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Vult von Steyern, Kristina; Björkman-Burtscher, Isabella; Höglund, Peter; Bozovic, Gracijela; Wiklund, Marie; Geijer, Mats

Published in:
European Radiology

DOI:
10.1007/s00330-012-2534-y

2012

Description and validation of a scoring system for tomosynthesis in pulmonary cystic fibrosis

Kristina Vult von Steyern[1], Isabella M Björkman-Burtscher[1], Peter Höglund[2], Gracijela Bozovic[1], Marie Wiklund[1] and Mats Geijer[1]

[1] Centre for Medical Imaging and Physiology, Skåne University Hospital, Lund, Lund University, Sweden.

[2] Competence Centre for Clinical Research, Skåne University Hospital, Lund, Sweden

Corresponding author:

Kristina Vult von Steyern

Centre for Medical Imaging and Physiology

Skåne University Hospital

221 85 Lund, Sweden

kristina.vult_von_steyern@med.lu.se

Phone +46 46-171000

Fax number +46 46-176165

Key words: Cystic fibrosis; pulmonary disease; radiography; scoring methods; tomography, X-ray

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ABSTRACT

Objectives: To design and validate a scoring system for tomosynthesis (digital tomography) in pulmonary cystic fibrosis.

Methods: A scoring system dedicated to tomosynthesis in pulmonary cystic fibrosis was designed. Three radiologists independently scored 88 pairs of radiographs and tomosynthesis examinations of the chest in 60 patients with cystic fibrosis and 7 oncology patients. Radiographs were scored according to the Brasfield scoring system and tomosynthesis examinations were scored using the new scoring system.

Results: Observer agreements for the tomosynthesis score were almost perfect for the total score with square-weighted kappa >0.90, and generally substantial to almost perfect for subscores. Correlation between the tomosynthesis score and the Brasfield score was good for the three observers (Kendall's rank correlation tau 0.68, 0.77 and 0.78). Tomosynthesis was generally scored higher as a percentage of the maximum score. Observer agreements for the total score for Brasfield score were almost perfect (square-weighted kappa 0.80, 0.81 and 0.85).

Conclusions: The tomosynthesis scoring system seems robust and correlates well with the Brasfield score. Compared with radiography, tomosynthesis is more sensitive to cystic fibrosis changes, especially bronchiectasis and mucus plugging, and the new tomosynthesis scoring system offers the possibility of more detailed and accurate scoring of disease severity.

Key points:

- *Tomosynthesis is more sensitive than conventional radiography for pulmonary cystic fibrosis changes*
- *The radiation dose from chest tomosynthesis is low compared with computed tomography*
- *Tomosynthesis may become useful in the regular follow-up of patients with CF*

INTRODUCTION

Tomosynthesis (digital tomography) is a low dose alternative to computed tomography (CT) in the evaluation of pulmonary cystic fibrosis (CF). In tomosynthesis multiple tomographic sections of the lungs have an appearance similar to radiography, with sharply depicted structures in each section and blurred structures outside the section (Fig. 1). This gives superior visualisation of for example metastases [1] compared with radiography and a more detailed assessment of CF pulmonary changes, such as mucus plugging and bronchiectasis [2].

Scoring of tomosynthesis studies with radiographic CF scoring systems [3-13] is not optimal because additional information gained from the sectional imaging in tomosynthesis cannot be accurately incorporated into the radiography scores, with loss of important image information. On the other hand, tomosynthesis does not show all the abnormal features used for CT scoring [14-22], such as ground glass opacities, regional emphysema, mosaic perfusion, or focal air trapping on expiratory images. Also, many CT scoring systems score individual bronchopulmonary segments or lobes, which cannot be accurately defined by tomosynthesis.

The purpose of this study was to describe and validate a CF scoring system dedicated to tomosynthesis. The scoring system was designed to score the whole spectrum of mild to severe pulmonary changes in CF with well-defined scoring parameters, illustrated with reference images, and aiming at high interobserver reliability as well as ease of use, with a straightforward calculation of the total score.

MATERIALS AND METHODS

Tomosynthesis technique

The radiographic study consists in each case of posteroanterior (PA) or anteroposterior (AP) tomosynthesis including a PA (or AP) chest radiograph, combined with a lateral radiograph. Tomosynthesis was performed with a commercially available product (Definium 8000; GE Healthcare, Chalfont St Giles, UK, and VolumeRAD; GE Healthcare), described in detail in several reports [1, 23-25]. Sixty low-dose projection images from tube angles from − 17.5° to +17.5° were used to reconstruct up to 60 coronal sectional images without overlap, with a nominal thickness of 3 mm for children and 4 mm for adults. Imaging time is approximately 10 s during a breath held on full inspiration. As small children cannot cooperate adequately tomosynthesis is currently only used in children around 8 years of age and older. Adults and teenagers are examined upright (PA) while children under 12 years are examined supine (AP), making it easier for them to be still and hold their breath, thus reducing motion artefacts.

Scoring system

Our scoring system evaluates chest tomosynthesis examinations, which consist of tomosynthesis including the scout radiograph and a lateral radiograph. The scoring form (Fig. 2) provides clearly defined for the severity and extent of five well-recognised pathological changes in CF: overinflation, bronchial wall thickening, parenchymal lesions, bronchiectasis and mucus plugging.

Score components

Overinflation is scored on the PA (or AP) and lateral radiographs. For the other scoring components the lungs are divided at the level of the first division of the left main bronchus, clearly seen on tomosynthesis sections (in most patients corresponding to the level of the minor fissure). Each lung quadrant is scored for bronchial wall thickening, parenchymal lesions (atelectases or consolidation), number and appearance of bronchiectatic bronchi, and large or small mucus plugs, using all tomosynthesis sections covering the quadrant in question. The proper scoring level is determined by comparing the findings with reference images in the Electronic Supplementary Appendix (two examples of scoring levels are shown in Fig. 3) and by relating to the score definitions given on the scoring form (Fig. 2), described in more detail below.

Overinflation is characterised by depression and flattening of the diaphragm, uplifted heart position, retrosternal lucency, sternal bowing, thoracic kyphosis and vascular oligaemia.

Bronchial wall thickening is defined as parallel linear densities or end-on circular densities, and is scored as none, present (when visible in lung regions peripheral to the central parts of the segmental bronchi) or marked.

The extent of **parenchymal lesions** (atelectases or consolidation) is scored by number and size of lesions, with lesion size related to the volume of the 7th thoracic vertebra (the depth is estimated by counting the number of sections including the vertebra).

Bronchiectasis is scored for both number and appearance of abnormalities [26-28] and is present when a non-tapering bronchus (cylindrical, varicose or cystic) is detected, when the broncho-arterial ratio is larger than 1, or when a visible bronchus is detected close to the pleura (less than 2 cm, depending on patient size). If a bronchiectatic bronchus divides into two dilated branches, only the branches are counted. Cylindrical bronchiectasis is a mildly and uniformly dilated bronchus, with a more or less straight outline. An only discretely

dilated bronchus with a straight outline is a subtle cylindrical bronchiectasis. A clearly dilated bronchus with a slightly irregular outline is markedly cylindrical. Varicose bronchiectasis is a moderately dilated bronchus with local constrictions, giving the airway an irregular or beaded outline. Cystic bronchiectasis is a severely dilated bronchus, with a ballooned appearance and strings of cysts or grape-like clusters in the peripheral part of the bronchus.

Mucus plugging is scored for the extent of large and small mucus plugs. Large mucus plugs are tubular opacities, with or without a branching pattern, or rounded opacities 5 mm in diameter or larger, differentiated from vessels by their continuity with bronchi. Small mucus plugs are small clustered nodular opacities less than 5 mm in diameter or tree-in-bud patterns [29, 30] in the periphery of the lobes. The extent of small mucus plugs is also determined relative to the volume of the 7th thoracic vertebra.

Maximum total score

The scoring components overinflation, parenchymal lesions, bronchiectasis and mucus plugging have five scoring levels (0–4). Bronchial wall thickening has three scoring levels (0–2–4). The most severe score is 4 for all scoring components and subcomponents. Overinflation is scored for both lungs together, all other scoring components for each quadrant. The maximum score is 4 for overinflation, 16 for bronchial wall thickening and parenchymal lesions, and 32 for bronchiectasis and mucus plugging, with a maximum total score of 100.

Validation of the scoring system

In a prospective study, approved by the local ethics committee (DNR 2008/268, 2008/670 and 2010/306) and with informed consent from all patients or legal guardians 31 children and teenagers with CF (13 boys, 18 girls, mean age 13, range 8–19 years) and 31 adults (17 men,

14 women, mean age 30, range 20–59 years) with CF were included. Forty-two patients were examined once, 17 patients twice and 3 patients three times (totally 85 examinations). Seven children and teenagers without CF (6 boys, 1 girl, mean age 13, range 8–19 years), screened for lung metastases with normal imaging findings, were included to provide normal base-line studies. Four paediatric CF tomosynthesis examinations were excluded for motion artefacts. Eighty-eight anonymised pairs of chest radiographs and tomosynthesis examinations from 67 patients were independently scored by two paediatric radiologists and one chest radiologist, aware that not all cases represented CF patients. The radiographs were scored first, using the Brasfield scoring system [6]. Then the corresponding tomosynthesis study was scored using the new tomosynthesis scoring system. Scoring forms for radiography [6] and tomosynthesis (Fig. 2) were filled out by all observers. Reference images similar to the Electronic Supplementary Appendix, but not from study cases, were provided illustrating the different score components and evaluation levels.

