



HAL
open science

Submillisievert Multiphasic Coronary Computed Tomography Angiography for Pediatric Patients With Congenital Heart Diseases

Julien Le Roy, H el ene Vernhet Kovacsik, Hamid Zarqane, Marie Vincenti, Hamouda Abassi, Kathleen Lavastre, Thibault Mura, Alain Lacampagne, Pascal Amedro

► **To cite this version:**

Julien Le Roy, H el ene Vernhet Kovacsik, Hamid Zarqane, Marie Vincenti, Hamouda Abassi, et al.. Submillisievert Multiphasic Coronary Computed Tomography Angiography for Pediatric Patients With Congenital Heart Diseases. *Circulation: Cardiovascular Imaging*, 2019, 12 (2), pp.e008348. 10.1161/CIRCIMAGING.118.008348 . hal-02005609

HAL Id: hal-02005609

<https://hal.science/hal-02005609>

Submitted on 10 Jun 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destin ee au d ep ot et  a la diffusion de documents scientifiques de niveau recherche, publi es ou non,  emanant des  tablissements d'enseignement et de recherche fran ais ou  trangers, des laboratoires publics ou priv es.

Submillisievert Multiphasic Coronary Computed Tomography Angiography for Pediatric Patients With Congenital Heart Diseases

BACKGROUND: The use of coronary computed tomography (CT) angiography in children with coronary artery anomalies is increasing. However, it remains technically demanding and the need to adapt acquisition parameters to a patient's cardiac characteristics has not yet been addressed. The aim of the study was to prospectively assess the feasibility of personalized multiphasic coronary CT angiography for pediatric patients.

METHODS: Fifty pediatric patients (mean age 6.1 ± 4.9 years) with coronary artery anomalies underwent a coronary CT angiography on a wide detector single-source CT equipment. Fifteen different acquisition patterns were used to trigger the acquisition at the best theoretical moment within the cardiac cycle. The appropriate pattern was automatically selected based on the patient's heart rate and heart rate variability, derived from the patient's ECG. Two independent radiologists qualitatively evaluated images.

RESULTS: All acquisitions fully answered the clinical question for a mean effective dose of 0.97 ± 0.34 mSv. Image quality qualified as good or excellent in 94% of cases (47/50). No examination was considered as not assessable but 6% (3/50) were scored as adequate for diagnosis. For these 3 patients, motion artifacts were the main cause of average image quality. No significant visual differences were reported between the different coronary arteries (mean score of 3.6 on a 4-point scale). No correlation between image quality and cardiac parameters were reported ($r = -0.19$ and $r = 0.00$, respectively for heart rate and heart rate variability).

CONCLUSIONS: Personalized multiphasic coronary CT angiography acquisitions could be performed with diagnostic quality for a dose equivalent of <4 months of natural background irradiation.

CLINICAL TRIAL REGISTRATION: URL: <https://www.clinicaltrials.gov>. Unique identifier: NCT03194763.

Julien Le Roy, MSc
Hélène Vernhet Kovacsik,
MD, PhD
Hamid Zarqane, MD
Marie Vincenti, MD
Hamouda Abassi, MSc
Kathleen Lavastre, MSc
Thibault Mura, MD, PhD
Alain Lacampagne, PhD
Pascal Amedro, MD, PhD

Key Words: artifacts ■ cardiac-gated imaging techniques ■ computed tomography angiography ■ congenital heart defects ■ diagnosis ■ pediatrics

CLINICAL PERSPECTIVE

Coronary computed tomography angiography has progressively replaced cardiac catheterization in nearly all situations involving coronary arteries among children with congenital heart disease and is now used as a diagnostic tool complementary to echocardiography. Performing coronary computed tomography angiography in such pediatric population is technically challenging, because of complex anatomies, breath-holding issues, uncontrolled movements, elevated heart rates, and visualization of small structures. Therefore, better (higher image quality) and safer (lower radiation dose) coronary computed tomography angiography practices are needed. Recent computed tomography technology allows further personalization of cardiac acquisitions and makes their application possible in daily clinical routine. The COROPEDIA trial provides a comprehensive set of parameters to perform pediatric coronary computed tomography angiography as a function of a patient's cardiac characteristics. Results suggest that duration and position of the acquisition window within cardiac cycle should be adapted to patient's heart rate and variability, to maximize structure visualization. Besides, carefully selected multiphasic acquisitions should be performed to provide more information to clinicians while keeping submillisievert dose levels.

Congenital heart disease (CHD) is the leading cause of congenital abnormalities (8/1000 of live births).¹ Coronary artery anomalies represent 0.17% of the overall pediatric population² and are associated with an increased risk of heart failure, valve disease, arrhythmia, or sudden death.³

Over the past 2 decades, coronary computed tomography angiography (CCTA) has progressively replaced cardiac catheterization in nearly all situations involving coronary arteries among children with CHD. This includes abnormal left or right coronary artery arising from the pulmonary artery, syncope or sudden death with suspected interarterial or intramural coronary artery, possible existence of a major coronary artery branch crossing the infundibulum before surgical repair of tetralogy of Fallot, and follow-up after surgical reimplantation of coronary arteries.^{4,5} In these situations, CCTA has progressively been used as a diagnostic tool complementary to echocardiography.^{5,6} As a non-invasive and widely available technique, CCTA provides superior spatial resolution with multiple reconstruction possibilities.⁶ It may be a good alternative to overcome the limited acoustic window and poor extracardiac structure visualization provided by echocardiography.⁶

The recent development of wide-detector scanner allows volumetric acquisitions within a single heartbeat, avoiding stair-step artifacts, reducing radiation exposure, and improving uniform contrast enhancement.⁷

However, CCTA performed on children still raises 2 major difficulties: (1) The use of ionizing radiation in young patients involves a highly radiosensitive population, potentially subject to multiple examinations during their follow-up^{2,8} and (2) There are technical issues related to young patients, such as breath-holding issues, uncontrolled movements during acquisition, elevated heart rates (HR), and visualization of small structures.

Technically, a cardiac CTA is currently performed in 3 ways depending on how the ECG data are used:

1. CTA without ECG synchronization: during the entire acquisition duration, the positions of the shifting vessels are averaged in a single reconstructed volume, causing important motion artifacts. Therefore, this technique is not suitable for coronary artery assessment in patients with a high HR, such as children with CHD,⁹ despite moderate delivered doses, from 0.5 to 4.8 mSv.^{7,10,11}
2. Retrospective ECG-gated acquisitions: ECG synchronization is only used retrospectively, at the reconstruction stage, to differentiate data coming from each cardiac phase separately. Every cardiac phase is reconstructed one at a time and is available with high image quality. It delivers a substantial amount of radiation, from 3 to 11 mSv^{8,12-14} for pediatric patients: its use should be limited to least performing CT scanners and applied with ECG dose modulation.
3. Prospective ECG-triggered acquisitions. The ECG synchronization is used to trigger irradiation at the right moment to select a specific cardiac phase. During other phases of low interest, irradiation can either be halted or only be reduced, leading to monophasic (without any padding) or multiphasic acquisition, respectively. Multiphasic acquisitions give more flexibility for diagnosis at the cost of an increased dose to the patient. Doses from 0.8 to 4 mSv have been reported for pediatric populations.^{6,8,13-15}

Prospective ECG-triggered monophasic acquisitions are well adapted to regular and moderate HR, such as in adult patients. However, children with CHD do not present equivalent cardiac characteristics; they have higher and unstable HR, involving faster coronary artery velocity.^{16,17} Coronary arteries are then harder to acquire without motion artifacts, because of the limited temporal resolution of CT. This may finally lead to 11% to 15% of nondiagnostic or suboptimal quality examinations.^{11,13,18}

Therefore, a hybrid method between monophasic and multiphasic acquisitions could combine the advantages of both techniques providing additional—but

strictly selected—cardiac phases compared with monophasic acquisitions, while maintaining irradiation at low dose levels compared with a regular multiphasic acquisition. Moreover, some studies have suggested adapting the acquisition window within the cardiac cycle as a function of patients' HR and HR variability.^{19–22} However, these studies did not include pediatric patients with the use of CT.

