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FULL PAPER

Comparison of digital tomosynthesis and chest radiography for the detection of pulmonary nodules: systematic review and meta-analysis

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Objective: To compare the diagnostic accuracy of digital tomosynthesis (DTS) with that of chest radiography for the detection of pulmonary nodules by meta-analysis.

Methods: A systematic literature search was performed to identify relevant original studies from 1 January 1976 to 31 August 31 2016. The quality of included studies was assessed by quality assessment of diagnostic accuracy studies-2. Per-patient data were used to calculate the sensitivity and specificity and per-lesion data were used to calculate the detection rate. Summary receiver-operating characteristic curves were drawn for pulmonary nodule detection.

Results: 16 studies met the inclusion criteria. 1017 patients on a per-patient basis and 2159 lesions on a per-lesion

basis from 16 eligible studies were evaluated. The pooled patient-based sensitivity of DTS was 0.85 [95% confidence interval (CI) 0.83–0.88] and the specificity was 0.95 (0.93–0.96). The pooled sensitivity and specificity of chest radiography were 0.47 (0.44–0.51) and 0.37 (0.34–0.40), respectively. The per-lesion detection rate was 2.90 (95% CI 2.63–3.19).

Conclusion: DTS has higher diagnostic accuracy than chest radiography for detection of pulmonary nodules. Chest radiography has low sensitivity but similar specificity, comparable with that of DTS.

Advances in knowledge: DTS has higher diagnostic accuracy than chest radiography for the detection of pulmonary nodules.

INTRODUCTION

Detection and characterization of pulmonary nodules are challenging tasks in thoracic imaging. Chest radiography is the most commonly used screening tool for pulmonary nodules. Its advantages include a short examination time, low cost and easy accessibility. However, nodules may be poorly visualized by chest radiography because it shows the three-dimensional chest as a two-dimensional image, resulting in anatomical overlap.^{1,2} Chest radiography shows high specificity (90–99%) according to confidence level for early detection of lung carcinoma, but the sensitivity is low (54–84%).³ CT shows higher sensitivity for nodule detection and it is currently the gold standard for the detection of pulmonary abnormalities and in particular pulmonary nodules. However, in comparison with chest radiography, CT is costly and it exposes patients to substantially higher radiation doses.^{4,5}

Digital tomosynthesis (DTS) is a type of limited-angle tomography that provides continuous coronal images

through the area of interest. Because it eliminates overlapping anatomy or composite artefact, DTS facilitates improved lesion detection, depth localization and contrast resolution compared with plain radiography,^{6,7} and compared with CT, the cost and radiation dose of DTS are lower.^{8–10} Therefore, DTS has been recommended by several authors as an alternative to both chest radiography and CT, and the greater diagnostic performance of DTS for detecting pulmonary nodules has been reported.^{9,11–13} However, differences in the diagnostic performance for detection of pulmonary nodules between chest radiography and DTS have not been clearly delineated. Thus, the purpose of this meta-analysis was to compare the diagnostic accuracy of DTS with that of chest radiography for the detection of pulmonary nodules.

METHODS AND MATERIALS

We performed an extensive database search to identify studies comparing DTS and radiography for detection of lung nodules. The study protocol was based on Cochrane

Review Methods¹⁴ and reported according to the Meta-analysis of Observational Studies in Epidemiology guidelines for reviews of observational studies.¹⁵

Search

On 31 August 2016, we searched Medline, Embase and the Cochrane Central Register of Controlled Trials with no restrictions on language, year or type of publication.

The search strategies were developed with following keywords and Medical Subject Headings (MeSH): (lung OR pulmonary OR bronchial) AND (neoplasm OR nodule OR lesion OR cancer OR carcinoma) AND (tomosynthesis). Search strategies were tailored to each database (Appendix A). After the initial electronic search, we manually searched reference lists from retrieved articles and relevant reviews for additional studies.

Study selection

We developed inclusion and exclusion criteria in advance. The inclusion criteria were as follows: (1) the study was performed with only human subjects; (2) the study evaluated pulmonary non-calcified nodules or nodular lesions (opacity or ground-glass nodules) in patients of all ages in any disease category; (3) the presence of nodules was confirmed by CT or clinical follow-up of at least 3 months; (4) radiography and DTS were performed within 4 weeks of each other; and (5) when data or subsets of data were present in more than one article, the most detailed or most recent article was chosen.

