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Effect of image reconstruction algorithms on volumetric and radiomic parameters of coronary plaques

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ABSTRACT

Background: Volumetric and radiomic analysis of atherosclerotic plaques on coronary CT angiography have been shown to predict high-risk plaque morphology and to predict patient outcomes. However, there is limited information whether image reconstruction algorithms and preprocessing steps (type of binning, number of bins used for discretization) may influence parameter values.

Methods: We retrospectively identified 60 coronary lesions on coronary CT angiography (CTA). All images were reconstructed using filtered back projection (FBP), hybrid (HIR) and model-based (MIR) iterative reconstruction. Plaques were segmented manually on HIR images and copied to FBP and MIR images to ensure identical voxels were analyzed. Overall, 4 volumetric and 169 radiomic parameters were calculated. Intra-class correlation coefficient (ICC) was used to assess reproducibility between image reconstructions, while linear regression analysis was used to assess the effect of preprocessing steps done before calculating radiomic metrics.

Results: All volumetric and radiomic metrics had ICC > 0.90 except for first-order statistics: mode, harmonic mean, minimum (0.45, 0.76, 0.84; respectively) and gray level co-occurrence (GLCM) parameters: inverse difference sum and sum variance (0.01, 0.04; respectively). Among GLCM parameters 90% were significantly affected by the type of binning and 100% by the number of bins. In case of gray level run length matrix parameters 100% of metrics were affected by both preprocessing steps.

Conclusions: Volumetric and radiomic statistics are robust to image reconstruction algorithms. However, all radiomic variables were affected by preprocessing steps therefore, showing the need for standardization before being implemented into everyday clinical practice.

1. TOC summary

Many findings support the additive value of volumetric plaque analysis in patients clinical evaluation. Furthermore, radiomics is emerging as a new tool to potentially further increase the diagnostic capabilities of coronary CT angiography. With initiatives to decrease radiation exposure, new image reconstruction algorithms have been developed. However, it is unknown whether image reconstruction has any effect on quantitative coronary CT angiography parameters. Our results show that both volumetric and radiomic parameters have excellent reproducibility with regards to different image reconstructions. However, all radiomic variables were affected by preprocessing steps before the calculation of the parameters showing the need for standardization.

2. Introduction

Volumetric analysis of coronary plaque composition on coronary CT angiography (CTA) has been shown to predict high-risk plaque morphology, assess hemodynamic significance of coronary lesions and to predict patient outcomes.[1–3] Radiomics has emerged as a new methodology to analyze radiological images.[4] By extracting large number of quantitative parameters from given regions of interest, big data databases can be built, where each abnormality is represented by hundreds and thousands of different parameters.[5,6] Recently, radiomic analysis of coronary plaques in CTA images was able to identify lesions showing

Abbreviations: CNR, contrast-to-noise ratio; CTA, coronary CT angiography; FBP, filtered back projection; GLCM, gray level co-occurrence matrix; GLRLM, gray level run length matrix; HIR, hybrid iterative reconstruction; HU, Hounsfield units; ICC, intra-class correlation coefficient; MIR, model-based iterative reconstruction; SD, standard deviation; SNR, signal-to-noise ratio

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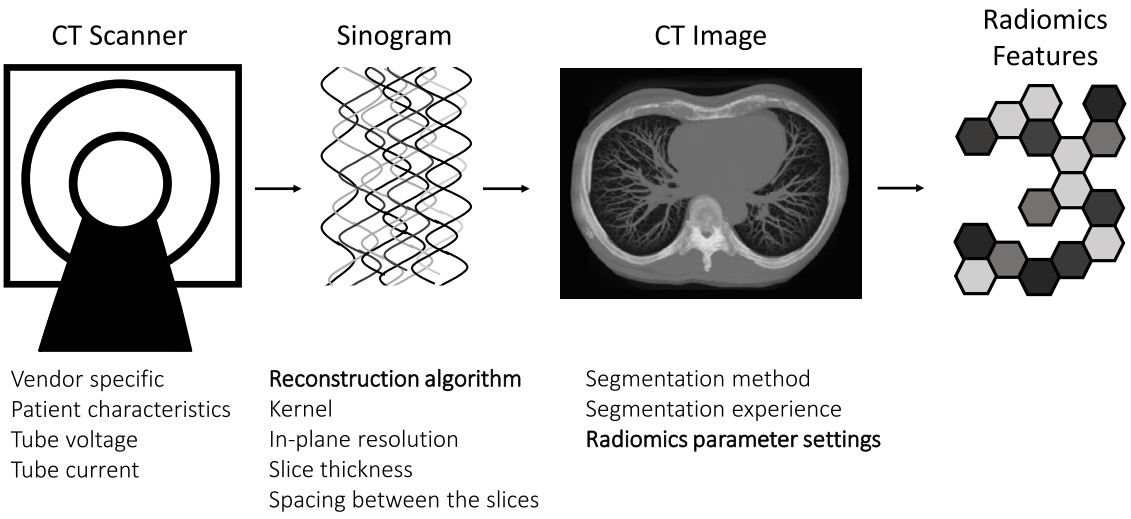