By combining these 2 novel aspects in a single acquisition protocol, the COROPEDIA trial (Observational Study for Feasibility and Performance of Sub-millisievert Coronary Computed Tomography Angiography for Coronary Artery Anomalies in Paediatric Patients) aimed to prospectively assess the feasibility of this new way of performing submillisievert CCTA on children with CHD.

METHODS

Study Design and Population

This cross-sectional study was performed from May 2017 to December 2017 in a tertiary care pediatric and congenital cardiology reference center (Montpellier University, France). Children with CHD younger than 18 years old and with a suspected or confirmed coronary artery anomaly were prospectively recruited. Only those requiring a CCTA as part of their follow-up were eligible. Children with absolute contraindication for angiography CT (allergy to iodinated contrast material) were not eligible.

Formal Aspects

The study was conducted in compliance with the Good Clinical Practices protocol and Declaration of Helsinki principles. It was approved by the French South-East III Ethics Committee (2017-A00909-44) and registered. Informed consent was obtained from all parents or legal guardians. The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

CT Pediatric Protocol

The existing protocol in our institution was used for this study. A complete physical examination and an ECG were systematically performed before CCTA. One hour before CCTA, eligible children with an HR above 70 beats per minute (bpm) received a single dose of β -blocker (propranolol 0.5 mg/kg, orally). When needed, on the pediatric cardiologist's recommendation, sedation was prescribed, using hydroxyzine (1 mg/kg, orally) and midazolam (0.2 mg/kg, orally). After CCTA, children were monitored (blood pressure, pulse) for 3 hours in the pediatric cardiology day hospital unit. The CT pediatric protocol does not require general anesthesia in our institution.

CT Technical Parameters

CCTA was performed on a single-source 512-slice CT (Revolution CT, General Electric Healthcare [GE], Milwaukee) using a wide detector aperture (160 mm), iterative reconstruction algorithm (Asir-V with 50% strength), and specific

reconstruction software reducing coronary motion artifacts (SnapShot Freeze).

A prospective ECG-triggered axial technique was performed within a single heartbeat for all patients. Low kV values were selected to maximize iodine contrast to noise ratio (70 kV for children weighing <12 kg; 80 kV for >12 kg and <35 kg; 100 kV for >35 kg).¹⁰

All patients were injected with an iodinated contrast medium (Iomeron 400 mg/mL at 2 mL per kg intravenously, Bracco s.p.a, Milan, Italy) followed by intravenous 10 mL of saline solution. Injection was manually triggered under the radiologist's supervision. Contrast material was infused with flow rates of 4, 3, or 1.5 mL/s through respectively 20, 22, or 24g intravenous antecubital catheters, selected on body size, and prioritizing smallest gauges.

Cardiac Gating Parameters

For every combination of patient's HR and HR variability, a specific acquisition scheme was designed to deliver irradiation at the best theoretical phase within the cardiac cycle. It was made up of one central phase, receiving the maximum irradiation dose (for an optimal image quality); and secondary phases, receiving only a fraction of this maximum dose (with reduced image quality).

To determine the position of the central phase within the cardiac cycle, we took the following factors into consideration: (1) a diastolic acquisition for patients with HR below 80 bpm, (2) a systolic acquisition for patients with HR above 80 bpm, (3) a widened acquisition window for patients with HR higher than 80 bpm or HR variability defined as variable or irregular, and (4) a shifting acquisition window towards the end of the R-R interval on the ECG with increasing HR (Figure 1).

Secondary phases which included between 25% and 85% of R-R interval were acquired with a reduced dose (20% of mA). The beginning (0%–25%) and the end (85%–100%) of R-R interval was not acquired (mA set to 0%).

Patient's HR variability was defined as (1) irregular when HR variability exceeded 6 bpm at least 4 times during ECG recording, (2) variable when HR variability exceeded 6 bpm 2 to 3 times during ECG recording, and (3) stable, otherwise.

Following these literature recommendations, a 15-scenario protocol was drafted as illustrated in Figure 2. Each irradiation scheme was optimized for a given HR range and HR variability. To ease its implementation in clinical routine, the Autogating system (GE Healthcare, Milwaukee) was used. It consists in an automatic selection among the 15 schemes, based on patient's ECG, and following the rules defined on the abscissa and ordinate of Figure 2. Two applications of this protocol are presented in Figures 3 and 4.

Irradiation

The dose delivered to patients was evaluated in terms of CT dose index and dose-length product. Effective doses were derived from chest conversion factors by Deak et al²³ using the following formula.

$$ED \text{ (mSv)} = DLP \text{ (mGy}\cdot\text{cm)} \cdot k \text{ (mSv}\cdot\text{mGy}^{-1}\cdot\text{cm}^{-1})$$

The CT dose index, dose-length product, and conversion factor were expressed for a 32 cm body phantom reference.

Situation	References	Recommended acquisition phase
Low to Moderate heart rates	(20,21)	Mid-end diastole
High to very high heart rates	(11,19-22,28)	End-systolic
Switching from diastolic to systolic acquisition	(11,19-21,27)	Between 70 et 85 bpm
Every heart rates	(20,21)	Phases from 0% to 25% and from 85% to 100% of the R-R interval to be avoided
Increasing heart rates	(19,21,28)	Motionless phase shifting towards the end of the R-R interval
Variable and Irregular heart rates	(24)	Widening of the acquisition window

Figure 1. Optimal cardiac phase for prospective ECG-gated acquisitions.

Literature recommendations about phase selection within the R-R interval as a function of patient's cardiac parameters.

Image Analysis

Reconstructed images were evaluated independently by 2 radiologists with 10 and 20 years of experience in cardiovascular imaging, respectively.

General image quality for diagnosis, noise perception in the main phase, motion and injection artifacts, were evaluated. All coronary segments were reviewed and gathered under the 4 main coronary artery groups, for scoring: right coronary artery (segments 1–4), left anterior descending artery (segments 6–10), left circumflex artery (segment 11–15), and left main coronary artery (segment 5). Every metric and the ability to visualize the entire coronary course were assessed by both radiologists following precise scoring criteria derived from previous publications²⁴ and reported in Table 1. Interobserver agreements were evaluated, and the mean score given by the 2 observers was finally considered.

The ability of CCTA to answer the initial clinical question was qualitatively evaluated by both radiologists (yes, partially, and no) taking into account: visualization of the ostia, presence of ostial stenosis, plication aspects, retrosternal course, presence and length of intramyocardial course, anomalous course

or origins of coronary arteries involving potential compression between the aorta and pulmonary trunk (Figures 5 through 7).

Statistical Analysis

Patient's characteristics were described with proportions for categorical variables and as mean±SD for quantitative variables.

Correlations between the score quantifying image quality, and cardiac parameters, age, dose (CT dose index), noise, and artifacts were calculated using the Spearman correlation coefficient. Correlation strength was expressed using Evans classification.²⁵ CIs were computed using the Fisher z transformation. Interobserver agreement was assessed with weighted kappa coefficients, using Landis and Koch criteria to characterize strength agreement.²⁶ Statistical analyses were performed at a conventional 2-tailed α level of 0.05 using SAS version 9.2 (SAS Institute, Cary, NC).