The titles and abstracts of all studies were independently reviewed according to the predefined inclusion criteria by two reviewers (JHK and KTK), who decided whether to select the studies for full-text review. The full studies were evaluated for relevance to the aims of the present study. In case of disagreement between the two reviewers, a third reviewer (KHL) joined the discussion. Appendix B lists the excluded articles with reasons for their exclusion.

Data extraction and quality assessment

The two reviewers (JHK and KTK) independently extracted relevant data from each study using a predefined data extraction form. The third reviewer (KHL) examined and confirmed the accuracy of the extracted data.

The following data were extracted from the included studies: (1) sample size; (2) a description of study population (including age and male/female distribution); (3) study design; (4) year of publication; (5) reference standard; and (6) author country. Data regarding projection type [posteroanterior (PA) view alone or with lateral view] were extracted for chest radiographs. For each study, we recorded the number of true-positive, false-positive, true-negative and false-negative findings for both DTS and chest radiography. If each study suggests two or more data sets by each independent reviewer separately, we extracted each data set.

We used the quality assessment of diagnostic accuracy studies-2 tool to appraise the methodological quality of the selected studies in four domains: patient selection, index test, reference standard and flow and timing.¹⁶ We decided that the risk of bias

for any domain was high when the answer to at least one signalling question was no. Two reviewers (JHK and KTK) independently assessed the included studies using this tool.

Statistical analysis

The main outcome of our study was a summary estimate of the sensitivity and specificity of DTS and chest radiography for nodule detection. However, the meta-analysis was based on the summary data provided in the source publications, either the number of true- and false-positive or true- and false-negative test results or detection rates. We regarded the differences in detection rates as secondary outcomes. For pooled sensitivity and specificity with 95% confidence intervals (CIs), data for the true-positive, true-negative, false-positive and false-negative values of each test in each study were entered into Meta-DiSc (XI Cochrane Colloquium, Madrid, Spain). The results of each index test (DTS and chest radiography) were displayed as forest plots and summary receiver-operating characteristic (SROC) curve. To determine the detection rates of each index test, data for the number of true positives in each study were entered into Review Manager 5.2 (The Nordic Cochrane Centre, Copenhagen, Denmark). The detection rate of DTS was compared with that of chest radiography and is presented as risk ratio with 95% CI using the Mantel-Haenszel random-effects model.

Factors of heterogeneity could not be rigorously investigated and hierarchical SROC curve models and bivariate model were not fitted because of the small number of studies. Inconsistency index (I^2) tests were used to test for statistical heterogeneity, irrespective of whether pooled specificity, sensitivity or risk ratio was calculated, as well as to assess heterogeneity across studies. When the clinical heterogeneity was present across studies or I^2 value was $\geq 50\%$, we controlled for heterogeneity by conducting subgroup analyses. We performed subgroup analysis according to different study population.

RESULTS

Literature search

Searches of the databases yielded 198 articles (Figure 1). A total of 151 studies remained after excluding duplicate articles. Of these, 123 articles were excluded because it was clear from the title and abstract that they did not fulfil the selection criteria. For the remaining 28 articles, we obtained full manuscripts and following scrutiny of these, we identified 16 potentially relevant studies. 12 studies were excluded (Appendix B): 6 of them because the total number of true-positive, false-positive, true-negative and false-negative results (per patient) or the detection rate (per lesion) were not provided; 3 studies because they presented data or subsets of data that were also presented in more recent articles, which were chosen instead; and 6 studies because only radiography or DTS was performed without reference CT scans. Finally, 16 studies were included in the review (Figure 1).

Study characteristics and patient populations

We could extract the total number of true positives, false positives, true negatives and false negatives from per-patient-based studies;^{10,12,17–21} however, we could not extract those from the per-lesion-based studies because of insufficient data.^{9,11,13,21–23}

Figure 1. Preferred reporting items for Systematic Reviews and Meta-analyses flow diagram for the meta-analysis.