Fig. 1. Descriptive figure of potential influencers of radiomic statistics. In our current investigation we wished to assess the effect of reconstruction algorithms and radiomic parameter settings (bold).

the qualitative napkin-ring sign with excellent diagnostic accuracy.[7] However, concerns have been raised regarding the reproducibility and robustness of quantitative metrics, as several different parameters may affect volumetric and radiomic parameters.[8–14] Applicability of a new diagnostic technique not only depends on its potential to identify pathologies, but also on its robustness to different clinical and technical settings. Therefore, the potential influence of these factors needs to be investigated, before the clinical value of these techniques can be decided.

Quantitative analysis of medical images consists of several steps. First, the pathology needs to be imaged using a scanner. Then specific acquisition parameters are used to create the sinogram. The images are reconstructed from the raw data using a given field of view, slice thickness, kernels and image reconstruction algorithms. From these images the lesion is segmented and volumetric and radiomic parameters are calculated. Potentially all of these variables may influence quantitative parameters (Fig. 1).

Regarding conventional quantitative metrics such as the Agatston-score, image reconstruction algorithms have been shown to significantly affect results and alter patient risk stratification.[15] However, little is known whether CT-based volumetric and radiomic features are affected by image reconstruction algorithms.

Therefore, our primary aim was to assess whether filtered back projection (FBP), hybrid (HIR) or model-based (MIR) iterative reconstruction have any significant effect on volumetric and radiomic parameters of coronary plaques. Furthermore, we sought to evaluate the impact of preprocessing steps: type of binning and the number of bins used for discretization on radiomic parameter values.

3. Methods

Institutional review board approved the study (SE TUKEB 1/2017) and due to the retrospective nature of the study informed consent was waived.

3.1. Study design, image acquisition and reconstruction

Between August 1st and October 31st, 2017 we retrospectively identified 20 non-calcified, 20 partially calcified and 20 calcified coronary atherosclerotic plaques of 60 patients (Age 60.4 ± 9.8; Female: n = 16) showing at least 25% stenosis on excellent image quality coronary CTA scans. We chose plaques showing greater than 25% stenosis as these plaque may be hemodynamically significant and prone to rupture and therefore be candidates of future volumetric and radiomic plaque analyses.[16,17] All images were acquired using a 256-slice scanner (Brilliance iCT 256, Philips Healthcare) with prospective ECG-triggered acquisition mode. Images were acquired in cranio-caudal direction during a single breath-hold in inspiration. Four-phasic injection protocol with 90–100 ml of Iomeprol contrast agent was used (Iomeron 400, Bracco Ltd) for the coronary CTA examinations.[18] Examinations were performed using 128 × 0.625 mm detector collimation, 270 ms gantry rotation time, 120 kV, mAs 250–300 depending on patient's body mass index and chest size. All images were reconstructed to a 512 × 512 matrix using a XCB kernel with a slice thickness of 0.8 mm and 0.4 mm spacing between slices. All images were reconstructed using FBP, HIR (iDOSE4 level 5, Philips Healthcare) and MIR (IMR level 2, Philips Healthcare). Demographic and image acquisition data can be found in Table 1.

