

Transthoracic needle biopsy of the lung

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Background: Image guided transthoracic needle aspiration (TTNA) is a valuable tool used for the diagnosis of countless thoracic diseases. Computed tomography (CT) is the most common imaging modality used for guidance followed by ultrasound (US) for lesions abutting the pleural surface. Novel approaches using virtual CT guidance have recently been introduced. The objective of this review is to examine the current literature for TTNA biopsy of the lung focusing on diagnostic accuracy and safety.

Methods: MEDLINE was searched from inception to October 2015 for all case series examining image guided TTNA. Articles focusing on fluoroscopic guidance as well as influence of rapid on-site evaluation (ROSE) on yield were excluded. The diagnostic accuracy, defined as the number of true positives divided by the number of biopsies done, as well as the complication rate [pneumothorax (PTX), bleeding] was examined for CT guided TTNA, US guided TTNA as well as CT guided electromagnetic navigational-TTNA (E-TTNA). Of the 490 articles recovered 75 were included in our analysis.

Results: The overall pooled diagnostic accuracy for CT guided TTNA using 48 articles that met the inclusion and exclusion criteria was 92.1% (9,567/10,383). A similar yield was obtained examining ten articles using US guided TTNA of 88.7% (446/503). E-TTNA, being a new modality, only had one pilot study citing a diagnostic accuracy of 83% (19/23). Pooled PTX and hemorrhage rates were 20.5% and 2.8% respectively for CT guided TTNA. The PTX rate was lower in US guided TTNA at a pooled rate of 4.4%. E-TTNA showed a similar rate of PTX at 20% with no incidence of bleeding in a single pilot study available.

Conclusions: Image guided TTNA is a safe and accurate modality for the biopsy of lung pathology. This study found similar yield and safety profiles with the three imaging modalities examined.

Keywords: Image guided lung biopsy; transthoracic needle aspiration (TTNA); computed tomography guided TTNA (CT guided TTNA); ultrasound guided TTNA (US guided TTNA); CT guided electromagnetic navigational TTNA

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Introduction

Image guided transthoracic needle aspiration (TTNA) of lung lesions has been a valuable diagnostic tool since it was first described in 1965 (1). Integral to the evolution of the technique has been the type of image guidance used to

direct the biopsy tool to the area of abnormality. As imaging technology has advanced, so has the type of guidance used: plain radiograph and fluoroscopy giving way to computed tomography (CT), ultrasound (US) guided procedures (2,3) and CT guided electromagnetic navigational-TTNA (E-TTNA).

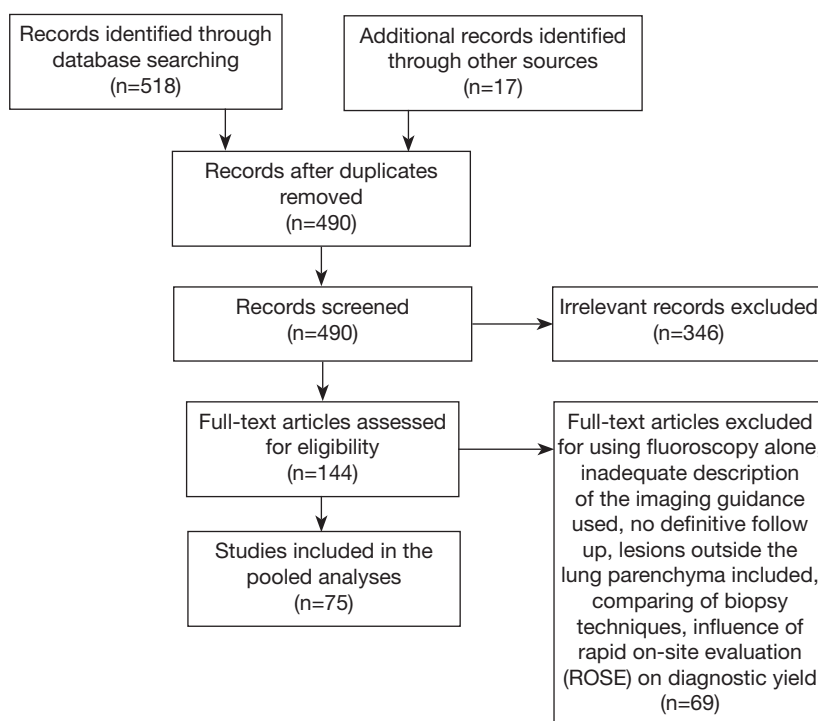


Figure 1 Flow diagram.