Statistics

Cohen's kappa with quadratic weighting [31] and percentage agreement were used for assessment of agreements between observers for total disease severity scores and subscores of the tomosynthesis score. The kappa coefficient may be translated into strength of agreement as ≤0=poor, 0.01–0.20=slight, 0.21–0.40=fair, 0.41–0.60=moderate, 0.61–0.80=substantial and 0.81–1=almost perfect [31]. Disagreement between two observers could be systematic or random. Quantification of the disagreement between paired ordered categorical classifications was done using a method by Svensson and Holm [32, 33]. Two types of systematic variation are possible: the fist due to overestimation or underestimation of the classifications, and the second due to the concentration of the classifications. Systematic overestimation (or

underestimation) occurs when an observer generally classifies cases as being more (or less) abnormal than another observer does. Systematic concentration occurs e.g. when an observer uses the middle part of the scale more frequently than another observer who uses the extremes of the scale more often. Overestimation or underestimation is reflected by the variable relative position (RP), and concentration by the variable relative concentration (RC). The possible values for RP and RC range from -1 to 1, with 0 indicating no systematic disagreement. The pattern of random differences was quantified using the variable of relative rank variance (RV). Random errors could be caused e.g. by guessing or losing concentration. The possible values for RV are between 0 and 1, with 0 indicating no random contribution. Kendall's rank correlation tau was used to assess the correlation between the total disease severity scores for tomosynthesis and radiography.

RESULTS

Overall observer performance

Observer agreements for the total disease severity score in the tomosynthesis scoring showed almost perfect correlation with kappa values >0.90 for the three pairs of observers (Table 1 and Fig. 4). The observer agreements for all subscores were also high (Table 1). The RV was close to zero for all subscores, thus the random differences between observers were low and the observers were consistent when scoring the examinations. The percentage agreement differed more because of some systematic differences between the observers. Observer 3 systematically scored slightly higher for number of bronchiectatic bronchi and large mucus plugs than the other two, generating a RP farther from zero when comparing these pairs. The other two observers had a higher agreement on the scoring levels for all subscores, with RP near zero for this pair of observers. The RC was generally near zero for all subscores for the three pairs of observers, thus the observers used the scoring levels in a similar way.

Judged by kappa values observer agreements regarding **overinflation** were for two pairs of observers substantial and for one pair moderate, although the percentage agreement was only approximately 0.5 (Table 1). A tendency towards somewhat higher RV for overinflation compared with other subscores was observed, but the systematic disagreement was very low. Expressed as kappa values, agreements for the score for **bronchial wall thickening** were almost perfect for two pairs of observers and substantial for one pair (Table 1). However, as can be seen from the values for RC, observer 1 used the scale somewhat differently from the other two. Observer agreements for **parenchymal lesions** were moderate for two pairs of observers and substantial for one pair, judged by kappa values, and no obvious systematic differences were noted (Table 1). Agreements for the number of **bronchiectatic bronchi** were

substantial for two pairs of observers and almost perfect for one pair, judged by kappa values. Agreements for the appearance of bronchiectasis were almost perfect for all three pairs of observers (Table 1). Observer 3 systematically scored slightly higher for number of bronchiectatic bronchi than the other two, generating a RP farther from zero when comparing these pairs. The agreements for large **mucus plugs** were almost perfect for two pairs of observers and substantial for one pair, judged by kappa values. The agreements for small mucus plugs were substantial for two pairs of observers and almost perfect for one pair (Table 1). However, some systematic differences between the observers were noted: observer 3 systematically scored slightly higher for number of large mucus plugs (RP), and observer 1 used the scale for small mucus plugs somewhat differently from the two others (RC).

Comparison tomosynthesis – radiography

Observer agreements for total disease severity scores were almost perfect for radiography [6] with kappa values 0.80, 0.81 and 0.85 for the three pairs of observers (Table 2, Fig. 5). The scoring results for tomosynthesis and for radiography showed good correlation between the total disease severity scores, and Kendall's rank correlation tau was 0.68, 0.77 and 0.78 for the three observers. Tomosynthesis was generally scored higher with regard to percentage of maximum score with mean tomosynthesis score for the three observers of 30% of the maximum score and mean Brasfield score of 24% of the maximum score (Fig. 6).

Diversity in the tomosynthesis scores was greater than with the Brasfield score (Figs. 6-8). Many patients who were scored normal for linear markings with radiography were scored for presence of bronchial wall thickening with tomosynthesis (Fig. 7). Patients without apparent nodular cystic lesions on radiographs had bronchiectasis or mucus plugs detectable with tomosynthesis; 14 patients (16%) were scored normal for nodular cystic lesions on

radiographs but were scored positive for bronchiectasis or mucus plugs with tomosynthesis by all observers (Fig. 8).

DISCUSSION

Tomosynthesis can show structures in more detail than radiography, and allows for a superior assessment of bronchiectasis and mucus plugging, which according to some authors [15, 34] are the most specific changes of CF pulmonary disease. This tomosynthesis scoring system is based on previously reported scoring systems for radiography [3-13] and CT [14-22]. Typical findings of CF pulmonary disease seen with tomosynthesis and evaluated with the scoring system are overinflation, bronchial wall thickening, parenchymal lesions, bronchiectasis and mucus plugging. As pulmonary lobes or bronchopulmonary segments are difficult to delineate with tomosynthesis, findings are instead scored per quadrant. In established CF radiography scoring systems [5, 6, 9] for example bronchiectasis and mucus plugging are rated subjectively for increasing severity, without definition of the scoring levels. To increase the accuracy of the tomosynthesis scoring system we created well-defined scoring levels, supported by reference images.

The extent of parenchymal lesions and small mucus plugs were evaluated in relation to the volume of the 7^{th} thoracic vertebra instead of the size of the scored area (which is common in CT scoring systems), owing to difficulties in estimating the relative involvement of the quadrants. Giving a measurement in centimetres would also be inadequate as the scoring system is designed to be used independent of patient age and size.

In most CT scoring systems bronchiectasis is rated for severity, i.e. bronchus diameter compared with the adjacent blood vessel, and extent [14, 16-19, 22]. In tomosynthesis this method is not optimal as the vessels in the periphery of the lungs are often difficult to define in patients with severe CF changes, which would make measurements unreliable. In the CT scoring system of Nathanson [15], on the other hand, bronchi affected by bronchiectasis are

scored for appearance (cylindrical, saccular or cystic) and for extent. In the proposed tomosynthesis scoring system bronchiectatic bronchi are rated for number and appearance. The whole lung volume is included in the tomosynthesis examinations and the contiguous tomosynthesis sections offer the ability to observe a bronchus in its full length and thereby assess the number and types of bronchiectatic lesions. In previous studies the number of abnormal airways found with high resolution CT has been shown to correlate with the degree of impairment of pulmonary function [28] and the classification of the type of bronchiectasis has been described as a useful index of disease severity [27].

Observer agreements for the total score in the tomosynthesis scoring showed almost perfect correlation and observer agreements for all subscores were generally high (Table 1, Fig. 4). The subscore of overinflation showed slightly lower observer agreements than the other subscores, probably due to the lack of quantification of scoring levels. The scoring of overinflation is performed by comparing with the reference images and is thus more subjective. There was only a slight systematic variation between observers for the subcomponents of the number of bronchiectatic bronchi and large mucus plugs but no random variation, thus showing that the scoring system is robust (Table 1).

Except for overinflation, the tomosynthesis score evaluates the four quadrants separately for all subscores with a total score of 16 for each component or subcomponent. In the Brasfield score for radiography [6] both lungs are rated simultaneously with a total score of 4 or 5 for each component. For example, with the Brasfield scoring system nodular cystic lesions are scored for both lungs with a maximum score of 4. In the tomosynthesis score bronchiectasis is scored for both number and appearance and mucus plugging is scored for both large and small mucus plugs, for each lung quadrant, with a maximum score of 64 for both lungs. Thus a higher diversity of scores in a patient population can be achieved with the tomosynthesis score (Figs. 6–8) giving the possibility of earlier detection of disease progression or alteration

of lung status. The tomosynthesis scoring system, having a higher maximum score, offers the possibility of a more detailed scoring of disease severity than radiography using the Brasfield scoring system. As tomosynthesis is more sensitive to pulmonary CF changes than radiography, the total disease severity scores were generally higher for tomosynthesis than for radiography with regard to percentage of the maximum score.

The scoring of a tomosynthesis examination takes approximately 5 to 15 min to perform, depending on the severity of changes and experience of the reader. Thus, the scoring system probably mainly will be used for yearly check-ups, for treatment evaluation in severe or complicated cases as well as for research and quality assurance projects. The total score is simply calculated by a summation of all subscores. In the Electronic Supplementary Appendix reference images are provided from cases where the observers agreed on the scoring levels.

The proposed tomosynthesis score correlates well with the Brasfield scoring system, with good observer agreements for the total disease severity score. The current study has shown at least as good observer agreements for the tomosynthesis score as for radiographs evaluated with the Brasfield score. The purpose of the study was to design and validate a scoring system for tomosynthesis, not to define when to perform tomosynthesis or CT, or compare advantages and disadvantages of these two methods, which will be the purpose of future research.

The limitations of tomosynthesis are mainly related to the present acquisition time of 10 s, under breath hold at inspiration, which restricts use in small children. According to our experience, however, the examination quality can be substantially increased by training the patients in breath-holding techniques before the examination, preferably even at home.

Localised air-trapping on expiratory images is well assessed with CT and is thought to reflect small airway disease that occurs early in the course of pulmonary CF disease [35], and may be a useful feature in assessing children with mild CF lung disease [22]. Unfortunately, this cannot be accurately evaluated with tomosynthesis.

