Impact of Hybrid Iterative Reconstruction on Agatston Coronary Artery Calcium Scores in Comparison to Filtered Back Projection in Native Cardiac CT

Einfluss der hybriden iterativen Rekonstruktion bei der nativen CT des Herzens auf die Agatston-Kalziumscores der Koronararterien

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Abstract

Purpose: To investigate whether the effects of hybrid iterative reconstruction (HIR) on coronary artery calcium (CAC) measurements using the Agatston score lead to changes in assignment of patients to cardiovascular risk groups compared to filtered back projection (FBP).

Materials and Methods: 68 patients (mean age 61.5 years: 48 male; 20 female) underwent prospectively ECG-gated, non-enhanced, cardiac 256-MSCT for coronary calcium scoring. Scanning parameters were as follows: Tube voltage, 120 kV; Mean tube current time-product 63.67 mAs (50 – 150 mAs); collimation, 2 × 128 × 0.625 mm. Images were reconstructed with FBP and with HIR at all levels (L1 to L7). Two independent readers measured Agatston scores of all reconstructions and assigned patients to cardiovascular risk groups. Scores of HIR and FBP reconstructions were correlated (Spearman). Interobserver agreement and variability was assessed with κ-statistics and Bland-Altman-Plots.

Results: Agatston scores of HIR reconstructions were closely correlated with FBP reconstructions (L1, R = 0.9996; L2, R = 0.9995; L3, R = 0.9991; L4, R = 0.986; L5, R = 0.9986; L6, R = 0.9987; and L7, R = 0.9986). In comparison to FBP, HIR led to reduced Agatston scores between 97 % (L1) and 87.4 % (L7) of the FBP values. Using HIR iterations L1 – L3, all patients were assigned to identical risk groups as after FPB reconstruction. In 5.4 % of patients the risk group after HIR with the maximum iteration level was different from the group after FPB reconstruction.

Conclusion: There was an excellent correlation of Agatston scores after HIR and FBP with identical risk group assignment at levels 1 – 3 for all patients. Hence it appears that the application of HIR in routine calcium scoring does not entail any disadvantages. Thus, future studies are needed to demonstrate whether HIR is a reliable method for reducing radiation dose in coronary calcium scoring.

Key Points:
- Agatston-Scores showed excellent correlation between HIR and FBP.
- The higher the HIR Level, the more Agatston scores deviated to lower values.
- No change in risk group assignment using Level 1 – 3.
- Change in risk group assignment when using HIR compared to FBP in 1.5 % (Level 4), 5.4 % (Level 5 – 7).

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Zusammenfassung

Ziel: Ziel dieser Studie war es zu prüfen, ob die Erfassung des Agatston-Scores durch hybride iterative Rekonstruktion (HIR) gegenüber der gefilterten Rückprojektion (FBP) zu einer Änderung der kardiovaskulären Risikogruppe führt.

Material und Methoden: 68 Patienten (mittleres Alter 61,5 Jahre; 48 Männer, 20 Frauen) erhielten eine prospektiv EKG-getriggerte native 256-MSCT des Herzens zum Kalziumscoring. Die Scanparameter waren wie folgt: Röhrenspannung 120kV, Röhrenstromzeitprodukt im Mittel 63,67 mAs (50 – 150 mAs); Kollimation 2 × 128 × 0.625 mm. Die Rohdaten wurden mittels FBP und HIR in allen Iterationssstufen (L1 – L7) rekonstruiert. Zwei unabängige Beobachter erfassten die Agatston-Scores der HIR- und FBP-Rekonstruktion und nahmen eine Einteilung in kardiovaskuläre Risikogruppen.
vor. Die Resultate wurden zwischen HIR und FBP korreliert (Spearman). Die Übereinstimmung und Variabilität zwischen den beiden Beobachtern wurde mittels χ-Statistik und Bland-Altman-Plots bestimmt.

**Ergebnisse:** Die Agatston-Scores der HIR korrelierten gut bis exzellennt mit den FBP-Rekonstruktionen (L1: \( R = 0.9996 \), L2: \( R = 0.9995 \), L3: \( R = 0.9991 \), L4: \( R = 0.9986 \), L5: \( R = 0.9986 \), L6: \( R = 0.9987 \) und L7: \( R = 0.9986 \)). Im Vergleich zu FBP führte die HIR zu niedrigeren Agatston-Scores zwischen 97 % (L1) und 87.4 % (L7). Bei niedrigen Iterationsstufen (L1 – L3) wurden alle Patienten in identische Risikokategorien eingeteilt wie bei FBP. Nur bei Verwendung der höchsten HIR-Stufen änderte sich die Gruppe bei 5.4 % der Patienten gegenüber FBP.

