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Assessment of left coronary artery beat-to-beat repositioning in order to propose an optimal acquisition window for coronary MRA

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Abstract

Introduction: Coronary magnetic resonance angiography (MRA) is a medical imaging technique that involves collecting data from consecutive heartbeats, always at the same time in the cardiac cycle, in order to minimize heart motion artifacts. This technique relies on the assumption that coronary arteries always follow the same trajectory from heartbeat to heartbeat. Until now, choosing the acquisition window in the cardiac cycle was based exclusively on the position of minimal coronary motion. The goal of this study was to test the hypothesis that there are time intervals during the cardiac cycle when coronary beat-to-beat repositioning is optimal. The repositioning uncertainty values in these time intervals were then compared with the intervals of low coronary motion in order to propose an optimal acquisition window for coronary MRA.

Methods: Cine breath-hold x-ray angiograms with synchronous ECG were collected from 11 patients who underwent elective routine diagnostic coronarography. Twenty-three bifurcations of the left coronary artery were selected as markers to evaluate repositioning uncertainty and velocity during cardiac cycle. Each bifurcation was tracked by two observers, with the help of a user-assisted algorithm implemented in Matlab (The Mathworks, Natick, MA, USA) that compared the trajectories of the markers coming from consecutive heartbeats and computed the coronary repositioning uncertainty with steps of 50ms until 650ms after the R-wave. Repositioning uncertainty was defined as the diameter of the smallest circle encompassing the points to be compared at the same time after the R-wave. Student's t-tests with a false discovery rate (FDR, q=0.1) correction for multiple comparison were applied to see whether coronary repositioning and velocity vary statistically during cardiac cycle. Bland-Altman plots and linear regression were used to assess intra- and inter-observer agreement.

Results: The analysis of left coronary artery beat-to-beat repositioning uncertainty shows a tendency to have better repositioning in mid systole (less than 0.84±0.58mm) and mid diastole (less than 0.89±0.6mm) than in the rest of the cardiac cycle (highest value at 50ms=1.35±0.64mm). According to Student's t-tests with FDR correction for multiple comparison (q=0.1), two intervals, in mid systole (150-200ms) and mid diastole (550-600ms), provide statistically better repositioning in comparison with the early systole and the early diastole. Coronary velocity analysis reveals that left coronary artery moves more slowly in end systole (14.35±11.35mm/s at 225ms) and mid diastole (11.78±11.62mm/s at 625ms) than in the rest of the cardiac cycle (highest value at 25ms: 55.96±22.34mm/s). This was confirmed by Student's t-tests with FDR correction for multiple comparison (q=0.1, FDR-corrected p-value=0.054): coronary velocity values at 225, 575 and 625ms are not much different between them but they are statistically inferior to all others. Bland-Altman plots and linear regression show that intra-observer agreement ($y=0.97x+0.02$ with $R^2=0.93$ at 150ms) is better than inter-observer ($y=0.8x+0.11$ with $R^2=0.67$ at 150ms).

Discussion: The present study has demonstrated that there are two time intervals in the cardiac cycle, one in mid systole and one in mid diastole, where left coronary artery repositioning uncertainty reaches points of local minima. It has also been calculated that the velocity is the lowest in end systole and mid diastole. Since systole is less influenced by heart rate variability than diastole, it was finally proposed to test an acquisition window between 150 and 200ms after the R-wave.

Key-words: coronary magnetic resonance angiography, acquisition window, beat-to-beat repositioning uncertainty, velocity

Introduction

Although death rates due to cardiovascular diseases continue to decline [1], coronary artery disease (CAD) remains the leading cause of death worldwide with more than 7 million deaths recorded in 2002 [2]. Currently the gold standard technique for CAD diagnosis is coronary angiography, which implies an invasive procedure involving x-ray exposure for both the patient and the operator as well as potential side effects attributable to the contrast agent [3]. An alternative is magnetic resonance imaging (MRI), or more precisely coronary magnetic resonance angiography (MRA) [4].

MRI is a medical imaging technique that uses the properties of the hydrogen nucleus to produce images of inner structures of the human body [5]. Nuclei carry a positive charge and, rotating on themselves, they create a magnetic moment called *spin*. When placing the patient in the MRI machine, the hydrogen nuclei are subjected to a strong static magnetic field called B_0, whose direction often define also the Z axis. This induces the spins to align themselves along the direction of B_0 but with two possible orientations: either in parallel or opposite of B_0. As a result slightly more than half of the spins are oriented in parallel to B_0, the rest are oriented in the opposite direction, leading to a small positive sum, called net magnetization M.
The hydrogen nuclei spin at a determined frequency called the Larmor frequency (ω_0), which depends on the type of nuclei involved and of the strength of B_0 ($\omega_0 = \gamma * B_0$, where γ = hydrogen gyromagnetic ratio = 42.6 MHz / T).
Sending radiofrequency pulses at the Larmor frequency allows interaction with the net magnetization, moving M progressively away from B_0 direction; this process is called *excitation*. At this point, M can be split into two components: one parallel to the Z-axis, M_z, and the other one lying in the XY plane, M_{xy}. M tends to return to the equilibrium, parallel to B_0, so M_{xy} returns to 0 and M_z returns to its initial value; this process is called *relaxation*. While M_{xy} relaxes, it also rotates, generating a radiofrequency signal that is detected by the MRI receiver coils placed around the patient. Additional magnetic fields are used on top of B_0 to codify the spatial information, for acquisition of images in three dimensions. These magnetic fields are called gradients, since their amplitudes vary as a function of their position in the scanner, along the three axes X, Y, and Z.
When MRI is used to image and highlight the vessel, it is called magnetic resonance angiography (MRA) and can be performed by using either a contrast agent, or the intrinsic properties of blood flow.

Coronary MRA has the great potential to be harmless because it does not use x-ray and is not invasive. However, data collection is time-consuming and sufficient image quality is hard to obtain because of the coronaries' continuous motion [6]. Indeed, their movement is due to heart contraction and relaxation and to respiratory diaphragm displacement; these two components can be analyzed separately. To overcome the respiratory movement, several techniques have been developed such as breath holding, navigator gating [7] and, more recently, self-navigation [8]. This work concerns only the treatment of the cardiac motion. The most preferred solution is to perform an ECG-triggered sequence [9]; this means image data are collected from consecutive heartbeats, always at the same time in the cardiac cycle. The position in the cardiac cycle where the data are acquired is called the acquisition window. This technique relies on the assumption that coronary arteries always follow the same trajectory from heartbeat to heartbeat. Until now, choosing the acquisition window in the cardiac cycle was based exclusively on the position of minimal coronary motion. Wang et al.

(1999) [10] and Johnson et al. (2004) [11] have used x-ray angiograms taken at 30 frames/s to find a period of low coronary motion in the cardiac cycle, that means less than 1mm displacement in any direction between succeeding frames. Both found a rest period in mid diastole but Johnson et al. established one in end systole too. Only Wang et al. (1999) have analyzed the coronaries' repositioning in the diastolic resting period [10], but nobody has focused on the analysis of their repositioning throughout the whole cardiac cycle. The primary goal of this study is therefore to analyze coronary artery repositioning throughout the entire cardiac cycle in order to test the hypothesis that there are moments during the cardiac cycle when the beat-to-beat repositioning is optimal. The repositioning uncertainty values in these time intervals were then compared with the intervals of low coronary motion. Finally, an optimal timing for ECG triggered MRA data acquisition that combines low coronary velocity and minimal coronary repositioning uncertainty was proposed.

Methods

The images used in this work were cine breath-hold x-ray angiograms, since it is the gold standard technique to analyze coronaries with high temporal and spatial resolution. They were collected from 11 patients who underwent elective routine diagnostic coronary angiography, in order to avoid additional radiation exposure. All participants gave their written informed consent prior to the procedure. The images were taken with a matrix of 512x512, a 0.32mm^2 pixel size and a temporal resolution of 15 frames/s on a Philips ALURA monoplanar FD10 (Philips Healthcare, Best, The Netherlands). Synchronous ECG was recorded over 2 to 5 consecutive heartbeats, depending on the duration of the diagnostic procedure.

Since the left coronary artery is the most frequently involved in myocardial infarction (55-70% of cases) [12], the bifurcations of the left coronary tree were selected as markers to evaluate the repositioning of the arteries and their velocity during the cardiac cycle. Images were taken in a left anterior view (LAO) and in a right anterior view (RAO) (Figure 1). Markers were chosen in the proximal and middle part of the heart since this is the most interesting part on the clinical point of view: occlusion occurs most frequently in the first centimeters [12] and vessels are big enough to allow intervention. The more distal part of the vessel is less important because, even if we would be able to detect lumen narrowing, it would be impossible to intervene. Not all the angiograms of each patient were used, because some contained either camera motion or diaphragmatic movement, which would distort the analysis of the intrinsic heart motion. One patient had a heart contraction that was asynchronous with the ECG; it was therefore considered an outlier and excluded from the analysis. Finally, 23 bifurcations were selected from 10 patients (mean±SD age 68.3±7.0 years), 10 on the left anterior descending coronary artery (LAD) and 13 on the left circumflex coronary artery (LCX).