RESULTS

Fifty pediatric patients (24 females, 26 males, 6.1±4.9 years old) were prospectively enrolled in the COROPE-

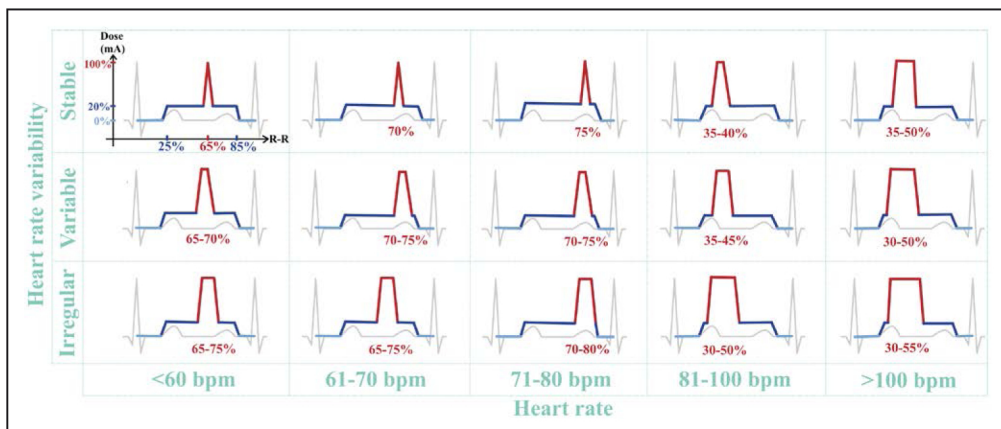


Figure 2. ECG-triggering patterns for every heart rate (HR) and HR variability combination (15 possibilities).

The figure shows X-ray tube current variations (ie, dose modulation) within a patient's cardiac cycle. The red line represents the central phase that receives the maximum dose for optimal image quality. Other cardiac phases (dark blue line) only receive 20% of the maximum dose producing reduced image quality. Phases from 0% to 25% and 85% to 100% are never acquired (light blue line).

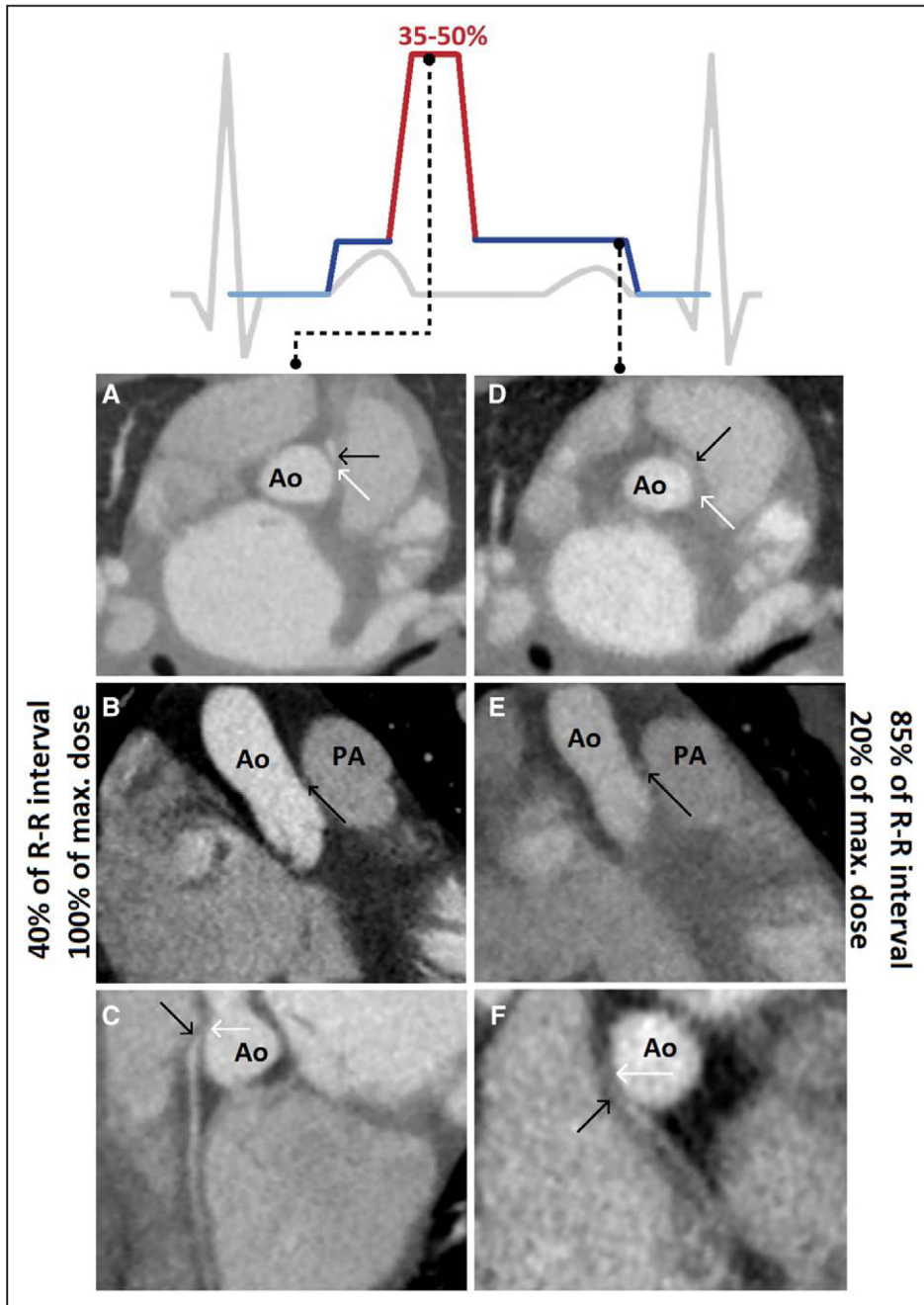


Figure 3. Preoperative coronary computed tomography angiography (CCTA) of a 1.5 year-old boy (heart rate [HR]=115 bpm; stable HR variability=4 bpm) before mitral surgery revealing an anomalous origin of the right coronary artery (RCA) presented at 2 different phases of the R-R interval (at 40% and 85% of the R-R interval).

This case will be further discussed in Figure 5. The axial (A), sagittal-oblique (B), and curved multiplanar (C) systolic reconstructions show a severe compression of the right ostium (white arrows), and of the RCA proximal segment (black arrows) between the aorta and the pulmonary artery. The axial (D), sagittal-oblique (E), and curved multiplanar (F) diastolic reconstructions reveal a lesser degree of these compressions, highlighting the importance of multiple phase acquisitions for dynamic information. We note the increase of noise between the 2 phases, due to the dose decrease between main and secondary acquisitions (100% and 20% of dose, respectively).

DIA clinical trial (Table 2). The underlying CHD requiring CCTA were, in descending order, transposition of the great arteries (n=13), tetralogy of Fallot (n=12), anomalous origin of coronary arteries (n=10, including 5 case of abnormal left coronary artery arising from the pulmonary artery), complex CHD (n=7), anomalous course of coronary arteries (n=4), ventricular septal defects

(n=3), and post-heart transplant checkup (n=1). All eligible children participated in the study, as no contraindication for CCTA occurred and all families gave their informed consent. All children received a β -blocker (propranolol 0.5 mg/kg, orally) and sedation with hydroxyzine (1 mg/kg, orally). An additional sedation by midazolam (0.2 mg/kg, orally) was necessary for 25

Table 1. Scoring Scale

Score	Diagnostic Performance Evaluation	Motion and injection, artifacts evaluation	Noise perception	RCA, LAD, LCX, LM evaluation
4	Excellent: no artifacts, unrestricted evaluation	No artifacts	Low noise	Clearly visualized, unrestricted evaluation
3	Good: minor artifacts, good diagnostic quality	Moderate artifacts	Moderate noise	Mildly blurred, good evaluation
2	Adequate: moderate artifacts, still acceptable for diagnostic	Important artifacts: without diagnosis interference	Important noise: without diagnosis interference	Moderately blurred, just acceptable for evaluation
1	Not assessable: severe artifacts impairing accurate evaluation	Severe artifacts: interfere with diagnosis	Important noise: interfere with diagnosis	Severely blurred, insufficient for evaluation

LAD indicates left anterior descending artery; LCX, left circumflex artery; LM, left main coronary artery; and RCA, right coronary artery.

children, all aged <6 years old. No child required under-vent general anesthesia. No adverse effect related to β -blockers, sedation, and the CCTA itself was reported.

