Published in final edited form as:

J Pharmacol Toxicol Methods. 2011 September ; 64(2): 151–157. doi:10.1016/j.vascn.2011.05.008.

In vivo imaging of rat coronary arteries using bi-plane digital subtraction angiography

Cristian T. Badea^a, Laurence W. Hedlund^a, Yi Qi^a, Brian Berridge^b, and G. Allan Johnson^a

^aCenter for In Vivo Microscopy, Duke University Medical Center, Durham, NC 27710, USA

^bGlaxoSmithKline Safety Assessment, 5 Moore Drive, Research Triangle Park, NC 27709, USA

Abstract

INTRODUCTION—X-ray based digital subtraction angiography (DSA) is a common clinical imaging method for vascular morphology and function. Coronary artery characterization is one of its most important applications. We show that bi-plane DSA of rat coronary arteries can provide a powerful imaging tool for translational safety assessment in drug discovery.

METHODS—A novel, dual tube/detector system, constructed explicitly for preclinical imaging, supports image acquisition at 10 frames/second with 88-micron spatial resolution. Ventilation, x-ray exposure, and contrast injection are all precisely synchronized using a biological sequence controller implemented as a LabVIEW application. A set of experiments were performed to test and optimize the sampling and image quality. We applied the DSA imaging protocol to record changes in the visualization of coronaries and myocardial perfusion induced by a vasodilator drug, nitroprusside. The drug was infused into a tail vein catheter using a peristaltic infusion pump at a rate of 0.07 ml/h for 3 mins (dose: 0.0875 mg). Multiple DSA sequences were acquired before, during, and up to 25 minutes after drug infusion. Perfusion maps of the heart were generated in MATLAB to compare the drug effects over time.

RESULTS—The best trade-off between the injection time, pressure, and image quality was achieved at 60 PSI, with the injection of 150 ms occurring early in diastole (60 ms delay) and resulting in the delivery of 113 microL of contrast agent. DSA images clearly show the main branches of the coronary arteries in an intact, beating heart. The drug test demonstrated that DSA can detect relative changes in coronary circulation via perfusion maps.

DISCUSSION—The methodology for DSA imaging of rat coronary arteries can serve as a template for future translational studies to assist in safety evaluation of new pharmaceuticals. Although x-ray imaging involves radiation, the associated dose (0.4 Gy) is not a major limitation.

Keywords

digital subtraction angiography; rat; coronary arteries

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Corresponding author: Cristian Badea, Center For In Vivo Microscopy, Box 3302 Duke University Medical Center, Durham, NC 27710, 919-684-7858, Cristian.Badea@duke.edu .

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Introduction

Preclinical imaging of small animal models has become an important component of biomedical, pharmaceutical, and genomic research programs. Imaging can be particularly useful for integrated (e.g. structure and function) approaches to the preclinical assessment of safety for novel therapeutics with the added benefit of functioning as a translational biomarker. To meet this need, the technology for in vivo, small animal imaging has advanced rapidly in recent years to include magnetic resonance microscopy (Johnson, Hedlund et al. 1992), micro-CT (Holdsworth and Thornton 2002), micro-ultrasound (Hoit 2001), micro-PET/SPECT (Herschman 2003), and optical methods based on fluorescence and bioluminescence (Ntziachristos, Ripoll et al. 2005). We and others have recently added x-ray-based digital subtraction angiography (DSA) (Buhalog, Yasuda et al. ; Lin, Samei et al. 2006; Badea, Hedlund et al. 2007; Badea, Drangova et al. 2008) to this imaging armamentarium.