**Schlussfolgerung:** Aufgrund der exzellenten Korrelation der Agatston-Scores nach FBP- und HIR-Rekonstruktion und den identischen kardiovaskulären Risikokategorien zwischen FBP- und HIR-Level 1 – 3 bei allen Patienten, scheint der Einsatz der iterativen Rekonstruktion unter diesen Bedingungen bei Kalziumscoring nicht von Nachteil zu sein. Weitere Studien müssen zeigen, ob sich die HIR auch als zuverlässige Methode zur Dosisreduktion bei Kalziumscoring eignet.

**Introduction**

Numerous studies have shown that Agatston scores computed from non-contrast cardiac CT can be used to generate risk stratification for acute cardiac events [1 – 4]. Compared to spiral imaging with retrospective EKG gating, sequential image acquisition with prospective EKG triggering is one of the most effective measures for reducing radiation dose [5, 6]. Various iterative reconstruction algorithms (IR) are seeing increased use alongside filtered back projection (FBP). IR allows a significant reduction in image noise. Although IR is based on complex computational steps, the CT images are generated on modern reconstruction computers without any significant loss of time.

The hybrid iterative reconstruction algorithm (HIR) used in this study reduces image noise by up to 50 – 76 %, while allowing image quality that is at least as good, if not better under certain circumstances [7 – 9]. As a result, radiation dose can be reduced by as much as 55 – 63 % [8].

To date very few studies have described the effects of IR-techniques on calcium score. Of these existing studies, only four are based on patient data [10 – 13], while the other studies constitute phantom studies. The latter describe no significant difference in Agatston scores when using HIR (iDose⁴) versus FBP [14, 15]. There are currently no published patient studies addressing the influence of iDose on calcium score in non-contrast cardiac CT.

This article examined whether a good correlation exists between the coronary artery Agatston scores obtained through filtered back projection and those obtained through hybrid iteration algorithm iDose⁴ such that using HIR would not result in an unintended change in cardiovascular risk stratification.

**Methods**

**Study population**

This retrospective study included 68 ambulant patients who underwent non-contrast cardiac CT for initial evaluation of risk of coronary artery disease (CAD) between November 2011 and June 2013. Inclusion criterion was initial evaluation for the risk of coronary artery disease (CAD) performed in a routine clinical setting.

The image data sets were irreversibly anonymized and analysed retrospectively. Because of the anonymized and retrospective evaluation of medical data for research purposes, the ethics committee of the Medical Association of North Rhine declared that neither ethical approval nor patient consent were necessary.

**Image acquisition**

The image data sets were acquired using non-contrast techniques on a 256 multi-row CT machine (Brilliance iCT, Philips Healthcare, Cleveland, OH, USA). The patients were examined in supine position. The upper end of the examination volume was located 1 – 2 cm beneath the tracheal bifurcation, while the bottom end was at the level of the diaphragm. Gantry rotation time was 0.67 and collimation was 128 × 0.625 mm while using the z-flying focal spot. The tube voltage was 120 kVp, and mean current time product was 63.67 mAs (range 50 – 150 mAs). Median heart rate at the start of examination was 59 bpm (SD 7.51 bpm). Patients with heart rates greater than 60 bpm received 50 – 100 mg metoprolol p.o. for premedication 30 to 60 seconds prior to examination. All image acquisition was performed using prospective electrocardiogram (EKG)-triggering during a low-motion blood pressure interval at 78 % [16]. The effective radiation dose was estimated by multiplying the dose length product (DLP) by the conversion coefficients (0.014 mSv×Gycm⁻¹×cm⁻¹) [17, 18].

**Image reconstruction**

The raw data was reconstructed in the levels L1 – L7 at a slice thickness of 2 mm and an increment of 2 mm in the axial plane using FBP as well as the hybrid iterative reconstruction algorithm “iDose⁴” (Fig. 3), thus yielding 8 data sets per patient. A heart kernel (CXB with window settings level 90 and width 750) was used at all times.