A large body of literature has subsequently explored the technique using CT and US. This literature has focused on the diagnostic accuracy of TTNA, modifications to the biopsy tools used, and the complications. The vast majority of the literature is large case series based with periodic pooled analyses, meta-analyses, and structured reviews of the test characteristics reported (4-7). These analyses have focused on the excellent diagnostic performance of TTNA for the diagnosis of peripheral lung cancer and have included an older and heterogeneous group of procedures guided by plain radiograph, fluoroscopy guided, CT guided, and US.

In this review, we summarize the recent available literature on CT guided and US guided TTNA for lung lesions. Furthermore, we report our case series using a novel electromagnetic navigational technology for TTNA (E-TTNA) and explore future directions in the field (8-10).

Methods

MEDLINE was searched from inception to October 2015 for all case series designed to describe the test characteristics and complications of TTNA of lung nodules using combinations of the medical subject headings (MeSH terms)

“computed tomography”, “ultrasound”, “transthoracic”, “needle aspiration”, “needle biopsy”, and “peripheral lung nodules”. Bibliographies and related articles of included studies were hand searched for additional reports. Research analyzing TTNA guided by fluoroscopy alone, an inadequate description of the imaging guidance used, inadequate confirmation of diagnosis, and analyses that included lesions from outside the lung parenchyma were excluded from our pooled analysis. Articles designed to compare biopsy techniques or examine the influence of rapid on-site evaluation (ROSE) on diagnostic yield were excluded. Non-English language articles were also excluded (*Figure 1*).

For the purposes of the pooled analysis, the overall diagnostic accuracy was defined as the number of true positives (true malignancy found on TTNA) and true negatives (confirmed benign lesions found on TTNA) divided by the number of biopsies done, provided that a definitive diagnosis was achieved based on clinical follow up and/or further invasive testing. Patients who underwent repeat biopsies had each biopsy counted separately. The pooled sensitivity and specificity of TTNA for malignancy was also calculated. If the subset of the test characteristics regarding malignancy were not available, overall diagnostic

sensitivity and specificity were reported as indicated in the tables. When reports had adequate diagnostic follow up for only a subset of their study population, the diagnostic accuracy, sensitivity for malignancy, and specificity for malignancy used in the pooled analyses were derived only from the subset with follow up. Primary data was extracted manually from each full text article. When articles calculated the test characteristics of TTNA only after excluding failed procedures (aborted or nondiagnostic) this was noted in the table. Similarly, the safety data was manually extracted and pooled from each full text manuscript.

Results

CT guided TTNA

Diagnostic accuracy

The vast majority of the literature focuses on the diagnostic yield of CT guided TTNA. Forty-eight articles using CT guidance met the inclusion and exclusion criteria based on the search strategy described above. The overall pooled diagnostic accuracy was 92.1% (9,567/10,383) and the sensitivity for detecting malignancy was 92.1% (7,343/7,975). The specificity for the diagnosis of malignancy approaches 100% with rare false positives (*Table 1*). Within each individual study, one factor consistently proposed as influencing the diagnostic accuracy of TTNA was lung lesion size. However, individual studies were mixed in validating lesion size as a predictor of diagnostic failure and were consistently under powered to detect a difference (14,17,20,22,28,30,31,33,36-39,41-44,52,58). When articles restricted to lung nodules ≤ 2 cm were analyzed with articles that reported diagnostic accuracy stratified by lesion size ≤ 2 cm, the pooled diagnostic accuracy was still excellent at 92.8% (2,521/2,718) and the pooled sensitivity for detecting malignancy was similarly high at 92.3% (1,497/1,622) (*Table 2*). When nodules were further stratified into ≤ 1 cm lesions the test characteristics did not decline significantly with a pooled diagnostic accuracy of 92.6% (638/689), and a pooled sensitivity for detecting malignancy at 88.7% (410/462).