Between 1 and 7 exams were conducted with each of the 15 scan protocols, and no deviation between expected and actual irradiation schemes was observed.

The mean HR was 89 ± 26 bpm under premedication. Patient's HR dropped by 3.4 ± 13.8 bpm on average, following the β -blocker administration.

All performed CCTA were adequate to fully answer the clinical question using an effective dose inferior to 1 mSv (0.97 ± 0.34 mSv). Ninety-four percent (47/50) of the examinations presented good or excellent image quality for diagnosis. No exam was considered as not assessable but 6% (3/50) were scored as adequate because of coronary motion artifacts. The main acquisition (Figure 2, red lines) successfully targeted the optimum phase within the R-R interval in 88% of cases (44/50). The remaining 6 patients, with optimum phase occurring during low signal acquisition

(Figure 2, dark blue lines), all had an HR between 76 and 85 bpm.

Correlations between image quality and other parameters are presented in Table 3. A moderate correlation was found between image quality degradation and image noise ($r=0.44$; $P<0.01$) or motion artifacts ($r=0.48$; $P<0.01$). A weak correlation with injection artifacts was also reported ($r=0.36$; $P<0.01$). Very weak to no correlation were found between image quality and cardiac parameters including mean HR ($r=-0.19$; $P=0.19$), maximum HR ($r=-0.13$; $P=0.34$), minimum HR ($r=-0.16$; $P=0.27$), and HR variability ($r=0.00$; $P=0.99$). No significant differences in visualization of left and right coronary artery segments were reported with 91%, 91%, 92%, and 91% of right coronary artery, left main coronary artery, left anterior descending artery, and left circumflex artery, respectively evaluated as good or excellent (Table 4). The entire length of the coronary tree, including proximal, middle, and distal segments, could be visualized in 100% of cases. A total of 46 coronary

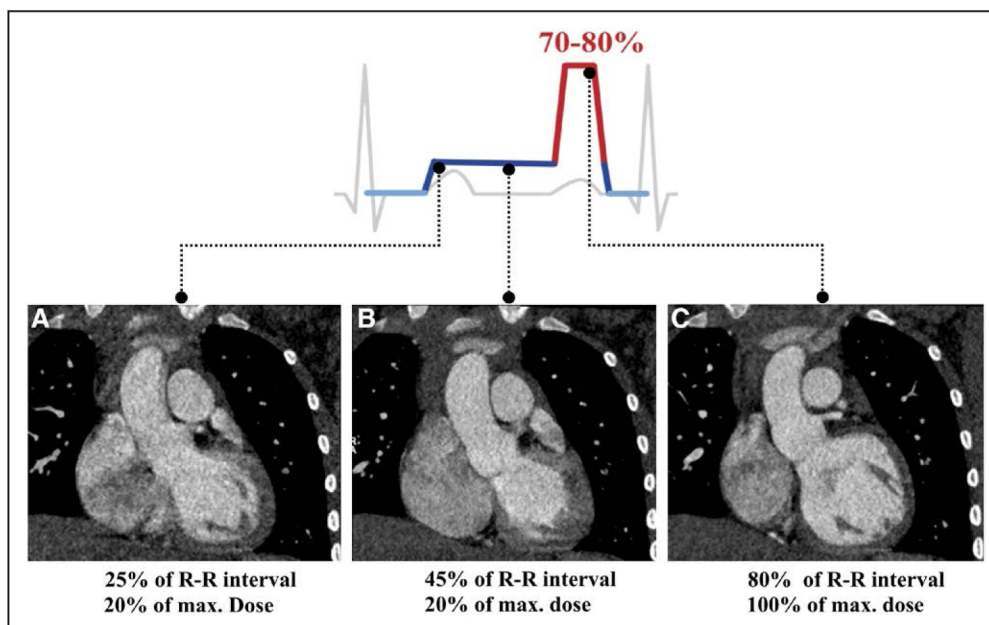


Figure 4. Coronary computed tomography angiography (CCTA) performed for abnormal left coronary artery arising from the pulmonary artery (ALCAPA) suspicion on a 9-year-old girl (heart rate [HR]=78 bpm, irregular HR variability=18 bpm).

Different phases are presented here: (A) at 25%, (B) at 50%, and (C) at 80% of the R-R interval. Maximum dose is delivered from 70% to 80%. On this main phase (C), the left coronary origin is observable. This is not the case at 40% of the R-R interval (B) because of important motion artifacts.

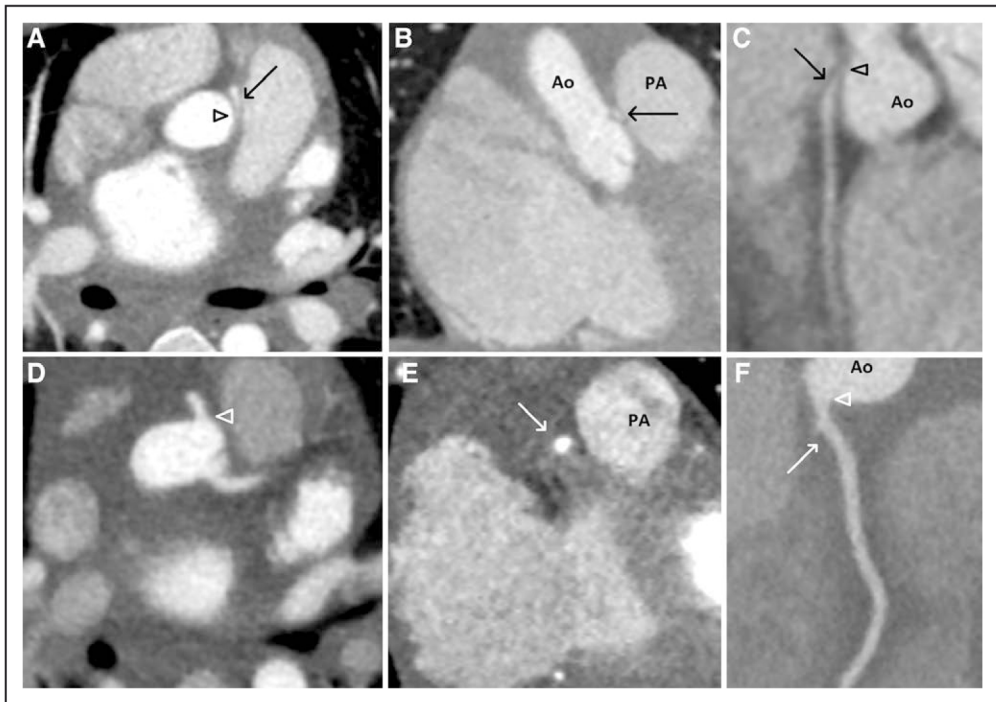


Figure 5. Preoperative coronary computed tomography angiography (CCTA) of a 1.5-year-old boy (heart rate [HR]=115 bpm; HR variability=4 bpm) before mitral valve and coronary anomaly surgical repair.

Axial (A), sagittal-oblique (B), and curved (C) reformations reveal an anomalous origin of the right coronary artery (RCA) arising from the left anterior sinus. We observe a compression of RCA origin (black arrow head) and proximal segment (black arrow) because of an aortic-pulmonary course. A replantation of the RCA origin on the right anterior sinus was performed during the mitral surgery. The axial (D), sagittal-oblique (E), and curved (F) reformations show the replantation of the RCA origin, now arising from the right anterior sinus, without interaortic-pulmonary course (white arrow), and without residual stenosis (white arrow head).

trees could be reconstructed with a score of 3 or more in every segment (good or excellent evaluation). The remaining 4 coronary trees had 1 segment or more with a score of 2 (moderately blurred, just acceptable for evaluation). No coronary tree with a nonevaluative segment was reported. The effective doses delivered to patients were not different among each age group (Table 5).