Drug-induced vascular injury is a particularly challenging drug safety concern for a number of reasons. Prominent among these are an incomplete understanding of the predictivity of preclinical models for clinical risk and lack of a sensitive and relevant translational biomarker strategy. Many of the best characterized preclinical models of vascular injury involve drugs that are vasoactive—i.e., induce vasoconstriction or vascular relaxation/vasodilation (Kerns, Arena et al. 1989; Dogterom, Zbinden et al. 1992; Hanton, Le Net et al. 1995; Loudon, Brott et al. 2006). In traditional preclinical safety paradigms, these effects are characterized by correlating changes in systemic blood pressure as a surrogate for vasoactivity with histologic evidence of lesions in blood vessels of various organ systems, including the heart. Paradoxically, these assessments are generally collected in separate study settings. Sensitive measures of systemic blood pressure are most often collected in single-dose telemetered animal safety pharmacology studies. Morphologic characterization of vascular injury, on the other hand, is done in repeat-dose studies from which representative tissues are collected for histologic examination. This paradigm lacks the ability to visualize tissue-specific vasoactivity where blood vessel lesions occur. Coronary arteries are a recognized site of drug-induced vascular injury in both rodents and non-rodents (Kerns, Arena et al. 1989; Dogterom, Zbinden et al. 1992; Loudon, Brott et al. 2006).

In many vascular studies, useful information can be obtained from two-dimensional (2D) digital subtraction angiography (DSA) projection images. First suggested by Mistretta et al. (Mistretta, Ort et al. 1973), DSA is now a routine clinical imaging modality and coronary artery DSA is one of its main applications (Struyven, Delcour et al. 1986). However, to date, there have been only limited studies using DSA for preclinical imaging (de Lin, Ning et al. 2008; Lin, Marshall et al. 2009). Yet, much potential exists for this modality given its ease of use, throughput, potential high speed, and relatively low cost. DSA can be based on either temporal subtraction or k-edge subtraction. The latter technique is based on the nonlinear differences in the attenuation of iodine with the x-ray beam energy. A k-edge describes a sudden increase in the attenuation coefficient of x-ray photons. K-edge DSA ideally requires imaging on both sides of the k-edge of iodine with monochromatic x-rays obtained using a synchrotron source as in (Schültke, Fiedler et al.). However, the need of a synchrotron limits the availability of such a method, since the majority of x-ray imaging systems are using polychromatic x-ray sources and are therefore, better suited for temporal subtraction. We report here methods for in vivo DSA based on temporal subtraction based on the injection of contrast agent and image acquisition before and after the contrast injection.

Coronary arteries in the rat have been previously visualized using synchrotron x-ray radiation (Matsushita, Hyodo et al. 2005; Matsushita, Hyodo et al. 2008). Although this approach provides very high resolution (13 microns), the studies were limited to ex vivo

Langerdorff heart preparations (Skrzypiec-Spring, Grotthus et al. 2007). Recently, Ishikura et al. (Ishikura, Hirayama et al. 2008) have shown three-dimensional (3D) real-time contrast echocardiography of rat coronary arteries. The image quality, however, is inferior compared to the x-ray-based imaging. In this work, we describe a bi-plane DSA system based on conventional x-ray tubes and CCD-based solid state detectors to image rat coronary arteries in vivo.

Our goal was to develop methods for imaging in rats that might provide translational information to assist safety assessment in drug discovery. We demonstrate that DSA can be used, not only for morphological evaluation of the coronary arteries, but also for assessing myocardial perfusion in a case study using the drug nitroprusside.