Another consistent factor proposed as affecting diagnostic yield was the presence of a ground glass opacity (GGO) component to the lesion being biopsied. However, when articles reporting test characteristics of TTNA of GGO were segregated (*Table 3*), the pooled diagnostic accuracy was still very high at 92.5%, and the pooled sensitivity for detecting malignancy was similar at 91.4% (30-32,35,38,39,50).

Several other factors were inconsistently associated with a lower diagnostic yield in univariate and multivariate analyses including lower lobe biopsy site (28,42,52), acquisition of two or fewer specimens (28), malignant lesions (28,52), benign lesions (25), pneumothorax (PTX) during procedure (52), and use of aspiration needle only (39). Regardless of this mixed data (15,23), a high pretest probability of malignancy is a consistent predictor of high diagnostic accuracy as benign lesions were the most difficult to definitively diagnose on TTNA. Articles that studied patients with a lower pretest probability of malignancy reported the lowest diagnostic yield (46,47).

Safety

A sizable amount of case-series data was also available on the safety of CT guided TTNA with seventeen articles identified as specifically describing the complications. Additionally, thirty-six articles designed to describe the test characteristics of CT guided TTNA also provided information on complications encountered (*Table 4*). Generally, the information regarding the most common complications is dominated by the largest, multi-centered case series with over 15,000 subjects (59).

Overall, PTX is the most common safety issue. PTX occurred with a pooled incidence of 20.5% (6,821/33,306) (*Table 4*). The overall pooled incidence of chest tube placement for PTX was 7.3% (2,178/29,930) but varied widely (range, 0-31.1%), likely owing to different and evolving management strategies.

Several risk factors for PTX have been proposed in univariate and multivariate analyses including coaxial stabilizing needle size (13,72), age (13,34,57,72,75), smaller lesion size (23,55,60,64,66,69), depth of lesion (22,23,34,41,53,55,60,62-66,69,72-75), wider trajectory angle (41,63), a higher forced vital capacity (22,63), supine position during biopsy (61), longer puncture time (68), needle passing through a pulmonary fissure (69,75), traversing aerated lung (69,71), emphysema within biopsy path (42,43,72,75), presence of emphysema (73,74), number of pleural surfaces crossed (42,72,75), number of punctures (22,34), anterior biopsy approach (72), posterior biopsy approach (72), lateral biopsy approach (34), and a less experienced operator (66). Once a PTX has occurred, several risk factors for chest tube placement have been consistently identified such as age (52,72), supine position during biopsy (52), benign lung lesion on final diagnosis (52), a history of chronic obstructive pulmonary disease (57,59,60,62,72), emphysema within biopsy path (75),

Table 1 Test characteristics for CT guided transthoracic needle biopsy for pulmonary lesions