Interobserver agreement was substantial for diagnostic image performance ($k=0.70$ [0.50–0.90]),

noise evaluation ($k=0.61$ [0.39–0.82]), artifact evaluation ($k=0.64$ [0.48–0.80]), and coronary tree segment assessment ($k=0.67$ [0.57–0.77]).

DISCUSSION

The COROPEDIA clinical trial assessed the feasibility and the performance of a selective multiphasic CCTA at low

Table 2. Patient Characteristics

	Age Class				
	Overall	0–1 y	1–6 y	6–10 y	10–17 y
Patient no.	50	13	12	13	12
Age, y	6.1±4.9	0.4±0.2	3.7±1.6	7.9±1.2	12.9±2.4
Height, m	1.1±0.4	0.6±0.1	1.0±0.1	1.2±0.1	1.5±0.1
Weight, kg	20.4±14.4	5.5±1.6	14.9±3.5	21.2±4.2	41.2±10.7
Mean HR, bpm*	90±26	123±13	91±19	69±11	72±10
Min HR, bpm†	80±27	112±15	84±22	59±14	62±11
Max HR, bpm‡	99±27	132±20	97±15	83±18	81±14
HR variability, bpm§	14±11	15±11	12±11	17±13	12±7
Scan length, cm	104±29	74±15	100±21	115±17	133±23

bpm indicates beats per minute; and HR, heart rate.

*Mean HR during acquisition.

†Minimum HR during acquisition.

‡Maximum HR during acquisition.

§HR variability during acquisition, defined as the difference between the average HR and the higher HR deviation recorded during the acquisition.

Table 3. Correlations Between General Diagnostic Image Quality and Cardiac Parameters, Age, Dose (CTDI), Noise, and Artifacts

Parameter	N	r_s^*	95% CI	P Value†
Minimum HR‡	50	-0.16	(-0.42 to 0.13)	0.27
Maximum HR‡	50	-0.13	(-0.40 to 0.15)	0.34
Mean HR‡	50	-0.19	(-0.44 to 0.10)	0.19
HR variability§	50	0.00	(-0.28 to 0.28)	0.99
Age	50	0.16	(-0.12 to 0.42)	0.24
CTDI	50	0.32	(0.05 to 0.55)	<0.05
Noise	50	0.44	(0.18 to 0.64)	<0.01
Motion artifacts	50	0.48	(0.07 to 0.57)	<0.01
Injection artifacts	50	0.36	(0.09 to 0.58)	<0.01

CTDI indicates computed tomography dose index; and HR, heart rate.

* r_s =Spearman rank correlation coefficient.

†A P value for a $H_0: r_s=0$; a P value <0.05 indicates a correlation coefficient significantly different from 0.

‡Minimum, maximum, and mean heart rates recorded during the acquisition.

§HR variability is defined as the difference between the average HR and the higher HR deviation recorded during the acquisition.

dose, from a cohort of 50 children with CHD requiring coronary artery imaging in their clinical follow-up. We used a wide detector single-source CT scanner, combined with a specific cardiac phase selection protocol, designed from a comprehensive literature review. To our knowledge, this study is the first to prospectively test a selective multiphasic acquisition protocol based on cardiac rhythm and variability. This approach gave the advantage of multiphasic acquisitions (more information for the clinician and reduced risk of acquiring cardiac phase with motion artifacts) as well as keeping dose to submillisievert levels by being selective on the multiphasic aspect.

Phase Selection as a Function of the Patient's Cardiac Characteristics

Performing CCTA on adults has been extensively studied.^{20,21,24,27} In a pediatric population, coronary artery diameters are smaller, velocities, and HR are higher; and the variability of cardiac rhythms from one patient to another is an important consideration (from 42 to 185 bpm in this study). Therefore, targeting the same car-

diac phase for all patients represents a limiting factor of CCTA image quality.^{16,28,29} As a result, to maximize chances of triggering the acquisition when coronary arteries are relatively motionless, it is crucial to adapt duration and positioning of the acquisition window within the R-R interval. Considering HR below 80 bpm, the least motion of the coronary artery is reached from mid to end diastole, when blood is passively flowing from the lungs into the left ventricle while the myocardium is at rest,^{20,21} but with increasing HR, this stability phase tends to shorten. The end-systolic phase then becomes the longest motionless phase.^{11,19-22,28} Thereby, a switch from a diastolic to a systolic acquisition should be applied for patients with HR above 70 to 90 bpm.^{11,19-21,27} In addition, as diastolic diastasis shortens with increasing HR, both diastolic and systolic stability phases tend to slightly shift towards the end of the cycle.^{19,21,28} Additionally, tachycardia and HR variability involve higher chances of missing the targeted phase, so that a wider acquisition window is recommended.²⁴ Independently of HR, cardiac phases between 0% to 25% and 85% to 100% of R-R interval present important motion, thus these should not be acquired, preserving the patient from unnecessary irradiation.^{20,21}

Selective Multiphasic ECG-Triggered Acquisitions

This protocol resulted in a mean delivered dose inferior to 1 mSv, with the ability to fully answer the clinical question for all patients. Very few CCTA studies have been conducted with pediatric patients with CHD. Most of them reported doses from 1.4 to 4 mSv.^{6,15} Some recent studies went further in dose reduction. Paul et al¹⁸ reported a dose of 0.26 mSv with end-systolic monophasic acquisitions. In 13% of cases, CCTA had to be performed again because of suboptimal image quality and inaccurate diagnosis. Habib Geryes et al¹³ used doses ranging from 0.8 to 3.1 mSv and reported 15% of examinations with significant artifacts. Finally with an effective dose of 1.3 mSv, Ben Saad et al¹¹ counted 11% of CCTA with no possible diagnosis, because of insufficient contrast, noise, respiratory motion, or cardiac motion. Neither suboptimal image quality nor sec-

Table 4. Coronary Artery Evaluation

Quality of Visualization	Score 4* (95% CI)	Score 3* (95% CI)	Score 2* (95% CI)	Score 1* (95% CI)	Mean Score (4) (95% CI)
RCA	67 (58-76)	24 (16-32)	9 (3-15)	0	3.6 (3.5-3.7)
LM	68 (59-77)	22 (14-30)	10 (4-16)	0	3.6 (3.5-3.7)
LAD	67 (58-76)	25 (17-33)	8 (3-13)	0	3.6 (3.5-3.7)
LCX	66 (57-75)	25 (17-33)	9 (3-15)	0	3.6 (3.5-3.7)

LAD indicates left anterior descending artery; LCX, left circumflex artery; LM, left main coronary artery; and RCA, right coronary artery.

*Score 4: clearly visualized, unrestricted evaluation; Score 3: mildly blurred, good evaluation; Score 2: moderately blurred, just acceptable for evaluation; and Score 1: severely blurred, insufficient for evaluation.

