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Harrison JK

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Image Quality and Coronary Blood Flow Assessment: The Influence of Radiographic Contrast

J. K. Harrison

The growth of percutaneous coronary intervention has been fostered by technological progress in many areas, including vast improvements in angiographic image quality. Achieving optimal outcomes in coronary intervention requires real-time review of detailed, high resolution images of the coronary vasculature.

The role of radiographic contrast in obtaining optimal coronary angiograms is often overlooked. We studied the image quality provided by 4 different contrast agents, using an *in-vitro* model to simulate coronary vessels. Phantom vessels, ranging from 0.5 to 3.0 mm in diameter, were filled with 1 of 4 contrasts, which varied with respect to chemical composition and iodine concentration. The contrast compounds employed were: 1. ioxaglate (320 mgI/ml), 2. iodixanol (320 mgI/ml), 3. iopamidol (370 mgI/ml), and 4. iomeprol (400 mgI/ml). Radiographic images of these contrast filled phantoms were obtained in a catheterization suite using a Phillips Digital Cardiac Imaging system.

Quantitative analysis of these image data demonstrated that the peak and mean videodensity was directly related to the iodine concentration of the agents being studied. Qualitative analysis of image pairs, graded by 8 angiographers blinded to the contrast used to generate them, demonstrated a clear preference for the images obtained with the higher iodine containing contrast agents. Whether the improvement in image quality demonstrated in this *in-vitro* study will translate into clinically important differences in human coronary arteriography requires further investigation. However, review of the recent literature suggests that image quality enhancement improves diagnostic accuracy in cardiac angiographic procedures, such as the detection of coronary thrombi and coronary dissection. *J Clin Basic Cardiol 2001; 4: 249-51.*

Key words: coronary angiography, angioplasty, radiographic contrast, myocardial perfusion

Invasive cardiology has grown exponentially over the last two decades, thanks in part to improvements in radiographic contrast agents. Cardiac catheterization and coronary angiography, procedures once considered to be fraught with considerable risk, have become commonplace. The relative safety and benefits of the procedures have allowed even small community hospitals to provide these services.

Improvements in diagnostic imaging, especially related to coronary angiography, have been part of the foundation for the tremendous growth and success of percutaneous coronary interventions. The high osmolar ionic contrast agents introduced in the 1950s and 60s had common toxic side effects including nausea, vomiting, severe bradycardia, hypotension, frequent ventricular fibrillation, pulmonary oedema, and occasional anaphylactic reactions. These early ionic agents have now been largely replaced by the non-ionic contrast agents introduced in the mid 1980s. These non-ionic contrast molecules have inherently lower osmolality than their ionic counterparts. Their improved tolerance has also been attributed to their large polar organic side chains, which serve to conceal their X-ray attenuating iodine atoms. These non-ionic agents have provided greater patient comfort and tolerance. These agents can now be employed, even in long cases involving complex coronary interventions, with relative disregard on the part of the operator for acute contrast complications. While renal toxicity continues to be a potential concern for all radiographic contrast agents, not solved by the non-ionic molecules, the cardiac rhythm and haemodynamic alterations common to the original ionic contrast agents have all but been eliminated by the newer non-ionic contrast molecules.

In addition to the improved tolerance of the newer contrast agents, many other factors have afforded the growth and success of percutaneous coronary interventions (PCI). Operator expertise and experience have probably been the most important factors in the success of PCI over the last two

decades. The tremendous technological advances in device and pharmacologic development are of clear and paramount importance as well. Additionally, the improvements in X-ray systems and angiographic image quality, which have occurred over this same period, have promoted the success of PCI.

Radiographic imaging systems have improved vastly over this period. Perhaps most important in this regard is the development and use of digital imaging systems. These systems allow the operator immediate playback and review of current and previous image sequences. Software enhancement of these digital angiographic images provides improved image quality compared with the analog images of a decade ago. Whether the iodine concentration of the contrast agent employed for coronary angiography influences image quality is unclear.