However, we could extract the total numbers of true positives and the total number of pulmonary nodules, which allowed us to calculate and analyze detection rates. Thus, we identified 7 studies (1017 patients) that presented per-patient results^{10,12,17–21} and 10 studies that presented per-lesion results (2159 lesions)^{9,11,13,21–27} for meta-analysis. Only one study included both per-patient- and per-lesion-based data.²¹

The characteristics of the included studies are presented in detail in Table 1. All studies except two studies, which were in Chinese language,^{17,23} were in English language. All studies had prospective design. Seven studies used both PA and lateral projections for chest radiography, while the others used only PA projections. CT served as the reference standard in 15 studies, while the remaining study included CT or clinical follow-up as the reference standard. All but four studies included an intervention group (pulmonary nodule) and a control group (no pulmonary nodule), and there were four studies that included patients with equivocal or abnormal findings, such as opacity or nodule, on chest radiography.^{18,19,24,26}

Quality assessment

Table 2 outlines the quality assessment of all studies included in the meta-analysis. In all studies but two studies,^{17,23} index test was defined as a low risk of bias. Risk of bias concerning patient selection was assessed high in all included studies because of the case-control design. Applicability of the index test and reference standard was scored as a low risk of bias in all studies. The item

“flow and timing” was assessed as high risk of bias or unclear in more than half studies, because the time from chest radiography until DTS was not mentioned or some patients received a different reference standard.

Summary estimate and subgroup analysis of sensitivity and specificity (per-patient studies)

Figure 2 shows the forest plot and SROC curves for sensitivity, specificity and 95% CI for DTS and chest radiography in each per-patient study. Individual sensitivities and specificities for nodule detection by DTS ranged from 62–100% and 81–100%, respectively, and for chest radiography, the individual sensitivities for nodule detection ranged from 17 to 85%, with specificities of 10–100%. The pooled sensitivity and specificity for nodule detection by DTS were 85% (95% CI 83–88%) and 95% (95% CI 93–96%), respectively, and the pooled sensitivity and specificity for nodule detection by chest radiography were 47% (44–51%) and 37% (34–40%), respectively. The results among studies that evaluated DTS were highly homogeneous, while those between studies that evaluated chest radiography were extremely heterogeneous. The SROC curves suggested that DTS has better diagnostic accuracy for pulmonary nodules than chest radiography.

The results of the subgroup analysis are shown in Figure 3. Two studies that included only patients with equivocal findings on chest X-ray were excluded from the subgroup analysis. DTS had a pooled sensitivity for nodule detection of 86% (95% CI

Table 1. Main characteristics of the included studies

Study	Year	Origin	Design	Number of patients (lesions)	Number of data sets	Radiography	Reference standard	Patient characteristics
Per patient								
Kim <i>et al</i> ¹⁰	2010	Korea	Prospective	100	2	PA	CT	Pulmonary mycobacterial disease
Sun <i>et al</i> ¹⁷	2010	China	Prospective	30	1	PA	CT	
Yamada <i>et al</i> ¹²	2011	Japan	Prospective	116	3	PA/lateral	CT	
Quaia <i>et al</i> ¹⁸	2014	Italy	Prospective	465	2	PA/lateral	CT or follow-up	Opacity and nodule on chest radiography
Galea <i>et al</i> ¹⁹	2015	UK	Prospective	78	1	PA/lateral	CT	Equivocal finding on chest radiography
Sharma <i>et al</i> ²⁰	2015	India	Prospective	70	2	PA	CT	Pulmonary mycobacterial disease
Dobbins III <i>et al</i> ²¹	2016	USA, Sweden	Prospective	158	1	PA/lateral	CT	
Per lesion								
Vikgren <i>et al</i> ⁹	2008	Sweden	Prospective	89 (131)	1	PA/lateral	CT	
Dobbins III <i>et al</i> ¹³	2008	USA	Prospective	21 (175)	1	PA	CT	
Quaia <i>et al</i> ²⁴	2010	Italy	Prospective	228 (251)	2	PA/lateral	CT	Opacity and nodule on chest radiography
Chen <i>et al</i> ²³	2011	China	Prospective	41 (260)	1	PA	CT	
Jung <i>et al</i> ¹¹	2012	Korea	Prospective	142 (237)	2	PA	CT	Colorectal cancer
Terzi <i>et al</i> ²²	2013	Italy	Prospective	132 (132)	1	PA	CT	Smokers
Kumar <i>et al</i> ²⁵	2015	India	Prospective	55 (110)	2	PA	CT	
Galea <i>et al</i> ²⁶	2015	UK	Prospective	78 (202)	1	PA	CT	Equivocal finding on chest radiography
Langer <i>et al</i> ²⁷	2016	USA	Prospective	82 (145)	1	PA/lateral	CT	Nodule size ≥ 4 mm
Dobbins III <i>et al</i> ²¹	2016	USA, Sweden	Prospective	158 (516)	1	PA/lateral	CT	

PA, posteroanterior.

