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Effect of Chest Computed Tomography Kernel Use on Emphysema Score in Severe Chronic Obstructive Pulmonary Disease Patients Evaluated for Lung Volume Reduction

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Keywords
Chronic obstructive pulmonary disease · Lung volume reduction · Chest computed tomography · Emphysema · Kernel

Abstract
Background: Chest computed tomography (CT) emphysema quantification is a vital diagnostic tool in patient evaluation for bronchoscopic lung volume reduction (BLVR). Smooth kernels for CT image reconstruction are generally recommended for quantitative analyses. This recommendation is not always followed, which may affect quantification of emphysema extent and eventually, treatment decisions. ***Objective:*** The main goal is to demonstrate the influence of CT reconstruction kernels on emphysema quantification in patients with severe COPD, considered for BLVR. ***Methods:*** Chest CT scans were acquired with one multi-detector CT system and reconstructed using three different kernels: smooth, medium smooth, and sharp. Other parameters were kept constant. Emphysema scores (ESs), meaning the percentage of voxels below −950 Hounsfield units, were calculated and compared to the smooth reference kernel using paired *t* tests. Bland-Altman plots were made to assess the biases and limits of agreement between kernels. ***Results:*** Ninety-eight COPD patient CT scans were analyzed. The sharp kernel had a systematic bias of 6.2% and limits of agreement of 16.6% to −4.2% compared to the smooth kernel. The medium smooth kernel had a systematic bias of 5.7% and limits of agreement of 9.2% and 2.2% compared to the smooth kernel. The ES differed, for a single patient, up to 18% for different kernels. ***Conclusions:*** Chest CT kernel reconstruction can lead to a significant difference in emphysema severity quantification. This may cause invalid treatment selection in COPD patients evaluated for BLVR. Standardization of a smooth CT kernel setting and/or normalization to a standard kernel is strongly recommended.

Introduction

Emphysema quantification using computed tomography (CT) densitometry is a vital diagnostic tool for evaluation for lung volume reduction (LVR) in patients suffering from chronic obstructive pulmonary disease (COPD). Emphysema quantification can be used to properly select the most suitable treatment target lobe. The target lobe is preferably highly emphysematous, hyperinflated, and air-trapped, and consequently contributes scarcely to gas exchange [1].

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Now that LVR can be performed bronchoscopically and, therefore, less invasively, this kind of treatment is implemented more often [2]. With its rise, the importance of accurate emphysema quantification increases as well. The treatment target lobe is most often required to have at least 30% emphysema [3]. Inaccurate emphysema measurements may lead to invalid target lobe selection. For example, a severely emphysematous lobe may be determined as relatively unaffected and may consequently not be selected or vice versa, potentially harming the patient.

One of the most frequently used emphysema quantifications is the "emphysema score." This score is the percentage of the number of voxels below a defined Hounsfield units (HU) threshold on an inspiratory CT scan, using a thin slice high-resolution CT reconstruction. The −950 HU threshold has been established by examination of pathological evidence for emphysema quantification [4, 5]. However, such a threshold does not account for the diversity of CT acquisition and reconstruction settings available such as the tube voltage, reconstruction kernel, and slice thickness used. It is known that these settings can have a significant influence on the measured percentage of voxels below the HU threshold [6, 7].

Kernels are reconstruction filters that are distinguished by the amount of spatial frequency filtering they perform. Spatial frequency filtering can be interpreted as giving weights to the sizes of structures in an image. A sharp kernel retains or accentuates high spatial frequencies, highlighting details at the cost of noise. A smooth kernel filters out the high spatial frequencies, and therefore, filters out noise at the cost of detail. Filtering the high spatial frequencies essentially has the effect of averaging voxels over a larger area. Given a scan with a normally distributed histogram, kernel choice does not severely impact the mean lung density. However, the standard deviation is impacted. Smooth kernels have a raised histogram compared to sharp kernels, and therefore, the standard deviation is decreased for smooth kernels compared to sharp kernels. Since the emphysema score is the proportion of voxels below −950 HU, this can lead to different emphysema scores for distinct kernels. In a similar way, a relatively large slice thickness averages over a larger area and thereby mitigates noise at the cost of detail, affecting emphysema scores as well [7].

