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Citation: AIP Advances **8**, 095005 (2018); doi: 10.1063/1.5030796
View online: https://doi.org/10.1063/1.5030796
View Table of Contents: http://aip.scitation.org/toc/adv/8/9
Published by the American Institute of Physics

Movement compensation during carbon dioxide coronary angiography: In-vitro validation

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(Received 26 March 2018; accepted 27 August 2018; published online 7 September 2018)

The aim of this in vitro study was to evaluate the feasibility of movement compensation for CO_2 coronary angiography. The use of CO_2 as a contrast medium for coronary angiography in a routine clinical setting is still premature. Nonetheless, the gas can solve most of the problems related to iodine contrast-induced nephropathy and can be safely used for patients with renal insufficiency. In a previous work [I. Corazza *et al.*, AIP Adv. **8**(1), 015225 (2018)], we demonstrated that an adequate setting of the CO_2 injection parameters (pressures and volumes) allows gas injection into the coronaries, avoiding reflux into the aorta and cerebral circulation. A mechanical mock simulating coronary circulation and movement was used to simulate different CO_2 injection conditions. Simultaneous acquisition of ECG and optical images allowed synchronous frame extraction for post-processing analysis, like masking and stacking processes. A single test with a radiological apparatus was done to demonstrate the feasibility of the technique. By injecting CO_2 at a pressure between the dicrotic notch and diastolic value, no reflux into the aorta was observed and the new software yielded final optical images of clinical quality after about 8 seconds of injection. The feasibility test under the X-ray apparatus gave promising results. CO_2 coronary angiography is still far from becoming a clinical standard, but our bench evaluation demonstrates that if the injection parameters are well-controlled and physiological values known, CO_2 can be used as a contrast agent not only for the lower part of the body, but also for the coronary arteries, respecting basic safety standards.
https://doi.org/10.1063/1.5030796

INTRODUCTION

CO_2 arteriography is currently undertaken only for the lower part of the body to avoid the potential risk of cerebral ischemia.[1–3] As iodine contrast is nephrotoxic, the possibility to extend CO_2 angiography to the coronary arteries could be of great benefit for patients with renal insufficiency.[1,4–7] To explore this scenario, we built a mechanical model of the coronary circulation to evaluate the relationship between CO_2 injection and hemodynamic parameters to avoid arterial reflux and minimize the risk of ischemia.[8,9] We previously demonstrated that an injection pressure (*InPs*) between the dicrotic notch and the diastolic value with a high resistance catheter can generate a lower injection flow than that of blood, thereby allowing safe injection without reflux into the aorta. In the wake of our encouraging results, we improved our system by adding a simulator of coronary movements

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to test the feasibility and accuracy of image reconstruction in dynamic conditions. Since the gas substitutes blood inside the vessel during CO_2 angiography, the duration of the procedure necessary to obtain a final stacked image of good clinical quality must be established to make this technique feasible in clinical practice and avoid ischemic injury. Common durations of balloon inflation during angioplastic procedures[10] were taken as reference values to avoid ischemic damage.

MATERIALS AND METHODS

A mechanical simulator of the cardiovascular system[8,11–13] was modified and the coronaries support was connected to the ventricular pump to allow a circular periodic movement. The system is fitted with a device to simulate the myocardial coronary constriction, producing a fully diastolic left coronary flow, as occurs in a physiological setting. The system is depicted in figure 1.

The pumping frequency was fixed at 72bpm, the stroke volume at 10ml, and the aortic pressure at 130/75mmHg (dicrotic pressure=120mmHg). Aortic and coronary blood flows were monitored by the electromagnetic Biotronex BL610 system with 7mm and 3mm probes. To inject CO_2 gas a Cordis® ARIMOD100cm, 2F catheter (1F=1/3mm) was used (hydraulic resistance: 80mmHg/ml/s.[8] Room temperature was 20°C and medical grade 99.8% CO_2 gas was used.

Ventricular, aortic and gas *InPs* were monitored by three Statham P23 transducers and conditioned with an Esaote EP12 polygraph. Analog signals were sampled, digitally converted and stored by the Anscovery System (Sparkbio Srl, Bologna, Italy). Video recording during injection was performed using a digital camera (model acA 1300- 75gc, Basler, Ahrensburg, Germany) interfaced with a Matrox Concord Card (Matrox, Dorval, Quebec, Canada) connected and synchronized to the Anscovery System,[14] positioned above the coronaries, back-lighted and filled with a red-colored saline solution. Video was acquired at a rate of 25fps and a frame dimension of 1280x1024 pixels.