All the x-ray angiograms were inspected in order to select the most visible bifurcations corresponding to the location criteria, which means along the proximal and middle segments of LAD and LCX. Then, each bifurcation was tracked with the help of a user-assisted algorithm implemented in Matlab (The Mathworks, Natick, MA, USA). Every point of the tracking was placed manually, frame per frame, on the bifurcation at the conjunction of two vessel walls on a zoomed color jet image of the area of interest (Figure 2). Using the synchronous ECG, the algorithm recognized the different heartbeats, compared the trajectories of the markers coming from consecutive heartbeats and computed the coronary repositioning uncertainty (Figure 3). Repositioning uncertainty was defined as the diameter of the smallest circle encompassing the points to be compared at the same time after the R-wave. The algorithm computed steps of 50ms until 650ms after the R-wave, which corresponded to the two patients with the fastest heart rate (89 and 92 beats per minute) and therefore the shortest R-R interval.
Two independent observers performed the tracking of the 23 bifurcations, with the R-wave of the ECG as the starting point. Six months later, observer 2 performed the tracking of the 23 bifurcations a second time. All data were exported from Matlab to Excel where the statistical analysis has been performed.

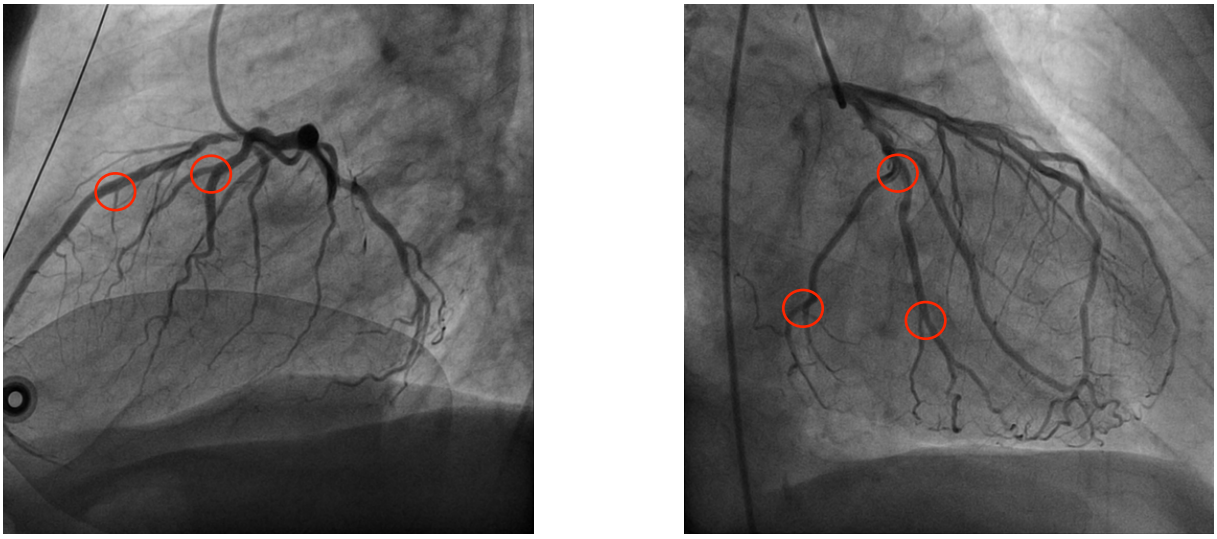

Figure 1: On the left, two bifurcations on the LAD taken in LAO view. On the right, three bifurcations on the LCX taken in RAO view.

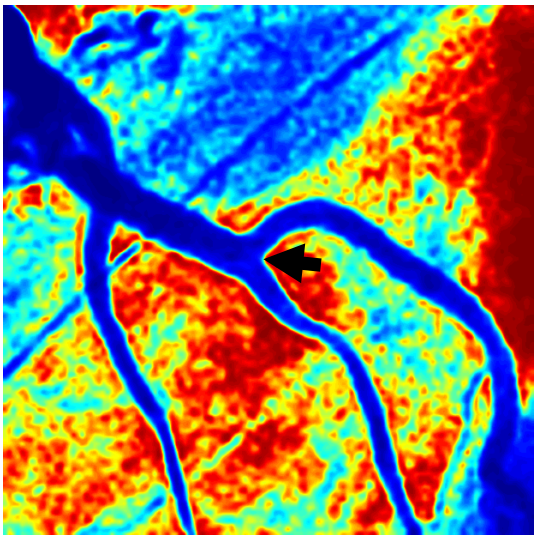

Figure 2: The arrow indicates where the marker was placed on the given bifurcation.

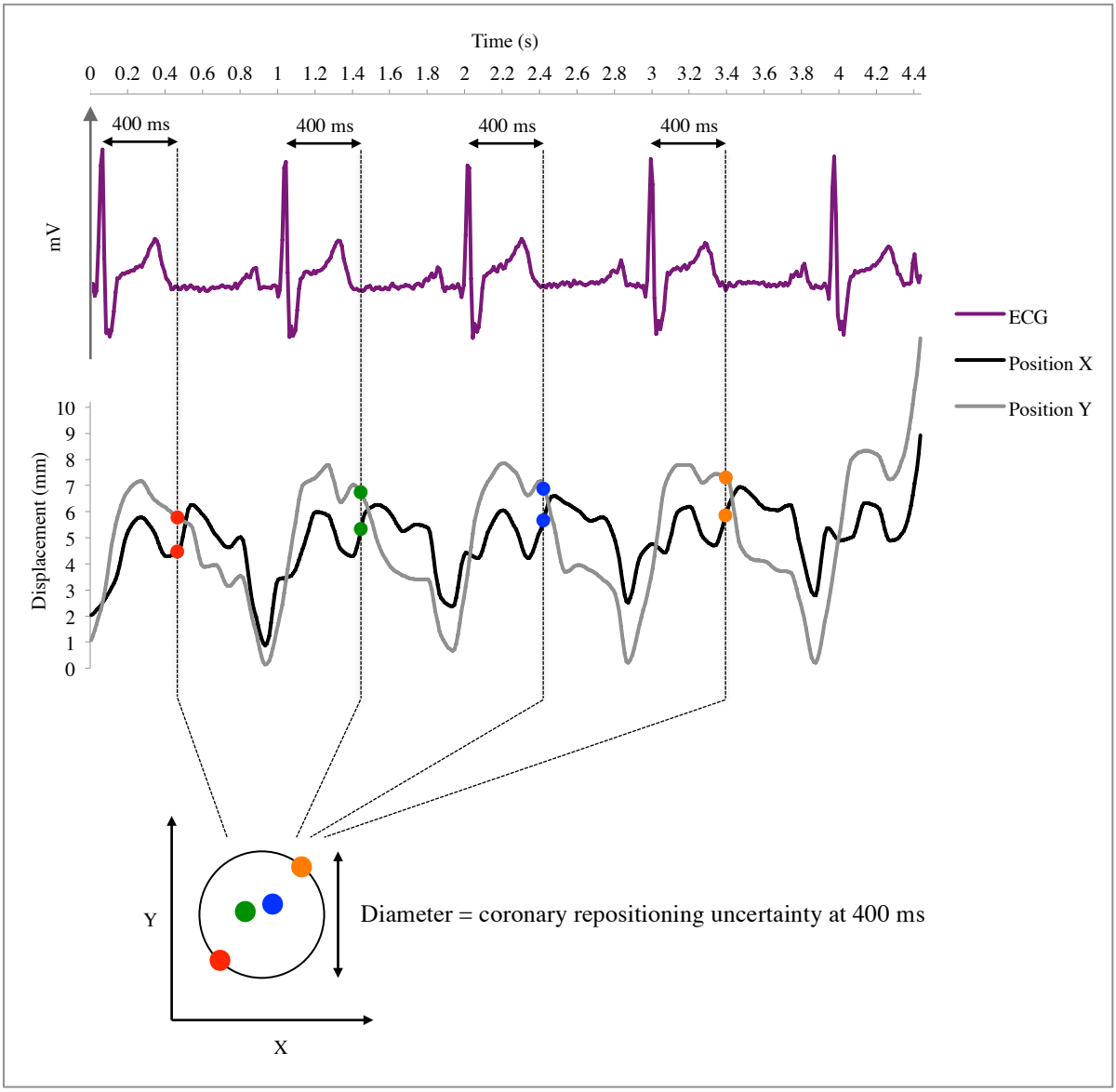

Figure 3: Example of measuring coronary repositioning uncertainty at 400ms after the R-wave of the ECG, following the tracking of a proximal LAD bifurcation. For each heartbeat, the algorithm implemented in Matlab detects the R-wave and records the position of the marker (X and Y coordinates) placed e.g. 400ms after the R-wave. Then it determines the smallest circle that includes all the markers placed 400ms after the R-wave. The diameter of this circle is then defined as the repositioning uncertainty at 400ms.

As Johnson et al. have shown that all parts of the coronary arteries move differently [11], all bifurcations have been considered as independent variables, although some of them belong to the same heart. Student's t-tests with a false discovery rate (FDR, q=0.1) correction for multiple comparison [13] were applied to see whether coronary repositioning varies statistically during cardiac cycle.

Calculating the average velocity on the second tracking of the observer 2 was done using the temporal derivative of the X and Y coordinates of each moving marker. The distance traveled of a single point was obtained by Euclidean distance. Student's t-tests with a FDR (q=0.1)

correction for multiple comparison were applied to see whether coronary velocity varies statistically during cardiac cycle. Johnson et al. [11] analyzed each cardiac cycle entirely and presented their results as a percentage of the cardiac cycle. The time scale of the present study was therefore converted in percent of 650ms in order to compare the results concerning the velocity evolution among patients. Since 8 out of 10 patients had an R-R interval longer than 650ms, the results were also presented as a percentage of 1.08±0.23 s, which corresponds to the mean R-R interval on the 23 bifurcations.