The Quantitative Imaging Biomarkers Alliance (QIBA) has a CT guideline in place for emphysema measurements. QIBA suggests that the spatial frequency dependence of the noise in the CT images should be matched to those typically found in smooth kernels and that a slice thickness is to be used of ≤1 mm [8]. However, this guideline is not always followed. In fact, a wide variety of reconstruction parameters is used [9]. Therefore, emphysema scores may differ between facilities and CT scanners, and, consequently, patient and/or lobe selection may not be optimal in every facility.

The effect of CT kernel reconstruction on emphysema quantification has been studied before [7]. However, this was performed in a small diverse patient cohort. The specific effect in a population of severe emphysematous COPD patients is unknown. Furthermore, no studies have been performed in a bronchoscopic lung volume reduction (BLVR) patient population, where precise emphysema quantification is critical [3].

The goal of this study is to demonstrate the effect of CT kernels on the emphysema score in a population of patients with severe COPD under evaluation for BLVR. A secondary goal is to determine the proportion of CT scans of patient referrals to our clinic that are suitable, according to the QIBA recommendations, for quantitative emphysema assessment.

Materials and Methods

Patients

We included COPD patients under evaluation for BLVR between October 2017 and October 2018, visiting the University Medical Center Groningen, the Netherlands. This research did not fall within the scope of the WMO (Medical Research involving human subjects act), but all patients gave written informed consent to the use of their data. For their BLVR evaluation, the patients had a clinical indication to perform both pulmonary function tests and an in/expiration CT scan. For this evaluation, we receive referrals from the entirety of the Netherlands.

Chest CT Acquisition and Quantification

Patients were breath-coached, by a standard voice recording, to maximum inspiration at CT acquisition (CT Somatom Definition Flash, Siemens Healthineers, Erlangen, Germany). Scans were reconstructed with three different kernels: B31f (smooth), B45f (medium smooth), and B60f (sharp) (Siemens Healthineers, Erlangen, Germany). The tube voltage was 100 kVp for patients below 80 kg, 120 kVp for patients between 80 and 110 kg, and 140 kVp for patients above 110 kg. The reference tube current was 75 mAs. The reconstructed slice thickness was 1 mm.

CT scans were quantitatively analyzed using automated, commercial software (LungQ, Thirona, Nijmegen, The Netherlands). This software segments the lungs and calculates the emphysema score based on that segmentation, based on −950 HU as threshold.

Evaluation of CT Scans of Patient Referral Cohort

For our secondary analysis on the quality of the referral CT scans, we included all externally made CT axial inspiration reconstructions that were sent to us for our BLVR evaluation at our center between May and December 2021. We excluded all coronal,

sagittal, maximum intensity, and minimum intensity projection reconstructions from this analysis. Additionally, scans using contrast were excluded, since the contrast increases the mean density of the parenchyma, which has an influence on the emphysema score as well [10, 11].

All included reconstructions were assigned to one of two categories, sharp and smooth. We chose for a dichotomy because strict kernel categories are difficult to define since there are four major vendors with a multitude of different kernels. Allocation of the kernels into one of the two categories was done on the basis of a study that sorted kernels from multiple vendors from smoothest to sharpest [12] and on visual assessment (see Table 1).

We assessed the number of scans that matched our inclusion criteria for each patient, and we evaluated the number of patients with a smooth kernel scan and/or a scan with a slice thickness smaller or equal to 1.0 mm, according to the protocol suggested by QIBA. Furthermore, we assessed the number of patients with a scan matching both criteria.

Statistics

The emphysema score distributions resulting from the different kernels were checked visually for normality and subsequently compared by paired *t* tests. Furthermore, Bland-Altman plots were made to assess the systemic and proportional bias. *p* values below 0.05 were considered significant. All statistical analyses were performed in SPSS version 28 (IBM Corporation, Armonk, NY, USA).

For all comparisons, we assumed that the smooth kernel represented the reference standard. This is based on the suggestions from QIBA.