83–89%) with 91% specificity (95% CI 88–94%). Chest radiography had a pooled sensitivity for nodule detection of 61% (56–65%) with 87% specificity (83–91%). The SROC curves again indicated that DTS had better diagnostic accuracy than chest radiography.

Nodule detection rates in per-lesion studies

Data acceptable for meta-analysis of per-lesion detection rates were available in 10 studies (Figure 4). Eight of these included patients with confirmed pulmonary nodule, and the nodule detection rate among these studies was 2.90 (95% CI 2.63–3.19,

Table 2. Summary of the quality assessment of diagnostic accuracy studies evaluation

Study	Year	Risk of bias				Applicability concerns		
		Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Kim et al ¹⁰	2010	High	Low	Low	Low	Low	Low	Low
Sun et al ¹⁷	2010	High	Unclear	Unclear	Unclear	Low	Low	Low
Yamada et al ¹²	2011	High	Low	Low	High	Low	Low	Low
Quaia et al ¹⁸	2014	High	Low	High	High	High	Low	Low
Galea et al ¹⁹	2015	High	Low	Unclear	Low	High	Low	Low
Sharma et al ²⁰	2015	High	Low	Low	Low	Low	Low	Low
Dobbins III et al ²¹	2016	High	Low	Low	High	Low	Low	Low
Vikgren et al ⁹	2008	High	Low	Low	High	Low	Low	Low
Dobbins III et al ¹³	2008	High	Low	Low	Unclear	Low	Low	Low
Quaia et al ²⁴	2010	High	Low	Low	High	High	Low	Low
Chen et al ²³	2011	High	Unclear	Unclear	Low	Low	Low	Low
Jung et al ¹¹	2012	High	Low	Unclear	Unclear	Low	Low	Low
Terzi et al ²²	2013	High	Low	High	High	Low	Low	Low
Kumar et al ²⁵	2015	High	Low	Unclear	Low	Low	Low	Low
Galea et al ²⁶	2015	High	Low	Unclear	Low	High	Low	Low
Langer et al ²⁷	2016	High	Low	Low	High	Low	Low	Low

heterogeneity test, $p = 0.32$; homogeneity $I^2 = 13\%$). The other two studies included patients who had equivocal results on chest radiography; in these, the nodule detection rate was 1.52 (95% CI 1.30–1.78, heterogeneity, $p = 0.85$; I^2 for homogeneity = 0).

DISCUSSION

We performed a systematic review and meta-analysis in order to obtain summary estimates and SROC curves supporting the diagnostic accuracy of DTS *vs* chest radiography for the detection of pulmonary nodules and showed that DTS was more accurate than chest radiography. In patient-based studies, DTS showed greater pooled sensitivity and specificity for pulmonary nodules, and nodule detection rates in lesion-based studies were higher.

Previous studies have touted DTS-based advances in diagnostic accuracy, reader confidence and interobserver agreement compared with plain chest radiography.^{9,12,28} DTS imaging excludes overlapping anatomy, such as vasculature and ribs, and allows a clear view of the lung parenchyma, increasing the conspicuity of pulmonary nodules and providing greater sensitivity.^{29,30} In addition to reductions in anatomical noise or composite artefacts, DTS provides greater depth and contrast resolution.⁷ Our findings for per-patient data showed that the

high diagnostic accuracy of DTS is complemented by greater homogeneity and consistency of results compared with chest radiography.