To test the accuracy of this method, inter- and intra-observer variability were assessed. Observer 1 implemented the algorithm and was experienced with the bifurcation tracking. For inter-observer comparison, only observer 2 second tracking was therefore used, since she was considered more experienced with the program than on the first tracking. Linear regression and Bland-Altman plots [14] were used to assess intra- and inter-observer agreement at 0, 150, 200, 400, 550 and 600ms after the R-wave of the ECG. Note that both tools have no threshold value that indicates whether the agreement is sufficient or not but they serve to appreciate how close the results are to a perfect agreement. For linear regression, perfect agreement would be all the points lying on the line of equality, that means a regression line with the formula X=Y and an R^2=1. Concerning Bland-Altman plots, the ideal would be to obtain a mean difference of 0 and the two lines representing mean±1.96SD the closest possible, since 95% of differences are supposed to be found between these two lines.

Results

Repositioning uncertainty

Observer 2 second tracking is the most relevant to present in details since it is the only one that is taken into account in all analyses of the study. In addition, observer 2 was then considered more experienced with the program than on the first tracking.

The analysis of the mean beat-to-beat repositioning uncertainty from observer 2 tracking (Figure 4) shows a tendency for better repositioning in mid systole (minimal value at 150ms = 0.77 ±0.46mm) and mid diastole (minimal value at 600ms = 0.76 ±0.49mm) than in the rest of the cardiac cycle (highest values: at 50ms = 1.15 ±0.62mm and at 350ms: 1.21 ±0.71mm). Student's t-tests with FDR correction for multiple comparison (q=0.1) also confirm that repositioning uncertainty during intervals 150-200ms and 550-600ms is statistically lower than at 50 and 350ms (Figure 5).

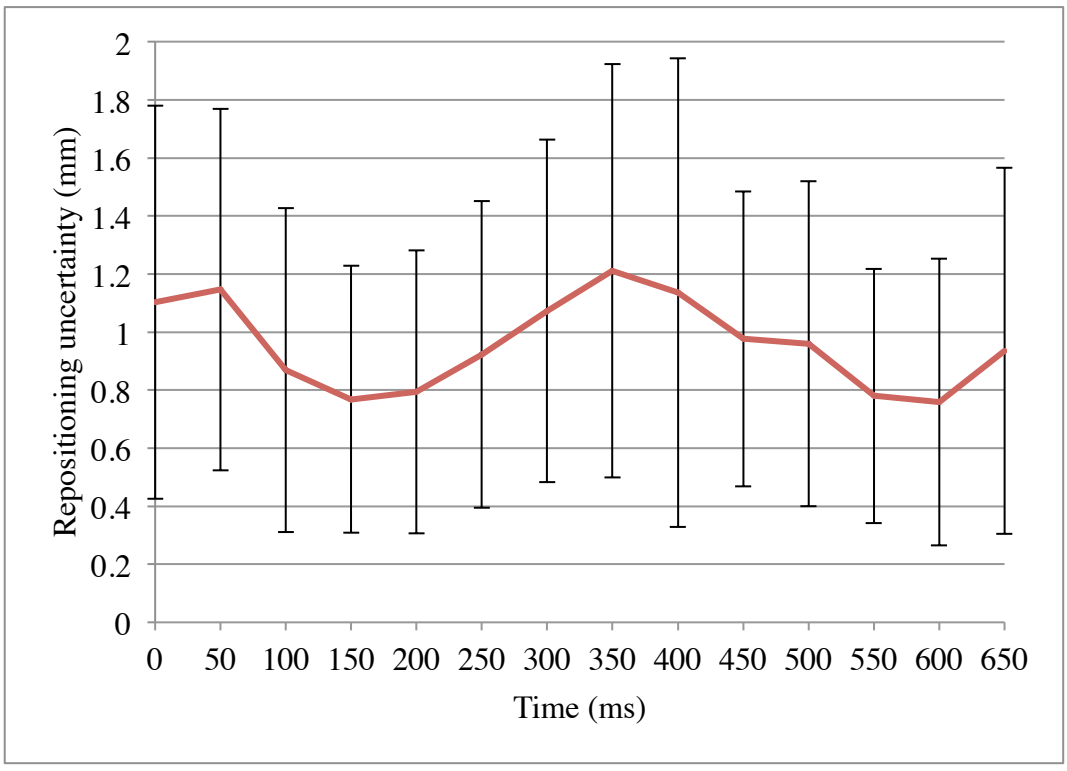

Figure 4: Mean coronary beat-to-beat repositioning uncertainty with standard deviation. Observer 2 second tracking.

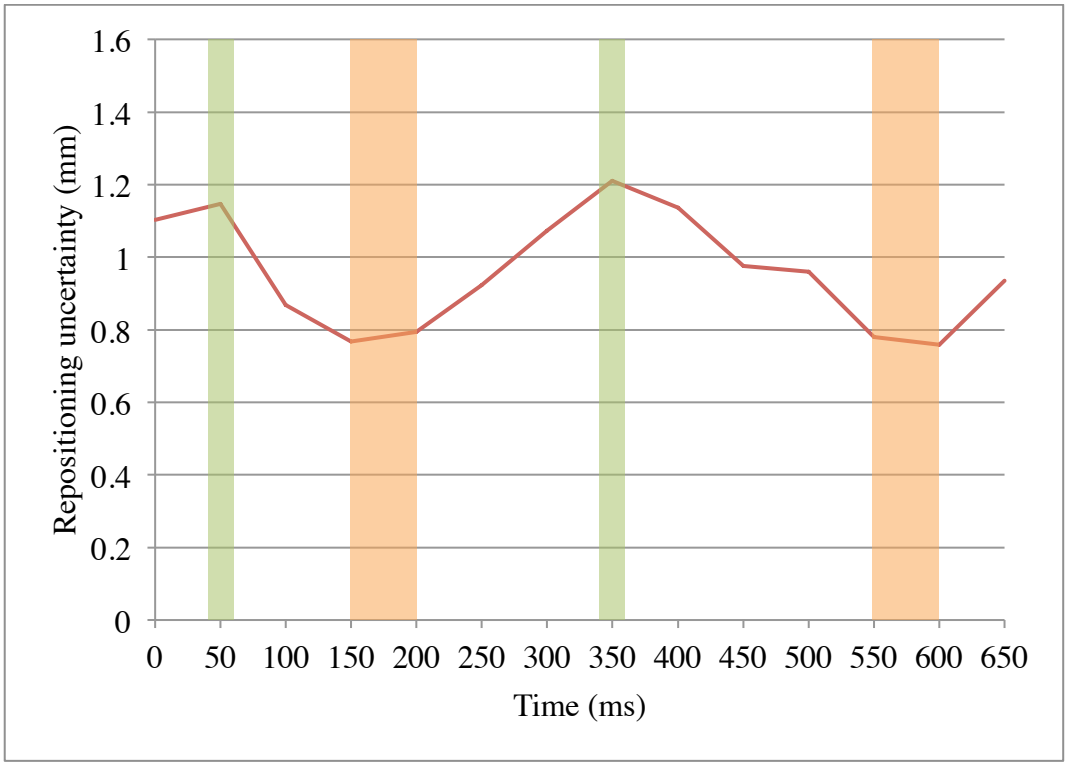

Figure 5: Mean coronary repositioning uncertainty from observer 2 second tracking. Repositioning uncertainty values during time intervals in orange are statistically lower than those in green. FDR-corrected p-value = 0.020

Coronary velocity

The analysis of the coronary velocity suggests that the heart has a tendency to move more slowly during end systole (lowest value at 225ms: 14.35 ±11.35mm/s) and mid diastole (lowest value at 625ms: 11.78 ±11.62mm/s) when compared to the rest of the cardiac cycle (highest value at 25ms: 55.96 ±22.34mm/s) (Figure 6). This was confirmed by Student's t-tests with FDR correction for multiple comparison (q=0.1, FDR-corrected p-value=0.054): velocities at 225, 575 and 625ms are not much different between them but they are statistically inferior to all others. Given the interest in the interval 150-200ms, it must be added that the velocity at 175ms (25.32 ±16.39mm/s) is statistically lower than those at 25-75-125ms (FDR corrected p-value=0.054).
Converting the time in percentage of the cardiac cycle for normalization, the two values of minimal velocity at 225 and 625ms correspond respectively to 34.62 and 96.15 % of 650ms. On the average R-R interval of 1.08±0.23s, these two values of minimal velocity are located at 20.93 and 58.14 %, respectively.