Table 1. Categorization of kernels

Vendor	Kernel	
	smooth	sharp
Philips	A	L
	B	IMR1,SharpPlus
	IMR1,Routine	YC
	IMR1,Soft Tissue	YA
Toshiba	FC02	FC30
	FC03	FC51
	FC08	FC56
	FC12	FC81
	FC17	FC86
	FC19	
Siemens	B26f	B60f
	B30f	B70f
	B31f	B90s
	B40f	Br58f
	B41s	Br59f
	Br36f	Br64f
	Br38f	Br59d
	Br40f	Br69d
	Br36d	Bl57f
	Br40d	Bl57d
	Bf37f	I70f
	Bf39f	
	Bl56f	
	I31f	
GE	Soft	Lung
	Standard	HD Lung

Results

We included 98 severe COPD patients, 72.4% were female, with a mean age of 61.6 (±7.6) years. Mean forced expiratory volume (FEV_1) was 28.3 (±8.5) % predicted, and residual volume (229.4 (±48.7) % predicted. The CT tube voltage used was 100 kVp for 73 patients, 120 kVp for 24 patients, and 140 kVp for 1 patient. The paired *t* tests showed significant differences in emphysema score between the smooth kernel and the other kernels. The mean ES for the smooth kernel was 33.3 (±9.2) %, for the medium smooth kernel 39.0 (±7.9) %, and for the sharp kernel 39.5 (±5.1) %. The ES for medium smooth kernel was a mean 5.69%-point (95% CI: −8.31 to −3.08%-point) higher than for the smooth kernel and for the sharp kernel this was a mean 6.20%-point (95% CI: −8.82 to −3.59%-point) higher than for the smooth kernel. The medium smooth kernel resulted in an average 0.51%-point (95% CI: −3.12 to 2.10%-point) lower ES than the sharp kernel. The overall trends are demonstrated in Figure 1. In this figure, a random selection of patients are included, for the clarity of the figure. The distribution of the emphysema scores was largest for the smooth kernel and smallest for the sharp kernel (Fig. 2).

Bland-Altman plots (Fig. 3, 4) demonstrate a systematic bias in the emphysema score, which are the mean differences between the kernels described above. The Bland-Altman plots demonstrated a proportional bias as well. As the sharpness of the kernel increases, the influence of noise increases as well, driving the emphysema scores more to a narrower range of emphysema scores. This is reflected in the Bland-Altman plots. For the population of severe COPD, evaluated for BLVR, the following holds: the lower the severity of emphysema, the higher the overestimation in the sharp kernel. The limits of agreement were 9.18 and 2.21 for smooth and medium smooth, 16.61 and −4.20 for smooth and sharp, and 7.84 and −6.82 for medium smooth and sharp.

Evaluation of CT Scans of Patient Referral Cohort

For this secondary analysis, we included 100 patients. Due to the exclusion of CT scans with iodine contrast scans 92 patients remained. Of the remaining scans, 89% included at least one reconstruction with

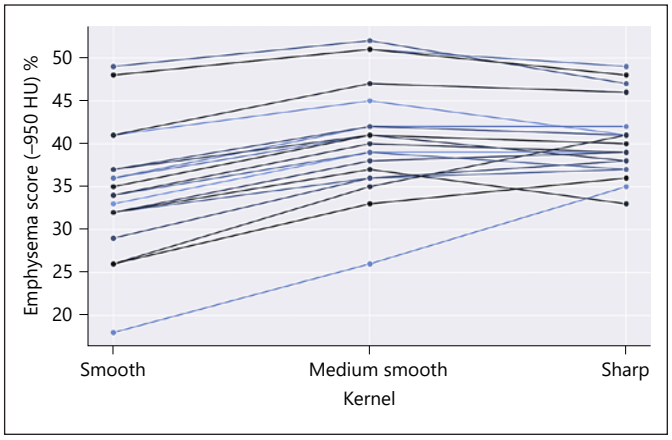

Fig. 1. Random selection of emphysema scores for smooth, medium smooth, and sharp kernels. This figure illustrates the overall trend.