Since the Anscovery System allows single frame extraction, the rising edge of the ECG signal was used as time reference. For each QRS complex, the frames corresponding to increasing delays from 0ms to 750ms with steps of 50ms were extracted. All the imaging operations on frames (filtering, DSA, stacking, etc) were made by dedicated and not commercial software developed in our laboratory with Microsoft Visual Studio 2015. The experimental protocol was structured as follows:

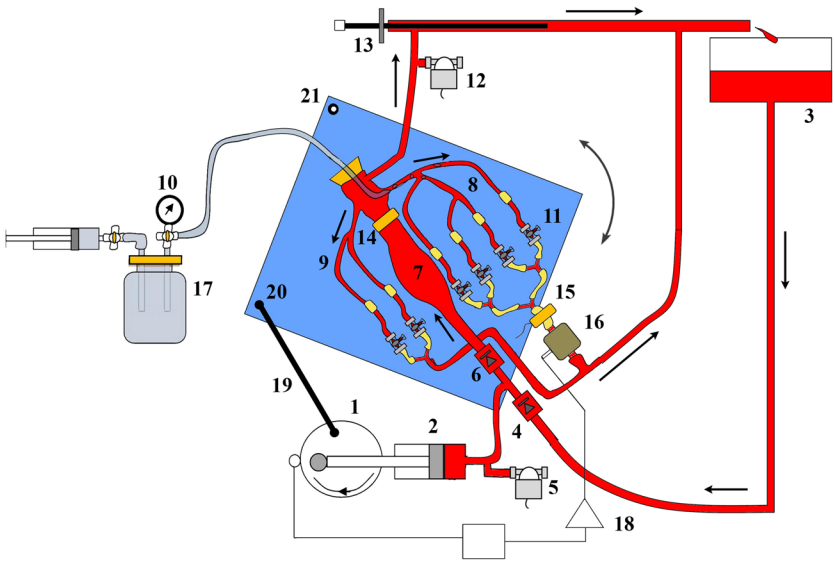

FIG. 1. Scheme of the cardiovascular model - (1) Motor, (2) Pumping syringe; (3) Atrium; (4) Mitral valve; (5) Ventricular pressure transducer; (6) Aortic valve; (7) Aorta; (8) Left coronary branch; (9) Right coronary branch; (10) Catheter; (11) Stopcocks; (12) Aortic pressure transducer; (13) Aortic hydraulic resistance regulator; (14) and (15) Electromagnetic flowmeter probes; (16) Electric valve; (17) Rigid chamber filled with CO_2; (18) Feedback circuit to drive the electric valve; (19) Moving arm connecting the motor to the (20) movable table with coronaries; (21) Rotation pivot.

(1) Acquisition of 1 minute of video recording and signals without injection (to create the mask for the Digital Subtraction Algorithm [DSA]);
(2) Start of injection at an initial reservoir pressure of 120 mmHg chosen to avoid reflux into the aorta.[8]
(3) Stop acquisition when the injection pressure drops below the diastolic pressure.
(4) Extraction of all the frames series from 0 to 750ms of delay with respect the to the rising edge of the ECG signal;
(5) Conversion of the frames into gray scale, 16 bit depth;
(6) For each series (delay from 0 to 750ms), creation of the mask by means extracted frames before injection (see point 1);
(7) Application of DSA to all the extracted series of frames after a shift/rotation correction to better superimpose the images;
(8) Stacking algorithm to create the final angiographic images for each series;
(9) Image filtering to enhance contrast and highlight the clinical information (thresholding, erosion and contrast improvement).[15]

Special attention was paid to the evaluation of the minimum number of frames necessary to have a complete and good final stacked image of the left coronary. Then, a case study in a radiological setting was done to demonstrate the feasibility of our proposal. An X-ray apparatus (Sias, Bologna, Italy) and a flat panel PaxScan 4030CB (Varian Medical System, Palo Alto, CA, USA) were used to acquire images of the coronaries of our mechanical mock. Since the images are acquired with a different system from that used for the optical images previously described, we developed and used a different algorithm based on a matrix correlation between selected ROIs to extract the synchronized frames. A frame rate of 25fps was set.

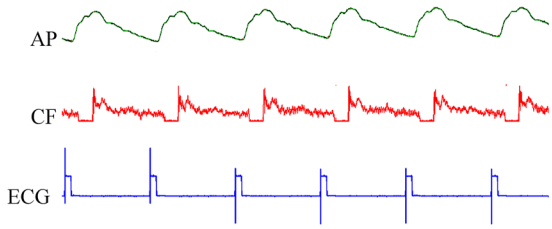

FIG. 2. Example of acquired signals: aortic pressure (AP); coronary flow (CF); ECG (the vertical blue lines represent the markers used to extract the frames of interest).