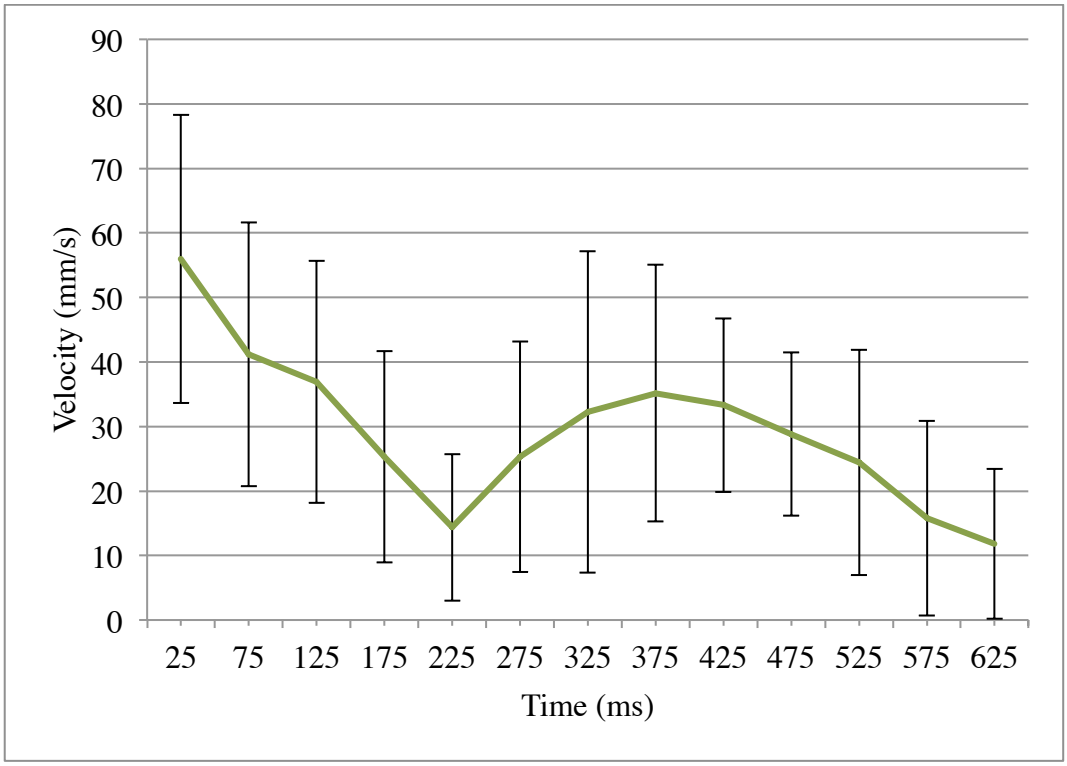

Figure 6: Mean coronary velocity with standard deviation

Intra-observer comparison

The average coronary repositioning uncertainty measured by observer 2 remained quite constant for both tracking analyses (Figure 7) (maximal difference = 0.18mm at 350ms). Note also that the standard deviation (SD) is large compared to the mean (maximal SD: second tracking at 400ms = ±0.81mm) but decreases where repositioning improves (minimal SD: second tracking at 550ms = ±0.44mm).

Compared to the second tracking, Student's t-tests with FDR correction for multiple comparison (q=0.1) on the first tracking show only two times, at 200 and 550ms, that provide statistically lower repositioning uncertainty than in early systole and early diastole (Figure 8), but it nevertheless proves that the pattern of repositioning is similar.

Intra-observer Bland-Altman plots (Figures 9 and 10) present better agreement during mid systole (Δ±1.96SD = 0.48mm at 150ms and 0.78mm at 200ms) and mid diastole (Δ±1.96SD = 0.70mm at 550ms and 0.60mm at 600ms) than in early systole (Δ±1.96SD = 0.87mm at 0ms) and early diastole (Δ±1.96SD = 1.01mm at 400ms). Linear regression (Figure 11) shows relatively high agreement at all times, regardless of repositioning: $y=0.96x+0.08$ with $R^2=0.89$ at 0ms, $y=0.97x+0.02$ with $R^2=0.93$ at 150ms, $y=1.19x-0.1$ with $R^2=0.92$ at 400ms, $y=0.90x+0.13$ with $R^2 = 0.84$ at 550ms.

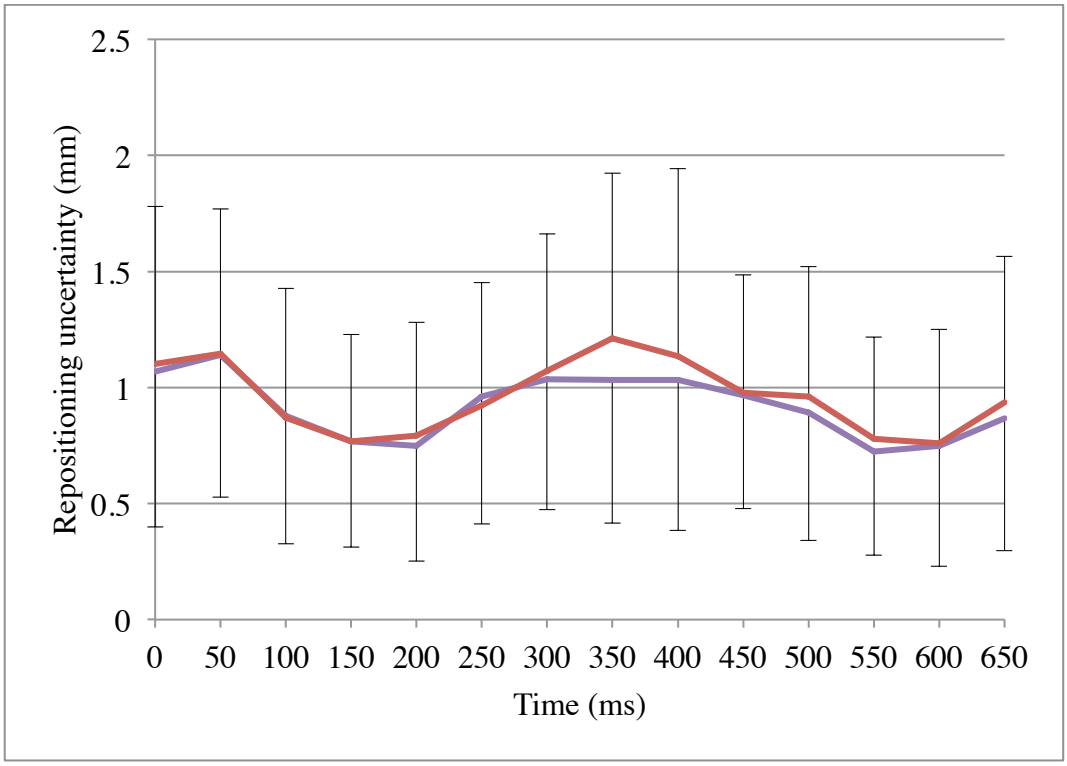

Figure 7: Mean coronary beat-to-beat repositioning uncertainty with standard deviation. In violet, observer 2 first tracking. In red, observer 2 second tracking.

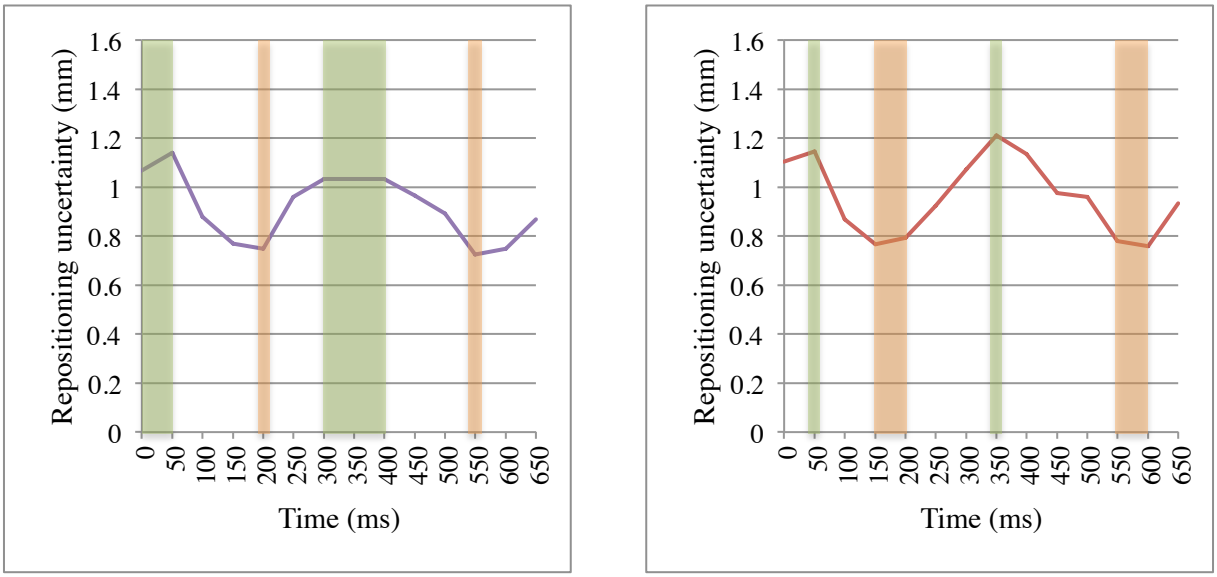

Figure 8: Repositioning uncertainty from observer 2 first tracking (on the left, FDR-corrected p-value=0.023) and second tracking (on the right, FDR-corrected p-value=0.020). Repositioning uncertainty values during time intervals in orange are statistically lower than those in green.