Dose considerations in radiological examinations are increasingly important as young patients with CF today may have a life expectancy of 40–50 years or more [36]. The effective adult dose from a PA and a lateral chest radiograph using a digital detector is approximately 0.04 to 0.05 mSv [24]. The effective dose from chest tomosynthesis has been reported to be 0.12 [1] to 0.13 [24] mSv for adults. In children 8 to18 years old (median age 13) at our institution the effective dose has been determined to be approximately 0.08 mSv for chest tomosynthesis and 0.04 mSv for chest radiography (PA and lateral views). Thus chest tomosynthesis results in an approximately 2- to 3-fold increase in effective dose compared with chest radiography. The role for CT as a routine assessment method in the management of CF lung disease is still controversial owing to dose issues and is under investigation [37-40]. As tomosynthesis exposes the patient to a comparatively low radiation dose of only about 10% of the dose from CT with low-dose protocols [41] and is performed on the same X-ray system as chest radiography (adding only about 1 min to the normal examination time), it may become useful in the regular follow-up of CF patients as well as in the everyday clinical practice.

In conclusion, the proposed tomosynthesis scoring system for pulmonary cystic fibrosis has been shown to be robust and correlates well with the total disease severity score of the Brasfield scoring system for radiography. Tomosynthesis is more sensitive to cystic fibrosis changes, in particular bronchiectasis and mucus plugging, and shows them in more detail than radiography. The tomosynthesis scoring system, with a higher maximum score than Brasfield

score, offers the possibility of a more accurate scoring of disease severity. Furthermore, the radiation dose from tomosynthesis is low. Considering these aspects we believe that tomosynthesis has the potential to become a useful tool in the regular follow-up of cystic fibrosis patients.

ACKNOWLEDGEMENTS

We thank Pär Wingren for his assistance in the development of the tomosynthesis scoring system, and Carina Fyledahl-Kastberg, for invaluable help in performing the tomosynthesis examinations and keeping the patient log.

REFERENCES

1. Vikgren J, Zachrisson S, Svalkvist A, et al. (2008) Comparison of chest tomosynthesis and chest radiography for detection of pulmonary nodules: Human observer study of clinical cases. Radiology 249:1034-1041.
2. Vult von Steyern K, Bjorkman-Burtscher I, Geijer M (2011) Tomosynthesis in pulmonary cystic fibrosis with comparison to radiography and computed tomography: a pictorial review. Insights Imaging. doi:10.1007/s13244-011-0137-9
3. Shwachman H, Kulczycki L (1958) Long-term study of one hundred five patients with cystic fibrosis: studies made over a five-to fourteen-year period. AMA J Dis Child 96:6-15.
4. Taussig L, Kattwinkel J, Friedewald W, et al. (1973) A new prognostic score and clinical evaluation system for cystic fibrosis. J Pediatr 82:380-390.
5. Chrispin A, Norman A (1974) The systematic evaluation of the chest radiograph in cystic fibrosis. Pediatr Radiol 2:101-105.
6. Brasfield D, Hicks G, Soong S, et al. (1979) The chest roentgenogram in cystic fibrosis: a new scoring system. Pediatrics 63:24-29.
7. Van der Put J, Meradji M, Danoesastro D, et al. (1982) Chest radiographs in cystic fibrosis. A follow-up study with application of a quantitative system. Pediatr Radiol 12:57-61.
8. Carty H (1987) The chest radiograph in cystic fibrosis in children and the role of other radiological techniques. J R Soc Med 80:38-46.
9. Weatherly M, Palmer C, Peters M, et al. (1993) Wisconsin cystic fibrosis chest radiograph scoring system. Pediatrics 91:488-495.

10. Conway S, Pond M, Bowler I, et al. (1994) The chest radiograph in cystic fibrosis: a new scoring system compared with the Chrispin-Norman and Brasfield scores. Thorax 49:860-862.

11. Cleveland R, Neish A, Zurakowski D, et al. (1998) Cystic fibrosis: a system for assessing and predicting progression. AJR Am J Roentgenol 170:1067-1072.

12. Koscik R, Kosorok M, Farrell P, et al. (2000) Wisconsin cystic fibrosis chest radiograph scoring system: validation and standardization for application to longitudinal studies. Pediatr Pulmonol 29:457-467.

13. Benden C, Wallis C, Owens C, et al. (2005) The Chrispin-Norman score in cystic fibrosis: doing away with the lateral view. Eur Respir J 26:894-897.

14. Bhalla M, Turcios N, Aponte V, et al. (1991) Cystic fibrosis: scoring system with thin-section CT. Radiology 179:783-788.

15. Nathanson I, Conboy K, Murphy S, et al. (1991) Ultrafast computerized tomography of the chest in cystic fibrosis: a new scoring system. Pediatr Pulmonol 11:81-86.

16. Maffessanti M, Candusso M, Brizzi F, et al. (1996) Cystic fibrosis in children: HRCT findings and distribution of disease. J Thorac Imaging 11:27-38.

17. Santamaria F, Grillo G, Guidi G, et al. (1998) Cystic fibrosis: when should high-resolution computed tomography of the chest be obtained? Pediatrics 101:908-913.

18. Brody A, Molina P, Klein J, et al. (1999) High-resolution computed tomography of the chest in children with cystic fibrosis: support for use as an outcome surrogate. Pediatr Radiol 29:731-735.

19. Helbich T, Heinz-Peer G, Eichler I, et al. (1999) Cystic Fibrosis: CT assessment of lung involvement in children and adults. Radiology 213:537-544.

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20. Robinson T, Leung A, Northway W, et al. (2001) Spirometer-triggered high-resolution computed tomography and pulmonary function measurements during an acute exacerbation in patients with cystic fibrosis. J Pediatr 138:553-559.

21. Oikonomou A, Tsanakas J, Hatziagorou E, et al. (2008) High resolution computed tomography of the chest in cystic fibrosis (CF): is simplification of scoring systems feasible? Eur Radiol 18:538-547.

22. Brody A, Klein J, Molina P, et al. (2004) High-resolution computed tomography in young patients with cystic fibrosis: distribution of abnormalities and correlation with pulmonary function tests. J Pediatr 145:32-38.

23. Dobbins J, Godfrey D (2003) Digital x-ray tomosynthesis: current state of the art and clinical potential. Phys Med Biol 48:R65-R106.

24. Bath M, Svalkvist A, von Wrangel A, et al. (2010) Effective dose to patients from chest examinations with tomosynthesis. Radiat Prot Dosimetry 139:153-158.

25. Sabol JM (2009) A Monte Carlo estimation of effective dose in chest tomosynthesis. Med Phys 36:5480-5487.

26. Reid L (1950) Reduction in bronchial subdivision in bronchiectasis. Thorax 5:233-247.

27. Lynch D, Newell J, Hale V, et al. (1999) Correlation of CT findings with clinical evaluations in 261 patients with symptomatic bronchiectasis. AJR Am J Roentgenol 173:53-58.

28. Barker A (2002) Bronchiectasis. N Engl J Med 346:1383-1393.

29. Rossi S, Franquet T, Volpacchio M, et al. (2005) Tree-in-Bud Pattern at Thin-Section CT of the Lungs: Radiologic-Pathologic Overview1. Radiographics 25:789-801.

30. Eisenhuber E (2002) The Tree-in-Bud Sign1. Radiology 222:771-772.

31. Landis JR, Koch GG (1977) The measurement of observer agreement for categorical data. Biometrics 33:159-174.

32. Svensson E, Holm S (1994) Separation of systematic and random differences in ordinal rating scales. Stat Med 13:2437-2453.

33. Svensson E, Starmark JE, Ekholm S, et al. (1996) Analysis of interobserver disagreement in the assessment of subarachnoid blood and acute hydrocephalus on CT scans. Neurol Res 18:487-494.

34. de Jong P, Lindblad A, Rubin L, et al. (2006) Progression of lung disease on computed tomography and pulmonary function tests in children and adults with cystic fibrosis. Thorax 61:80-85.

35. de Jong P, Tiddens H (2007) Cystic fibrosis specific computed tomography scoring. Proc Am Thorac Soc 4:338-342.

36. Swedish National Board of Health and Welfare (Socialstyrelsen) (2010) Ovanliga diagnoser, cystisk fibros. http://www.socialstyrelsen.se/ovanligadiagnoser/cystiskfibros. Accessed 15 June 2010

37. Aziz Z, Davies J, Alton E, et al. (2007) Computed tomography and cystic fibrosis: promises and problems. Thorax 62:181-186.

38. Cooper P, MacLean J (2006) High-resolution computed tomography (HRCT) should not be considered as a routine assessment method in cystic fibrosis lung disease. Paediatr Respir Rev 7:197-201.

39. Tiddens H (2006) Chest computed tomography scans should be considered as a routine investigation in cystic fibrosis. Paediatr Respir Rev 7:202-208.

40. de Jong P, Nakano Y, Lequin M, et al. (2004) Progressive damage on high resolution computed tomography despite stable lung function in cystic fibrosis. Eur Respir J 23:93-97.

41. Lucaya J, Piqueras J, Garcia-Pena P, et al. (2000) Low-dose high-resolution CT of the chest in children and young adults: dose, cooperation, artifact incidence, and image quality. AJR Am J Roentgenol 175:985-992.