3.2. Image quality measurements

For image quality assessment, we measured the signal-to-noise ratio (SNR), which was defined as the mean coronary luminal CT attenuation in Hounsfield units (HU) adjacent to the lesion divided by the standard deviation of the CT number in the aorta measured in a region of interest

Table 1
Patient characteristics, scan parameters and plaque characteristics.

Demographics	n = 60
Age (years)	60.4 ± 9.8
Female gender, n (%)	16 (27%)
BMI (kg/m^2)	27.7 ± 4.3
Heart rate (bpm)	62.2 ± 7.1
Cardiovascular risk factors	
Hypertension n (%)	40 (67%)
Diabetes mellitus n (%)	18 (30%)
Dyslipidemia n (%)	34 (57%)
Current smoker n (%)	30 (50%)
Scan parameters	
Total DLP (mGy x cm)	358 ± 87
Pixel spacing (mm)	0.40 ± 0.04
Plaque characteristics	
Lesion length (mm)	15.0 ± 7.4
Lesion volume (mm^3)	125.1 ± 79.1

Data is presented as average and standard deviation or frequency and percentage as appropriate.
BMI: body mass index; DLP: dose length product.

at least 2 cm^2 at the level of the left main. Contrast-to-noise ratio (CNR) was defined as: the mean luminal HU minus the perivascular HU at the site of the plaque divided by the standard deviation of the aortic HU. All measurements were performed on a clinical workstation (IntelliSpace portal, Philips Healthcare) on all analyzed images by a fellow (BS, 5 years of experience).

3.3. Segmentation and data extraction

An expert reader (PMH, 12 years of experience) manually segmented the coronary plaques on HIR image using a dedicated software tool (QAngioCT Research Edition; Medis medical imaging systems bv).[19] HIR images were chosen as they are available for each vendor and are most frequently used for plaque analysis. Voxels containing plaque tissue were extracted as a DICOM image with dimensions identical to the original image using a dedicated software (QAngioCT 3D workbench, Medis medical imaging systems bv). This DICOM image was used as a mask to select the same voxels from all three reconstructions. Using the same segmentation ensured that only the change in voxel values attributable to different image reconstructions affected the results. For volumetric plaque analysis, voxels were grouped into calcified plaque volume (> 130 HU), high attenuation (90–129 HU), intermediate attenuation (30–89 HU) and low attenuation (< 30 HU) non-calcified plaque volumes.[20]

3.4. Calculation of radiomic parameters

Segmented images were sent to a core laboratory for radiomic analysis (Pictologics Ltd.). Overall, 44 first-order metrics describing the distribution of HU values, 114 gray level co-occurrence matrix (GLCM) parameters enumerating the frequency at which similar HU values co-occur next to each other, and 11 gray level run length matrix (GLRLM) features quantifying the prevalence of many similar voxel values in a line next to each other, were calculated based-on a prior publication.[7] Before calculation of GLCM and GLRLM statistics, images need to be preprocessed. To calculate parameters describing the spatial heterogeneity of a lesion, HU values need to be first discretized into given ranges (bins), since minimal differences in HU value have little effect on heterogeneity and therefore can be considered similar values. Therefore, replicate images were created by discretizing the voxel HU values either to equally sized bins where the discrete bins span equal ranges (i.e. 10–20; 20–30; 30–40; etc.) or to equally probable bins, where equal proportion of data are present in each bin (i.e. 10%; 10%; 10%; etc.). Radiomic parameters were calculated on all three reconstructions. GLCM and GLRLM parameters were calculated using with 2, 4, 8, 16, 32, 64, 128 and 256 number of bins both for equally sized and equally probable binning. This resulted in 2 × 8 variations for each reconstruction of each plaque. Therefore, for first-order statistics 3 × 60 (number of reconstruction × number of plaques) = 180 values, for GLCM and GLRLM 3 × 60*2 × 8 (number of reconstructions × number of plaques × number of different types of discretizations × number of different bins) = 2880 different values were available for each radiomics parameter.