Study	Year	No.	Type of biopsy	Sensitivity (%)	Specificity (%)	Diagnostic accuracy (%)	Lesion sizes (cm)	Other
Larscheid (11)	1998	109*	22 or 23-G TTNA	91	100	89	<1 to >6	
Lopez Hänninen (12)	2001	79	TTCNB 20-G	96	100	95	0.5-6	
Geraghty (13)	2003	676*	TTNA 18 or 19-G	91	99	94	<1 to >2	
Yankelevitz (14)	1997	114	TTNA 20 or 22-G	94	100	75	≤3	
Charig (15)	2000	185	TTCNB 14, 18, or 20-G	93	100	94	1.3-11.2	
Hirose (16)	2000	50	TTCNB 18-G	89	100	90	0.8-6	
Arslan (17)	2002	294	TTNA 22-G	88	100	82	1 to >6	
Lucidarme (18)	1998	89*	TTCNB 18-G	93	100	90	0.9-8	
García Río (19)	1994	84	TTNA	76	100	82	1.8-4	
Wallace (20)	2002	57*	TTNA 20 to 22-G	82	100	88	≤1	
Laurent (21)	2000	66*	TTCNB 20-G	91	100	91	<2	
		132*	TTCNB 20-G	96	100	96	>2	
Ohno (22)	2003	162	TTNA 22-G	87	100	77	≤2	
Heyer (23)	2008	172	TTCNB 16-G	93	100	95	0.8-7.6	
Montaudon (24)	2004	605	TTCNB 20-G	92	99	94	Range	
Yeow (25)	2003	631	TTCNB 16 to 20-G	93	98	94	Range	
Priola (26)	2007	612	TTNA 21, 20-G, or TTCNB 18-G	90	99	83	<1 to 11	
Bladt (27)	2006	66*	TTCNB	81	100	84	<1 to >3	
Hiraki (28)	2009	1000	TTCNB 20-G	94	99	95	<1 to >3	
Inoue (29)	2012	66*	TTCNB 20-G	95	100	95	0.5-3.5	Pure GGO
Hur (30)	2009	28	TTNA 20 to 22-G	71	100	82	0.8-2.8	GGO
Yamauchi (31)	2011	67	TTCNB	97	100	97 [‡] (2)	0.6-4.7	GGO
Yamagami (32)	2013	85	TTCNB	88	100	91	0.4-3	GGO
Yamagami (33)	2004	22	mixed	93	100	95	0.7-2	Difficult lesions
Yang (34)	2015	311	TTCNB 18-G	95	97	93	≤3	
De Filippo (35)	2013	78*	TTNA 20-G	86	100	86	0.7-3	Some GGO
Ng (36)	2008	47*	TTNA 22-G	68	100	79	≤1	
Zhuang (37)	2013	102	TTNA 18 or 20-G	96	98	96	1-7	Cavitary lesions
Kim (38)	2008	43*	TTCNB 18 or 20-G	92	100	91 [‡] (7)	0.9-3.1	GGO
Choi (39)	2013	268*	Mixed, all 20-G	93	99	95 [‡] (27)	<1	Some GGO
Hayashi (40)	1998	52	TTCNB 18 or 20-G	100	100	96	<3	
Li (41)	2013	169	TTCNB 20-G	90	100	94	≤2	
Lee (42)	2014	1153	TTCNB 18-G	96	100	97	0.5-13	
Choi (43)	2012	173	TTCNB 18-G	97	100	98 [‡] (10)	≤2	
Choo (44)	2013	107	TTCNB 18-G	97	100	98 [‡] (9)	≤1	Virtual CT scan
Lima (45)	2011	89*	TTNA 25-G	94	82	84	Not reported	
Mesurolle (46)	2003	85	TTNA 18, 19, or 21-G	82	100	81	0.9-9	Head & neck CA
Yankelevitz (47)	1998	48	TTNA 20 or 22-G	94	100	67	<3	Negative bronch
Yu (48)	2002	52	TTCNB 18 or 20-G	97	100	97 [‡] (1)	1.8-15	

Table 1 (continued)

Table 1 (continued)

Study	Year	No.	Type of biopsy	Sensitivity (%)	Specificity (%)	Diagnostic accuracy (%)	Lesion sizes (cm)	Other
Floridi (49)	2014	95	TTCNB 20-G	91	100	93 [‡] (5)	0.7-14	
Lu (50)	2012	52*	TTCNB 20-G	94	100	94	≤3	GGO
Laspas (51)	2008	409	TTNA 21 or 23-G	92	98	93 [‡] (40)	0.6-10	
Takeshita (52)	2015	750	Mixed	91	99	93 [‡] (10)	0.9-3.9	
Uskül (53)	2009	134	TTNA 22-G	83	100	84	1.3-11	
Niu (54)	2015	84	TTCNB 20-G	86	100	89	0.5-12	Pleural lesions
Loh (55)	2013	367*	Mixed	96	100	97	0.6-12.3	
Lee (56)	2012	94	Mixed	93	100	91	0.8-12	
Yaffe (57)	2015	173*	TTCNB 18-G	94	92	94	0.9-3.9	
Jiao de (58)	2014	110	TTCNB 16-G	97	100	97 [‡] (2)	0.6-15	
Pooled analysis				92.1		92.1		

* , subset of a larger population with adequate follow up; ‡ , excludes nondiagnostic biopsies (number of biopsies excluded). CT, computed tomography; TTNA, transthoracic needle aspiration; TTCNB, transthoracic core needle biopsy; GGO, ground-glass opacities.

presence of emphysema (52,74), smoking history (59), lesion depth (52,63,72), lateral biopsy approach (72), posterior biopsy approach (72), number of pleural surfaces crossed (72), needle passing through a pulmonary fissure (75), and wider trajectory angle (63). However, many of these biologically plausible risk factors are only inconsistently associated with PTX and chest tube placement, likely owing to the heterogeneity of methods and lack of consistent controlling for confounding (15,37,42,56,61,62,67,68,73,74).