FIGURE LEGENDS

Fig. 1. A 32-year-old man with cystic fibrosis. The mean total Brasfield score for the three observers for the posteroanterior (a) and lateral radiograph was 10.7 (48.5% of the maximum score). The mean total score for tomosynthesis was 69.3. On two tomosynthesis sections (b and c) marked bronchial wall thickening, bronchiectasis and extensive mucus plugging can be seen

Fig. 2 a, b. The scoring form of the tomosynthesis cystic fibrosis scoring system (two pages)

Fig. 3 a, b. Examples of reference images for scoring of the appearance of bronchiectasis (a) and extent of small mucus plugs (b) from the Electronic Supplementary Appendix

Fig. 4. Comparison of total disease severity scores for tomosynthesis between observers (observer 1 vs. observer 2: black squares and observer 1 vs. observer 3: red triangles)

Fig. 5. Comparison of total disease severity scores for radiography between the observers (observer 1 vs. observer 2: black squares and observer 1 vs. observer 3: red triangles)

Fig. 6. Comparison of the total disease severity scores for radiography and tomosynthesis in percentage of the maximum score for the three observers (observer 1: black dots, observer 2: green squares and observer 3: red triangles)

Fig. 7. Comparison of the scores for linear markings on radiographs and bronchial wall thickening on tomosynthesis sections for the three observers (observer 1: black dots, observer 2: green squares and observer 3: red triangles)

Fig. 8. Comparison of the scores for nodular cystic lesions (NCL) on radiographs with the sum of the scores for bronchiectases and mucus plugging (BMP) on tomosynthesis sections

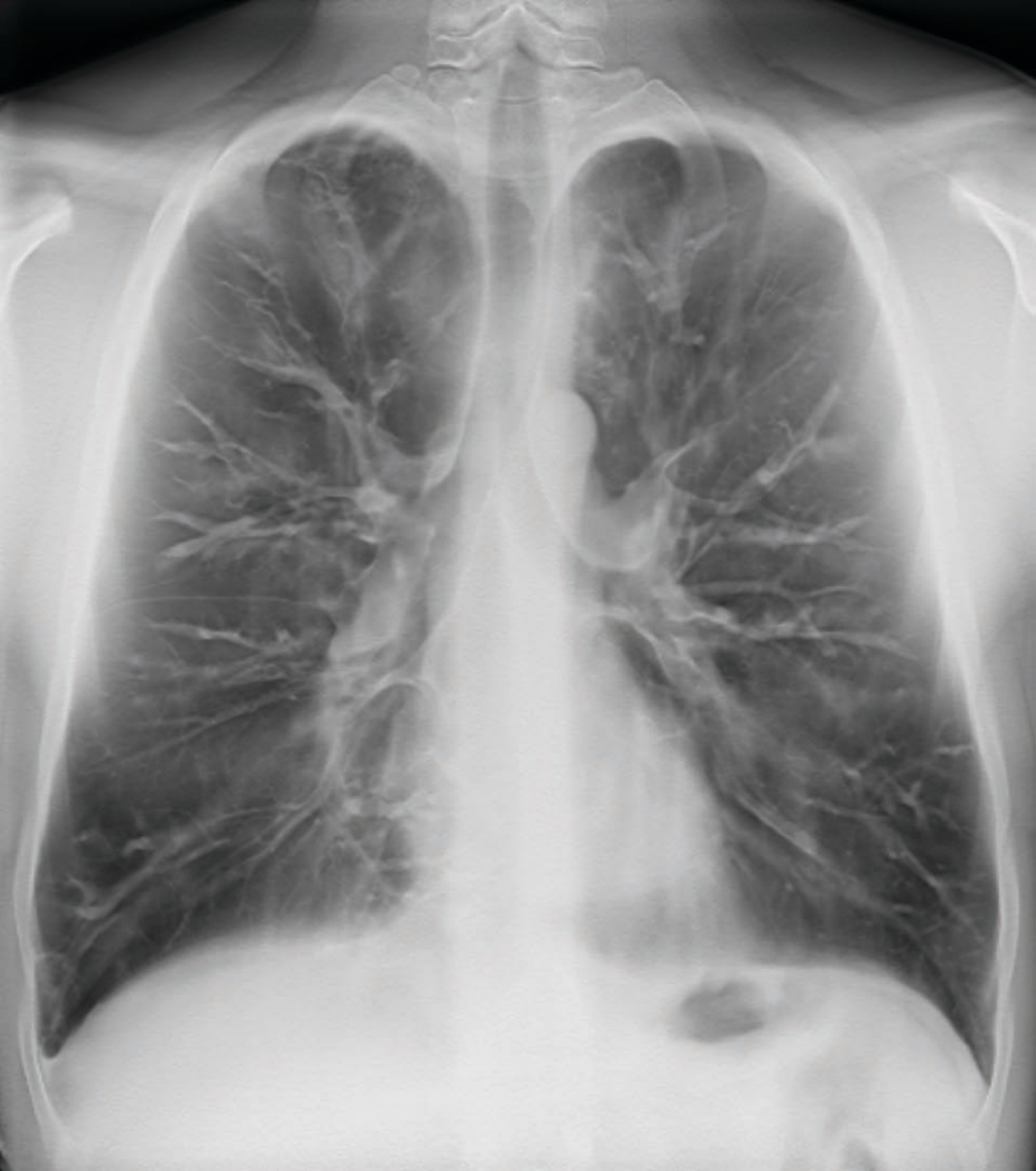
for the three observers (observer 1: black dots, observer 2: green squares and observer 3: red triangles)

Table 1. Comparisons of the total scores and subscores for tomosynthesis for the three pairs of observers. For each score the values in the first row represent observer 1 vs. observer 2, in the second row observer 1 vs. observer 3, and in the third row observer 2 vs. observer 3

Score	Possible range (all quadrants)	Square-weighted kappa	Relative rank variance	Percentage agreement	Relative position	Relative concentration
Total	0-100	0.90	0.021	0.52	-0.022	-0.025
		0.91	0.011	0.44	0.079	-0.11
		0.90	0.016	0.45	0.10	-0.099
Overinflation	0-4	0.71	0.024	0.57	0.040	0.054
		0.61	0.069	0.49	0.018	0.034
		0.56	0.075	0.52	-0.023	-0.019
Bronchial wall thickening	0-16	0.76	0.052	0.44	0.00026	-0.11
		0.82	0.037	0.56	0.0048	-0.13
		0.84	0.037	0.53	0.0045	-0.013
Parenchyma	0-16	0.74	0.019	0.67	0.029	-0.027
		0.58	0.063	0.63	-0.029	-0.074
		0.59	0.061	0.63	-0.057	-0.051
Number of bronchiectases	0-16	0.93	0.029	0.32	-0.021	0.059
		0.79	0.052	0.19	0.26	-0.076
		0.75	0.051	0.13	0.29	-0.16
Severity of bronchiectases	0-16	0.93	0.040	0.34	-0.010	0.012
		0.93	0.029	0.26	0.055	0.15
		0.92	0.041	0.25	0.047	0.13
Large mucus plugging	0-16	0.88	0.0024	0.75	-0.094	-0.052
		0.82	0.020	0.57	0.16	-0.050
		0.65	0.016	0.58	0.25	0.0053
Small mucus plugging	0-16	0.84	0.027	0.49	-0.041	-0.11
		0.75	0.057	0.44	0.058	-0.19
		0.78	0.052	0.42	0.094	-0.079

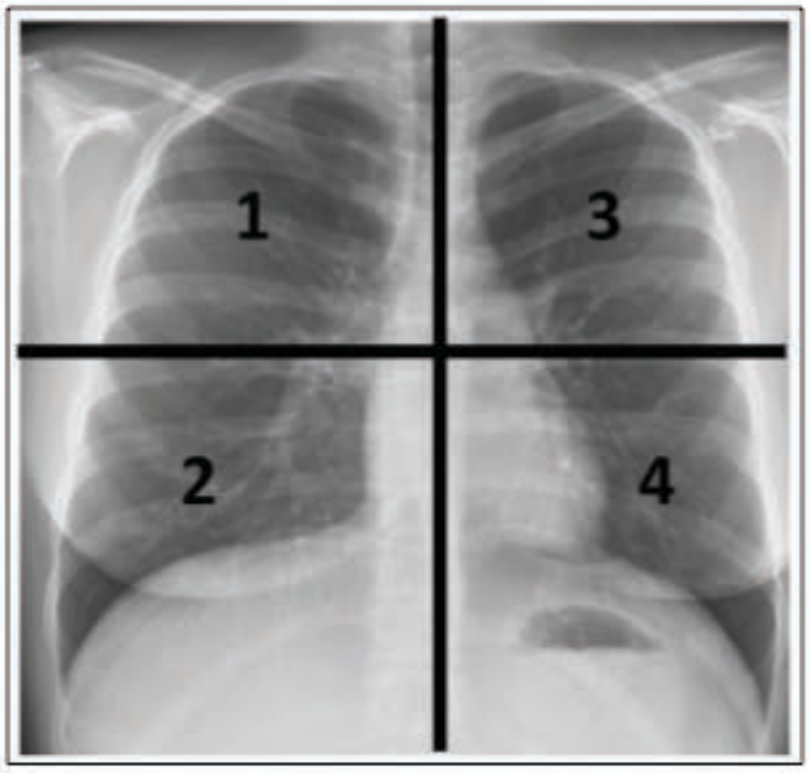
Table 2. Comparisons of the total scores for radiography for the three pairs of observers. In the first row the values represent observer 1 vs. observer 2, in the second row observer 1 vs. observer 3, and in the third row observer 2 vs. observer 3

Score	Square-weighted kappa	Relative rank variance	Percentage agreement	Relative position	Relative concentration
Brasfield score	0.85	0.023	0.53	0.0075	-0.037
	0.80	0.053	0.39	-0.016	-0.17
	0.81	0.070	0.32	-0.028	-0.14



The tomosynthesis cystic fibrosis scoring form

Patient name	
Patient ID	
Study date	
Study ID	
Scorer	
Scoring date	
Total score (max 100)	



4 lung quadrants:

The lungs are divided at the level of the first division of the left main bronchus

1= Right upper
2= Right lower

3= Left upper
4= Left lower

1) OVERINFLATION

Both lungs are scored (PA/AP and lateral radiographs)
Overall impression (0-4):

0 ☐ None
1 ☐ Mild
2 ☐ Moderate
3 ☐ Severe
4 ☐ Very severe

Score:
(max 4)

2) BRONCHIAL WALL THICKENING

Parallel line densities or end-on circular densities.
Normally bronchi peripheral of the central part of the segmental bronchi are ***not*** *visible on tomosynthesis sections.*

Rate each quadrant for bronchial wall thickening (0-4)

Quadrant 1
0 ☐ None
2 ☐ Present
4 ☐ Marked

Quadrant 3
0 ☐ None
2 ☐ Present
4 ☐ Marked

Quadrant 2
0 ☐ None
2 ☐ Present
4 ☐ Marked

Quadrant 4
0 ☐ None
2 ☐ Present
4 ☐ Marked

Sum of scores:
(max. 16)

3) PARENCHYMAL LESIONS

Rate each quadrant for atelectasis or consolidation (0-4)

Small consolidation *is defined as less than the volume of the 7th thoracic vertebra.*

Quadrant 1
0 ☐ None
1 ☐ = b
2 ☐ = c
3 ☐ = d
4 ☐ = e

Quadrant 3
0 ☐ None
1 ☐ = b
2 ☐ = c
3 ☐ = d
4 ☐ = e

b) 1-2 small areas of consolidation or thin atelectases*

c) 3-4 small areas of consolidation or atelectases*

d) 5-6 small areas of consolidation or atelectases*

e) Dense infiltration, little or no area of normal lung is seen

***or a larger area of equivalent size**

Quadrant 2
0 ☐ None
1 ☐ = b
2 ☐ = c
3 ☐ = d
4 ☐ = e

Quadrant 4
0 ☐ None
1 ☐ = b
2 ☐ = c
3 ☐ = d
4 ☐ = e

Sum of scores:
(max. 16)

4) BRONCHIECTASIS

A non-tapering bronchus (cylindrical, varicose or cystic); or broncho-arterial ratio > 1; or a visible bronchus close to the pleura.
If a bronchiectatic bronchus divides into two dilated branches, only the branches are counted.