Materials and Methods

I. Dual source/detector x-ray system

We have developed a unique, dual tube/detector radiographic system that allows high-resolution imaging with high photon fluence rate, and integrated motion control, i.e. imaging is synchronized to respiratory and cardiac activity to reduce the motion artifacts. The system is also used for micro-CT, which was described previously (Badea, Johnston et al. 2008). The CT system uses two Varian A197 x-ray tubes (Varian Medical Systems, Palo Alto, CA) with dual focal spots of 0.3/0.8 mm. The tubes are commonly used in clinical angiography, which requires high instantaneous flux and large heat capacity. Two Epsilon High Frequency x-ray generators (EMD technologies Quebec, Canada) are used to control both x-ray tubes. The system has two detectors with a $\text{Gd}_2\text{O}_2\text{S}$ phosphor (XDI-VHR 2 115 mm, Photonic Science, East Sussex, UK) with pixel size of 22 microns, 115-mm input taper size, and 4008×2672 image matrix. Both detectors allow on-chip binning of up to 8×8 pixels, and sub-area readout to allow higher-speed readout of 10 frames/second, i.e. a temporal resolution of 100 ms. The high-performance x-ray tubes/generators provide short (10 ms) exposures that minimize motion blur with sufficient flux to fill the 14 bits of the detector digitizer. The x-ray tubes and detectors are stationary in the horizontal plane with the subject positioned vertically on a rotatable stage between the tubes/detector. The source-to-subject distance (702 mm), subject-to-detector distance (100 mm), and a source-to-detector distance (802 mm), results in a geometric blur of the focal spot that matches the Nyquist sample at the detector (Badea, Hedlund et al. 2004). X-ray settings for DSA imaging were 80 kVp, 160 mA, and 10 ms per exposures. The x-ray generators, tubes, detectors, and injector are controlled by a sequencer application written in LabVIEW (National Instruments, Austin, TX) to provide precise cardio-respiratory gating of each image.

II. Micro-injector

For contrast injection, we used a custom-built, power micro-injector consisting of a computer-controlled solenoid valve attached to the contrast injection catheter and a heated contrast agent reservoir, which is powered by N_2 at up to 90 PSI (de Lin, Ning et al. 2008). The high power pressure driving the injection is necessary to compensate for the small caliber lumen and high resistance of the injection catheters (3 Fr). The high power is also needed to achieve the high flow velocity for bolus injections. This device reproducibly injects volumes as little as 6 μL at 1 to 2 $\mu\text{L}/\text{ms}$. The contrast agent we have used is Isovue containing 370 mg/ml iodine (Isovue-370, Bracco Diagnostics Inc, Princeton, NJ). The contrast agent was heated to the body temperature of the rat, eliminating thermal shock and reducing contrast viscosity.

III. Animal preparation

The animal procedures were approved by the Duke Institutional Animal Care and Use Committee. We used 10 male 11-12 week-old SAS-SD rats (Charles-River Wilmington, MA). Animals were first anesthetized with Nembutal (Ovation Pharmaceuticals Inc., Deerfield, IL) with an IP dose of 60 mg/kg). The rats were perorally intubated (18 ga catheter, BD Medical Systems, UT) and mechanically ventilated at 80 breaths per minute using an in-house developed ventilator (Hedlund and Johnson 2002).

A PE-50 catheter (Access Technologies, Skokie, IL) was inserted into the right common carotid artery and advanced into the aortic arch. The catheter tip was positioned just cranial to the aortic valve using real-time blood pressure guidance. As the catheter was advanced, the diastolic pressure dropped to zero indicating the tip was in the left ventricle, then the catheter was slowly withdrawn until the normal systolic/diastolic pressure appeared, which indicated that the tip was in the aorta just beyond the aortic valve, and finally, the catheter was withdrawn an additional 3 to 5 mm to position within the ascending aorta and secured in this final position.

During imaging, anesthesia was maintained with isoflurane (1-1.5%. Halocarbon Laboratories, River Edge, NJ) delivered by mechanical ventilation. Normal body temperature was maintained using heat lamps and a feedback PID controller (Cole-Parmer, Chicago, IL) using input from a rectal thermistor. Pediatric electrodes were taped to the footpads for ECG (Ambu, Glen Burnie, MD). A pneumatic pillow on the thorax recorded breathing motion (Coulbourn Instruments, Whitehall, PA). All physiologic signals were acquired with LabLine V amplifiers (Coulbourn Instruments) and were displayed on a computer using a custom LabVIEW application.

IV. Imaging sequence

A custom sequence-controller application implemented in LabVIEW was used to synchronize x-ray exposure and contrast injection with cardiac activity (ECG) and ventilation. The bolus injection time and duration are precisely synchronized with the x-ray exposure by this controller (see Figure 1). The sequence starts by spinning the high-speed x-ray rotor, stopping ventilation during end-expiration, and acquiring a set of non-contrast images at a specific delay after the ECG R wave; these images are used to create the mask. Without interruption, this is followed by a bolus injection of contrast (about 150 ms duration) at the same delay time after the R wave, and then a series of post-injection images is obtained also at the same time in the cardiac cycle. After the last image, ventilation is restarted. The entire sequence is completed in 8 seconds with 30 images acquired over 30 consecutive heartbeats. The total radiation dose associated with a single injection bi-plane DSA sequence that includes 30 images is 0.04 Gy. The time of delay after the R wave is set to occur in diastole, at the time when the aortic valve is closed, and when flow is greatest in the coronary arteries.