**Image evaluation**

Each image was evaluated at a workstation (Extended Brilliance Workspace (EBW), Philips, Best, Holland) independently by two radiologists with 2 and 15 years experience, respectively, in cardiac CT imaging. The calcium score was analysed for FBP and each HIR iteration level using semi-automated software (Heartbeat CS, Philips, Best, Holland). Structures having a density over 130 Hounsfield units (HE) were saved colour-coded by the software. Anatomical classification by coronary vessel (right coronary artery, main stem of the left coronary artery as well as left anterior descending artery and left circumflex artery) was performed manually. The Agatston calcium score [1] was computed automatically.
Data analysis and statistics
Medians (M) and standard deviations (SD) were computed for patient and CT acquisition parameters. Correlation analyses were performed (Spearman) for the purpose of comparing the Agatston scores following reconstruction by means of FBP and HIR and using different iteration levels. Differences between FBP and HIR at various iteration levels were checked for significance using Wilcoxon matched pair test. A significant difference was assumed for a p-value < 0.05. Medians and interquartile distance were computed. Risk stratification was performed, and patients were assigned to different risk groups on the basis of Agatston scores. In this process, the intervals described by Rumberger et al. were used on the one hand: Agatston score < 10 compared to FBP decreases as iteration level increases. Although the degree of calcification visually appears to be the same or is more prominent due to the noise reduction, there is a tendency toward a decrease starting with the 4th iteration level (L4) when quantification is performed.
Calcium score analysis
For 12 patients, no coronary calcifications were detected in the FBP (Agatston score = 0). A separate evaluation was thus performed for patients with an Agatston score of 0 as well as > 0 following reconstruction with FBP. All patients with a score of 0 in FBP also exhibited a score of 0 for the seven HIR-levels. In patients with Agatston scores > 0, there was a tendency for Agatston scores to decrease and exhibit greater statistical spread as iteration increased (Table 2, Fig. 1). The differences between FBP and HIR level 7 were statistically significant when the Agatston scores were examined (p < 0.001) but not when the risk groups listed below were taken into consideration (p = 0.25) (Fig. 2a). On average, all measured Agatston scores (min. 0 – max. 1880) decreased to 97% (L1), 94% (L2), 93% (L3), 91% (L4), 90% (L5), 88% (L6) and 87% (L7) compared to FBP (100%) (Fig. 2b). Fig. 2b shows a sharp decrease in percentage between FBP and L7 in five patients with low Agatston scores (< 15.68).
If patients are divided into risk groups based on the FBP Agatston value, the values in risk group 1 (Agatston score > 0 – 10) measured using HIR (Level 7) lie at the middle 57.29% of the values measured using FBP, while those of risk group 2 (> 10 – 100) lie at 89.71%, those of risk group 3 (> 100 – 400) at 90.94% and those of risk group 4 (> 400) at 90.40% of the FBP values.
In addition to the strong percentage deviations found with low Agatston score, there were also two patients with higher Agatston scores (691 and 645, respectively) exhibiting a remarkable decrease in values when using HIR Level 7 (78.5% and 80.7%, respectively) compared to FBP. When the plaques in the particular coronary arteries of these two patients were subjected to sub-analysis, reconstruction with FBP of the right coronary artery (RCA) revealed bordering artefacts which the software incorrectly measured as plaques (RCA FBP 617 and 170, respectively) and which could not be corrected manually. With noise-reducing L7 reconstruction, the artefacts were no longer visible, thus yielding measured values for the RCA of 477 (77%) and 79 (47%), respectively.
After the results were grouped according to coronary vessel, the greatest percentage-based deviations appeared in cases of more minor calcification load, while the lowest deviations appeared in cases of higher calcium load. Differences, for example due to differing frequency of motion artefacts between the left and right coronary artery, were not ascertained.
There were no patients – previously yielded a positive Agatston score after FBP reconstruction – whose scores decreased to 0 after HIR. However there were some plaques that were no longer detected due to being just below the threshold value. If viewed without the scoring software, these changes are visible only as weak hyperdensities. For example, a “plaque” in the LAD of a patient measuring 0.46 (130 HE) in FBP, measures 0 (128 HE) in L7.
Nevertheless, there is excellent correlation between the Agatston scores measured in all iteration levels with HIR and the values following FBP (Fig. 3.) The correlation coefficient was > 0.99 for all iteration levels.
In 24 of 448 cases (5.4%) the value measured for each iteration level was higher than for the next lower iteration level or FBP. In two cases it was observed that the total score following reconstruction with iDose4 Level 1 was higher than using standard FBP (FBP 203.13 and L1 204.01, and 225.46 and 229.89, respectively). However, this did not result in any changes in risk group assignment or risk percentile.

Table 1  Patient demographics and CT acquisition parameters.