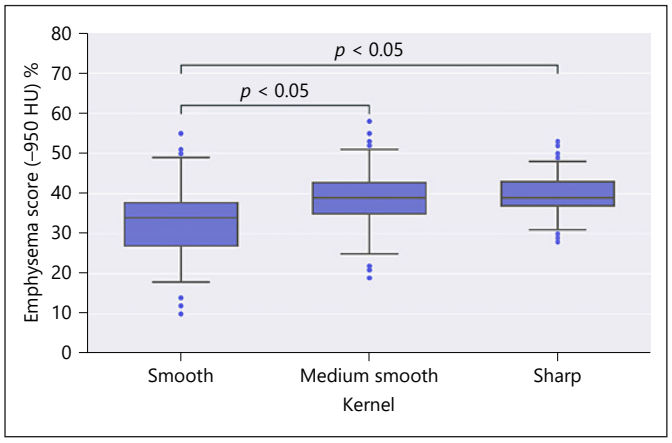

Fig. 2. Emphysema score as measured by the smooth, medium smooth, and sharp kernels.

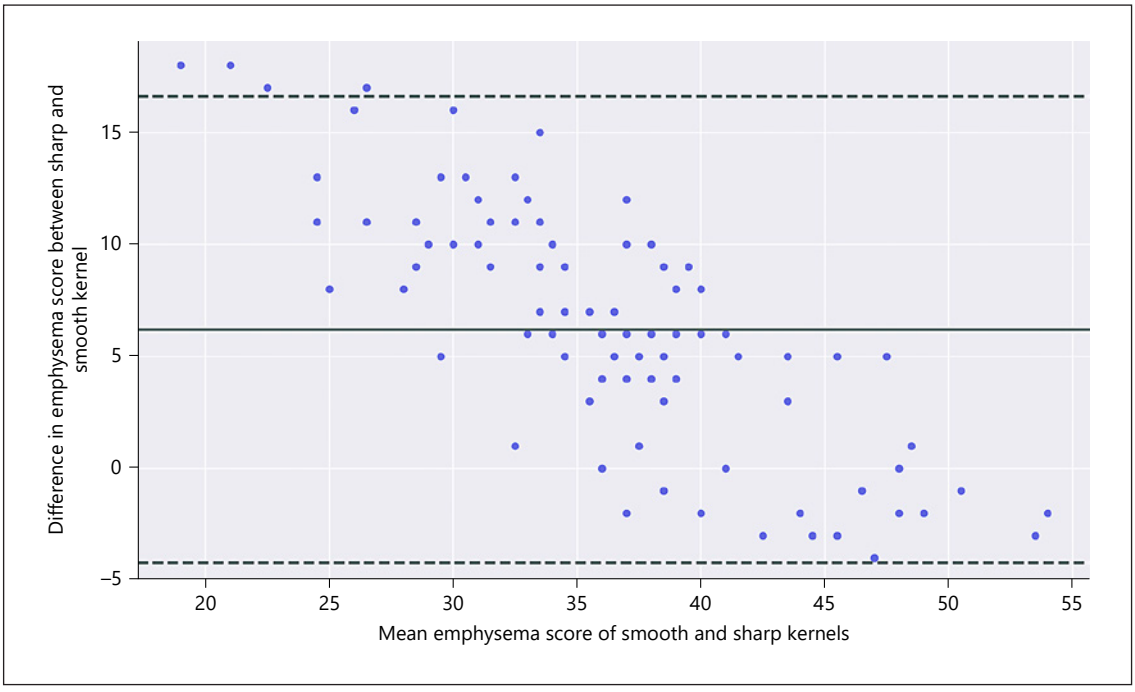

Fig. 3. Bland-Altman of the emphysema score (–950 HU) comparing the sharp kernel to the smooth kernel.

smooth kernel. Furthermore, 88% included at least one scan with a slice thickness of 1.0 mm or lower. However, overall, only 40% included at least one scan with both criteria met and were therefore suitable for reliable QCT analysis according to QIBA. Figure 5 shows the flowchart of inclusion.