In our system, a separate PC computer is dedicated to each imaging chain providing high-speed image capture directly to memory. Each system has 8GB of on-board memory that serves as fast frame storage. Each camera bins the data at 4×4 in the camera controller to allow the highest frame rate. At the conclusion of each imaging sequence, data are downloaded to another computer where MATLAB routines perform the requisite post-processing for image subtraction. As shown in Figure 2, the pre-contrast mask obtained by averaging is subtracted from the post-contrast images resulting in display of only the opacified vascular structures such as the aorta and coronary arteries.

V. Protocol optimization

A set of experiments was performed to test and optimize the sampling and image quality for coronary artery DSA.

Critical elements of a coronary arteries DSA experiment included:

- a. Position of the tip of the contrast agent injection catheter
- b. Contrast agent volume and injection pressure
- c. Time of injection during the cardiac cycle

The volume of contrast agent injected depends on the injection duration and N_2 pressure. We have tested injection times from 75 to 300 ms and pressures from 20 to 80 PSI. We measured a series of volumes of delivered contrast agent by collecting and then weighing samples. The density of Isovue 370 was used to convert mass to volume. Finally, we tested how the time of injection during the cardiac cycle affected quality of visualization of the coronary arteries based on maximum enhancement. The start of injection was delayed from the R wave by 0%, 30%, and 60% of the RR interval.

VI. DSA-based assessment of nitroprusside (NP) effects on coronary arteries

Our goal was to use coronary artery DSA to measure changes in flow in relation to drug exposure. To test our capability to measure such changes, we used sodium nitroprusside (NP, Nitropress, Hosira, Inc, Lake Forest, IL) as a model compound. NP is a smooth muscle relaxant causing vasodilation of peripheral arteries and veins. NP is also known as a coronary artery vasodilator in humans (Yeh, Gosselin et al. 1977). NP at a concentration of 25 mg/ml was infused into a tail vein catheter using a peristaltic infusion pump (Pegasus Vario, Instech Solomon, Plymouth Meeting, PA) at a rate of 0.07 ml/h for 3 minutes (dose: 0.0875 mg). Multiple DSA sequences were acquired before, during, and up to 25 minutes after NP infusion using 113 microL of contrast per sequence. With such a small volume of contrast per sequence, imaging could be repeated several times without significantly changing blood volume. For these NP studies, a pulse oximeter (Starr-Life Science, Oakmont, PA) was used to record physiologic parameters, such as pulse distension (relative peripheral artery pressure), heart rate, oxygen saturation, breathing rate, and breath distention (measure of breathing difficulty).

Perfusion maps of the heart were generated in MATLAB to compare the drug effects over time. We computed perfusion using the Mullani-Gould formulation (Mullani and Gould 1983). Typically, perfusion (i.e., blood flow in a voxel) is calculated as the peak enhancement divided by the area under the time density curve for the arterial input. The arterial input was obtained by selecting a region of interest in the aorta. Similar to (Tilkemeier and Wackers, 2006), the planar DSA images can be used for segmental perfusion assessment. In essence, the myocardium images can be divided into regions of interest for which average perfusion values can be computed and compared between multiple runs in the same animal or between multiple animals, and Student t-test can be used for a statistical comparison.