This issue was recently investigated using an *in-vitro* model at Duke University Medical Center. Phantoms of coronary vessels were created by drilling precise cylinders of various diameters in Lucite blocks. The lumen diameters varied from 0.5 to 3.0 mm to simulate diameters typical of coronary vessels. The coronary phantoms were filled with one of four commercially available contrast agents: iodixanol, ioxaglate, iopamidol and iomeprol. These contrast agents vary in iodine concentration: the first two contain 320 mgI/ml, iopamidol contains 370 mgI/ml and iomeprol contains 400 mgI/ml. The contrast filled phantoms were imaged using a Phillips Digital Cardiac Imaging catheterization laboratory, standardly used for clinical coronary angiography. Digital images were obtained at four X-ray settings ranging from 65 to 108 kVp. Images were obtained in the straight anterior-posterior projection. A 1 cm grid was simultaneously imaged for measurement standardization. These coronary phantom image sequences were repeated with each of the 4 contrast agents, at the four different X-ray settings.

The images so obtained were analyzed quantitatively with respect to image videodensity and lumen diameter. Peak and

From the Division of Cardiology, Duke Medical Center, Durham, U.S.A.

Correspondence to: J. Kevin Harrison, MD, Associate Professor of Medicine, Division of Cardiology, Box 3331, Duke University Medical Center, Durham, N. C. 27710, U.S.A.; e-mail: harri015@mc.duke.edu

mean videodensity was measured across the contrast filled phantom vessel. Using edge detection software developed in our laboratory, lumen diameters were measured and compared to the known diameter of the coronary phantom.

The peak videodensity of the contrast filled lumen was directly related to the iodine concentration of the contrast agent. This was true regardless of the lumen diameter or X-ray parameter. Peak and mean videodensity averaged 6 % greater in the iomeprol-400 mgI/ml images compared with the iopamidol-370 mgI/ml images. Videodensity of the iomeprol images averaged 16 % greater than either of the 320 mgI/ml contrast agents. In addition, images obtained with 400 mgI/ml contrast more closely approximated the known luminal diameter of the vessel phantoms, although this difference between contrast agents did not reach statistical significance.

In addition to these quantitative analyses, qualitative assessment of the images was performed. Eight experienced coronary angiographers evaluated 72 image pairs. The image pairs were displayed side by side on a single monitor. The image pairs were selected from the phantom image sequences of a particular lumen diameter and given X-ray setting. Image pairs represented coronary phantoms filled with contrast of different or the same iodine concentration. The angiographers, blinded to how the coronary phantom images differed, were asked to judge the left panel image quality superior, inferior or the same as the image quality of the right panel. The results of this qualitative image quality analysis are summarized in Table 1.

Thus, while one might have anticipated that image videodensity measured quantitatively would be related to the iodine concentration of the contrast agent, the qualitative difference in image quality was striking. This qualitative difference was most profound when comparing images obtained with 400 vs 320 mgI/ml contrast. Whether the finding of this *in-vitro* investigation will hold true for clinical coronary angiography requires further investigation. Some interesting considerations can already be made.

To date, very little attention has been paid to image quality as a function of contrast iodine concentration in human clinical trials. The study of Schrader and colleagues is of interest in this regard [1]. The primary endpoint of the study, the clinical outcome of percutaneous coronary intervention patients randomized to the use of iomeprol vs ioxaglate, was not different. Iomeprol and ioxaglate vary with respect to iodine concentration; 350 vs. 320 mgI/ml, respectively. Interestingly, angiographic differences were seen between the iomeprol and ioxaglate groups. Despite similar patient demographics, coronary thrombus prior to coronary intervention was detected more frequently in the iomeprol group compared to the ioxaglate patients (4.2 % vs 2.7 %, respectively, $p = 0.04$). Coronary dissection following intervention was visualized more frequently as well in the iomeprol patients compared with the ioxaglate group (30.2 % vs 25.0 %, respectively, $p = 0.01$).