Conclusion

In this population of severe COPD patients evaluated for BLVR, we showed that the kernel choice has a significant impact on the quantified emphysema score. Sharp kernels do not provide an accurate measurement of emphysema. This population especially requires accurate

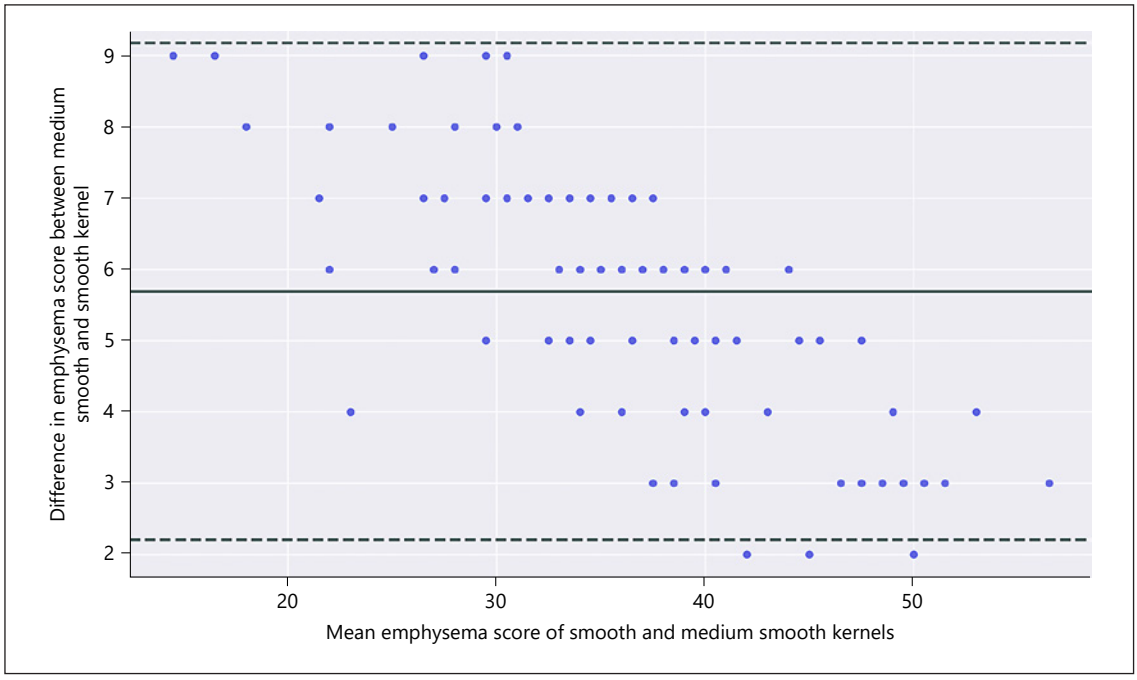

Fig. 4. Bland-Altman of the emphysema score (−950 HU) comparing the medium smooth kernel to the smooth kernel.

emphysema measurements for the BLVR evaluation, since BLVR targets the most emphysematous and hyperinflated lobes [1].

We have demonstrated that sharper kernels show a smaller distribution in emphysema scores between patients compared to smooth kernels, which is in agreement with other studies [7, 13] and is in line with the expectations based on qualitative differences in emphysema between patients. Sharp kernels, therefore, have a decreased differentiation between patients when compared to smooth kernels. This is visible as well in the Bland-Altman plots, which show a clear systemic and proportional bias. All scores are more similar to one another. The effects of noise are more pronounced and ultimately the voxels designated as emphysema may be more noise than actual emphysema.

Another way of understanding this is that the histogram of a sharp kernel is relatively more flattened than a smooth kernel, meaning that it has a larger standard deviation. Therefore, the place of the emphysema threshold within in the histogram has a relatively lower impact on the measured score compared to a smooth kernel histogram.