Results

Examples of cine display of DSA images are available as animations in the movie supplement to this manuscript. Each animation shows the first pass of the bolus of the contrast agent. For each injection, we generated two movies corresponding to the orthogonal bi-plane views. Static frames from such a cine-sequence are shown in Figure 3. These sequences demonstrate the importance of catheter tip position. In the Figure 3A,B series, the

tip is very close to the aortic valve and apparently blocking the orifice of the left coronary artery. In Figure 3C,D series, the catheter tip is farther from the aortic valve allowing complete filling of both coronary arteries, as seen in the first frame (first heartbeat) following contrast injection. The left (LCA) and right coronary arteries (RCA) are clearly seen.

The effect of micro-injection pressure and duration on contrast volume is illustrated in Figure 4, and the actual volume delivered is shown in Figure 5. Coronary artery visualization generally improves by increasing both injection duration and/or driving pressure (Figure 4). At a given injection duration, volume increases linearly with pressure. We selected to use 60 PSI for 150 ms as the best trade-off for providing adequate image quality, while minimizing volume of contrast injected (113 microL, see Figure 5). While 80 PSI for 150 ms provided a slight improvement in image quality, the higher pressure resulted in retrograde flow of contrast into the left ventricle.

Figure 6 shows images acquired at different delay times from the QRS complex, when the contrast agent was injected using 60 PSI for 150 ms. The RR-interval was about 200 ms. The maximum contrast DSA images show some improvement with the added delays.

Figures 7 and 8 illustrate the use of DSA to detect changes in coronary artery circulation. Figure 7A compares the same maximum-enhanced DSA image at different sequences during the NP experiment. The start of NP infusion is considered as time point 0 seconds. The -5 minute image is before NP infusion. The images at 2 and 3 minutes were acquired during the NP infusion. The rest of the images were acquired after infusion was stopped. The first 7 frames of the pre-drug (-5 minutes) and +8 minutes post-drug DSA sequences are compared in Figure 7B and 7C. Note how NP caused an increase in myocardial perfusion. The supplement movie for this manuscript compares DSA sequences in the same animal -5 minutes before and +8 minutes after NP infusion.

During the NP infusion, we witnessed a drop in pulse distension (relative peripheral artery pressure) which later returns to pre-drug levels. Unexpectedly, the heart rate also dropped by approximately 9%, but returned to the pre-drug levels in about 15 minutes. The arterial oxygen saturation remained above 98% during the whole experiment, suggesting that the suspended respiration during the injection of contrast did not affect the animal.

Finally, myocardial perfusion maps for the NP experiment are shown by Figure 8. Since DSA is not able to provide 3D information, the display values are given in arbitrary values, but can be used to compare qualitatively the changes that occurring over different DSA sequences. Maximum myocardial perfusion values are shown at the +8 minutes time point.

Discussion and Conclusions

Imaging coronary arteries in a rat is very challenging due to their small size and fast physiologic motion of the heart and respiration. These challenges are hard to overcome with commercial small animal x-ray or micro-CT systems that are using micro-focus x-ray tubes for which the exposures should be sufficiently long in time for an adequate signal to noise ratio. We have been able to achieve this goal by building an x-ray-based imaging system that uses x-ray tubes with large focal spot (clinical angiography tubes) able to deliver very short exposures (10 ms) with adequate flux (Badea, Hedlund et al. 2004). The short exposures are needed to freeze the cardiac and respiratory motion using the gating strategies. Of equal importance to our approach is the micro-injector that is able to deliver controlled amounts of contrast with high accuracy and precision (de Lin, Ning et al. 2008). But the most important, is the integration of all these components in a single system.

In the armamentarium of preclinical methods accepted for the evaluation of morphology of coronary arteries, conventional histology is still the most used method due to its low cost. TTC staining can be used to detect myocardial infarct size (Lie, Pairolero et al. 1975) and fluorescent microspheres for myocardial perfusion estimations (Ytrehus, Liu et al. 1994). However, these methods are post-sacrifice techniques. Imaging can sometimes provide an alternative approach but in general, at higher cost. 3D micro-CT is the x-ray-based method able to provide the morphology of the coronary arteries as shown by (Beighley, Thomas et al. 1997). However, this approach involves ex-vivo imaging of the casted heart limiting the use of such methods to the possibility of extracting real time flow information on transitory effects associated with drug exposure. Cine-MRI with 3D coronary angiography has also been proven to be the appropriate diagnostic tool to characterize the rat model of coronary artery stenosis. However, in those studies, 3D MR angiography has been performed in isolated hearts (Nahrendorf, Hiller et al. 2003).