Table 5. Overall and Age-Dependent Dose and Image Quality Evaluation (Mean±SD)

	Overall	Age Class			
		0–1 y	1–6 y	6–10 y	10–17 y
Patient no.	50	13	12	13	12
Dose					
CTDI, mGy	2.8 ±1.3	1.9±0.4	2.3±0.8	3.5±1.7	3.6±1.2
DLP, mGy·cm	31.5±21.2	13.8±3.5	21.9±6.7	41.5±21.3	49.2±22.5
ED, mSv	1.0±0.3	1.0±0.3	0.9±0.3	1.0±0.5	1.0±0.3
Image quality					
Overall	3.6±0.6	3.5±0.5	3.5±0.8	3.6±0.6	3.7±0.3
Noise	3.5±0.5	3.3±0.5	3.4±0.5	3.6±0.5	3.6±0.3
Artifacts					
Motion	3.5±0.6	3.4±0.6	3.4±0.8	3.5±0.6	3.8±0.3
Injection	3.7±0.4	3.5±0.5	3.8±0.4	3.8±0.3	3.8±0.4

CTDI indicates computed tomography dose index; DLP, dose-length product; and ED, effective dose.

ond acquisition occurred in the COROPEDIA trial (0%; CI [0%–7.11%]). This differs significantly from the results previously discussed. Two reasons could explain this difference: first, triggering acquisitions during the coronary artery motionless phase, defined as a function of the patient's cardiac characteristics, increases

chances of getting images free of motion artifacts. Second, because of multiphase approach, cardiac phases from 25% to 85% of the R-R interval were reconstructed, even when acquired with low signal (only 20% of the dose was delivered during secondary phases). This expands chances of getting an interpretable phase

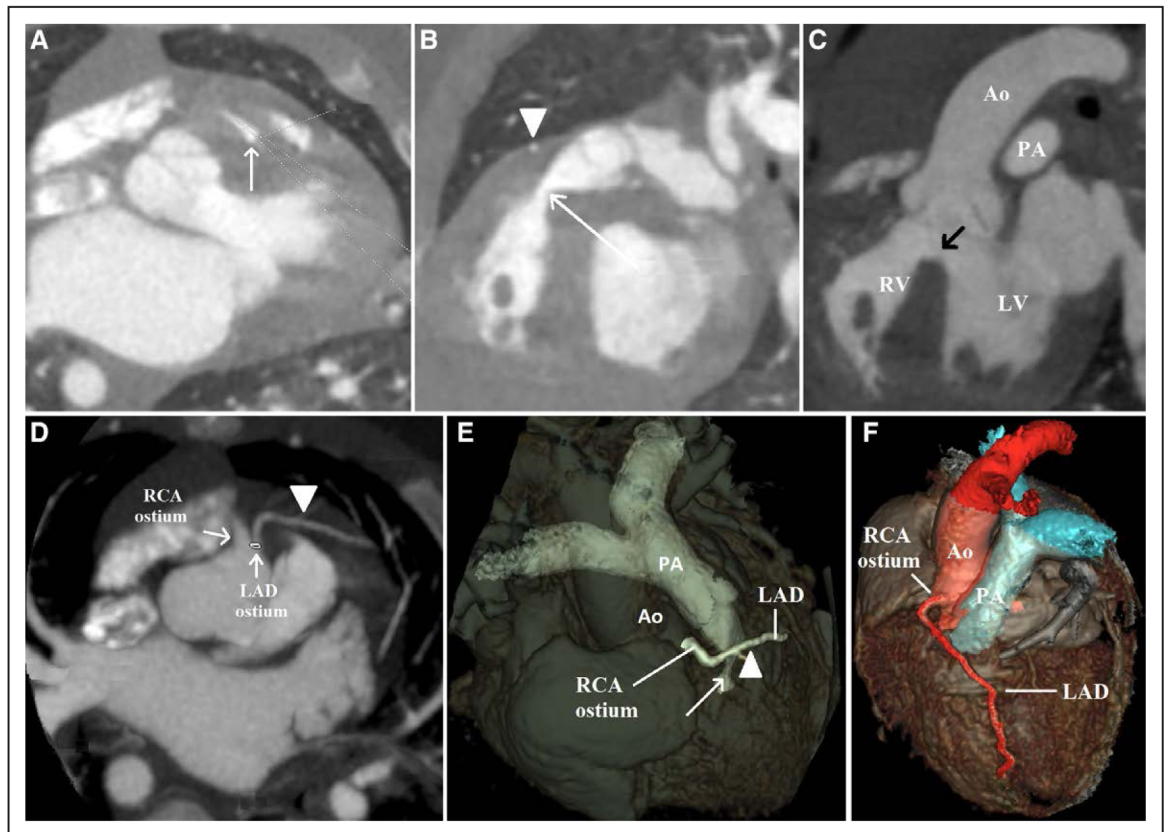


Figure 6. Preoperative coronary computed tomography angiography (CCTA) of a 6-month-old girl (heart rate [HR]=117 bpm, HR variability=18 bpm) undergoing surgery for tetralogy of Fallot repair.

The infundibular stenosis (white arrow) is shown in an axial view (A), an oblique-sagittal plane (B), and a volume rendered (E). A membranous ventricular septal defect (black arrow) is observed in an oblique-sagittal view (C). We also note an anomalous origin of the left anterior descending (LAD) artery (D) arising from the right anterior sinus (white circle) with a preinfundibular course (B, D, and E: white arrowhead). F, Volume rendered showing a single LAD course in the interventricular sulcus.

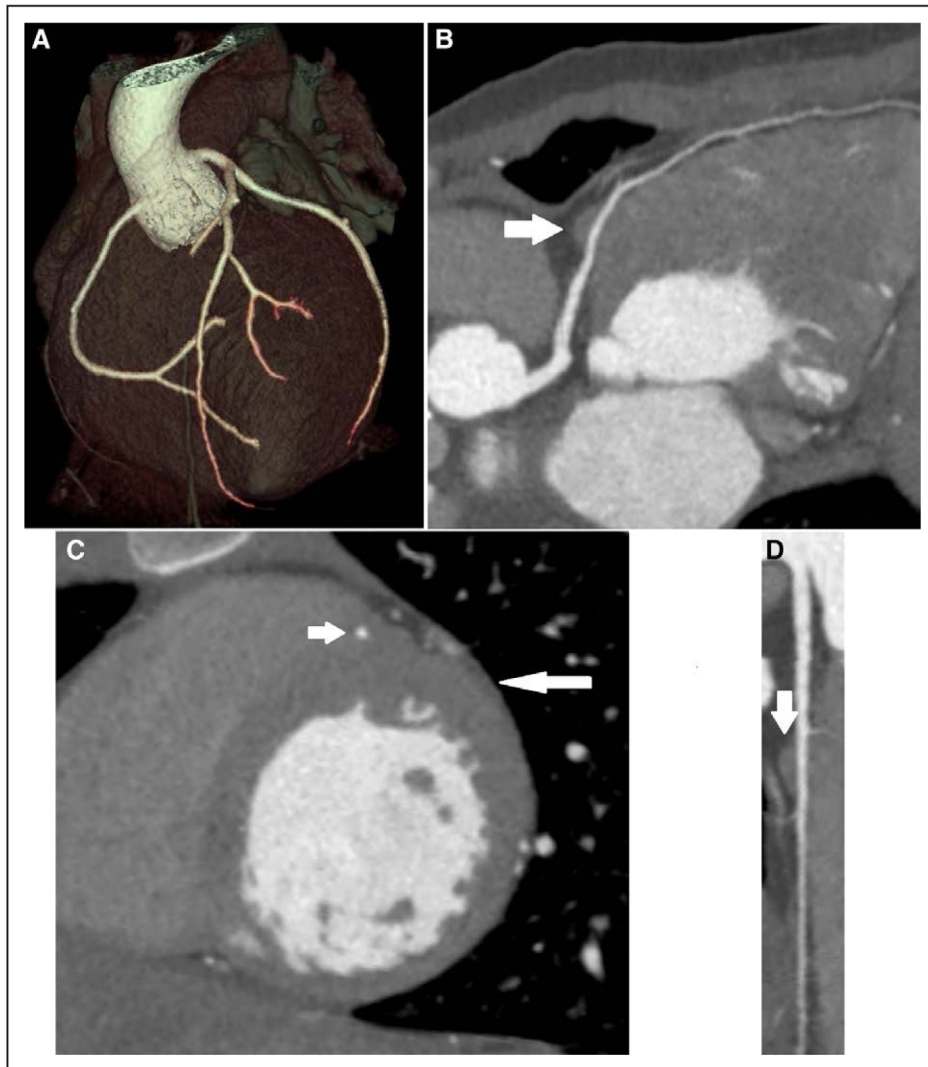


Figure 7. Coronary computed tomography angiography (CCTA) (heart rate [HR]=52 bpm, HR variability=7 bpm) in a 12-year-old male with chest pain during exercise: hypertrophic cardiomyopathy and intramyocardial coronary course (small white arrows). **A**, Volume-rendered image of whole coronary tree. **B**, Curved multiplanar reformation. **C**, Cross-sectional reformation showing an anterolateral thickening of the left ventricle wall (long white arrow). **D**, Stripe reconstruction of the left anterior descending artery (LAD) course.