The main effect of using a sharper than recommended kernel is overestimation of relatively low amounts of emphysema. This may impact the treatment since the cutoff for the minimal amount of emphysema is roughly 30% at −950 HU [3]. Therefore, a patient may not qualify for treatment when assessed by a smooth kernel reconstruction and simultaneously qualify for treatment when as-

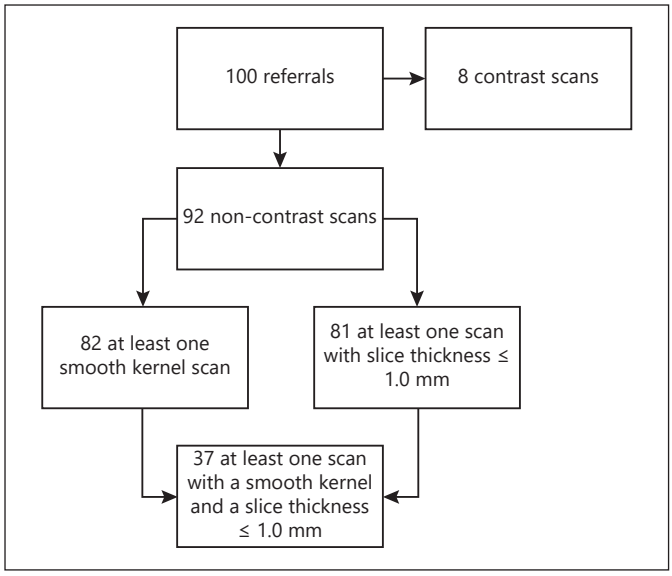

Fig. 5. Flowchart that shows the numbers of suitable scans, according to QIBA.