Thus, the diagnostic output was greater with iomeprol than with ioxaglate (Tab. 2). Himi et al. have demonstrated that a further increase in iodine concentration up to 400 mg/ml (osmolality, 720 mosmol/kg; viscosity, 12.6 mPa \cdot s) is associ-

ated with further improvement. In 20 patients undergoing diagnostic cardiac catheterisation, densitometric measurements on the left coronary artery revealed that the radiographic density of iomeprol 400 was 13 % greater than that of iomeprol 350 [2]. These data suggest that as little as a 10–15 % increase in iodine concentration may provide a visible, and clinically significant, difference in clinical coronary angiography. The issue of contrast iodine concentration has the potential to be of even greater clinical relevance as we move to smaller, 5 and 4 Fr, coronary catheters. The answer to this question awaits a randomized comparison of human coronary angiograms obtained with contrast agents of varying iodine concentration.

Finally, while a great deal of attention has been paid over the last 2 decades to the visualization of epicardial coronary anatomy and lesion morphology, several recent studies have shifted the focus downstream [3–5]. These studies have focused their attention on the coronary microvascular circulation as assessed by coronary angiography. Coronary flow in the epicardial vessels, as semi-quantitatively assessed using the TIMI flow score, has been shown to be related to mortality in studies evaluating reperfusion strategies for acute myocardial infarction [6]. In attempts to further quantify these epicardial flow rates, the TIMI frame count has been used for research purposes and has been shown to contain similar prognostic information [7].

In 1998, van't Hof and colleagues reported that contrast assessment of the coronary microvasculature contained prognostic information beyond what one could determine from the epicardial TIMI flow score [4]. They studied the coronary arteriograms of 777 acute myocardial infarction patients treated with primary angioplasty. They graded the intensity of the myocardial contrast blush distal to the infarct vessel using a semi-quantitative score from 0 to 3 (Tab. 3). These authors showed that the intensity of the myocardial blush so graded was inversely related to the infarct size, and was directly related to left ventricular ejection fraction and 30 day survival.

Gibson and colleagues similarly related angiographic contrast blush to mortality following acute myocardial infarction [5]. They studied the coronary angiograms of 762 acute myocardial infarction patients treated with thrombolytics, either TNK or tPA, in the TIMI 10B trial. They graded the contrast blush distal to the infarct lesion using a semi-quantitative scale. This blush score differed somewhat from the score of van't Hof (Tab. 3). This score graded contrast blush based on the entrance and clearance time of the contrast

Table 1. Qualitative image quality as a function of iodine concentration; *in-vitro* analysis of 8 angiographers grading 72 image pairs

	Superior	Same	Inferior
Iomeprol 400 vs:			
Iopamidol 370	43 %	52 %	5 %
Iodixanol 320	82 %	16 %	2 %
Ioxaglate 320	90 %	7 %	3 %

Table 2. German iomeprol vs ioxaglate trial

	Iomeprol (n = 1001)	Ioxaglate (n = 999)	P
IC-Thrombus pre-PCI	4.2 %	2.7 %	0.04
Post-PTCA Dissection	30.2 %	25.0 %	0.01
Stent use	31.6 %	25.7 %	0.004

Table 3. Myocardial blush grades

Grade	van't Hof et al. [3]	Gibson et al. [4]
0	No contrast blush	No contrast entry into microvasculature
1	Minimal contrast blush	Slow microvasculature contrast entry, fails to exit
2	Moderate contrast blush	Delayed entry and exit of microvasculature contrast
3	Normal contrast blush	Normal entry and exit of microvasculature contrast