A) Rate each quadrant for the NUMBER of bronchiectatic bronchi (0-4)

Quadrant 1
0 ☐ None
1 ☐ 1-5
2 ☐ 6-10
3 ☐ 11-15
4 ☐ >15

Quadrant 3
0 ☐ None
1 ☐ 1-5
2 ☐ 6-10
3 ☐ 11-15
4 ☐ >15

Quadrant 2
0 ☐ None
1 ☐ 1-5
2 ☐ 6-10
3 ☐ 11-15
4 ☐ >15

Quadrant 4
0 ☐ None
1 ☐ 1-5
2 ☐ 6-10
3 ☐ 11-15
4 ☐ >15

Sum of scores:
(max. 16)

B) Rate each quadrant for the APPEARANCE of the widest bronchiectasis (0-4)

Cylindrical (A, B) = *bronchi are mildly and uniformly dilated, with a relatively straight outline.*

Subtle cylindrical (A) = *discretely dilated, straight outline*

Markedly cylindrical (B) = *clearly dilated, slightly irregular outline*

Varicose (C) = *bronchi are moderately dilated and local constrictions give the airway an irregular or beaded outline.*

Cystic (D) = *bronchi are severely dilated giving the airways a ballooned appearance, with strings of cysts or grape-like clusters in the peripheral part of the bronchi.*

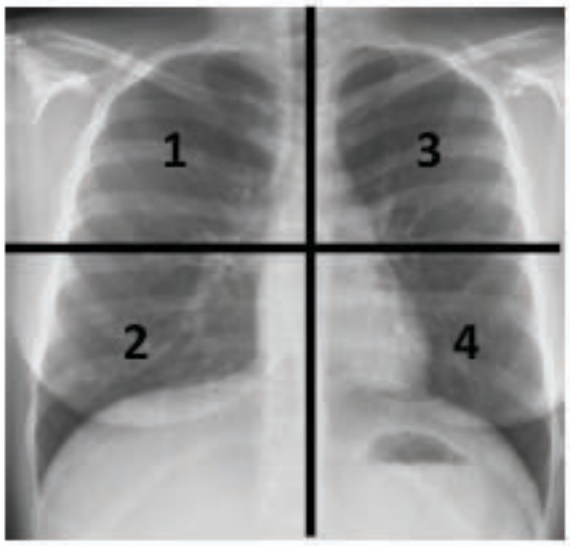
Quadrant 1
0 ☐ Not applicable
1 ☐ Subtle cylindrical
2 ☐ Markedly cylindrical
3 ☐ Varicose
4 ☐ Cystic

Quadrant 3
0 ☐ Not applicable
1 ☐ Subtle cylindrical
2 ☐ Markedly cylindrical
3 ☐ Varicose
4 ☐ Cystic

Quadrant 2
0 ☐ Not applicable
1 ☐ Subtle cylindrical
2 ☐ Markedly cylindrical
3 ☐ Varicose
4 ☐ Cystic

Quadrant 4
0 ☐ Not applicable
1 ☐ Subtle cylindrical
2 ☐ Markedly cylindrical
3 ☐ Varicose
4 ☐ Cystic

Sum of scores:
(max. 16)



4 lung quadrants:

1= Right upper
2= Right lower

3= Left upper
4= Left lower

5) MUCUS PLUGGING

A) Rate each quadrant for LARGE mucus plugs (0-4)

Large mucus plugs *are tubular opacities with or without a branching pattern or rounded opacities,* ***≥ 5mm****, differentiated from vessels by their continuity with bronchi.*

Quadrant 1
0 ☐ None
1 ☐ In 1-2 bronchi
2 ☐ In 3-4 bronchi
3 ☐ In 5-6 bronchi
4 ☐ In ≥7 bronchi

Quadrant 3
1 ☐ None
2 ☐ In 1-2 bronchi
3 ☐ In 3-4 bronchi
4 ☐ In 5-6 bronchi
5 ☐ In ≥7 bronchi

Quadrant 2
0 ☐ None
1 ☐ In 1-2 bronchi
3 ☐ In 3-4 bronchi
4 ☐ In 5-6 bronchi
5 ☐ In ≥7 bronchi

Quadrant 4
0 ☐ None
1 ☐ In 1-2 bronchi
2 ☐ In 3-4 bronchi
3 ☐ In 5-6 bronchi
4 ☐ In ≥7 bronchi

Sum of scores:
(max. 16)

B) Rate each quadrant for SMALL mucus plugs (0-4)

Small mucus plugs *are seen as clustered small nodular opacities (<5mm) or as a tree-in-bud pattern in the periphery of the lobes.*
A minor area *is defined as less than the volume of the 7th thoracic vertebra.*

Quadrant 1
0 ☐ none
1 ☐ = b
2 ☐ = c
3 ☐ = d
4 ☐ = e

b) Clustered small mucus plugs in **1-2 minor areas***

c) Clustered small mucus plugs in **3-4 minor areas***

d) Clustered small mucus plugs in **5-6 minor areas***

e) Clustered small mucus plugs in **≥7 minor areas***

*** or a larger area of equivalent size**

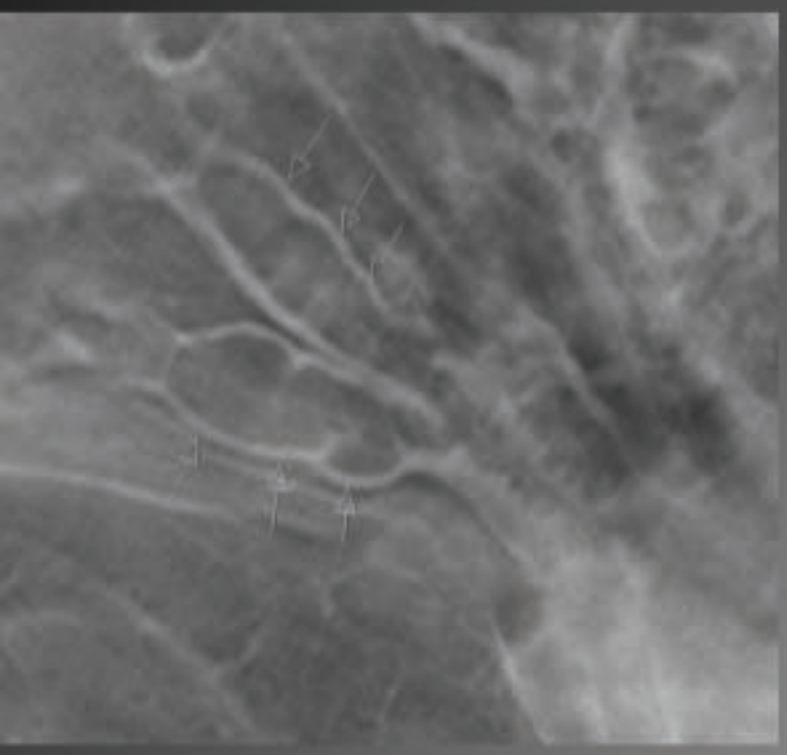
Quadrant 3
0 ☐ none
1 ☐ = b
2 ☐ = c
3 ☐ = d
4 ☐ = e

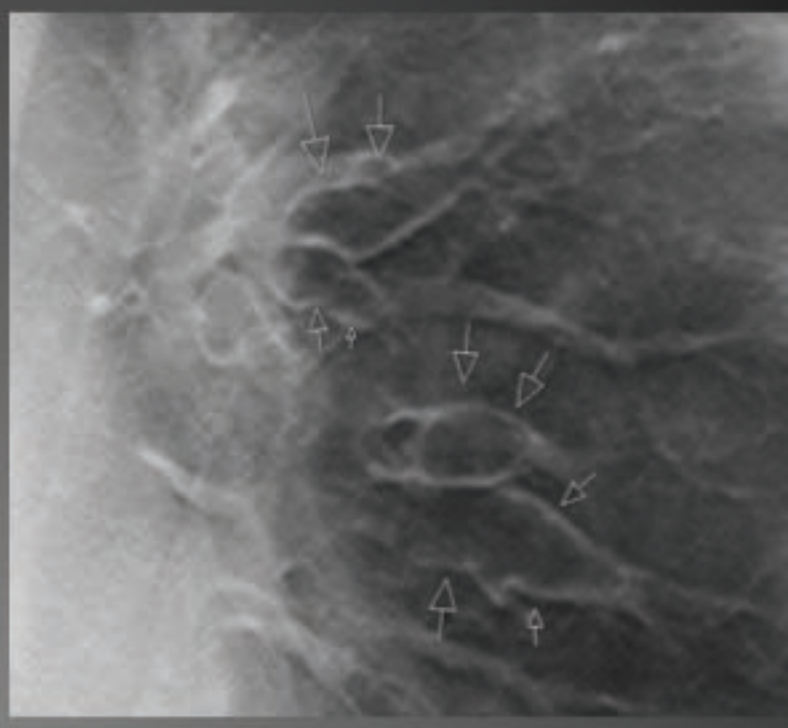
Quadrant 2
0 ☐ none
1 ☐ = b
2 ☐ = c
3 ☐ = d
4 ☐ = e

