

# UCLA

## UCLA Previously Published Works

### Title

Comparison of contrast enhancement, image quality and tolerability in Coronary CT angiography using 4 contrast agents: A prospective randomized trial

### Permalink

<https://escholarship.org/uc/item/33g54973>

### Authors

Honoris, Lily  
Zhong, Yan  
Chu, Edwin  
et al.

### Publication Date

2015-05-01

### DOI

10.1016/j.ijcard.2015.03.240

Peer reviewed

ClinicalTrials.gov Identifier: NCT01534975

**Comparison of contrast enhancement, image quality and tolerability in**

**Coronary CT angiography using 4 contrast agents: A prospective Randomized Trial**

*Lily Honoris, Yan Zhong, Edwin Chu, David Rosenthal, Dong Li, Franklin Lam, Matthew J Budoff*

Contact Information: Matthew Budoff, MD

1124 W Carson St

Torrance, CA 90502

[mbudoff@labiomed.org](mailto:mbudoff@labiomed.org)

310 222-4107

Fax (310) 787-0448

Key Words – contrast, iodine, cardiac CT, coronary ct angiography

Cardiac CT Angiography (CCTA) is a robust method for detecting obstructive CAD, with high sensitivity and specificity. Accuracy in analyzing coronary stenosis is reliant on quality of CCTA images and is largely heart rate dependent.<sup>1,2</sup> Several studies have suggested that low-osmolality contrasts affect heart rate variability, through hyperemia due to their interaction with endothelial cells and injection pain.<sup>3,4</sup> Iso-osmolality contrasts may not cause dilution which can degrade and affect intravascular enhancement. The beneficial effects of non-ionic contrast agents on image quality and resolution of CCTA and patient satisfaction is not well studied. We hypothesized that while image brightness varies by iodine content, both low-osmolality and iso-osmolality contrasts will yield high image quality and good safety profile. We undertook a prospective randomized trial to compare image quality, safety and patient tolerability between four contrasts with varying iodine contents: low-osmolal iohexol (350 mg I/mL) and iopamidol (370 I/mL) with two concentrations of iso-osmolal iodixanol (270 I/mL and 320 I/mL) during cardiac CT angiography.

513 sequential subjects undergoing outpatient CCTA for evaluation of CAD in a single CT scanning center were enrolled into the study (mean age 57+/-11 years). Patients randomly received one of 4 different contrast agents: iodixanol 270, iodixanol 320, iohexol 350 or iopamidol 370. The CT readers (Level 3 cardiologists) were blinded to the contrast administration used. Inclusion Criteria: >18 years old, undergoing contrast-enhanced CCTA examination, provided written informed consent. Exclusion criteria: renal insufficiency (GFR<50), known contrast allergy, pregnancy or prior revascularization. A 64-detector MDCT (Lightspeed VCT, GE healthcare, Milwaukee, USA) was used for image acquisition and scanning protocols followed the prior studies protocols(5,6). A research assistant collected a survey quantifying side effects of different contrasts: flushing, headache, nausea, and pain at

injection site as mild, moderate or severe. Readers, blinded to the contrast media used, assessed image quality by measuring contrast enhancement in aorta, myocardium, left main, proximal Left Anterior Descending, proximal and distal Right Coronary arteries. Standardized regions of interest were used (1 cm) in the ascending aorta, mid-LV ventricle and left atrium on axial slices. The largest region of interest in each coronary artery was used (manually drawn on axial slices). Heart rate(HR) variability during the scan was evaluated. A comparison of the degree of contrast enhancement of the coronary lumen, as well as their differences on each of the contrast agents were measured, stratified by 100 kVp and 120 kVp acquisition. The image quality of 17 coronary artery segments was graded by two cardiologists in consensus with the use of a four-point scale (1= excellent, 2=good, 3=fair , 4= poor enhancement) blinded to contrast agent administration.