<table>
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<tr>
<td>number of male/female patients (total) 48/20 (68)</td>
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<td>age in years, median ± SD 60.94 ± 8.51</td>
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<td>heart rate, median ± SD 58.51 ± 7.51</td>
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<td>tube voltage (kV) 120</td>
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<td>tube current, median ± SD (spread) 63.67 ± 20.2 (50 – 150)</td>
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<tr>
<td>CTDIvol (mGy), median ± SD 4.94 ± 2.68</td>
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<td>DLP (mGy/cm), median ± SD 74.42 ± 36.86</td>
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<td>effective dose (mSv), median ± SD 1.04 ± 0.52</td>
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Table 2  Parameters of the calculation of the Agatston score.

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Fig. 1  Example of an Agatston score level 1.
Fig. 2a  Multivariate analyses were performed using statistics software (Prism, Graph Pad Software, Version 6.0c).
Effect on risk stratification

In 92.9 % of HIR reconstructions (all iteration levels), assignment to risk group according to Rumberger et al. was identical to that of FBP reconstruction [2]. In the case of four patients (7.14 %) there was discrepancy between FBP and HIR in terms of assignment to risk group (Table 3).

With regard to iteration level, L1, L2 and L3 yielded no change in risk group assignment compared to FBP. At higher iteration levels, specifically in the case of 2 of 56 patients (1.6 %) at L4, 3 of 56 patients (5.4 %) at L5, L6 and L7, the lower measured Agatston score led to the patient being assigned instead to the next lowest risk group (Fig. 2a).

Using the risk percentiles according to McClelland resulted in no change in cardiovascular risk for these four patients [20]. However, when factoring in the total collective there is also a change in risk percentiles between HIR and FBP for three patients (5.4 %). The computed risk percentile decreased for one patient from the 75th percentile (FBP, L1, L2, L4) to the 50th percentile (L5, L6, L7) and in a second patient from the 75th (FBP, L1, L2, L3) to the 50th percentile (L4, L5, L6 and L7). In the case of a third patient, observer A measured an Agatston score of 21.12 following reconstruction with FBP, which corresponds to the 50th percentile, while observer B measured 15.68, corresponding to the 25th risk percentile. For both observers, the patient was assigned to the 25th percentile following iterative reconstruction (L1 – L7).

Interobserver agreement

The Bland-Altman diagrams of the Agatston scores of both observers showed good agreement both for FBP and HIR taking into consideration a greater standard deviation when using HIR (Fig. 4). Assignment to cardiovascular risk groups according to Rumberger on the basis of the Agatston scores issued by the two observers was identical to a weighted $\kappa$ of 1.00 for both FBP and HIR. Because of the good agreement between the two observers the results of observer A are presented in this study unless indicated otherwise.

Radiation dose

The average volume CT dose index (CTDIvol) was 5.27 mGy ± 2.09, while the DLP was 74.21 mGycm ± 27.03, resulting in an effective radiation dose of 1.04 mSv ± 0.38.

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<td>398.31</td>
<td>392.09</td>
<td>383.06</td>
<td>75th</td>
</tr>
</tbody>
</table>

Table 3. Agatston scores of patients in whom HIR resulted in a change of the risk group classification.

Table 2. Agatston score results (CAC).

n = number of patients in the respective risk group. median, 25th percentile, 75th percentile, lowest and highest value for the Agatston score for each reconstruction algorithm (FBP and L1-L7). Results from observer 1, observer 2 showed similar results.
Discussion

For valid risk stratification for cardiovascular events, it is important that the measured Agatston scores are reproducible and have only minimal variability. Our study showed that the Agatston scores following HIR correlated excellently with the FBP values on all iteration levels and that there is very good agreement between the measurement values of two independent observers. Although the measured Agatston scores gathered with HIR tended to decrease and exhibit greater statistical spread as iteration level increased, all patients were assigned to the correct risk category compared to the reference standard FBP when HIR iteration levels 1–3 were used.

Schindler et al. yielded comparable median Agatston scores with FBP (76.0) and SAFIRE (76.4) when using the iterative reconstruction algorithm SAFIRE (Siemens, Forchheim, Deutschland), resulting in 107 of 110 remaining in the same clinical risk group [11]. In our study, patients were assigned to the same risk groups at least for the lower iteration levels (L1–L3). At the higher levels L4–L7, a smaller percentage (1.6% for L4 and 5.4% for L5–L7) was reclassified into the next lowest risk group. The in some cases higher Agatston scores in L1–L7 compared FBP or the next lowest level resulted in no change in risk group assignment. It can be assumed that these changes apparently have no clinical relevance. Using iterative reconstruction reduces, for one, “blooming” artefacts, which are visible in FBP [21]. Although FBP reconstruction was used as reference standard, artefact superimposition could possibly lead to incorrectly high values that overestimate the true calcium load. One reason that this is possible is because the Agatston score was initially described for EBCT. Becker et al. demonstrated excellent agreement between MDCT and EBCT. However they also showed that MDCT has a systematic error with regard to calcium score [22].