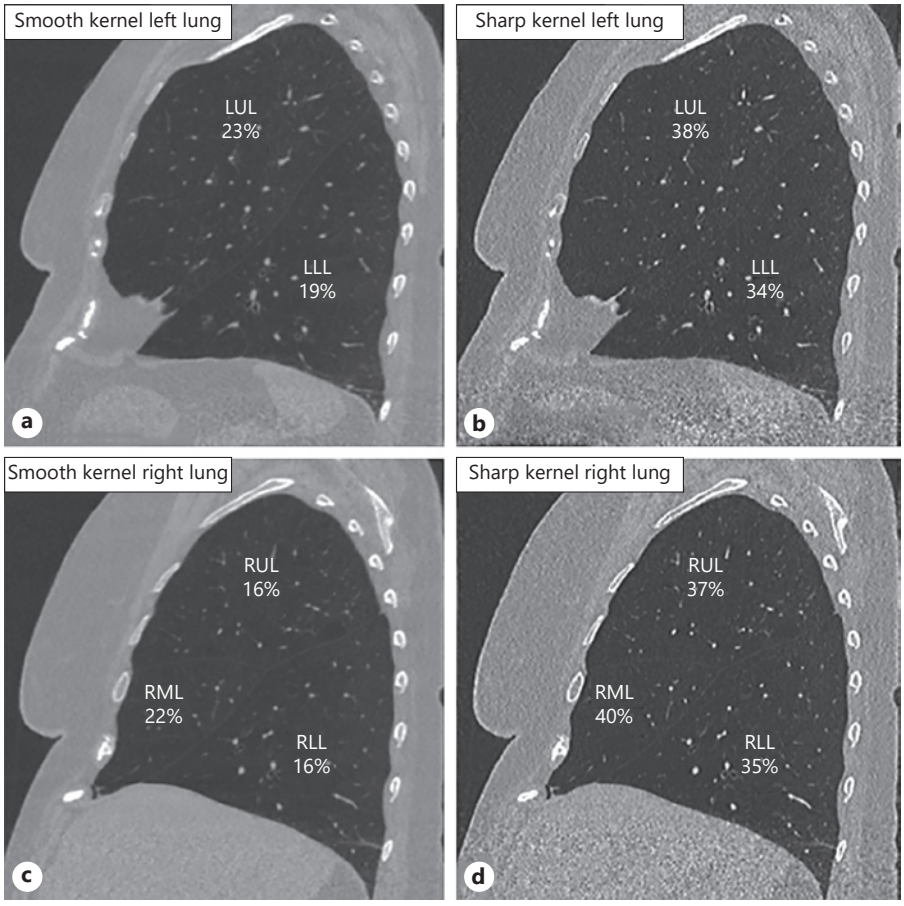

Fig. 6. Sagittal slices of a smooth and sharp kernel reconstruction of one scan, with added emphysema scores for every lobe. Demonstrating that lobes can be seen as targets for BLVR in the sharp reconstruction, due to emphysema scores that are higher than 30%. While simultaneously not being targets in the smooth kernel reconstruction. **a** Smooth kernel left lung, with a left upper lobe emphysema score of 23%, and a left lower lobe score of 19%. **b** Sharp kernel left lung, with a left upper lobe score of 38%, and a left lower lobe score of 34%. **c** Smooth kernel right lung, with a right upper lobe score of 16%, a right middle lobe score of 22%, and a right lower lobe score of 16%. **d** Sharp kernel right lung, with a right upper lobe score of 37%, a right middle lobe score of 40%, and a right lower lobe score of 35%.

sessed by a sharper kernel reconstruction (see example patient in Fig. 6). Another potential consequence is that the selected target lobe may differ between reconstructions. This discrepancy between the provided treatment, as a result of difference in CT reconstruction parameters, is undesirable. However, it should be noted that treatment evaluation should not be solely based on a quantitative measure of emphysema, but on a visual assessment of the emphysema as well.

The evaluation of the retrospective referral CT evaluation cohort indicated that only 40% of the patients sent to our clinic include a scan that is both a smooth kernel reconstruction and has a slice thickness of 1.0 mm or lower, and thus suitable for emphysema QCT analysis according to QIBA. It should be noted, however, that these reconstructions were not necessarily made with the intention of a quantitative emphysema analysis. It would however be preferable to change this to a situation so that every chest CT series of a COPD patient includes a reconstruction suitable for emphysema quantification, especially with a growing importance and use of emphysema quantification, specifically in the case of BLVR. Standard inclusion of a emphysema quantification suitable reconstruction may prevent the need for another CT scan in our clinic. This would achieve a cost reduction without impeding the diagnostic capabilities needed for a BLVR evaluation. Furthermore, this would reduce the radiation exposure of patients.

It is challenging to determine what the most suitable CT settings are for quantitative emphysema analysis. Retaining high spatial frequencies may appear to offer additional information on the lung parenchyma status of the patient, at least for visual evaluation. However, in practice, this information cannot be differentiated from the noise exhibiting similar spatial frequencies. Human observers are more capable in this regard, and these kernels are therefore more suited for qualitative assessments. However, for quantitative assessments, it is better to filter higher frequencies and only retain larger structures that more likely reflect reality. Minimizing noise is thus preferable. We and others have demonstrated that the use of softer kernels leads to a larger distribution in emphysema

scores between patients, which increases the ability for differentiation and, therefore, provides a more optimal reconstruction kernel for a standard protocol. This is corroborated by a meta-analysis by Crossley et al. [9], which recommends soft kernel use for and a slice thickness of 2.5–5 mm, such that noise is minimal as well due to an averaging effect. Increasing the slice thickness lowered the emphysema score in their cohort, similar to relatively low emphysema scores in smooth reconstruction kernels compared to more sharp kernels [7]. Furthermore, QIBA advises that the spatial frequency dependence of the noise is matched to those typically found in soft kernels [7]. However, QIBA suggests using a slice thickness of ≤1 mm, promoting the retention of information in that regard, opposed to Crossley et al. [9] who recommend a larger slice thickness. QIBA's recommendation in this regard is likely due to the fact that Genevois et al. [4, 5] used 1 mm slice thickness to establish the −950 HU threshold.

Possibly, sharp kernels combined with iterative reconstruction or noise reduction software may as well be suitable for emphysema scoring. A study looking into the effects of iterative reconstruction demonstrated that the use of a sharp kernel may be applicable with iterative reconstruction since iterative reconstruction suppresses noise as well [13]. Ultimately, the issue is that HU are not solely dependent on the physiology of a patient, but on a whole set of parameters that need to be stable or controlled for before reliable inferences can be made about the physiology on the basis of HU thresholding.