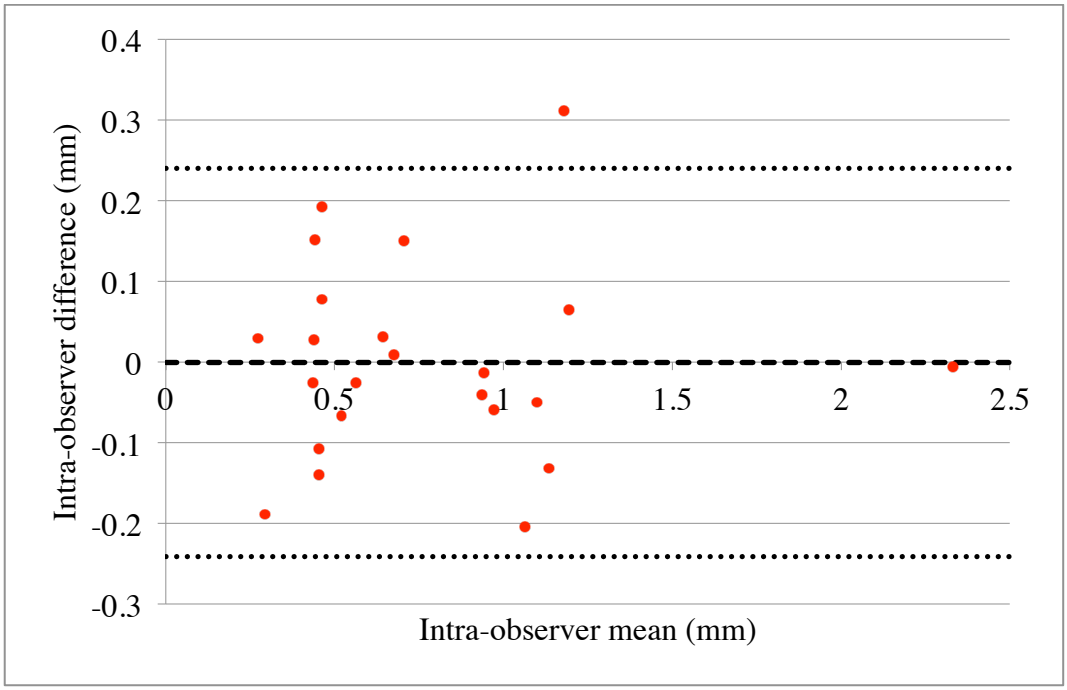

Figure 9: Intra-observer Bland-Altman plot at 150ms (dashed line = mean difference, dotted line = mean difference ±1.96SD). Mean difference = -0.0004mm, Mean difference +1.96SD = 0.24mm, Mean difference -1.96SD = -0.24mm.

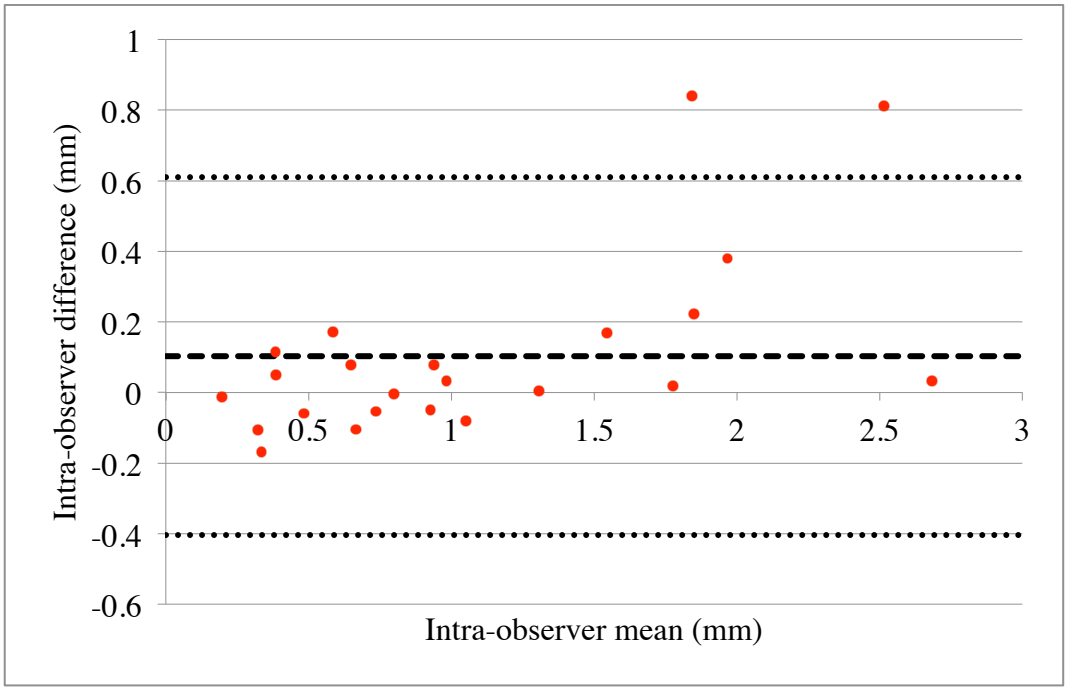

Figure 10: Intra-observer Bland-Altman plot at 400ms (dashed line = mean difference, dotted line = mean difference ±1.96SD). Mean difference = 0.10mm, Mean difference +1.96SD = 0.61mm, Mean difference -1.96SD = -0.40mm.

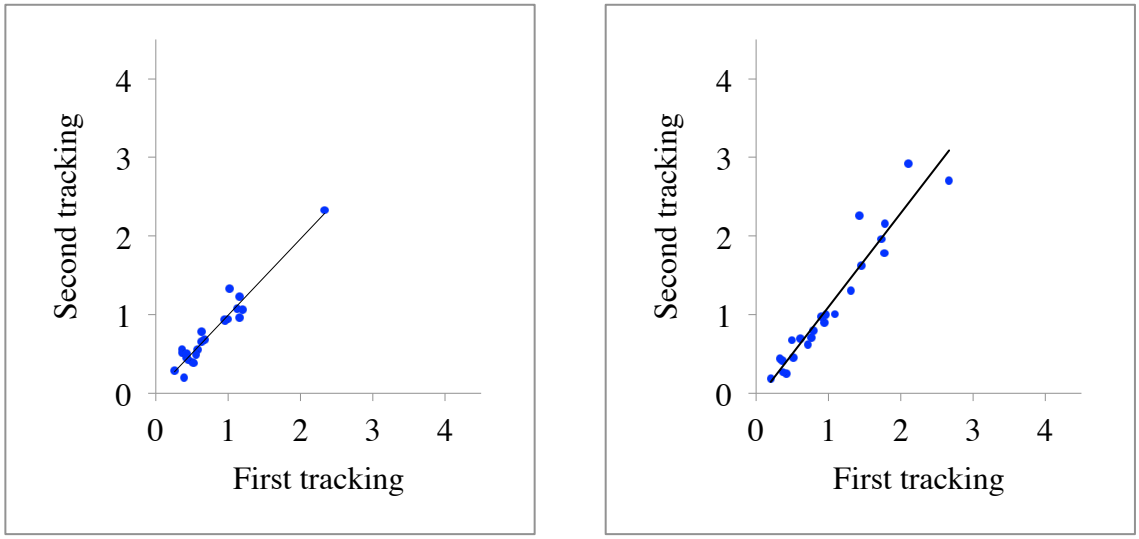

Figure 11: Intra-observer linear regression at 150ms (on the left, y=0.97x+0.02, R^2=0.93) and 400ms (on the right, y=1.19x-0.1, R^2=0.92). X-axis = Repositioning uncertainty observer 2 first tracking (mm). Y-axis = Repositioning uncertainty observer 2 second tracking (mm).

Inter-observer comparison

The analysis of the mean beat-to-beat repositioning uncertainty from observer 1 and observer 2 tracking (Figure 12) shows a tendency for improved repositioning uncertainty in mid systole (minimal value: observer 2 at 150ms = 0.77 ±0.46mm) and mid diastole (minimal value: observer 2 at 600ms = 0.76 ±0.49mm) when compared to the rest of the cardiac cycle (highest values: observer 1 at 50ms = 1.35 ±0.64mm and observer 1 at 400ms: 1.31 ±0.97mm). Observer 1 had systematically higher repositioning uncertainty values than observer 2, however both found a very similar pattern of repositioning. Note also that the standard deviation (SD) is large compared to the mean (maximal SD: observer 1 at 400ms = ±0.97mm) but decreases where repositioning improves (minimal SD: observer 2 at 150ms = ±0.46mm and observer 2 at 550ms = ±0.44mm).

Compared to observer 2, Student's t-tests with FDR correction for multiple comparison (q=0.1) on observer 1 tracking also show two intervals, from 150 to 200ms and from 550ms to 600ms, that provide statistically lower repositioning uncertainty than in early systole and early diastole (Figure 13), confirming that the pattern of repositioning is similar between independent observers.

Inter-observer Bland-Altman plots (Figures 14 and 15) present better agreement during mid systole (Δ±1.96SD = 1.10mm at 150ms and 1.14mm at 200ms) and mid diastole (Δ±1.96SD = 1.53mm at 550ms and 1.35mm at 600ms) than in early systole (Δ±1.96SD = 2.03mm at 0ms) and early diastole (Δ±1.96SD = 2.10mm at 400ms). Linear regression (Figure 16) shows a modest agreement among the observers at all times regardless of repositioning: y=0.7x+0.2 with R^2=0.51 at 0ms, y=0.8x+0.11 with R^2=0.67 at 150ms, y=0.7x+0.22 with R^2=0.69 at 400ms, y=0.56x+0.29 with R^2 = 0.53 at 550ms.