Subjects' characteristics were collected prior to CCTA acquisition and heart rate was captured before and following contrast delivery and the results are shown in Table 1. The vascular enhancement using the different contrast agents: iohexol, iopamidol and iodixanol all show clear delineation between enhancement in lumen, calcified and non-calcified plaques. Mean vascular enhancement across all segments measured are highest in iopamidol followed by iohexol, iodixanol 320 and iodixanol 270 respectively ( $p < 0.002$ ). Image quality (4 point scale) was highest with Iodixanol 320 and 270 (3.27/4.0), and lower with Iohexol (3.20) and Iopamidol (3.07),  $p = 0.09$ , table 3. Although iopamidol yield the brightest vascular enhancement, the images obtained using iohexol and iodixanol were similarly of high image quality and interpretable. The most commonly cited side effects was flushing and most frequently caused by iopamidol (78%; 95% CI 59-87%) followed by iohexol (72%; 95% CI 55-85), iodixanol 320 (58%; 95% CI 44-79%), iodixanol 270 (46%; 95% CI 36-56%) respectively (all  $p < 0.01$ ). Other commonly cited

side effects include injection site pain, headache and nausea which are infrequently reported across all contrast agents. Heart rate variability was lowest among the Iodixanol 320(2.5 +/- 3.0), followed by Iodixanol 270(3.4 +/- 5.2), Iohexol 350(4.1 +/- 5.0) and Iopamidol 370(4.9 +/- 5.8),  $p < 0.001$ .

This trial is the first study comparing four different contrast agents with varying iodine contents for CCTA. In over 500 consecutive patients enrolled, we found that enhancement in aorta, LV cavity, myocardium and image noise of aorta showed no statistically significant differences between iodixanol and iohexol (table 2), however image quality and heart rate variability were the lowest with iso-osmolar and highest with low-osmolar agents (table 3). Iopamidol yield the brightest vascular enhancement, presumably by having the most iodine content. However, this bright vascular enhancement is at the expense of having the most side effects, (ie flushing) and the most heart rate variability. Among our subjects, there were no differences in image quality using the four agents, so one could use a lower iodine content contrast to enhance safety and tolerability without compromising image quality. This also confirms an earlier study by Cademartiri et al.[7] which evaluated iodixanol 320 versus iohexol 350 for coronary artery enhancement in 16-MDCT and found no significant difference (mean  $333 \pm 51$  H vs  $320 \pm 55$  H, respectively). Iodixanol, despite a lower iodine concentration than iohexol, still provides similar enhancement[8]. In this study, iohexol offered better vascular enhancement compared to iodixanol, even though they were all of diagnostic image quality. Iohexol has a relative cost reduction over iopamidol, with less side effects and less heart rate variability, but higher rates of flushing than both concentrations of iodixanol (Table 3). Iodixanol has the lowest rates of flushing, moderate-to-severe pain and warmth (9-11). Our study confirmed that Iodixanol resulted high image quality with the lowest rates of adverse

events, such as flushing and heart rate variability. Several studies reported that iodixanol showed less HR changes during cardiac angiography than iopamidol (12-14). In a randomized study of 300 patients, iodixanol 320 showed less HR changes compared to iohexol 350 during the scan. The current study supports this finding.

Cardiac CT requires reliable and consistent heart rates, agents that reduce heart rate variability are good options. Iodixanol 270 had the lowest rates of flushing and heart rate variability. The use of a reconstructive software such as iterative reconstruction and lowered KVp (e.g., 100Kv) with iodixanol 270 may provide additional benefit of lower radiation and lower CM exposure minimizing adverse events, while maintaining image quality. This study was not powered to evaluate renal toxicity of different contrast agents, however many studies exist demonstrating the nephro-toxicity of different agents[15]. Given that data is now emerging that use of CT angiography improves outcomes[16] and obstructive disease rates during cardiac catheterization [17], utilization of this technique will continue to rise.

Iso-osmolar and low-osmolar contrast media yield high image quality. Flushing is the most commonly cited side effects after intravenous contrast delivery and iodixanol yielded the lowest incidence. This study shows that adequate quality images may be achieved with lower iodine concentration which may have important safety and tolerability implications.