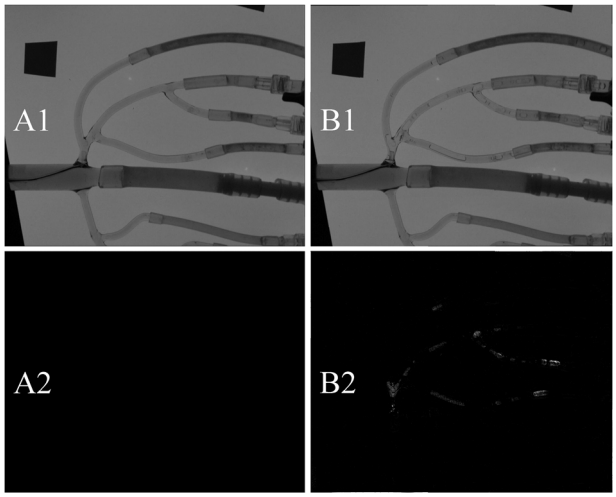

FIG. 3. Examples of extracted frames (A1, B1) and post processing elaboration. A1 is the mask used for DSA. Line 2 shows the result after DSA.

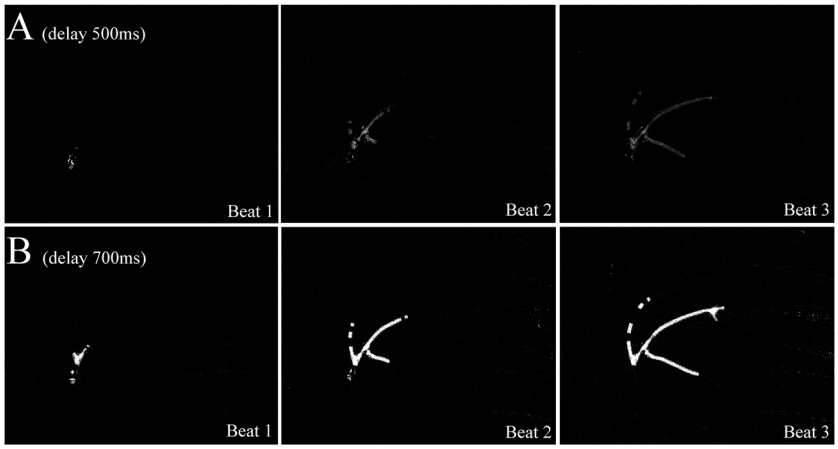

FIG. 4. Subtracted images of three frames of the first consecutive three beats at different delays. Line A corresponds to a delay of 500ms and line B a delay of 700ms.

RESULTS

Figure 2 shows an example of acquired signals (ECG, aortic pressure and coronary flow).

Since the coronaries dimensions and resistances were settled to be in a physiological range and the arterial pressure values are physiological, the measured mean coronary flow (≈1.5ml/s) results in a physiological range.

Figure 3 presents some examples of gray-converted frames corresponding to the arising phase of the ECG at different times with the corresponding subtracted images.

Figure 4 shows the result of DSA of two series of frames corresponding to three consecutive beats at different delays (500 and 70ms) with respect to the rising part of the ECG waves. Since