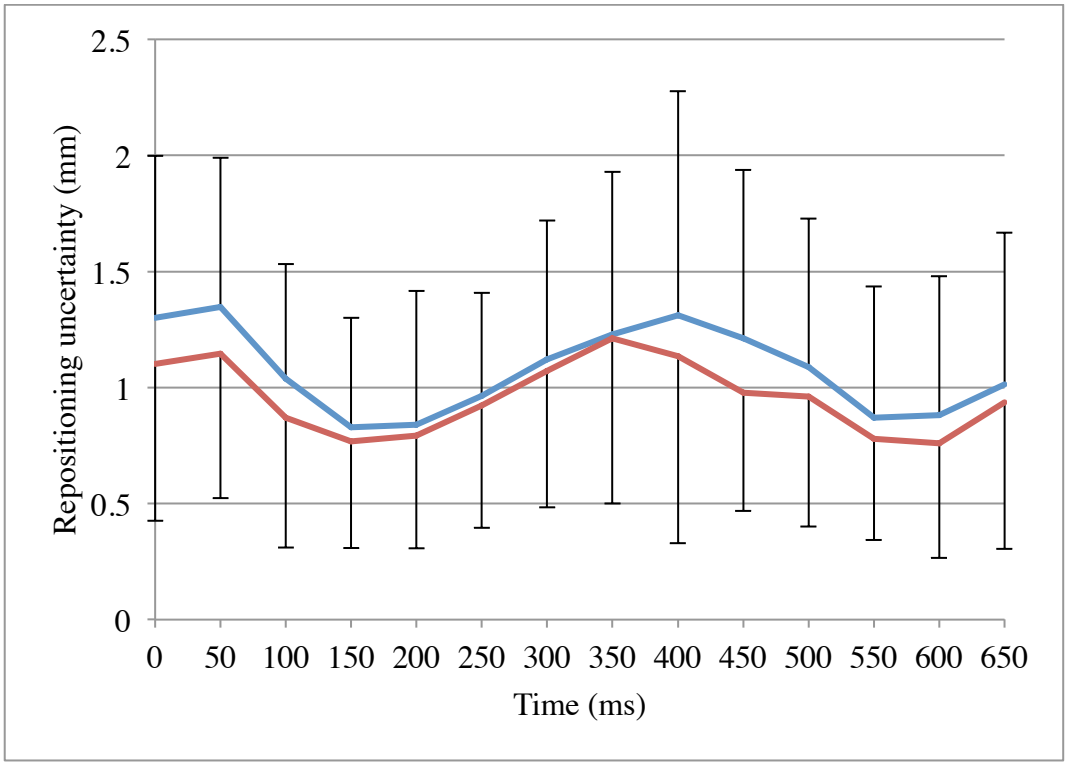

Figure 12: Mean coronary beat-to-beat repositioning uncertainty with standard deviation. In blue, observer 1. In red, observer 2 second tracking.

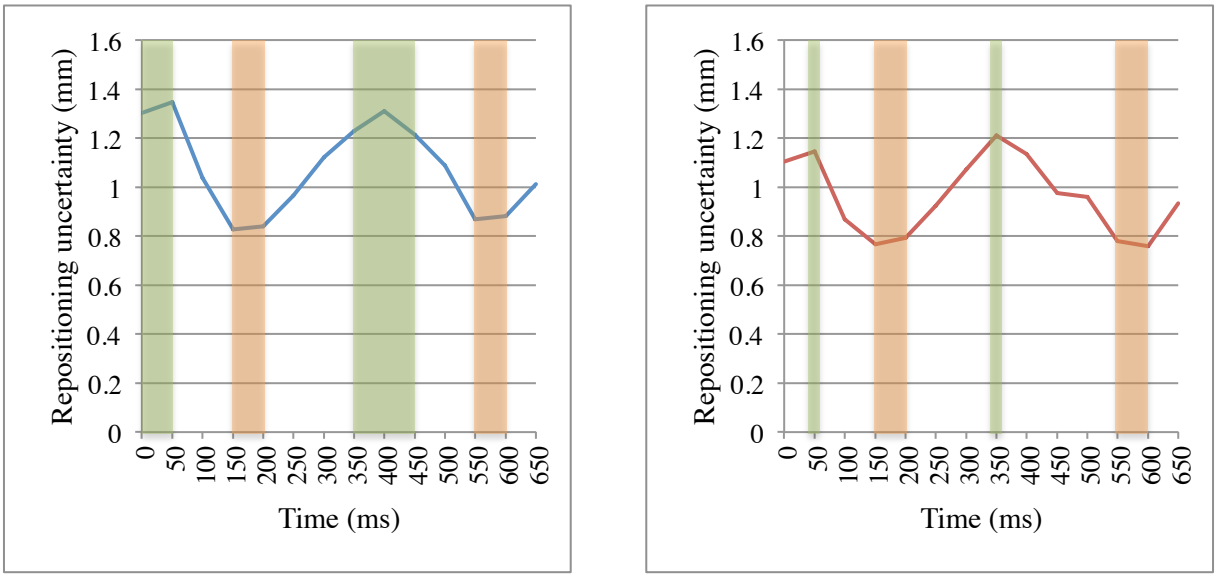

Figure 13: Repositioning uncertainty from observer 1 (on the left, FDR-corrected p-value=0.033) and observer 2 second tracking (on the right, FDR-corrected p-value=0.020). Repositioning uncertainty values during time intervals in orange are statistically lower than those in green.

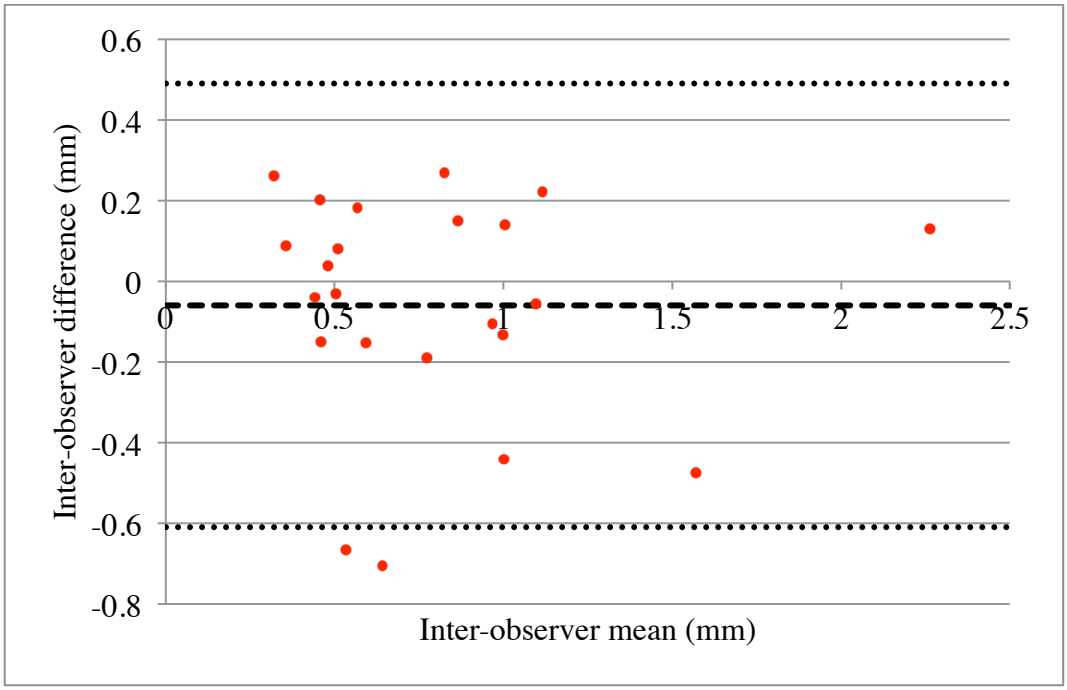

Figure 14: Inter-observer Bland-Altman plot at 150ms (dashed line = mean difference, dotted line = mean difference ±1.96SD). Mean difference = -0.06mm, Mean difference +1.96SD = 0.49mm, Mean difference -1.96SD = -0.61mm.

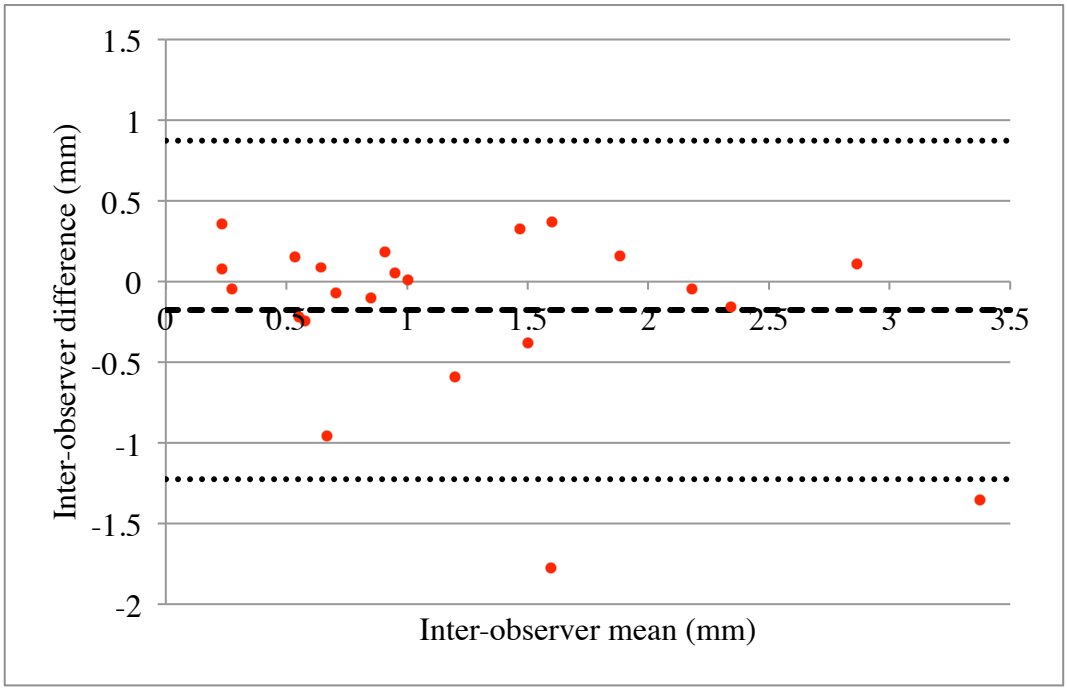

Figure 15: Inter-observer Bland-Altman plot at 400ms (dashed line = mean difference, dotted line = mean difference ±1.96SD). Mean difference = -0.18mm, Mean difference +1.96SD = 0.87mm, Mean difference -1.96SD = -1.22mm.