## References:

1. Giesler T, Baum U, Ropers D. [Noninvasive visualization of coronary arteries using contrast-enhanced multidetector CT: influence of heart rate on image quality and stenosis detection](#). American Journal of Roentgenology. 2002;179: 911-916.
2. Matt D, Scheffel H, Leschka S. [Dual-source CT coronary angiography: image quality, mean heart rate, and heart rate variability](#). American Journal of Roentgenology. 2007;189: 567-573.
3. Thompson BH, Stanford W. Evaluation of cardiac function with ultrafast computed tomography. Radiologic Clinics of North America. 1994;32:537–551.
4. Stanford W, Galvin JR, Weiss RM, Hajduczuk ZD, Skorton DJ. Ultrafast computed tomography in cardiac imaging: a review. [Seminars in Ultrasound, CT, MR](#). 1991;12(1):45–60.
5. Budoff MJ, Dowe D, Jollis JG, Gitter M, Sutherland J, Halamert E, Scherer M, Bellinger R, Martin A, Benton R, Delago A, Min JK. Diagnostic Performance of 64-Detector Row Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Prospective Multicenter ACCURACY (Assessment by Coronary Computed Individuals Without Known Coronary Artery Disease: Results From the Tomographic Angiography for Evaluation of Coronary Artery Stenosis in Angiography) Trial. J Am Coll Cardiol. 2008;52(21):1724-32.
6. Budoff MJ, Shittu A, Hacıoglu Y, Gang E, Li D, Bhatia H, Alvergue J, Karlsberg RP. Comparison of Transesophageal Echocardiography Versus Computed Tomography for Detection of Left Atrial Appendage Filling Defect (Thrombus). Am J Cardiol 2014;113(1):173-7.
7. Cademartiri et al. Intravenous contrast material administration at helical 16-detector row CT coronary angiography: effect of iodine concentration on vascular attenuation. Radiology. 2005 Aug;236(2):661-5.
8. Tsai, I, Lee, T, Tsai WL, et al. Contrast Enhancement in Cardiac MDCT: Comparison of Iodixanol 320 Versus Iohexol 350. American Journal of Roentgenology. 2008;190:W47-53
9. Hill JA, Cohen MB, Kou WH, et al. Iodixanol: a new isosmotic nonionic contrast agent compared with iohexol in cardiac angiography. Am J Cardiol. 1994;74:5 7-63
10. Choi TY, Woo V, Gupta M, Sourayanezhad S, Li D, Mao SS, Budoff M. Comparison of iodixanol 320 and iohexol 350 in image quality during 64-slice multidetector computed tomography: Prospective randomized study. Int J Cardiol. 2012;158:134-8. PMID: 22560910
11. Matthai WH Jr, Kussmaul WG 3rd, Krol J, Goin JE, Schwartz JS, Hirshfeld JW Jr. [A comparison of low- with high-osmolality contrast agents in cardiac angiography. Identification of criteria for selective use](#). Circulation. 1994 Jan;89(1):291-301. PMID: 8281660
12. Andersen PE, Bolstad B, Berg KJ, Justesen P, Thayssen P, Kloster YF. Iodixanol and ioxaglate in cardioangiography: a double-blind randomized phase III study. Clin Radiol 1993;48(4):268–72.

13. Hill JA, Cohen MB, Kou WH, et al. Iodixanol, a new isosmotic nonionic contrast agent compared with iohexol in cardiac angiography. *Am J Cardiol* 1994;74(1):57–63.
14. Christensen JD, Meyer LT, Hurwitz LM, Boll DT. Effects of iopamidol-370 versus iodixanol-320 on coronary contrast, branch depiction, and heart rate variability in dual-source coronary MDCT angiography. *Am J Roentgenol* 2011;197:W445–51.
15. Biondi-Zoccai G, Lotrionte M, Thomsen HS, Romagnoli E, D'Ascenzo F, Giordano A, Frati G. Nephropathy after administration of iso-osmolar and low-osmolar contrast media: evidence from a network meta-analysis. *Int J Cardiol*. 2014 Mar 15;172(2):375-80.
16. Budoff MJ, Liu S, Chow D, Flores F, Hsieh B, Gebow D, DeFrance A, Ahmadi N. Coronary CT angiography versus standard of care strategies to evaluate patients with potential coronary artery disease; effect on long term clinical outcomes. *Atherosclerosis* 2014;237:494-498.
17. Patel MR, Dai D, Hernandez AF, et al. Prevalence and predictors of nonobstructive coronary artery disease identified with coronary angiography in contemporary clinical practice. *Am Heart J* 2014;167:846-852.e2.