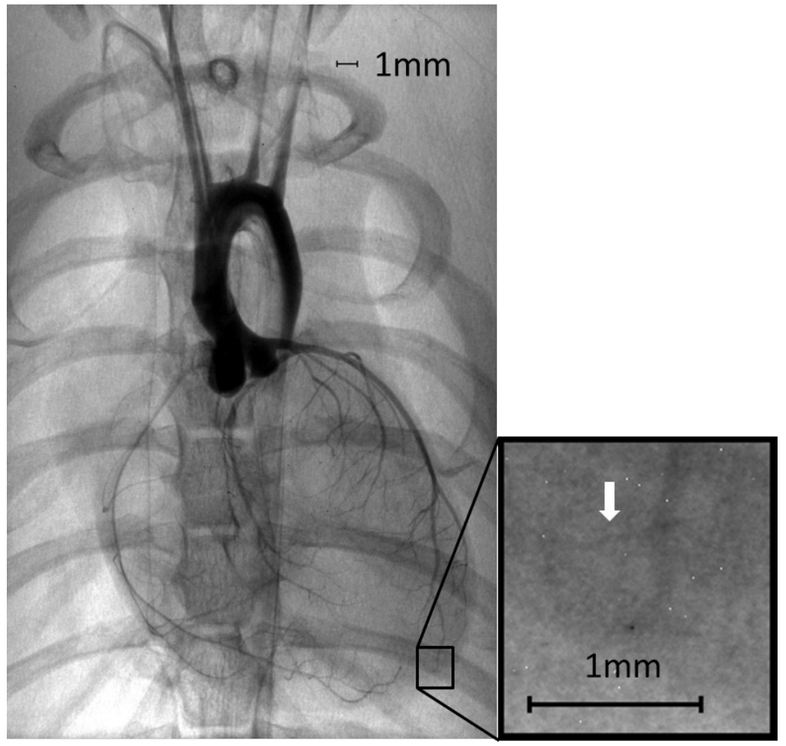

Figure 2: In vivo rat SRCA using ATP. White arrow shows a small branch which is 45 μm in diameter.

ATP is used clinically to treat paroxysmal supraventricular tachycardia. In addition, ATP is sometimes used to induce temporary heart asystole to permit precise endograft placement during thoracic endovascular aortic repair. Because our simple method slows the motion of the rat heart, clear images with high spatial, density, and temporal resolutions can be obtained from in vivo rat SRCA. This method can evaluate the coronary arteries of small animals with rapid heart rates, such as rats and mice. However, ATP has a vasodilator action and therefore this method is unsuitable for evaluation of vasodilatory potency. Nevertheless, we believe that our method is extremely useful for morphologic evaluation of the coronary arteries in small animals. We plan next to use in vivo rat SRCA to compare coronary arteries between normal and diabetic rats. These data could be helpful in evaluating endothelial dysfunction in diabetic rats. Clinically, this new technology may help researchers to investigate the proliferation of collateral arteries in ischemic heart disease and of new blood vessels in regenerative medicine in the near future.

In conclusion, our results demonstrate the effectiveness of SRCA for visualizing the coronary artery in an in vivo rat. Our method of using a bradycardic agent was simple and could improve the temporal resolution of SRCA.

REFERENCES

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