Alternatively, (Ishikura, Hirayama et al. 2008) have shown three-dimensional (3D) real-time contrast echocardiography of rat coronary arteries. But, the image quality is inferior due to low resolution. The nuclear imaging techniques could provide myocardial blood flow and metabolism information, but no 3D morphological information on coronary arteries, due to the lack of resolution (Thomas, Bal et al. 2008).

As shown here, DSA can be used to image the coronary arteries and follow changes in cardiac perfusion through the course of a drug (nitroprusside) infusion. Our DSA images clearly show the main branches of the coronary arteries in an intact beating heart. Because the images are obtained in-vivo using bi-plane geometry, the correct spatial positions, and orientation of the arteries in reference to the rest of the body are clear. The approach has its own challenges such as catheter placement, injection volume, injection timing in relation to the cardiac cycle, and the physiologic support and monitoring of the animal. Positioning the catheter tip and timing of contrast injection for imaging the coronary arteries proved to be challenging (see Figure 3). The optimal placement for the catheter tip should be several millimeters cranial to the aortic valve. If the catheter tip is too close to the aortic valve, it could possibly block a coronary artery orifice and obstruct flow to that artery. On the other-hand, if the tip is too far above the aortic valve, the injected contrast will be diluted by the blood volume between the tip and the roots of the coronary arteries. Timing of the sequence of image acquisitions also poses challenges. For optimal imaging quality, the contrast injection must occur during diastole when the aortic valve is closed so contrast enters the coronary arteries.

Finally, the use of an invasive catheter could be a limitation of coronary artery DSA, but we note that indwelling catheters are possible (Bechtold, Vernon et al. 2008) that will allow such studies to become longitudinal.

As shown in Figure 8, the temporal sequence associated with DSA can be used to assess perfusion of the myocardium. Time attenuation curves can be constructed for each pixel from each DSA sequence to qualitatively follow the effects of drugs or treatments on coronary artery flow. Thus, DSA can provide both anatomical and functional information on the coronary arteries and myocardial perfusion. DSA is, however, not a tomographic imaging method so the data is relative, not absolute blood flow. The perfusion maps show approximately double values for the myocardium at +8 minutes after drug compared with the -5 minutes pre-drug set (Figure 8). As seen in the NP experiment, coronary artery DSA studies may involve multiple DSA consecutive imaging runs to assess a drug transitory effect. But, even with 10 DSA imaging runs, the radiation dose is only about 0.4 Gy, a fraction of the LD 50/30 which in rats has been reported to be in approximately 7.1 Gy (Kouzmanova, Ivanov et al. 1997). The method is elegant in its simplicity. By

carefully controlling the sequence, e.g. injection volume, timing, respiration, one can produce a functional imaging biomarker that can be very sensitive to drug-induced changes in flow.

DSA is a method with high potential for imaging in drug-induced vascular injury studies. Drug-induced vascular injury seen in nonclinical toxicity studies is a significant drug development concern because of a lack of understanding of animal model-human patient concordance and lack of sensitive translational biomarkers. This toxicity is seen in both rodent and non-rodent animal species, and is most commonly associated with molecules that cause vasodilation or vasoconstriction (i.e. vasoactive molecules) (Greaves 2000; Loudon, Brott et al. 2006). Also, drug-induced myocardial injuries occasionally occur with a regional distribution in the heart that suggests an ischemic origin (e.g. subendocardial, left ventricular, apical predilections). Unlike clinical situations, these injuries frequently occur in the absence of coronary artery occlusion. Current nonclinical methods do not allow direct visualization of drug-induced changes in vascular tone or structural integrity with non-invasive methods that might be translational to the clinical setting. DSA enables a more direct evaluation of vascular tone and integrity of coronary arteries where vascular injury can occur in rodents (Yuhás, Morgan et al. 1985).