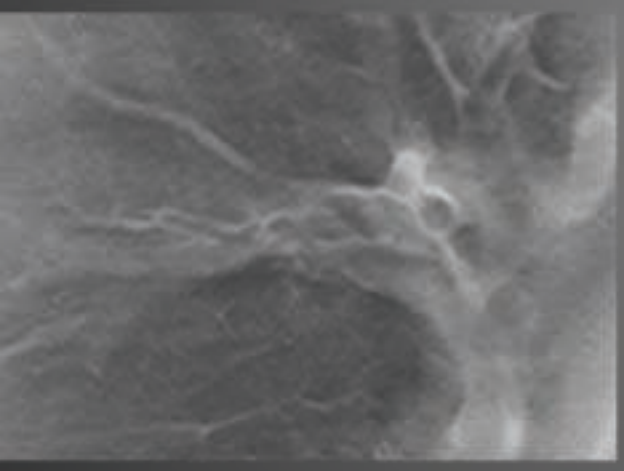
Quadrant 4
0 ☐ none
1 ☐ = b
2 ☐ = c
3 ☐ = d
4 ☐ = e

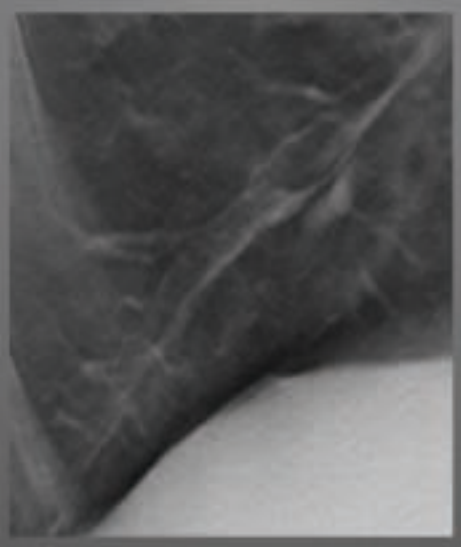
Sum of scores:
(max. 16)