3.5. Statistical analysis

Categorical variables are presented as frequencies and percentages, while continuous variables are shown as averages and standard deviations (SD). Intra-class correlation coefficient (ICC) was calculated to assess the reproducibility of the radiomic parameters with regards to different reconstructions. ICC values greater than 0.80 were considered good, values above 0.90 were considered to have excellent reproducibility. To assess which parameters have an independent influence on radiomic values, we conducted linear regression analysis. Models included plaque composition (non-calcified, partially calcified, calcified) and reconstruction algorithms where HIR was considered as reference. In addition, for GLCM and GLRLM parameters the type of binning and the number of bins were also added to the model. Beta (β) and p values are reported for each independent variable. ΔR^2 was calculated for each independent variable by subtracting the R^2 value calculated when considering all variables except the given variable from the regression model which considered all variables. ΔR^2 was calculated as an effect size measure, to show the proportion of variance attributable to a given parameter. In case of radiomic parameters, due to the large number of outcome parameters, results are summarized on Manhattan plots, where the given statistical results (ICC or ΔR^2) are plotted on the y axis while the radiomic parameters are lined up on the x axis in consecutive order and color coded based-on which family of radiomic metrics they belong to.[21] All statistical calculations were done in the R environment. A p value of $p < 0.05$ was considered statistically significant.

4. Results

The distribution of image quality parameters for FBP, HIR and MIR were as follows: aorta SD (50.3 ± 13.3; 31.3 ± 7.2; 27.1 ± 6.1), lumen mean HU (515.4 ± 94.2; 515.6 ± 94.4; 511.5 ± 94.9), pericoronary fat mean HU (−93.7 ± 35.6, −91.9 ± 28.6, −85.4 ± 25.6), CNR (13.1 ± 4.9, 20.4 ± 5.5, 32,7 ± 9.4) and SNR (11.1 ± 4.2, 17.4 ± 5.1, 28.1 ± 8.7). Aorta SD, CNR and SNR had low ICC values between image reconstructions (0.46, 0.60, 0.63; respectively), while lumen and pericoronary fat mean HU had excellent and good reproducibility (0.99, 0.83; respectively). Image reconstruction had a significant effect on aorta SD, CNR and SNR values with large ΔR^2, while lumen or pericoronary fat mean HU values were unaffected by the different algorithms. Detailed results of image quality reproducibility can be found in Table 2.

All volumetric plaque parameters showed excellent reproducibility (ICC > 0.97; all). None were affected by the type of image reconstruction. Detailed results of plaque volume reproducibility can be found in Table 3.

Regarding radiomic parameters, all had excellent reproducibility (ICC > 0.90) except for:first-order parameters: mode, harmonic mean

Table 2
Reproducibility of image quality parameters.

Parameter	ICC	FBP β	FBP p	MIR β	MIR p	ΔR^2	R^2 total
Aorta SD	0.46	19.04	< 0.0001	−11.98	< 0.0001	0.63	0.63
Lumen mean HU	0.99	−0.19	0.99	−4.20	0.81	0.00	0.02
Pericoronary fat mean HU	0.83	−1.85	0.74	6.40	0.25	0.01	0.04
CNR	0.60	−7.32	< 0.0001	12.85	< 0.0001	0.62	0.63
SNR	0.63	−6.26	< 0.0001	11.21	< 0.0001	0.60	0.60

ICC and linear regression models were calculated to assess the degree to which reconstruction algorithms might affect image quality parameters. ΔR^2 represents R^2 change if image reconstruction is added to the model considering plaque composition. R^2 total represents R^2 values for models considering both plaque composition and image reconstruction.

CNR: contrast-to-noise ratio; FBP: filtered back projection; HU: Hounsfield unit; ICC: intra-class correlation coefficient; MIR: model-based iterative reconstruction; SD: standard deviation; SNR: signal-to-noise ratio.

Table 3
Reproducibility of plaque volumes.

Parameter	ICC	FBP β	FBP p	MIR β	MIR p	ΔR^2	R^2 total
Low attenuation non-calcified plaque	0.98	−0.31	0.90	−2.43	0.31	0.01	0.28
Intermediate attenuation non-calcified plaque	0.98	−1.37	0.68	1.24	0.70	0.00	0.24
High attenuation non-calcified plaque	0.98	0.05	0.97	0.32	0.84	0.00	0.24
Calcified plaque	1.00	1.63	0.87	0.86	0.93	0.00	0.26

ICC and linear regression models were calculated to assess the degree to which reconstruction algorithms might affect plaque volumes. ΔR^2 represents R^2 change if image reconstruction is added to the model considering plaque composition. R^2 total represents R^2 values for models considering both plaque composition and image reconstruction.
FBP: filtered back projection; ICC: intra-class correlation coefficient; MIR: model-based iterative reconstruction.