Another DSA application could be ischemic heart disease. The paper by (Csonka, Kupai et al. 2010) presents different techniques to measure infarct size in clinical and preclinical studies. We have previously published on delayed enhancement micro-CT imaging to estimate both the size of the infarct as well as cardiac function (Nahrendorf, Badea et al. 2007). Dobutamine induced cardiac stress can be also assessed with micro-CT imaging (Badea, Hedlund et al. 2011). Our imaging system can, in fact, be used for combined micro-CT and DSA imaging (Badea, Hedlund et al. 2006). Therefore, we could conceivably design experiments that would use DSA to visualize rapid changes in coronary circulation and myocardial perfusion; and use micro-CT for 3D morphological information and to estimate cardiac function measures such as cardiac output, ejection fraction, stroke volume.

Finally, the proposed DSA imaging method has the advantage that can be readily translated to the clinical setting providing yet one more valuable imaging tool for assessing drug safety and toxicity from rodent to man.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

All work was performed at the Duke Center for In Vivo Microscopy, an NIH/NCRR national Biomedical Technology Research Center (P41 RR005959), with additional support from NCI (U24 CA092656).

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Figure 1.

For coronary artery DSA in the rat, an imaging sequence starts by bringing the x-ray anode rotor up to speed and suspending ventilation at end-expiration. The interval between each R wave is ~ 300 ms. Each 10-ms exposure and subsequent camera readout is initiated at the same delay after the peak R wave. A series of non-contrast images are acquired to create the mask. A 150-ms injection of Isovue is triggered followed by the acquisition of post-contrast injection images, again at the same point in the cardiac cycle. The whole sequence lasts about 8-10 seconds yielding a stack of 30 different frames.

Figure 2.

A dedicated image pipeline has been developed in MATLAB to automatically process the serial DSA images. We generate the average mask from pre-injection frames and subtract it from the post-contrast images to produce the vascular only DSA images.

Figure 3.

The effect of catheter tip position on visualizing coronary arteries is illustrated for two different animals. (A) and (C) are ventral/dorsal projections, and (B) and (D) are lateral projections. In first animal (A, B), the catheter tip appears to be touching the cranial surface of the aortic valve (red arrow) and apparently obstructing the orifice of the left coronary artery, whereas in second animal (C, D), the tip of the catheter (blue arrow) is well above the valve, and both arteries and branches are clearly seen.

Figure 4.

DSA images corresponding to the heartbeat with the maximum enhancement of the coronary arteries selected for tests where either the injector pressure or the time for injection were varied. Note that the best trade-off between the injection time, pressure, and image quality is achieved at 60 PSI, 150 ms injection (see green square).

Figure 5.

The injected volume is linearly related to the pressure driving the injector and the injection duration. A visual inspection of Figure 4 favors the image corresponding to 60 PSI, 150 ms corresponding to a volume of injected contrast agent of 113 microL. This volume is sufficient.

Figure 6.

The tests involved multiple injections (60 PSI, 150 ms) at different delay times from the R peak. The RR-interval was approximately 200 ms. Note that the visualization is slightly improved when the injection occurs early in diastole, 60 ms delay.

Figure 7.

These DSA images illustrate the effects of nitroprusside (NP) infusion on coronary arteries. Row A shows selected images before NP infusion (–5 minutes), during NP infusion (2 to 3 minutes), and after infusion has stopped (5 to 20 minutes). Note that dilation of the coronary arteries occurs within minutes of infusion and persists for at least 7 minutes after cessation of NP infusion, and after 17 minutes, the coronary arteries have returned to pre-infusion caliber. Row B shows the first 7 frames of the pre-infusion sequence (–5 minutes) and row C shows the first 7 images of the 8-minute sequence. In row C, after the first frame, note the evidence for myocardial perfusion as the ventricular walls are darkened.

Figure 8.

Perfusion maps from the study shown in Figure 7. Note the maximum perfusion occurs in the 8-minute sequence, 5 minutes after cessation of NP infusion. 25 minutes later, the perfusion levels have returned to pre-infusion levels.