Sharper deviations in Agatston score when expressed in percent generally appear between HIR and FBP the lower the obtained score, particularly in the risk group with a score < 10. However, the clinical relevance of such minor lesions has to be questioned [23]. According to Vliegenthard et al., an elevated risk of cardiovascular events is present only at Agatston scores > 100 [19]. Real plaque can be differentiated from artefacts partly with the aid of HIR. There are currently no published patient studies on the influence of iDose on calcium score in non-contrast cardiac CT. A phantom study conducted by Murazaki et al. [15] as well as CT-angiography studies performed on phantoms [14] and phantom studies on plaque volume [24, 25] can be used for comparison. In their CTA study, Takx et al. demonstrated for one that the HIR algorithm improves objective image quality, while having no influence on the quantitative analysis of coronary plaque volume, the analysis of calcium plaque composition or statements on vascular lumen [25]. In a phantom study, Murazaki et al. demonstrated that there are no significant differences in Agatston score derived from FBP (50 mAs) and iDose (15 mAs) when the same tube voltage is used [15]. Using CT-systems of other manufacturers and their iteration algorithms led in some cases to different results compared to our study (see also [12]). For one, a scanner-to-scanner variability of Agatston score is described [26]. The use of different iteration algorithms is also a possible cause [27]. The hybrid iterative reconstruction algorithm iDose4 (Philips, Brest, Holland) we employed initially functioned in the CT raw data space. The raw data with the most noise are identified and corrected, while edges are retained. For this purpose, a “maximum likelihood denoising” algorithm based on Poisson distribution is applied [28]. In contrast, the technique employed by Gebhardt et al., ASIR (GE Healthcare, Chalfont St. Giles, United Kingdom), is based on a complete iteration in image data space. The significant decrease in mean Agatston scores to 709.2 with 100 % ASIR versus 837.3 with FBP described by this group of researchers can thus be attributed possibly to the different place of action of the iteration steps.

In our study, there was consistently good correlation (R > 0.99 for all levels) without any flattening of the regression lines (Fig. 3). In contrast to the study by van Osch et al., our study had no patients with a score of 0 following HIR that had been > 0 in FBP. The number of patients with a score of 0 with ASIR increased by 13 % overall [13].

Bland-Altman-Plots. The figures show a good agreement between both observers with lower statistical spread for FBP compared to L3 and L7.
Limitations
The limitation of our study is that it was a retrospective single-centre study. The study was limited to one CT device and the use of the manufacturer’s associated HIR algorithm. The FBP reconstruction algorithm was used as reference standard, since a histological validation was not possible and other diagnostic procedures (e.g. intravascular ultrasound, IVUS) were not indicated. In our prior phantom study [9] we showed that HIR did not change the Hounsfield units of calcium. It is therefore unnecessary to adjust the threshold value for detecting calcium plaque. A lower calcium score due to differing density values for structures containing calcium is thus ruled out as a cause. Instead, reduced image noise was observed with increasing iteration. Utsunomiya et al. demonstrated the same results in a different, albeit smaller, patient study using the same iteration algorithm [14, 24].

Outlook
Further studies are needed to show whether acquisition with lower dose and HIR can yield the same Agatston score as obtained with higher dose and FBP and to what degree dose can be potentially reduced. Radiation exposure by non-invasive detection of coronary calcification with cardiac CT currently lies between 1 and 3 mSv [16, 29]. New low-dose studies are also describing values of 0.18 mSv per examination [30]. At the same time development continues, and there are already new iterative reconstruction algorithms that must be tested.

Conclusion
In our study, the employed HIR algorithm was used at the same radiation dose up to L3 without resulting in a relative change in risk group assignment or risk percentiles. Agatston scores tended to decrease as iteration increased, with good to excellent correlation with FBP always being maintained. Our examinations on a Philips CT system allow us to conclude that reliable values can be expected when using HIR up to iteration level 3. Additional studies are needed to demonstrate whether the acquisition with lower dose and HIR yields the same results obtained with higher dose and FBP. This would allow the potential for major further dose reduction.

Clinical Relevance of the Study
- Because the Agatston scores show excellent correlation between HIR and FBP, HIR has clinical application at least at low iteration levels (Level 3).
- There was no change in risk group assignment or risk percentiles up to a maximum iteration level 3, while it must be kept in mind that Agatston scores show slight decrease as iteration level increase.
- There was excellent agreement between the two observers for both FBP and all HIR iterations, suggesting good reproducibility of the measurements.

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