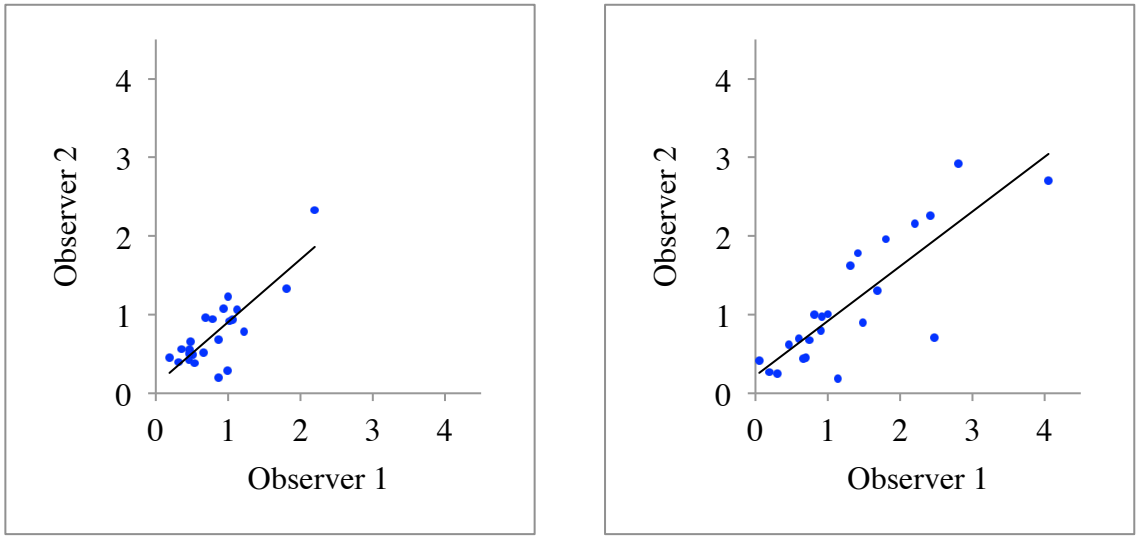

Figure 16: Inter-observer linear regression at 150ms (on the left, y=0.8x+0.11, R^2=0.67) and 400ms (on the right, y=0.7x+0.22, R^2=0.69). X-axis = Repositioning uncertainty observer 1 (mm). Y-axis = Repositioning uncertainty observer 2 second tracking (mm).

Overall, intra-observer agreement was better than inter-observer since the maximal differences (mean±1.96SD) are smaller, R^2 higher and regression line closer to the line of equality.

Discussion

The present study showed that beat-to-beat in-plane repositioning of proximal and middle left coronary artery segments is improved during mid systole (less than 0.84±0.58mm) and mid diastole (less than 0.89±0.6mm) when compared to the rest of the cardiac cycle. For comparison, Wang et al. [10] have used biplane angiography to assess beat-to-beat 3D repositioning in mid diastole and have determined that it amounts to 0.5mm or less. Even if the standard deviation is not indicated, this result remains considerably smaller than the two values found in mid systole and mid diastole in the present work. This may seem surprising because one would expect to obtain lower values of repositioning uncertainty by analyzing cardiac motion only in 2D versus 3D, since the 3D adds an extra dimension in which the repositioning uncertainty appears and must be taken into account. Comparison of methods used in both studies can help to understand the difference in their results. First, Wang et al studied a cohort of selected patients with normal ventricular function and without significant coronary artery disease. Secondly, they only analyzed motion of the very proximal bifurcations. However, these two points do not completely explain the difference in results, since the method of Wang et al. also has its limitations compared to the present work; first, instead of using a conversion through the image resolution, they converted the landmark position in mm using a comparison with the catheter, which is more subject to errors. Secondly, they estimated the position in the cardiac cycle considering the periodicity of the landmarks movement instead of using a synchronous ECG. It should also be noted that Wang et al gave little indication of the method and no information on statistical analysis of repositioning.
Although all tracking data present a similar motion pattern and statistically better repositioning in mid systole and mid diastole, inter-observer Bland-Altman plots and linear regression suggest a modest agreement between independent observers. Indeed, the averaged maximum inter-observer difference (mean±1.96SD) on 0, 150, 400 and 550ms is 1.69mm, which is a lot considering the fact that the diameter of a coronary artery is 3-5mm [15]. Figure 12 and inter-observer Bland-Altman plots clearly show that observer 1 had systematically higher repositioning uncertainty values than observer 2, so there is a bias. A possible explanation could be the fact that the number of heartbeats to be considered at the end of each tracking was determined according to a personal judgment, to keep maximum independence between the two observers. The comparison of the results from all tracking separately revealed that, in 3 of 23 bifurcations, observer 1 counted one more heartbeat and, in 1 of 23 bifurcations, he counted two more. The observer 2 had put these five heartbeats aside because she considered there was not enough contrast agent for precise tracking. This means observer 1 has added images of lower quality to his data, which made the tracking less accurate and probably increased the repositioning uncertainty. This explanation is supported by the fact that the points of greatest inter-observer difference on the Bland-Altman plots corresponded most often to the four bifurcations considered over a longer period by observer 1. It should nevertheless be noted that intra-observer agreement is higher than inter-observer agreement. Indeed, the averaged maximum intra-observer difference (mean±1.96SD) on 0, 150, 400 and 550ms is 0.77mm. These few points suggest that a better consensus on how to analyze the data is needed to improve the reproducibility of the method.

The velocity analysis revealed that coronary velocity is high immediately after the R-wave of the ECG (max 55.96±22.34mm/s at 25ms) and decreases gradually, reaching a first minimum in end systole (min 14.35±11.35mm/s at 225ms). Then the velocity increases again in early diastole (max 35.16±19.88mm/s at 375ms) and finally decelerates to 11.78±11.62mm/s at

625ms, the second minimal value in the cardiac cycle. Karwatowski et al. [16] have used MRI to evaluate regional left ventricular long-axis motion in healthy subjects. They showed a similar velocity pattern but with higher values, which may be related to the fact that young healthy subjects were used and that the measurement was performed in the direction of maximum coronary displacement as seen in a long axis view. Johnson et al. [11] analyzed the position and the duration of rest periods in the cardiac cycle using biplane diagnostic x-ray angiography. Two periods of low coronary displacement were found at 34±8% and 72±5% of the cardiac cycle. In the present study, the first time point of minimal coronary motion was found at 34.62%, and the second at 96.15%. This apparent discrepancy in diastole is, however, related to the different methods of normalization. Johnson et al. have expressed each cardiac cycle in percentage, whereas in the present study, it was chosen to analyze the first 650ms of each cardiac cycle, regardless of the heart rate. This method was preferred because the programming of the MRI is in milliseconds and not in percentage of cardiac cycle. In this study, the average R-R interval of the 23 bifurcations was 1.08±0.23s. On this mean R-R interval, the two lowest velocity values at 225 and 625ms are located at 20.93 and 58.14 %, which is similar to the values found by Johnson et al.

In the present work, it has been demonstrated that there are periods in the cardiac cycle, in mid systole and mid diastole, where repositioning uncertainty reaches points of local minima. It has also been calculated that the velocity is the lowest in end systole and mid diastole. To take advantage of all the results and propose an optimal timing for image acquisition, both coronary velocity and repositioning uncertainty need to be considered (Figure 17).

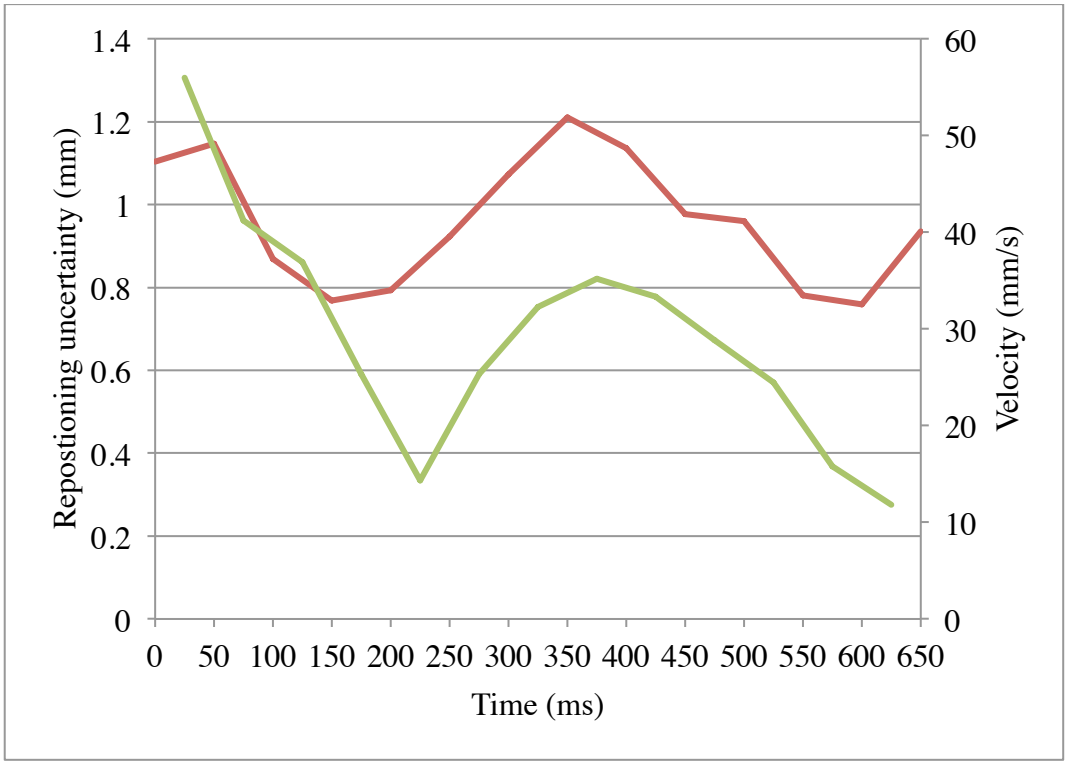

Figure 17: Beat-to-beat repositioning uncertainty vs velocity evolution. In red, mean repositioning uncertainty observer 2. In green, mean velocity observer 2.