whenever the main phase did not provide the expected results (coronary motion artifacts, sudden child's agitation, or crying). This was the case in 6 patients of our study, in whom a low signal phase presented higher diagnosis quality than the main phase. The HR of these patients, all between 76 and 85 bpm, suggests that 80 bpm might not be the optimum limit to switch from diastolic to systolic acquisitions. Yet, no clear trend implying increasing or lowering this threshold appeared in our study, suggesting that the best phase in patients with HR close to 80 bpm might be either diastolic or systolic, depending on individuals.

Delivered Doses

No differences in effective doses were reported, regardless of patients' age group. Dose-length product increased with body size, due to higher scan length and

X-ray absorption in larger bodies. Conversely, conversion factors decreased as a function of the patient's age because of lower dose contribution to radiosensitive organs (lung, liver, etc) because of increased patient cross section.²³ Therefore, in our study, effective doses remained steady through age groups.

Image Quality

Image quality slightly improved with age, while noise and motion artifacts were reduced. Fewer uncontrolled movements and larger size of cardiac structures could lead to these slight differences. For the 3 patients with adequate image quality only, motion artifacts remained the limiting factor, as reported previously.^{11,19} In our study, image noise and injection artifacts correlated to image quality; however, this did not lead to any inferiority in diagnostic quality, unlike other studies.¹¹ The

lack of breath holding did not lead to any limitation in image quality, neither. Children had the peripheral intravenous catheter placed before moving to the imaging department to avoid patient's agitation. Acquisitions only started when the child was calm on the table, to reduce respiratory artifacts. Additionally, coronary arteries shifting by respiration should be less than by cardiac pulsation.^{12,30}

Correlations Between Image Quality and Patients' Cardiac Characteristics

Some studies reported a correlation between HR³¹ or HR variability²⁷ and image quality. This is not the case in our study, and the CI from our analysis suggests that it is unlikely that an important correlation exists between image quality and cardiac parameters. Acquisition windows adapted to patient's HR and HR variability together with the multiphasic aspect of our acquisitions might have helped to reduce the negative impact of high HR and HR variability on image quality. In this study, we used the existing protocol in our institution, for example, children with an HR above 70 bpm received a single dose of β -blocker. Our results suggest that β -blockers might not be necessary, but this needs to be evaluated in further studies.

Coronary Artery Segment Visualization

Surprisingly, we found no significant visualization differences between right coronary artery, left main coronary artery, left circumflex artery, and left anterior descending artery. Other studies have reported that left circumflex artery and right coronary artery were more subject to myocardium movements, resulting in difficulties in visualizing these particular segments.^{16,17,29} About lower HR, a common point of least motion is established for all coronary segments at mid diastole. Nevertheless, this common interval no longer exists at higher HR (>75 bpm).^{16,21,28} Therefore, we made the assumption that this lack of visual quality differences between coronary segments in our study might be because of the multiphasic aspect of the protocol. Regardless of patient's HR, every coronary segment might be visualized in its own motionless phase, in case the main acquisition did not provide satisfactory vessel visualization.

Limitations

This study aimed to represent a typical pediatric population requiring CCTA, as part of their follow-up. Patients were gathered into 4 homogeneous groups, for analysis. Yet, the heterogeneity of our CHD population may represent a limit of the study. Although our cohort only included pediatric patients, CCTA care management is different when considering newborns,

infants, or adolescents. Our study revealed important variability in terms of cardiac parameters, breath-holding capacities, and morphology. However, the use of a multiphasic protocol, with the acquisition window adapted to patient's HR and HR variability led to significant diagnostic confidence for clinicians while maintaining low radiation dose for all patients. The COROPEDIA clinical trial assessed this possibility. Yet, additional studies are necessary to refine this model, leading to fully personalized CCTA examinations for children with CHD.

Conclusions

For the first time in a pediatric population, the COROPEDIA clinical trial assessed the feasibility and the performance of a selective multiphasic CCTA at low dose, based on prospectively ECG-triggered examinations. This study defined a comprehensive set of parameters to perform pediatric CCTA as a function of a patient's cardiac characteristics. Despite difficult acquisition conditions in pediatrics (HR up to 185 bpm, irregular rhythms, and coronary artery diameters under 2 mm), all examinations fully answered the clinical question, for a radiation dose equivalent to <4 months of natural background irradiation.

Correspondence

Julien Le Roy, MSc, Pediatric and Congenital Cardiology Department; Montpellier University Hospital; 371 Ave du Doyen Giraud, 34295 Montpellier, France. Email j-le_roy@chu-montpellier.fr

Affiliations

Pediatric and Congenital Cardiology Department, M3C Regional Reference CHD Center, CHU Montpellier, France (J.L.R., M.V., H.A., K.L., P.A.). PHYMED-EXP, University of Montpellier, CNRS, INSERM, CHU Montpellier, France (J.L.R., M.V., A.L., P.A.). Radiology Department, CHU Montpellier, France (H.V.K., H.Z.). Epidemiology and Clinical Research Department, University of Montpellier, INSERM, CHU Montpellier, France (T.M.).

Sources of Funding

This study was supported by Montpellier University Hospital Clinical Research Program (UF 9785).

Disclosures

None.

REFERENCES

1. Bernier PL, Stefanescu A, Samoukovic G, Tchervenkov CI. The challenge of congenital heart disease worldwide: epidemiologic and demographic facts. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu.* 2010;13:26–34. doi: 10.1053/j.pcsu.2010.02.005
2. Davis JA, Cecchin F, Jones TK, Portman MA. Major coronary artery anomalies in a pediatric population: incidence and clinical importance. *J Am Coll Cardiol.* 2001;37:593–597.