There were two patient-based studies in our analysis that included patients who had equivocal findings on chest radiography.^{18,19} The results of these studies were inconsistent compared with other studies in our analysis, and we speculated that the study design might have decreased the number of true negatives and affected the specificity results. Therefore, we performed a subgroup analysis excluding these two studies. In it, both DTS and chest radiography showed more consistent results. In particular, the pooled specificity of chest radiography was markedly increased. This subgroup analysis confirmed that DTS had higher sensitivity (86 *vs* 61%) than chest radiography, but showed that both had relatively similar specificity (91 and 87%) for nodule detection. This finding was consistent with those of previous studies that have shown chest radiography to be highly specific for early detection of lung nodules, especially malignant lesions,³ and it may support the continued use of chest radiography as a low-cost and easily accessible screening tool. In addition, Dobbins et al²¹ showed that both DTS and chest radiography had low sensitivity compared with other studies. This study included small nodules <6 mm up to about

Figure 2. Individual study estimates of patient-based sensitivity and specificity of digital tomosynthesis (DTS) (a) and chest radiography (b) for the detection of pulmonary nodules: per-patient summary receiver-operating characteristic (SROC) curves for DTS and chest radiography are showing that DTS exhibited greater diagnostic accuracy vs chest radiography. AUC, area under the curve; CI, confidence interval; SE, standard error.

80% of the reference standard, whereas other studies included those up to 43–64%.^{9,12,25}

Regarding the eight lesion-based studies, we compared detection rates rather than sensitivity and specificity because we were able to extract only the number of true positives and the total number of nodules from all but three of them.^{24–26} However, the inability to extract the number of true-positives, false-positives, true-negatives and false-negatives could be a significant drawback to our study, as this is essential when assessing the appropriateness of utilizing a technique for clinical use. In our meta-analysis, some studies which used CT as the reference standard did not suggest the true-negative number, because they demonstrated only the true-positive number of nodules detected with DTS and chest radiography among nodules detected with CT.^{13,22,23} In other studies, sensitivity was estimated on a per-lesion basis,^{9,11,21,27} but specificity was exclusively estimated on per-patient basis. Thus, we inevitably analyzed the detection rate from lesion-based data because we considered those information could be significant for evaluating the diagnostic value for the detection of pulmonary nodule despite definite limitations. The meta-analysis for lesion-based studies was performed using two groups. The first group included studies with an intervention group (patients with pulmonary nodules) and a control group (subjects with no nodule) and the second group consisted of studies that included patients with equivocal chest radiography. In the first group, the DTS/chest radiography nodule detection ratio

was 2.90 and in the second group, it was 1.52. The lower detection rate in the second group may be because it included patients with equivocal radiography results.

The results of quality assessment showed a high risk of bias in the patient selection domain, most likely because the majority of the studies were case-control studies that were designed as preliminary evaluations of the diagnostic performance of DTS and had small numbers of included patients. Such studies may have exaggerated the diagnostic accuracy of DTS. Moreover, we found that several of the studies in our analysis showed a high risk of bias in the reference standard because the reference tests were performed according to the result of the index tests rather than as a baseline study, which may have introduced a diagnostic review bias. The risk of bias in the flow and timing domains was also high in several (7/16) studies because they excluded up to 20% of patients, mainly because of poor imaging quality. Finally, as noted earlier, there was one study that did not have the same reference standard. This study included a large number of patients and therefore used clinical follow-up and CT as the reference standards, which could have resulted in overestimated sensitivity and specificity.

Because we focused on the diagnostic performance of DTS in our study, we did not suggest results about the radiation dose of each modality. However, we could obtain some information from some literature through our systematic review. Three studies

Figure 3. Estimates of patient-based sensitivity and specificity of digital tomosynthesis (DTS) (a) chest radiography (b) the detection of pulmonary nodules by subgroup analysis that excluded two studies that included only patients with equivocal findings on chest X-ray: per-patient summary receiver-operating characteristic (SROC) curves for DTS and chest radiography are indicating that DTS exhibited better diagnostic accuracy than chest radiography. AUC, area under the curve; CI, confidence interval; SE, standard error.

suggested that the estimated mean effective doses for chest radiography, DTS and CT were 0.06–0.10, 0.05–0.21 and 2–6.9 mSv, respectively.^{24,25,27} Also, several studies demonstrated the effective dose of each modality for standard patient in each study protocol,^{9–12,21} and we found that the radiation dose for DTS was approximately twice that for chest radiography and DTS required a much smaller radiation dose in comparison with CT.