Two intervals, from 150 to 200ms and from 550 to 600ms are best candidates for coronary MRA data acquisition because of minimal repositioning uncertainty and relatively low coronary velocity.
Several studies have suggested placing the acquisition window in mid diastole because of the relative quiescence of the heart during a relatively long period of time [10, 11]. However, it needs to be considered that the systolic duration is much less affected by R-R variability than its diastolic counterpart. When the heart rate increases, systole is shortened less than diastole. This phenomenon is particularly pronounced in patients with systemic hypertension, coronary, valvular or dilated heart disease [17]. This observation is very important for coronary MRA since the interval between R-wave and the acquisition window, the trigger delay, is programmed in advance and remains fixed. If the heart rate of the patient changes during the examination, the acquisition window placed initially in mid diastole may no longer be optimal and images will be blurred. In combination with the results found in this study, it advances the hypothesis that coronary MRA during the interval ranging from 150 to 200ms will lead to improved image quality. However, and considering the shorter duration of quiescence in systole as compared to diastole, a higher temporal resolution is needed for systolic imaging and a prolonged scanning time has to be considered.
A few studies have already tested the image acquisition in systole. Duerinckx and Atkinson [18] compared images acquired in mid systole (trigger delay 150ms, data acquisition 117ms) to images acquired in mid diastole (trigger delay 500ms, data acquisition 117ms) using 2D breath-hold coronary MRA in normal volunteers. According to their results, the quality of images taken in systole was almost similar to those taken in diastole. As the two trigger delays used in this work are very close to those proposed in the present study, it would be interesting to see if a data acquisition period of 50ms instead of 117ms changes the image quality in favor of systole or not. Gharib et al. [19] relied on several studies, including that of Johnson et al. [11], to compare images taken at end systole (mean trigger delay 305±60ms, acquisition window 35ms) to those acquired in mid diastole (mean trigger delay 668±85ms if acquisition window = 35ms, mean trigger delay 642±106ms if acquisition window = 75ms) by using parallel imaging (sensitivity encoding [SENSE]) at 3T. They found no significant differences in image quality and concluded that data acquisition in end systole is a valid alternative in patients with heart rate variability or short diastolic rest period. In this work, they tested a short acquisition window (35ms) in end systole whereas in the present study it is also proposed a short acquisition window (50ms) but in mid systole. A future step could be the comparison of images taken in mid systole to those taken in end systole to determine if a better repositioning with a slight compromise in coronary velocity, as proposed in this study, may be more advantageous for image quality than targeting the lowest coronary velocity. Finally, Uribe et al. [20] have used dual cardiac phase imaging to retrospectively compare images acquired in end systole to those acquired in mid diastole among children suffering from congenital heart disease. They found that some segments of coronary arteries are better visible in end systole than in mid diastole. These few studies demonstrate the growing interest of the scientific world in the acquisition of images in systole and the knowledge added through this study further promotes the notion and stimulates research of systolic imaging to further improve image quality.

The present work contains several limitations that need to be taken into account. First, cardiac motion has been studied using data from x-ray coronary angiography, that is to say a 2D technique, while the heart is moving in 3D. As the antero-posterior movement of bifurcations has not been considered, coronary repositioning uncertainty and velocity calculated with this method may have been underestimated. Secondly, as the x-ray coronary angiograms were acquired for diagnostic purposes, the results may have been influenced by conditions

affecting heart motility. On the other hand, this cohort of patients is also an advantage, since our final goal is to propose coronary MRA to people with potential cardio-vascular disease who require medical examination. Thirdly, some difficulties inherent to the method have also posed problems. The lack of contrast on some images rendered the tracking of the bifurcation imprecise and a significant part of the data had to be excluded due to movement of the camera or the diaphragm during angiography. In the end, 10 patients were selected, which is little to represent a population, but remains comparable to the studies of Wang et al. (13 patients) [10] and Johnson et al. (15 patients) [11]. Moreover, angiograms used in this work allowed an analysis of only 2 to 5 consecutive heartbeats, as they were performed for diagnostic purposes. Finally, several studies [10, 11] have shown that cardiac motility varies consistently between patients. It is therefore difficult to identify an average behavior without large standard deviations.

In conclusion, the present study demonstrated that there are periods in the cardiac cycle, in mid systole (150 to 200ms) and mid diastole (550 to 600ms), where beat-to-beat left coronary artery repositioning uncertainty reaches two points of minima. It has also been calculated that the times of lowest velocity are located in end systole (at 225ms) and mid diastole (575 to 625ms). Since systole is less influenced by heart rate variability than diastole, it was finally proposed to test an acquisition window between 150 and 200ms after the R-wave.

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References

1. Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, et al. Heart disease and stroke statistics--2011 update: a report from the American Heart Association. Circulation. 2012 Jan 3;125(1):e2–e220. Epub 2011 Dec 15.
2. Mackay J, Mensah G. The Atlas of Heart Disease and Stroke [Internet]. Geneva: World Health Organization; 2004. Available from: http://www.who.int/cardiovascular_diseases/resources/atlas/en/print.html
3. Moscucci M. Complications of Cardiovascular Procedures: Risk Factors, Management, and Bailout Techniques. Philadelphia: Lippincott Williams & Wilkins; 2010. p181-213.
4. Kim WY, Danias PG, Stuber M, Flamm SD, Plein S, Nagel E, et al. Coronary magnetic resonance angiography for the detection of coronary stenoses. N Engl J Med. 2001 Dec 27;345(26):1863-9.
5. Ridgway JP. Cardiovascular magnetic resonance physics for clinicians: part I. J Cardiovasc Magn Reson. 2010 Nov 30;12:71.
6. Van Geuns RJ, Wielopolski PA, De Bruin HG, Rensing BJ, Hulshoff M, Van Ooijen PM, et al. MR coronary angiography with breath-hold targeted volumes: preliminary clinical results. Radiology. 2000 Oct;217(1):270-7.
7. McConnell MV, Khasgiwala VC, Savord BJ, Chen MH, Chuang ML, Edelman RR, et al. Comparison of respiratory suppression methods and navigator locations for MR coronary angiography. Ajr Am J Of Roentgenol. 1997 May;168(5):1369–75.
8. Stehning C, Börnert P, Nehrke K, Eggers H, Stuber M. Free-breathing whole-heart coronary MRA with 3D radial SSFP and self-navigated image reconstruction. Magn Reson Med. 2005 Aug;54(2):476–80.
9. Fischer SE, Wickline SA, Lorenz CH. Novel real-time R-wave detection algorithm based on the vectorcardiogram for accurate gated magnetic resonance acquisitions. Magn Reson Med. 1999 Aug;42(2):361–70.
10. Wang Y, Vidan E, Bergman GW. Cardiac motion of coronary arteries: variability in the rest period and implications for coronary MR angiography. Radiology. 1999 Dec;213(3):751–8.
11. Johnson K, Patel S, Whigham A, Hakim A, Pettigrew R, Oshinski J. Three-Dimensional, Time-Resolved Motion of the Coronary Arteries. J Cardiovasc Magn Reson. 2004;6(3):663-73.
12. Moore KL, Dalley AF. Anatomie médicale: Aspects fondamentaux et applications cliniques. 2e éd. Bruxelles: De Boeck & Larcier s.a. ; 2007. p.141-169.
13. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. Journal of the Royal Statistical Society Series B Methodological [Internet]. 1995;57(1):289–300. Available from: http://www.jstor.org/stable/2346101
14. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet. 1986 Feb 8;1(8476):307–10.
15. Kamina P. Anatomie clinique - Thorax, abdomen – Tome 3. 2e éd. Paris: Maloine; 2007. p. 114-118.
16. Karwatowski SP, Mohiaddin R, Yang GZ, Firmin DN, Sutton MS, Underwood SR, et al. Assessment of regional left ventricular long-axis motion with MR velocity mapping in healthy subjects. J Magn Reson Imaging. 1994 Mar-Apr;4(2):151–5.
17. Bombardini T, Gemignani V, Bianchini E, Venneri L, Petersen C, Pasanisi E, et al. Diastolic time – frequency relation in the stress echo lab: filling timing and flow at different heart rates. Cardiovascular Ultrasound. 2008 Apr 21;6:15.
18. Duerinckx A, Atkinson DP. Coronary MR angiography during peak-systole: work in progress. J Magne Reson Imaging. 1997 Nov-Dec;7(6):979-86.
19. Gharib AM, Herzka D a, Ustun AO, Desai MY, Locklin J, Pettigrew RI, et al. Coronary MR angiography at 3T during diastole and systole. J Magn Reson Imaging. 2007 Oct;26(4):921–6.
20. Uribe S, Hussain T, Valverde I, Tejos C, Irarrazaval P, Fava M, et al. Congenital heart disease in children: coronary MR angiography during systole and diastole with dual cardiac phase whole-heart imaging. Radiology. 2011 Jul;260(1):232–40. Epub 2011 Apr 14.