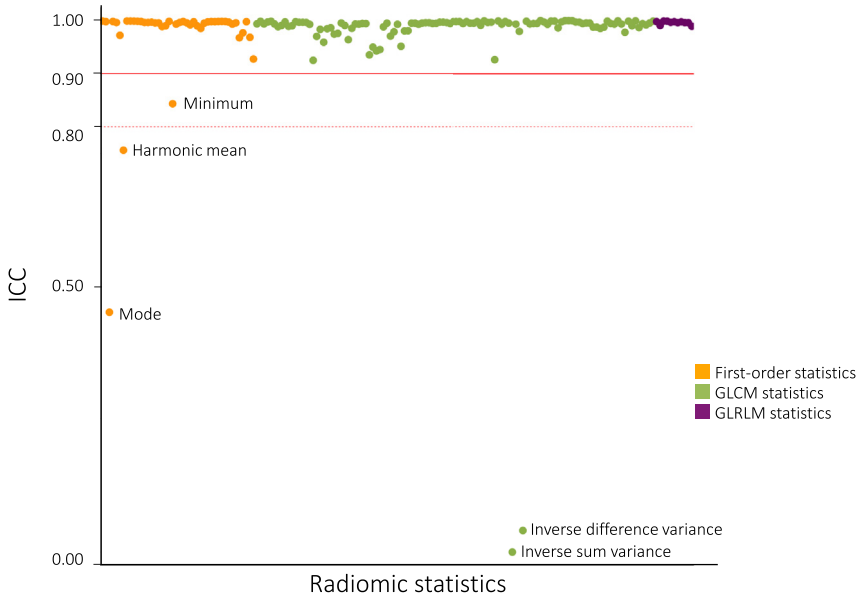

Fig. 2. Manhattan plot of intra-class correlation values of radiomic parameters. Radiomic parameters are lined up on the x axis and color coded based-on which family of radiomic metrics they belong to, while their corresponding intra-class correlation value is plotted on the y axis. ICC: intra-class correlation coefficient

and minimum (ICC: 0.45, 0.76; 0.84, respectively), and GLCM parameters: inverse difference sum and sum variance (ICC: 0.01, 0.04; respectively). Manhattan plot of ICC values can be found in Fig. 2.

Linear regression analysis showed that the type of binning i.e equal sized or equally probable binning, was a significant predictor of radiomic values for 90% (103/114) of all GLCM parameters. Among GLCM parameters ΔR^2 values attributable to the type of binning were smaller than 0.25 in 87% (99/114) of the radiomic parameters. 3% (3/114) had ΔR^2 changes between 0.25 and 0.49, and 2% (2/114) had changes between 0.50 and 0.75. Even though all GLRLM parameters were significantly affected by binning type ($p < 0.05$, all), the ΔR^2 attributable to adding binning type to the regression model only minimally changed the R^2 values ($\Delta R^2 < 0.04$ for all). Results are summarized in Fig. 3.

The number of bins to which HU values were discretized before the calculation of radiomic parameters, significantly affected the values for all GLCM and GLRLM parameters. Among GLCM, 61% (70/114) of the parameters had a $\Delta R^2 < 0.25$ if the number of bins was added to the model. 16% (18/114) produced ΔR^2 between 0.25 and 0.49, 17% (19/114) between 0.50 and 0.74 and 6% (7/114) of all parameters had R^2 change values greater than 0.75. Regarding GLRLM parameters, 4 parameters' ΔR^2 was less than 0.25 when the number of bins was added to the regression model. 4 statistics produced R^2 changes between 0.25 and 0.49, while in case of 3 parameters the ΔR^2 was more than 0.75. Results are summarized in Fig. 4.