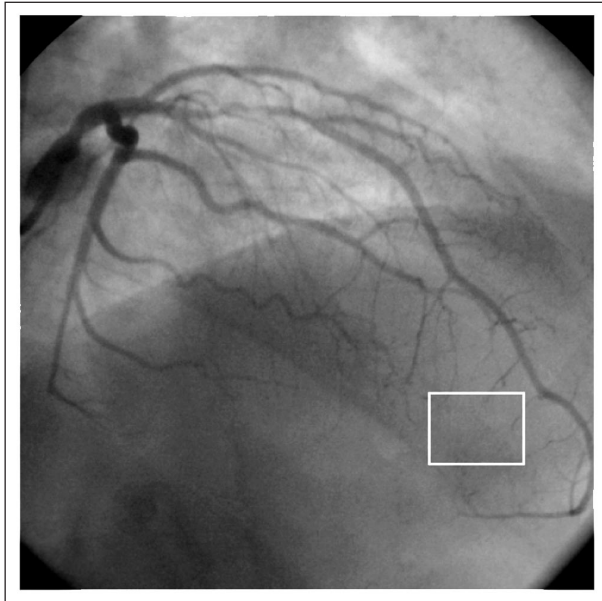


Figure 1. Left coronary angiogram in the right anterior oblique projection demonstrating stenosis in the proximal left anterior descending coronary artery. The box defines a region of interest, downstream to the coronary lesion, in which myocardial contrast blush can be measured.

blush. Using this scoring system, myocardial tissue perfusion of the distal coronary bed, graded by radiographic contrast blush, was found to be inversely related to 30 day mortality. They also reported that, in the group of patients with normal epicardial coronary flow, defined by TIMI 3 flow, prognosis could be better defined by myocardial blush score.

Thus, advances in coronary imaging over the last two decades have promoted the growth and success of non-surgical coronary intervention. Recently, the emphasis has shifted further downstream, from analysis of epicardial vessel morphology and flow, to an assessment of the coronary microvasculature using contrast coronary angiography. Further refinement of the assessment of myocardial contrast blush, employing computer assisted algorithms to quantify blush intensity and washout rates, may provide a tool for defining regional myocardial tissue perfusion (Figs. 1 and 2). Such a quantitative myocardial perfusion tool would be of great merit. Such measurements would be useful in research studies designed to improve the outcome of coronary reperfusion strategies and percutaneous coronary interventions. Such a metric, if rapid and reproducible, could even be employed routinely on a clinical basis to help the interventionalist define the state of the myocardium before, during and following coronary intervention.

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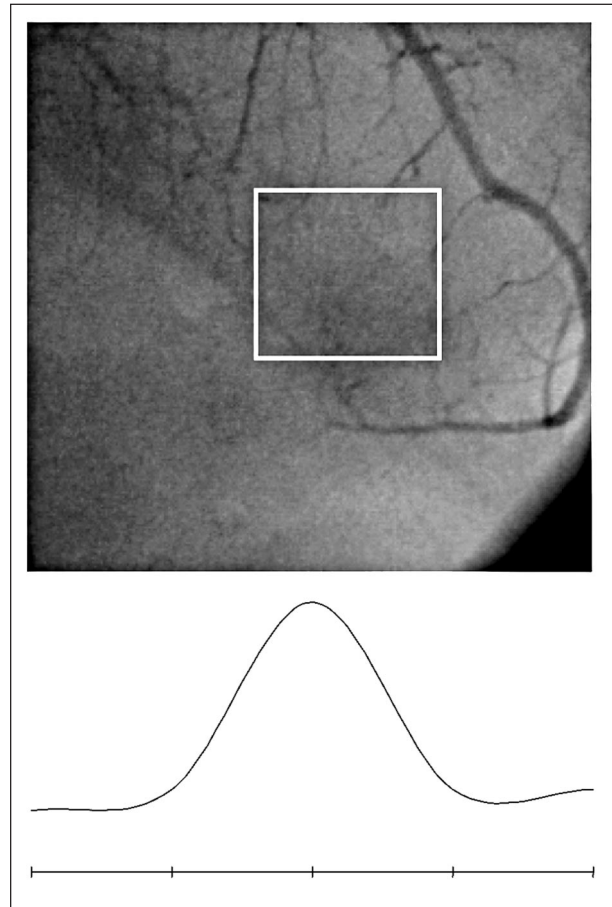


Figure 2. Upper panel: Magnified view of the region of interest (ROI) shown in Figure 1. Lower panel: Mean videodensity in the ROI plotted as a function of time.

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