Strengths and limitations

We believe this is the first meta-analysis that evaluates and summarizes the diagnostic performance of DTS vs chest radiography for the detection of pulmonary nodules. This meta-analysis had several strengths. We performed a robust literature search in collaboration with an information specialist that included a comprehensive search of major scientific databases and reference lists of reviews and articles. In addition, we selected studies according to strict inclusion criteria that were assessed by two independent reviewers, and we assessed the methodological quality of the studies included in the diagnostic meta-analysis.

The meta-analysis also had some limitations. First, the number of included studies was relatively small, although it was sufficient for performing the meta-analysis. Small numbers of involved studies and lack of raw data information could preclude accurate comparison between DTS and chest radiography. However, as

DTS is a newly emerging imaging modality, all included studies were published between 2008 and 2016. We aimed to include all available studies concerning the usefulness of DTS in the detection of pulmonary nodules.

Next, our meta-analysis was limited by the potential for publication bias. We could not evaluate publication bias because of the small number of available studies. Traditional assessments of publication bias have low power for diagnostic studies and can lead to seriously misleading results related to the lack of proper determinants of bias in these types of studies.³¹

Third, the studies included in our analysis had limited methodological quality. We chose demanding criteria for our quality assessment of diagnostic accuracy studies—2 evaluation. In particular, in eight studies, we could not determine whether the reference tests were interpreted independently of the index tests, which may have introduced diagnostic bias, specifically overestimation of the diagnostic accuracy. While preference for the use of gold standard diagnostic tests as screening tools may be unavoidable in clinical practice, it should not be the norm in studies of diagnostic accuracy. Adequate quality assessment requires accurate reporting in the primary studies, and the substantial number of items that were scored “unclear” in our analysis indicates a need for further improvement in this regard.

Figure 4. A forest plot is showing the lesion-based detection rates of digital tomosynthesis (DTS) and chest radiography for pulmonary nodules. CI, confidence interval; M-H, confidence interval.

Fourth, the presence of clinical heterogeneity associated with varying projection views among chest radiographs or the inclusion of patients with other clinical findings hinders generalization of the results. However, some degree of heterogeneity was unavoidable because there was heterogeneity in characteristics of the study populations and among imaging methodologies and methods of reference testing. When we performed a subgroup analysis according to different study populations, we were able to demonstrate increased homogeneity of per-patient-based results. The per-lesion studies also showed relatively consistent results when they were analyzed in two groups according to different study populations. However, this subgroup analysis after excluding these two studies has some drawbacks. Equivocal findings are used as real terms and are more true to regular chest radiography findings in routine daily practice and those studies included patients with equivocal

findings on chest radiography. Thus, these analyses may overestimate the specificity reported clinically.

In conclusion, our meta-analysis showed that DTS has consistently high diagnostic value for the detection of pulmonary nodules. On the other hand, chest radiography exhibited similar specificity but low sensitivity, comparable with that of DTS with considerable heterogeneity. Additional research, including randomized controlled trials in larger populations, are needed to confirm the diagnostic performance, cost efficiency and radiation dose of DTS in comparison with other modalities. Studies of diagnostic accuracy for lung cancer or lung metastases would also be useful.

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APPENDIX A

MEDLINE

- (1) tomosynthesis[tiab] 939
- (2) [Lung(tiab) OR pulmonary(tiab) OR Bronchial(tiab)] AND [Neoplasm(tiab) OR nodule(tiab) OR lesion(tiab) OR cancers(tiab) OR Neoplasms(tiab) OR nodules(tiab) OR lesions(tiab) OR cancer(tiab) OR Carcinoma(tiab) OR Carcinomas(tiab)] 241405
- (3) {[“Lung Neoplasms”(MeSh)] OR [“Lung/diagnosis”(MeSh) OR “Lung/radiography”(MeSh)]} OR “Lung/pathology”(Mesh) 259871
- (4) 2 OR 3 365201
- (5) 1 AND 4 84

EMBASE

- (1) tomosynthesis:ab,ti 1075
- (2) (Lung:ab,ti OR pulmonary:ab,ti OR Bronchial:ab,ti) AND (Neoplasm:ab,ti OR nodule:ab,ti OR lesion:ab,ti OR cancers:ab,ti OR Neoplasms:ab,ti OR nodules:ab,ti OR lesions:ab,ti OR cancer:ab,ti OR Carcinoma:ab,ti OR Carcinomas:ab,ti) 332652
- (3) 'lung tumor'/exp 320031
- (4) 2 OR 3 441079
- (5) 1 AND 4 112