3. Eckart RE, Scoville SL, Campbell CL, Shry EA, Stajduhar KC, Potter RN, Pearse LA, Virmani R. Sudden death in young adults: a 25-year review of autopsies in military recruits. *Ann Intern Med.* 2004;141:829–834.
4. Goo HW, Park IS, Ko JK, Kim YH, Seo DM, Park JJ. Computed tomography for the diagnosis of congenital heart disease in pediatric and adult patients. *Int J Cardiovasc Imaging.* 2005;21:347–365; discussion 367. doi: 10.1007/s10554-004-4015-0
5. Ou P, Celermajer DS, Calcagni G, Brunelle F, Bonnet D, Sidi D. Three-dimensional CT scanning: a new diagnostic modality in congenital heart disease. *Heart.* 2007;93:908–913. doi: 10.1136/hrt.2006.101352
6. Goitein O, Salem Y, Jacobson J, Goitein D, Mishali D, Hamdan A, Kuperstein R, Di Segni E, Konen E. The role of cardiac computed tomography in infants with congenital heart disease. *Isr Med Assoc J.* 2014;16:147–152.
7. Jadhav SP, Gollriz F, Atweh LA, Zhang W, Krishnamurthy R. CT angiography of neonates and infants: comparison of radiation dose and image quality of target mode prospectively ECG-gated 320-MDCT and ungated helical 64-MDCT. *AJR Am J Roentgenol.* 2015;204:W184–W191. doi: 10.2214/AJR.14.12846
8. Ghoshhajra BB, Lee AM, Engel LC, Celeng C, Kalra MK, Brady TJ, Hoffmann U, Westra SJ, Abbara S. Radiation dose reduction in pediatric cardiac computed tomography: experience from a tertiary medical center. *Pediatr Cardiol.* 2014;35:171–179. doi: 10.1007/s00246-013-0758-5
9. Goo HW, Park IS, Ko JK, Kim YH, Seo DM, Yun TJ, Park JJ. Visibility of the origin and proximal course of coronary arteries on non-ECG-gated heart CT in patients with congenital heart disease. *Pediatr Radiol.* 2005;35:792–798. doi: 10.1007/s00247-005-1482-y
10. Herzog C, Mulvihill DM, Nguyen SA, Savino G, Schmidt B, Costello P, Vogl TJ, Schoepf UJ. Pediatric cardiovascular CT angiography: radiation dose reduction using automatic anatomic tube current modulation. *AJR Am J Roentgenol.* 2008;190:1232–1240. doi: 10.2214/AJR.07.3124
11. Ben Saad M, Rohnean A, Sigal-Cinqualbre A, Adler G, Paul JF. Evaluation of image quality and radiation dose of thoracic and coronary dual-source CT in 110 infants with congenital heart disease. *Pediatr Radiol.* 2009;39:668–676. doi: 10.1007/s00247-009-1209-6
12. Tsai IC, Lee T, Chen MC, Fu YC, Jan SL, Wang CC, Chang Y. Visualization of neonatal coronary arteries on multidetector row CT: ECG-gated versus non-ECG-gated technique. *Pediatr Radiol.* 2007;37:818–825. doi: 10.1007/s00247-007-0512-3
13. Habib Geryes B, Calmon R, Khraiche D, Boddaert N, Bonnet D, Raimondi F. Radiation dose reduction in paediatric coronary computed tomography: assessment of effective dose and image quality. *Eur Radiol.* 2016;26:2030–2038. doi: 10.1007/s00330-015-4032-5
14. Podberesky DJ, Angel E, Yoshizumi TT, Toncheva G, Salisbury SR, Alsip C, Barelli A, Egelhoff JC, Anderson-Evans C, Nguyen GB, Dow D, Frush DP. Radiation dose estimation for prospective and retrospective ECG-gated cardiac CT angiography in infants and small children using a 320-MDCT volume scanner. *AJR Am J Roentgenol.* 2012;199:1129–1135. doi: 10.2214/AJR.12.8480
15. Ihlenburg S, Rempel O, Rueffer A, Purbojo A, Cesnjevar R, Dittrich S, Gloeckler M. Dual source computed tomography in patients with congenital heart disease. *Thorac Cardiovasc Surg.* 2014;62:203–210. doi: 10.1055/s-0033-1349791
16. Lu B, Mao SS, Zhuang N, Bakhsheshi H, Yamamoto H, Takasu J, Liu SC, Budoff MJ. Coronary artery motion during the cardiac cycle and optimal ECG triggering for coronary artery imaging. *Invest Radiol.* 2001;36:250–256.
17. Shim SS, Kim Y, Lim SM. Improvement of image quality with beta-blocker premedication on ECG-gated 16-MDCT coronary angiography. *AJR Am J Roentgenol.* 2005;184:649–654. doi: 10.2214/ajr.184.2.01840649
18. Paul JF, Rohnean A, Elfassy E, Sigal-Cinqualbre A. Radiation dose for thoracic and coronary step-and-shoot CT using a 128-slice dual-source machine in infants and small children with congenital heart disease. *Pediatr Radiol.* 2011;41:244–249. doi: 10.1007/s00247-010-1804-6
19. Zhang W, Bogale S, Gollriz F, Krishnamurthy R. Relationship between heart rate and quiescent interval of the cardiac cycle in children using MRI. *Pediatr Radiol.* 2017;47:1588–1593. doi: 10.1007/s00247-017-3918-6
20. Araoz PA, Kirsch J, Primak AN, Braun NN, Saba O, Williamson EE, Harmsen WS, Mandrekar JN, McCollough CH. Optimal image reconstruction phase at low and high heart rates in dual-source CT coronary angiography. *Int J Cardiovasc Imaging.* 2009;25:837–845. doi: 10.1007/s10554-009-9489-3
21. Seifarth H, Wienbeck S, Püsken M, Juergens KU, Maintz D, Vahlhaus C, Heindel W, Fischbach R. Optimal systolic and diastolic reconstruction windows for coronary CT angiography using dual-source CT. *AJR Am J Roentgenol.* 2007;189:1317–1323. doi: 10.2214/AJR.07.2711
22. Herzog C, Abolmaali N, Balzer JO, Baunach S, Ackermann H, Dogan S, Britten MB, Vogl TJ. Heart-rate-adapted image reconstruction in multidetector-row cardiac CT: influence of physiological and technical prerequisites on image quality. *Eur Radiol.* 2002;12:2670–2678. doi: 10.1007/s00330-002-1553-5
23. Deak PD, Smal Y, Kalender WA. Multisection CT protocols: sex- and age-specific conversion factors used to determine effective dose from dose-length product. *Radiology.* 2010;257:158–166. doi: 10.1148/radiol.10100047
24. Scheffel H, Alkadhi H, Plass A, Vachenaue R, Desbiolles L, Gaemperli O, Schepis T, Frauenfelder T, Schertler T, Husmann L, Grunenfelder J, Genoni M, Kaufmann PA, Marincek B, Leschka S. Accuracy of dual-source CT coronary angiography: first experience in a high pre-test probability population without heart rate control. *Eur Radiol.* 2006;16:2739–2747. doi: 10.1007/s00330-006-0474-0
25. Evans JD. *Straightforward Statistics for the Behavioral Sciences.* Pacific Grove, CA: Brooks/Cole Publishing; 1996.
26. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics.* 1977;33:159–174.
27. Leschka S, Wildermuth S, Boehm T, Desbiolles L, Husmann L, Plass A, Koepfli P, Schepis T, Marincek B, Kaufmann PA, Alkadhi H. Noninvasive coronary angiography with 64-section CT: effect of average heart rate and heart rate variability on image quality. *Radiology.* 2006;241:378–385. doi: 10.1148/radiol.2412051384
28. Husmann L, Leschka S, Desbiolles L, Schepis T, Gaemperli O, Seifert B, Cattin P, Frauenfelder T, Flohr TG, Marincek B, Kaufmann PA, Alkadhi H. Coronary artery motion and cardiac phases: dependency on heart rate – implications for CT image reconstruction. *Radiology.* 2007;245:567–576. doi: 10.1148/radiol.2451061791
29. Achenbach S, Ropers D, Holle J, Muschiol G, Daniel WG, Moshage W. In-plane coronary arterial motion velocity: measurement with electron-beam CT. *Radiology.* 2000;216:457–463. doi: 10.1148/radiology.216.2.r00au19457
30. Kang EJ, Lee J, Lee KN, Kown H, Ha DH, Kim RB. An initial randomised study assessing free-breathing CCTA using 320-detector CT. *Eur Radiol.* 2013;23:1199–1209. doi: 10.1007/s00330-012-2703-z
31. Ünal E, Yıldız AE, Güler E, Karcaaltincaba M, Akata D, Kılınçer A, Atlı E, Topçuoğlu M, Hazırolan T. Comparison of image quality and radiation dose between prospectively ECG-triggered and retrospectively ECG-gated CT angiography: establishing heart rate cut-off values in first-generation dual-source CT. *Anatol J Cardiol.* 2015;15:759–764. doi: 10.5152/akd.2014.5720