5. Discussion

Our results show that both volumetric and radiomic parameters have excellent reproducibility with regards to different image reconstructions indicating that quantitative plaque analysis can be confidently performed on any kind of image reconstruction. However, the type of binning and the number of bins used significantly affects radiomic parameters, therefore reporting the type of binning and number of bins used for radiomic analysis is needed. Furthermore, this emphasizes the need for standardization of radiomic analyses to achieve reproducible results and for radiomics to translate into everyday clinical practice.

Applicability of a new diagnostic technique not only depends on its potential to identify pathologies, but also on its robustness to different clinical and technical settings. In recent years iterative reconstruction algorithms became standard in clinical care as they allow significant reduction of radiation dose without significant compromise in image quality.[22] While the quality of radiological images has improved through the reduction of noise, concerns have been raised as to whether the novel reconstruction techniques have any effect on quantitative image analysis. Agatston-score, one of the earliest quantitative CT metrics has been shown to significantly change with new iterative reconstruction techniques, which also has impact on patients' cardiovascular risk assessment.[15,23,24] However interestingly, quantitative plaque volumes seem to be less affected.[25,26] Differences can be more attributable to the accuracy of automatic segmentation algorithms rather than the voxel values themselves.[27] Our research methodology of using one segmentation on all three image reconstructions ensures that only

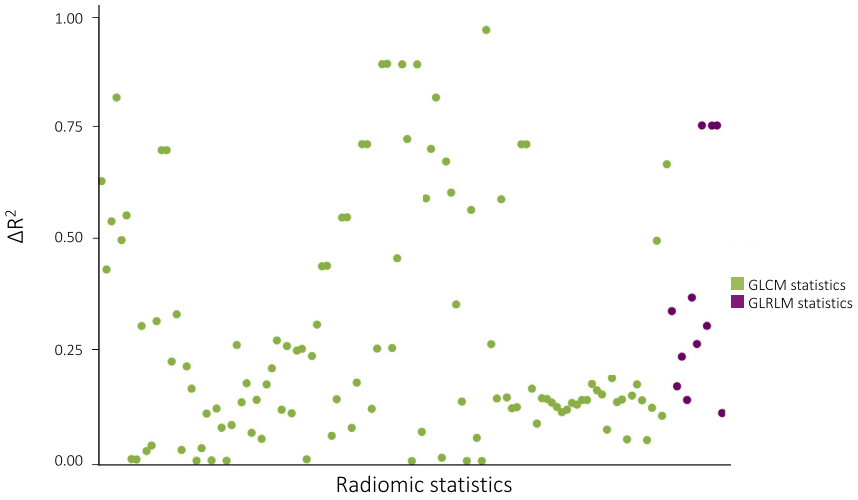

Fig. 3. Manhattan plot of ΔR^2 values when the preprocessing step: type of binning was added to the regression model. Radiomic parameters are lined up on the x axis and color coded based-on which family of radiomic metrics they belong to, while the corresponding ΔR^2 values are plotted on the y axis representing the amount of variation that can be attributable to the preprocessing step: type of binning in case of that given radiomic parameter.

the effect of the reconstruction algorithms are investigated regardless of the image segmentation. Our results confirm that volumetric plaque analysis has excellent reproducibility with respect to the different image reconstructions. However, there is little information as to whether radiomic parameters are affected by image reconstruction.

As radiomics has proven to help grade malignancies, classify lesions into histological categories and predict patient outcomes,[28–31] more and more attention is drawn to the reproducibility of such findings. Altazi and colleges has shown, that positron emission tomography (PET) based radiomic features using different reconstructions show variation regarding reproducibility.[10] Among 79 investigated features only inverse difference and inverse difference momentum showed ICC values > 0.90. Similarly, Shiri et al. investigated the effect of different PET reconstruction settings.[32] Among 100 different radiomic parameters, only 47 had very small variation. Interestingly, in our dataset only 3% of parameters had values below 0.90. Based on our results, CT based radiomic parameters seem to be more robust to different reconstructions as compared to PET. Our findings imply that new iterative reconstruction techniques can be used interchangeably, as they have minimal effect on calculated metrics. Therefore, new knowledge gained from radiomic studies can be applied across different reconstruction algorithms. Furthermore, previous images can also be used to increase radiological registries, as inferences gained from previous images reconstructed using FBP will result in similar results as if they would have been reconstructed using novel HIR or MIR techniques.