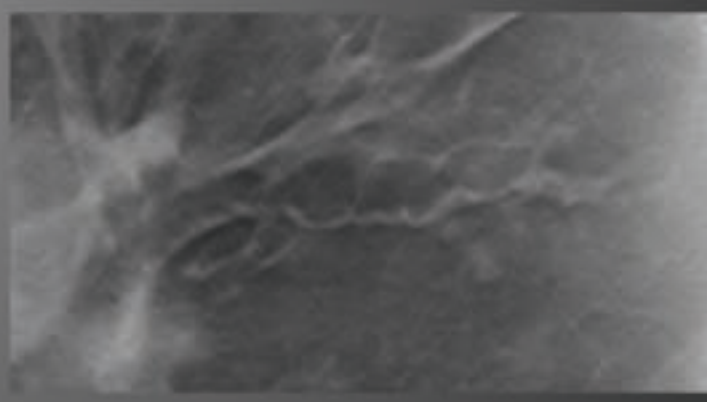
4B) 3 p. = Bronchiectasis, varicose

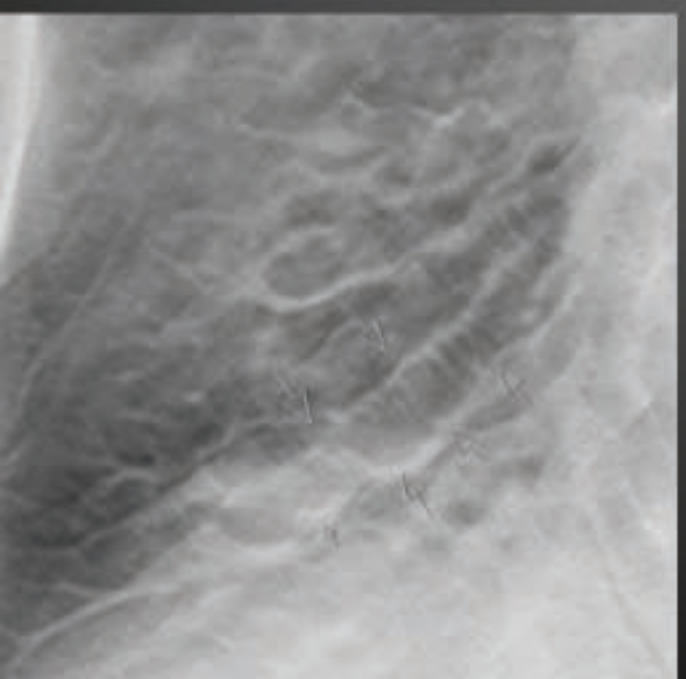


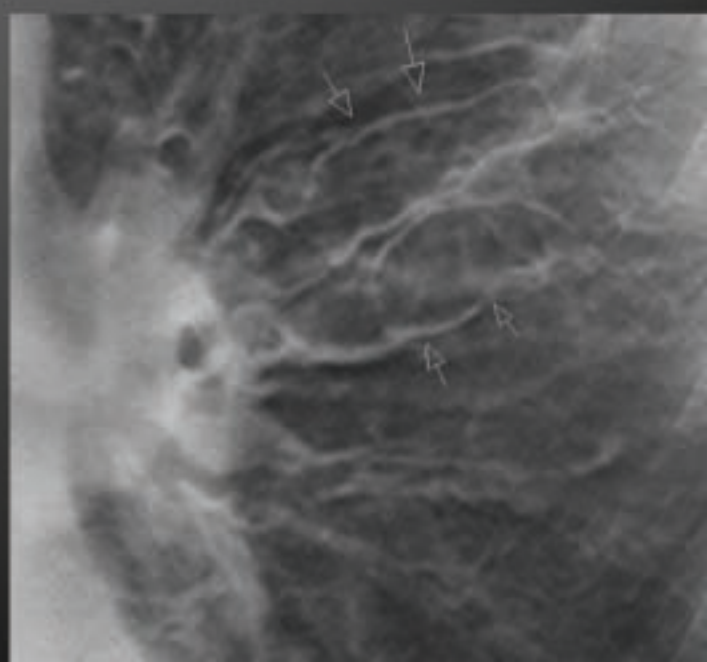




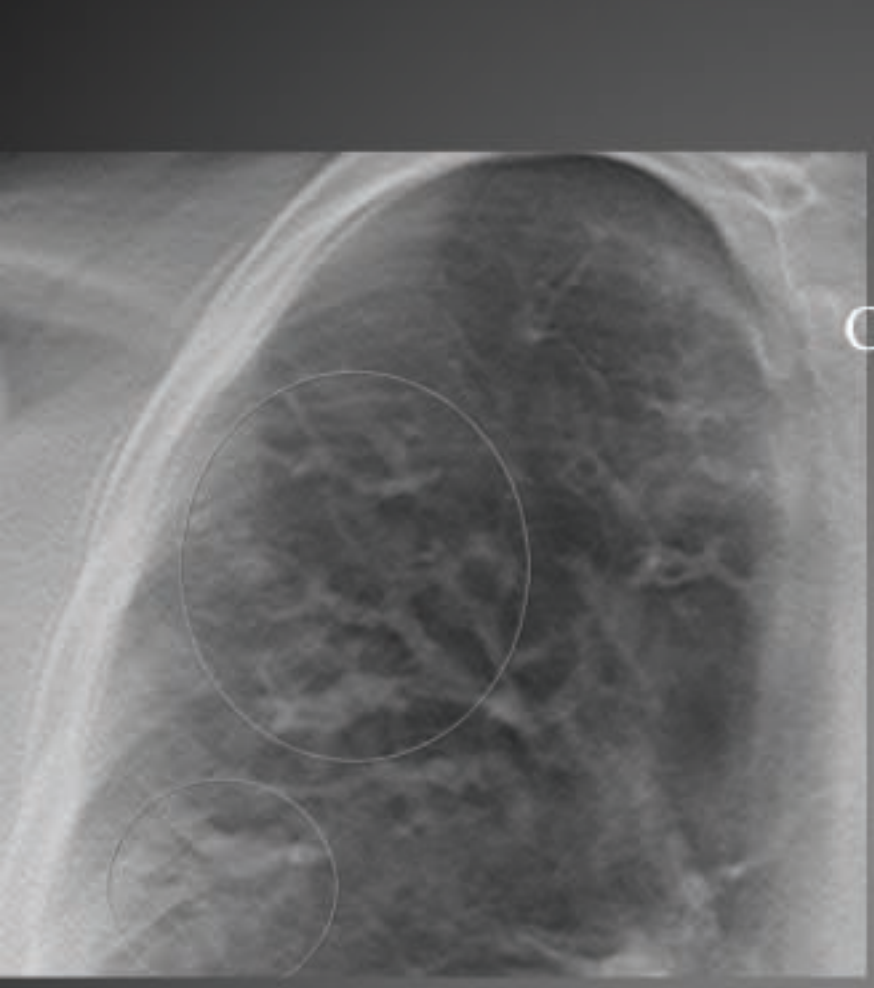






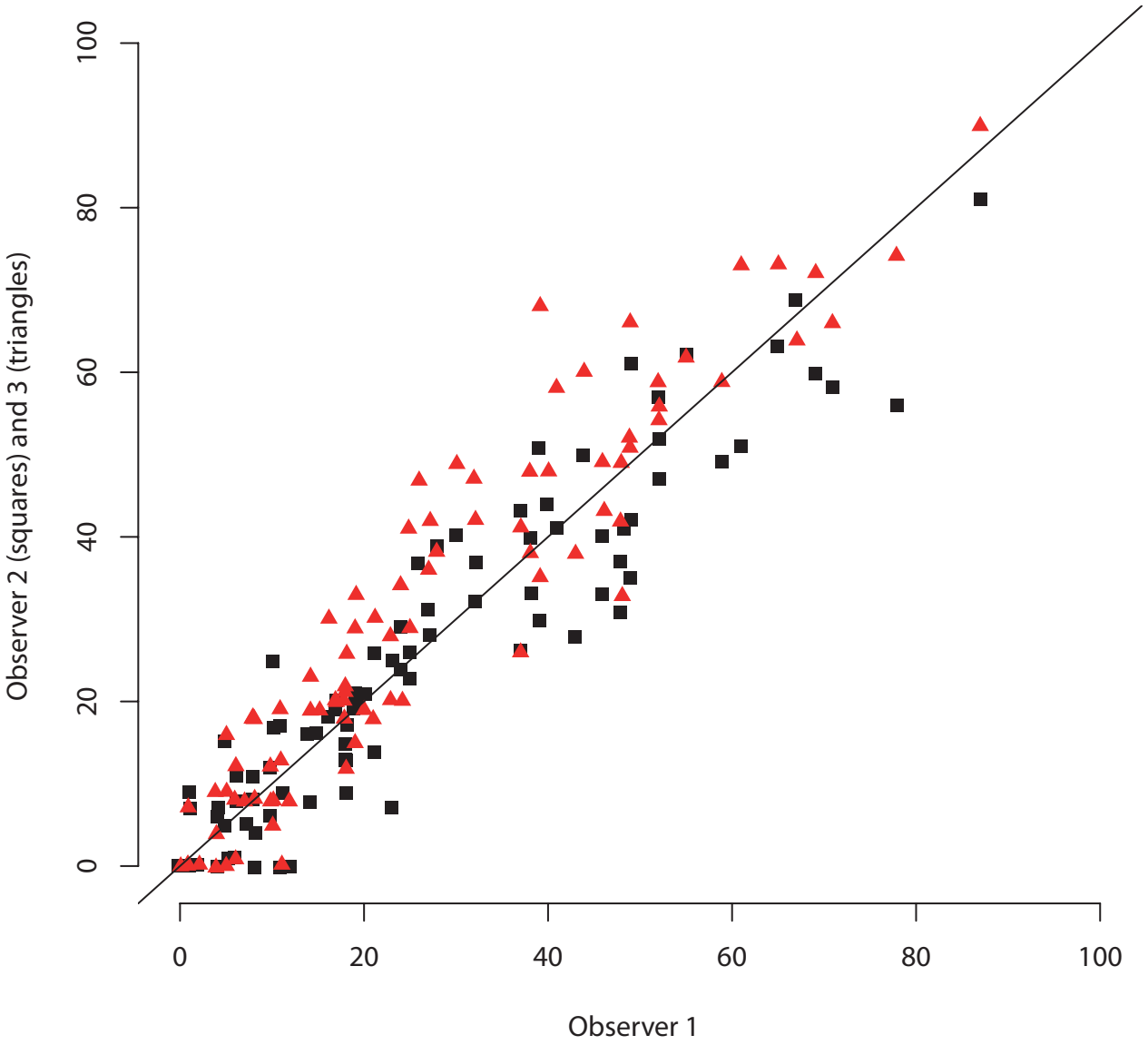


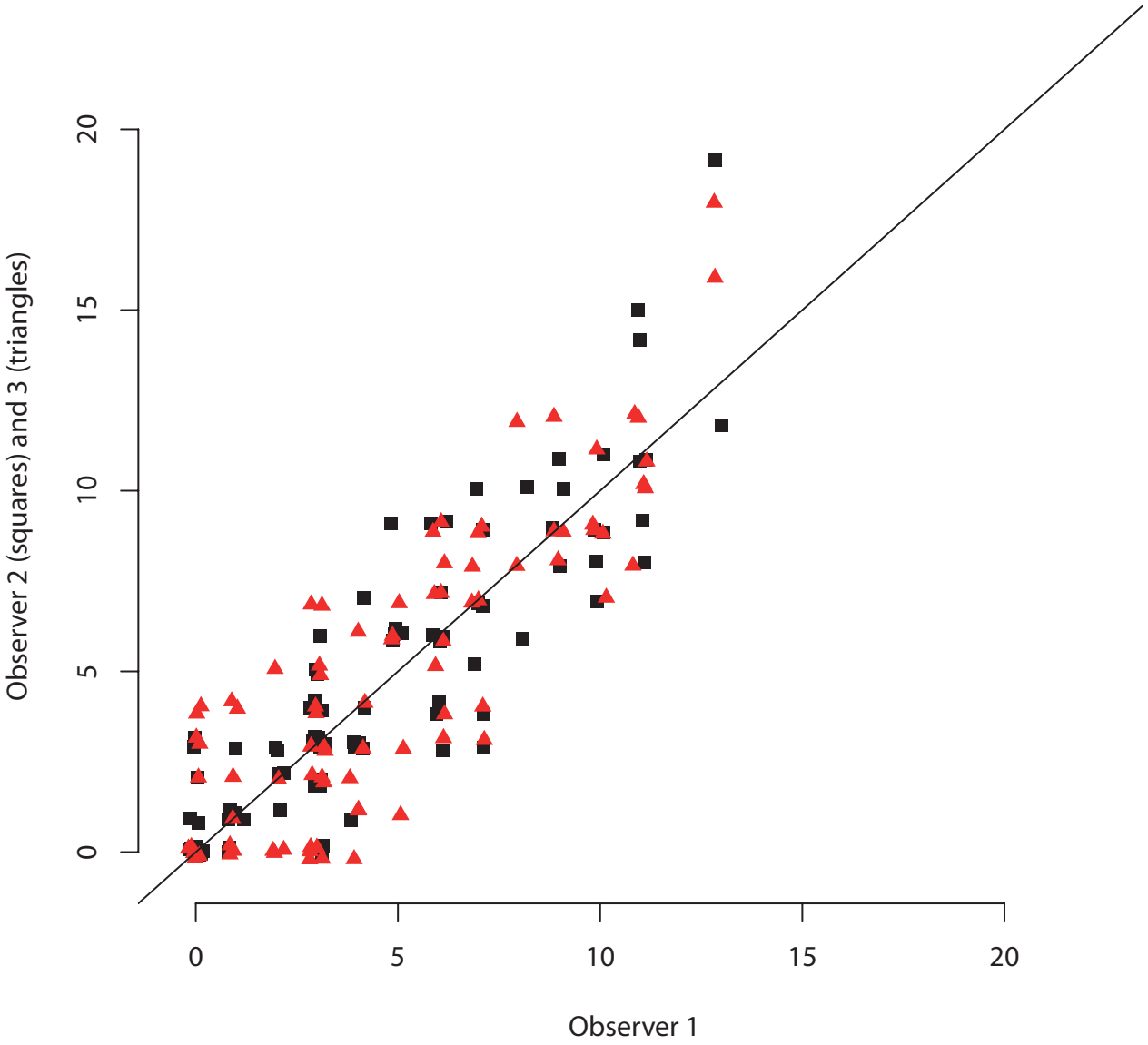
5B) 2 p. = Small mucus plugs, 3-4 minor areas (c)