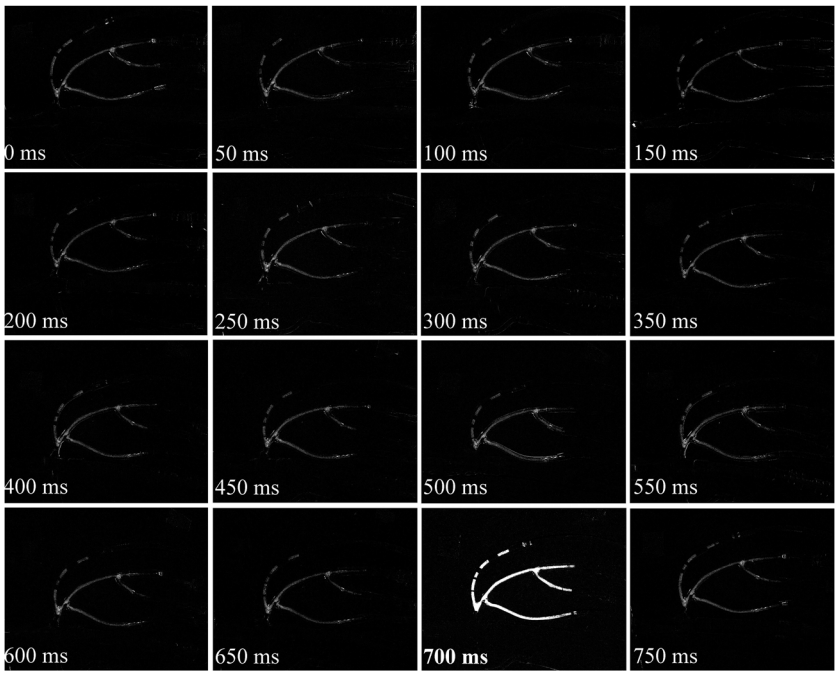

FIG. 5. Stacked images of the first five beats at the different delays (0 to 750ms). (The image with a delay of 700ms was contrasted since it is the forerunner of the one showed in figure 6).

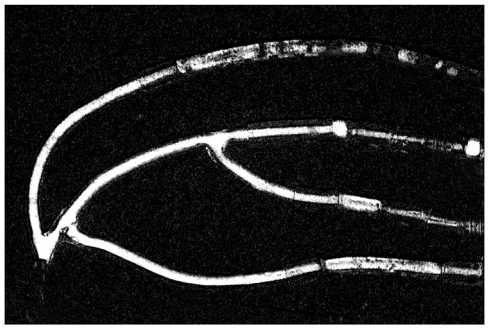

FIG. 6. Final stacked image at a delay of 700ms.

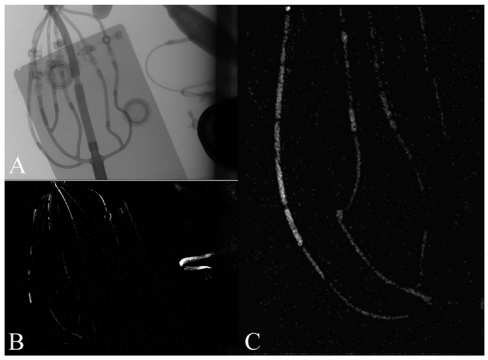

FIG. 7. Example of images acquired with an angiographic system. (A): A frame after flat-field correction; (B) Same frame after DSA; (C) Final image of the left coronary.

both the delays considered correspond to the diastolic phase when coronary flow is not zero, bubble dimensions and positions change in time and beat-by-beat.

Figure 5 shows the frames series obtained after the stacking the frames with different delays (from 0 to 750ms) of the first five consecutive beats. The coronary movements are visible. Figure 6 shows the final image after ten beats (about 8s total duration) obtained by stacking all the frames at the same delay (700ms). Considering the pressure decay inside the reservoir during 8s, the injected gas useful to produce the final image was of about 4ml.

To test the feasibility of our proposal a single image on a radiological setting was acquired and the results are shown in Figure 7. The presented image refers to the stacking process of 11 beats (about 9s of injection).

DISCUSSION

CO2 arteriography is currently confined to the lower part of the body to avoid the risk of gas reflux to the brain. In our previous work,[8] we demonstrated that a fine control of the injection parameters (pressures and flows), with respect to hemodynamic criteria reduces risk of reflux and allows angiography of the coronary arteries.

This study focused on the problem related to coronary movements. Peripheral vessels are in a fixed position and any movement is related to the patient (for example, due to patient pain). This makes the imaging procedures (DSA and stacking) quite straightforward. Moreover, the protocols implemented on commercial X-ray machines compensate for small movements to obtain better images.

Working with the coronaries, the movement of the heart during contraction becomes a major problem for accurate DSA and stacking. The X-ray images must always be extracted at the same times during the cardiac cycle by synchronizing frame extraction to a reference signal (i.e. ECG). To

test this hypothesis, we acquired optical video recording of the coronaries during CO_2 injection in a moving mechanical model of the cardiovascular system. Frames corresponding to different delays (0 to 750ms) with respect to the rising phase of the simulated ECG were extracted and a final image of the coronaries obtained for each coronary position (Figure 5). Although the stacked image in Figure 6 still presents noise and problems related to the light reflexes on the glass tubes, it correctly shows the coronary lumens and demonstrated the feasibility of the procedure. This image was obtained after ten beats (about 8s of total duration) and this time is quite low and adequate to avoid ischemic damage.[10]

Similar indications arise from the case study in a radiological setting. Although the radiological parameters (kV and mA) were not optimized, the results show that coronary imaging is possible (see Figure 5) after a low number of beats, avoiding ischemic damage. We tested our hypothesis at a frame rate of 25fps and an in-depth evaluation of the radiological results at lower rates (i.e. 10fps) is necessary. But by correctly selecting frames and compensating vessel movements angiography with CO_2 seems possible.