COCHRANE

- (1) tomosynthesis:ab,ti,kw 29
- (2) (Lung OR pulmonary OR Bronchial) AND (Neoplasm OR nodule OR lesion OR cancers OR Neoplasms OR nodules OR lesions OR cancer OR Carcinoma OR Carcinomas):ab,ti, kw 13992
- (3) MeSH descriptor: (Lung Neoplasms) explode all trees 5604
- (4) MeSH descriptor: (Lung) explode all trees and with qualifier (s): (Pathology - PA, Radiography - RA) 501
- (5) 2 or 3 or 14336
- (6) 1 AND 5 2

APPENDIX B

STUDIES EXCLUDED FROM THE META-ANALYSIS

Total numbers of true positives, false positives, true negatives and false negatives per patient or detection rate per lesion were unclear (six studies):

- (1) Kim SM, Chung MJ, Lee KS, Kang H, Song IY, Lee EJ, et al. Digital tomosynthesis of the thorax: the influence of respiratory motion artifacts on lung nodule detection. *Acta Radiol* 2013; **54**: 634–9.
- (2) Lee XW, Leong S, Marshall H, Ayres J, Mohamed O, Bowman R, et al. Pulmonary nodule detection by junior medical staff is improved by digital tomosynthesis compared to chest x-ray. *J Thorac Oncol* 2013; **8**: S971–2.
- (3) Leong SC, Bowman RV, Yang IA, Marshall HM, Bennett JA, Fong KM. Thoracic digital tomosynthesis: a single centre experience. *J Thorac Oncol* 2012; **7**: S175–6.
- (4) Battezzati G, Gollini P, Rahnama S, Cortese G. Use of digital tomosynthesis in pulmonary mycobacterial disease: a preliminary experience. *J Thorac Imaging* 2012; **27**: W146.
- (5) Nechaev VA, Vasiliev AY. Capabilities of Tomosynthesis in Diagnosing Chest Diseases and Injuries. *Sovrem Tehnol V Med* 2016; **8**: 59–65.
- (6) Quaia E, Baratella E, Poillucci G, Gennari AG, Cova MA. Diagnostic impact of digital tomosynthesis in oncologic patients with suspected pulmonary lesions on chest radiography. *Eur Radiol* 2016; **26**: 2837–44.

Data or subsets of data were present in more than one article (three studies):

- (1) Quaia E, Baratella E, Cioffi V, Casagrande F, Maria AC. Analysis of the clinical impact of chest digital tomosynthesis in the management of patients with suspected pulmonary lesions on chest radiography. *J Thorac Imaging* 2011; **26**: W105.
- (2) Quaia E, Baratella E, Casagrande F, Cioffi V, Cova MA. Digital tomosynthesis as a diagnostic tool to exclude pseudolesions in patients with suspected thoracic lesions on chest X-ray radiography. *J Thorac Imaging* 2012; **27**: W128.
- (3) Quaia E, Baratella E, Cernic S, Lorusso A, Casagrande F, Cioffi V, et al. Analysis of the impact of digital tomosynthesis on the radiological investigation of patients with suspected pulmonary lesions on chest radiography. *Eur Radiol* 2012; **22**: 1912–22.

X-ray or DTS was performed without reference CT scan (three studies):

- (1) Zachrisson S, Vikgren J, Svalkvist A, Johnsson AA, Boijesen M, Flinck A, et al. Effect of clinical experience of chest tomosynthesis on detection of pulmonary nodules. *Acta Radiol* 2009; **50**: 884–91.
- (2) Bertolaccini L, Viti A, Tavella C, Priotto R, Ghirardo D, Grosso M, et al. Lung cancer detection with chest digital tomosynthesis: results from the SOS observational study. *J Thorac Oncol* 2014; **9**: S15.
- (3) Bertolaccini L, Viti A, Tavella C, Priotto R, Ghirardo D, Grosso M, et al. Lung cancer detection with digital chest tomosynthesis: first round results from the SOS observational study. *Ann Transl Med* 2015; **3**: 67.