A way of controlling for this issue is using a standard protocol. This means that all parameters of influence on emphysema quantification should be equalized for all scans taken for the purpose of emphysema quantification. Important parameters are slice thickness, dose and kernel, and tube voltage. However, due to the multitude of vendors active in the CT market, complete homogenization of the protocol will never be perfect. This is especially true for kernels since every vendor uses their own types of kernels for which the methods are not fully transparent. Kernel choice can, however, be similar. It is unclear to what extent similarity of the kernels is enough and to what extent kernels are similar, which is reflected in the difficulty of categorizing kernels. QIBA already has such a protocol, but as we have shown with our analysis this is not often adhered to in routine clinical practice. The cause for this is likely that such a protocol as that from QIBA describes the kernel choice necessarily in terms that specify the amount of noise and not a clear selection of kernels.

Another possibility is to normalize the CT scans to an external reference standard [14–16]. An optimal kernel can be selected, which may be determined by comparison with pathology. Subsequently, all kernels can be converted to that kernel. When utilizing this approach, we speculate that it is probably best to first approach the optimal protocol with a similar kernel, since the normalization can remain closer to the original and is therefore less artificially altered. However, the downside of this method is that such a process is usually not fully transparent. Therefore, it may make unforeseen errors that cannot be traced to their source or it may be unclear that an error has occurred. Thus, such a method may be more suitable for evaluating already made scans.

In this study, the tube voltage varied as well. This is included in the protocol to adjust to the size of the patient in an effort to minimize dose. This variation may have had an impact on the emphysema scores, due to the previously mentioned effects on HU. However, this does not impact the analysis performed in this study, since the tube voltage does not differ within patients. Furthermore, any analysis into the tube voltage variation was beyond the scope of the study.

In conclusion, our study found that, in agreement with similar studies, the emphysema score is kernel dependent and the difference in emphysema score between kernels is strongly related to the emphysema score magnitude. This study is unique in the regard that it is performed in a population that is severely affected by COPD and under evaluation for BLVR. The accuracy of emphysema scoring in this population is especially important, due to the importance of finding a potential target lobe. In this regard, the differences in emphysema scores between kernels are highly problematic.

We furthermore demonstrated that a large proportion of externally made CT scans, sent to us for evaluation, is unsuitable for emphysema quantification according to the recommendations of QIBA. Generally, such scans are not performed with the intention of emphysema quantification; however, we would argue that a suitable reconstruction should be added more standardly to prevent excess CT scans.

These findings illuminate the need for stricter adherence to a protocol, like the recommendation by QIBA. It is important to use a reconstruction algorithm that mitigates the detrimental effects of noise and, therefore, filters high-frequency spatial information to some extent. This extent should be similar for all clinics quantitating emphysema. Additionally, normalization of CT scans to a reference standard is an option that may be most suitable for already made scans.

Statement of Ethics

This research did not fall within the scope of the WMO (Medical Research involving human subjects act). All patients have given written informed consent to the use of their data.

Conflict of Interest Statement

Rozemarijn Vliegenthart has received payment or honoraria for lectures at Bayer and Siemens Healthineers and received an institutional research grant from Siemens Healthineers outside of the submitted work. Hendrik Joost Wisselink is supported by a grant from the Dutch Royal Academy of Sciences. All other authors have no conflicts of interests to declare.

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Author Contributions

Jens T. Bakker: performed data gathering, statistical analyses, drafting of the manuscript, and approved the final version. Karin Klooster: helped conceive the idea, revised the manuscript several times, made substantial contributions to the design and interpretation of the work, and approved the final version. Hendrik Joost Wisselink: made substantial contributions to the design and interpretation of the work, revised the manuscript several times, and approved the final version. Gert Jan Pelgrim: made substantial contributions to the design and interpretation of the work, revised the manuscript several times, and approved the final version. Rozemarijn Vliegenthart: made substantial contributions to the design and interpretation of the work, revised the manuscript several times, and approved the final version. Dirk-Jan Slebos: helped conceive the idea, revised the manuscript several times, made substantial contributions to the design and interpretation of the work, revised the manuscript several times, and approved the final version. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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