Obviously our results are strictly related to the rigorous control of the gas injection parameters. The procedure may be very difficult to perform in a clinical setting due to the hemodynamic parameters (heart rate, pressures, flows) changing beat to beat.

Our main simulation was done with an optical system and only a simple feasibility test with an experimental low power (15 kW) RX apparatus (fixed kV and mA). Next step will be a protocol on animal model (pigs), with operative problems very complex, mainly for technological set (angiographic high power apparatus). In this perspective, in this phase the analysis was focused to optimize aspect which probably will arise in the animal testing: pressure monitoring, arterial catheter introduction, heart rate monitoring, precise pressure gas injection, respiration control, arrhythmias, etc. This is necessary also for the ethical committee approval.

CONCLUSIONS

Despite our work was eased since it was done with a fully controlled mechanical mock of the cardiovascular system and mainly with optical images, the results demonstrate that a correct and strict settings of the injection and clinical parameters together with a powerful frames extraction tool and imaging software make coronary angiography with CO2 feasible and reliable.

The small quantity of injected gas (4ml) and the small amount of frames (about 10) to obtain a good final image are promising to implement CO2 angiography on humans, in a safe clinical environment. Next steps to be made to reach this result are: (1) optimization of vessels imaging, deepening the relationships between injection and hemodynamic parameters, so to face all the problems related with human physiology, such as not constant heart rate, arrhythmias, different aortic and ventricular pressures and flows, respiration patterns and, obviously the presence of pathologies; (2) animal testing to study all the operative problems related to RX apparatus commonly used in cardiological laboratories and to properly test the evidences highlighted in step 1; (3) human testing. The first step is the currently object of interest of our research group.

A long and difficult road lies ahead before our results can be implemented in a real clinical setting. Nonetheless, our preliminary findings are promising and pave the way for CO_2 coronary angiography on nephropathic patients in the not-too-distant future.

[1] J. G. Caridi and I. F. Hawkins, J. Vasc. Interv. Radiol. JVIR **8**, 383 (1997).
[2] P. B. Dimakakos, T. Stefanopoulos, A. G. Doufas, M. Papasava, A. Gouliamos, D. Mourikis, and H. Deligiorgi, AJNR Am. J. Neuroradiol. **19**, 261 (1998).
[3] C. R. Lambert, E. J. de Marchena, M. Bikkina, and B. K. Arcement, Clin. Cardiol. **19**, 461 (1996).
[4] E. Criado, L. Kabbani, and K. Cho, J. Vasc. Surg. **48**, 527 (2008).
[5] M. Fujihara, D. Kawasaki, Y. Shintani, M. Fukunaga, T. Nakama, R. Koshida, A. Higashimori, Y. Yokoi, and on behalf of the CO_2 Angiography Registry Investigators, Catheter. Cardiovasc. Interv. **85**, 870 (2015).
[6] I. F. Hawkins, K. J. Cho, and J. G. Caridi, Radiol. Clin. North Am. **47**, 813 (2009).
[7] F. Liistro, G. Falsini, and L. Bolognese, Ital. Heart J. Off. J. Ital. Fed. Cardiol. **4**, 668 (2003).
[8] I. Corazza, N. Taglieri, E. Pirazzini, P. L. Rossi, A. Lombi, F. Scalise, J. G. Caridi, and R. Zannoli, AIP Adv. **8**(1), 015225 (2018).
[9] I. Corazza, P. L. Rossi, G. Feliciani, L. Pisani, S. Zannoli, and R. Zannoli, Phys. Medica-Eur. J. Med. Phys. **29**, 33 (2013).

[10] M. Saha, P. Poliacikova, A. de Belder, S. Holmberg, M. Clarke, R. Rajani, and D. Hildick-Smith, J. Invasive Cardiol. **25**, 28 (2013).
[11] R. Zannoli, I. Corazza, and A. Branzi, Phys. Med. **25**, 94 (2009).
[12] R. Zannoli, I. Corazza, P. Cacciafesta, and A. Branzi, J. Mech. Med. Biol. **5**, 369 (2005).
[13] I. Corazza, D. Bianchini, E. Marcelli, L. Cercenelli, and R. Zannoli, J. Biomech. **47**, 1618 (2014).
[14] I. Corazza, G. Barletta, P. Guaraldi, A. Cecere, G. Calandra-Buonaura, E. Altini, R. Zannoli, and P. Cortelli, Comput. Methods Programs Biomed. **117**, 267 (2014).
[15] R. C. Gonzalez and R. E. Woods, *Digital Image Processing*, 3rd ed. (Prentice Hall, 2007).