Even though radiomic statistics seem to be robust to reconstruction algorithms, the type of voxel binning and the number of bins used for discretization have a significant effect on the statistical values. Similar results have been reported when assessing the impact of different number of gray level discretizations on PET images.[10,11] Only two GLCM and GLRLM parameters were found to be highly reproducible. In our dataset all parameters were significantly affected by the number of bins. Furthermore, in 41% (51/125) of the examined parameters, more than 25% of the radiomic metrics' variation could be attributed to changes in the number of bins used for calculation of the parameters. In addition we found that 90% of GLCM parameters and 100% of GLRLM parameters were also affected by the way the binning was performed. However, only in case of 5 parameters could the type of binning explain more than 25% of the parameters variation. Our results emphasize the need for standardization of radiomic analysis, as differences in calculation of the metrics can cause significant changes in the radiomic statistics. Furthermore, precise reporting of all parameter setting used for radiomic calculations is needed to achieve reproducible results. However, these findings do not mean, that radiomic statistics are unreliable due to the significant influence of parameter settings used for calculations. Rather they highlight the fact that each radiomic statistic can be calculated in many different ways which can lead to very different results, which urges standardization of radiomics.

Our study has some limitations. There were only a limited number of plaques analyzed (n = 60) and only excellent image quality scans were selected retrospectively, which might cause a selection bias and decrease the generalizability of our results. The reconstruction algorithms used are specific to the vendor, therefore using other manufacture's algorithms might lead to different results. Furthermore, both HIR

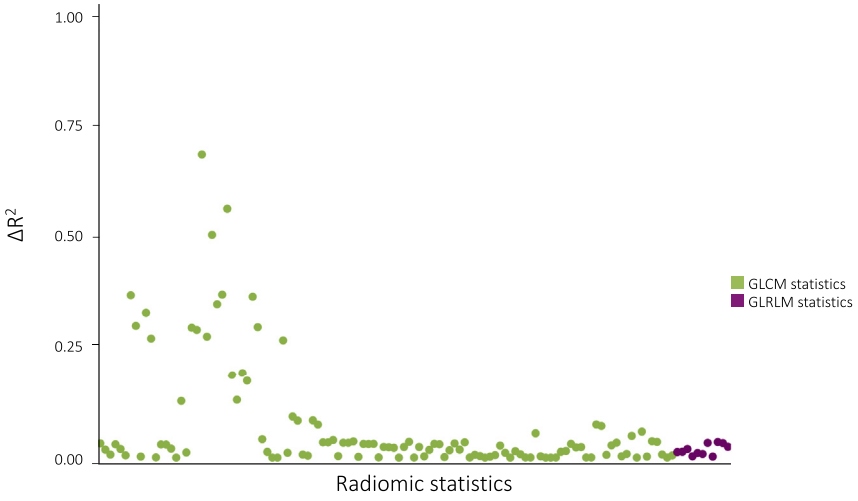

Fig. 4. Manhattan plot of ΔR^2 changes when the preprocessing step: number of bins used for discretization was added to the regression model. Radiomic parameters are lined up on the x axis and color coded based-on which family of radiomic metrics they belong to, while the corresponding ΔR^2 values are plotted on the y axis representing the amount of variation that can be attributable to the preprocessing step: number of bins used for discretization in case of that given radiomic parameter.

and MIR have different levels of possible iterations. We limited our analysis to mid-range levels in both cases (iDOSE[4] level 4; IMR level 2), as they are most commonly used in everyday practice. However, using different iteration levels would might lead to different results.

In conclusion, all volumetric and the majority of radiomic parameters are unchanged using different image reconstruction algorithms. However, radiomic features are significantly affected by how the discretization of HU values was done before calculation and therefore, precise reporting of used methods is needed. Our results, emphasize the need of standardization of radiomic analysis to achieve robust reproducible results which can be implemented into everyday clinical practice.

Conflicts of interest

Márton Kolossváry and Pál Maurovich-Horvat are shareholders in Pictologics Ltd. Which did the radiomic calculations.

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