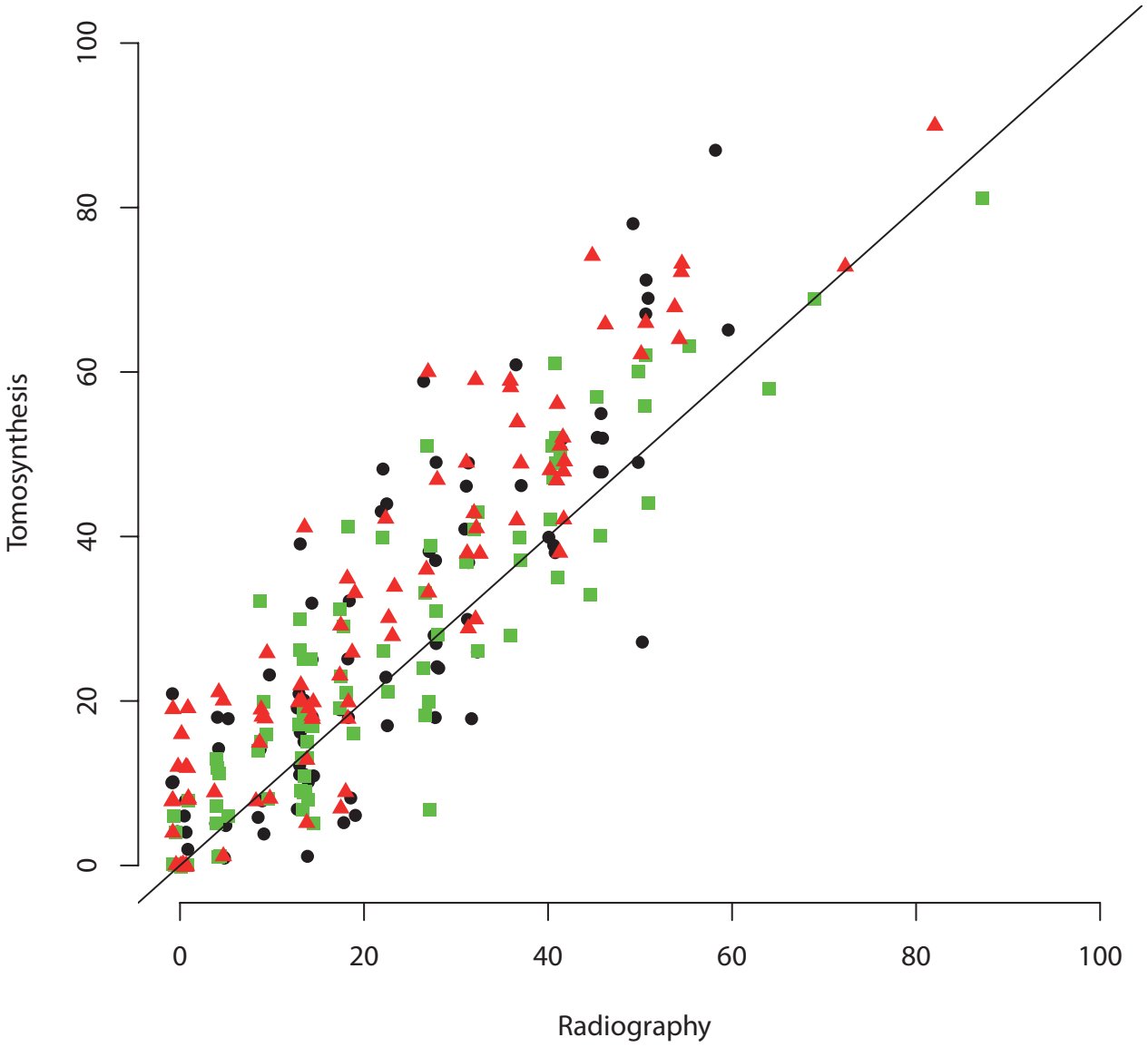


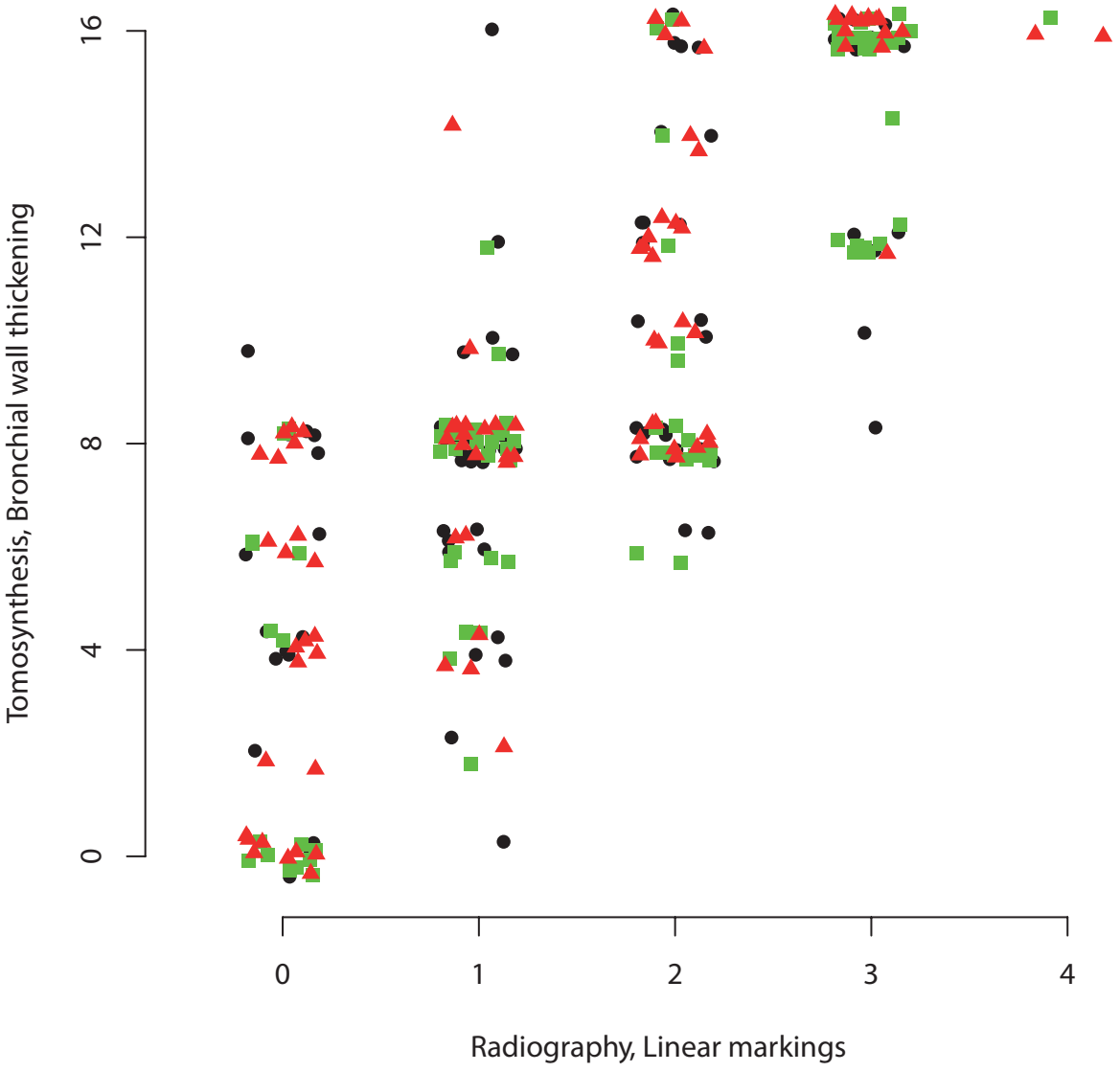
Case 1

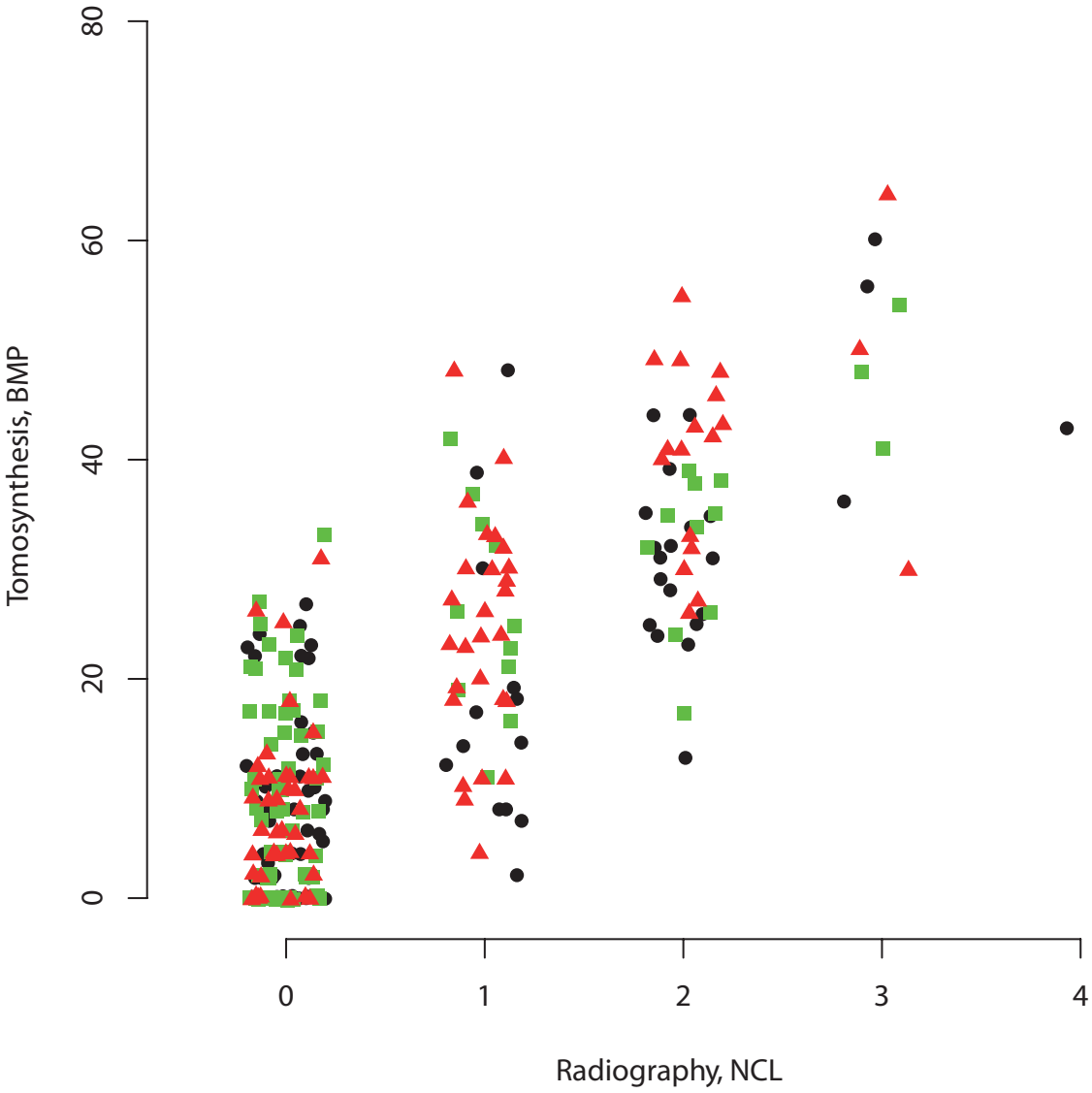
Case 2


Observer 2 (squares) and 3 (triangles)
0
20
40
60
80
100
0
20
40
60
80
100
Observer 1


Observer 2 (squares) and 3 (triangles)
0
5
10
15
20
0
5
10
15
20
Observer 1


Tomosynthesis
0
20
40
60
80
100
Radiography
0
20
40
60
80
100


Tomosynthesis, Bronchial wall thickening
0
4
8
12
16
0
1
2
3
4
Radiography, Linear markings


Tomosynthesis, BMP
0
20
40
60
80
0
1
2
3
4
Radiography, NCL