Clinically significant hemorrhage is the next most common complication with a pooled incidence of 2.8% (609/22,313) when defined as hemoptysis, hemothorax, hypotension, chest wall hematoma, or symptoms prompting imaging. These clinically significant hemorrhages were considerably less common than evidence of hemorrhage on screening post biopsy CT scan (41,56,68), and PTX (Table 4). Proposed risk factors for any hemorrhage included depth of lesion (41,55,68), number of times the pleura was punctured (68), GGO being biopsied (42,43), and size of the lesion (55,68). Other very rare complications such as cardiac or respiratory arrest, shock, seeding of malignant cells in the biopsy tract, and hemothorax have been reported (76-78). The dreaded complication of air-embolism occurs very rarely with an estimated incidence of 0.02% to 0.07% (52,79).

US guided TTNA

Diagnostic accuracy

There is considerably less data available describing US

guided TTNA for lung lesions. A total of ten studies met the inclusion and exclusion criteria for the pooled analysis (Table 5). Lesions amenable to US guided TTNA were abutting the pleura such that aerated lung did not reflect the US beams before the lesion was visible. The overall pooled diagnostic accuracy was similarly high at 88.7% (446/503), and the sensitivity for detecting malignancy was 91.5% (366/400). The specificity for the diagnosis of malignancy also approached 100% (Table 5).

Small lesions were biopsied with only mixed evidence that lesion size affected diagnostic yield (81,89). Pleural adhesion with a lack of lung sliding was also proposed as increasing diagnostic yield (89). As discussed above, a higher pretest probability of malignancy consistently increased the diagnostic yield as benign lesions were more difficult to definitively diagnose (83-89).

Safety

US guided TTNA was generally very well tolerated with a pooled incidence of PTX of 4.4% (22/503). This compared favorably to CT guided TTNA, however, US guided lesions are inherently more peripheral. Therefore, PTX is less likely regardless of biopsy method used. To our knowledge, the only comparison of US guided and CT guided TTNA reported retrospectively by Sconfienza *et al.* (90) did find a lower PTX rate with US guidance when biopsying consecutive peripheral lung lesions (14.7% *vs.* 5.8%). Pleural adhesions with a lack of lung sliding were proposed as protective against PTX (89).

Table 2 Test characteristics for CT guided transthoracic needle biopsy for pulmonary lesions ≤ 2 cm

Study	Year	No.	Type of biopsy	Sensitivity (%)	Specificity (%)	Diagnostic accuracy (%)	Lesion sizes (cm)	Other
Studies including data for nodules ≤ 2 cm								
Yankelevitz (14)	1997	69*	TTNA 20 or 22-G	90	100%	NA	≤ 2	
Arslan (17)	2002	20*	TTNA 22-G	NA	NA	95	1 to ≤ 2	
Wallace (20)	2002	57*	TTNA 20 to 22-G	82	100	88	≤ 1	
Laurent (21)	2000	66*	TTCNB 20-G	91	100	91	< 2	
Ohno (22)	2003	162	TTNA 22-G	87	100	77	≤ 2	
Hiraki (28)	2009	582*	TTCNB 20-G	94	100	95	≤ 2	
Hur (30)	2009	20*	TTNA 20 to 22-G	69	100	80	≤ 2	GGO
Yamauchi (31)	2011	50*	TTCNB	95	100	96	≤ 2	GGO
Yamagami (33)	2004	22	mixed	93	100	95	0.7-2	Difficult lesions
Ng (36)	2008	47*	TTNA 22-G	68	100	79	≤ 1	
Zhuang (37)	2013	78*	TTNA 18 or 20-G	97	93	96	< 2	Cavitary lesions
Kim (38)	2008	23*	TTCNB 18 or 20-G	94	100	91	< 2	GGO
Choi (39)	2013	268*	Mixed, all 20-G	93	99	95 [‡] (27)	< 1	Some GGO
Li (41)	2013	169	TTCNB 20-G	90	100	94	≤ 2	
Lee (42)	2014	485*	TTCNB 18-G	94	100	96	≤ 2	
Choi (43)	2012	173	TTCNB 18-G	97	100	98 [‡] (10)	≤ 2	
Choo (44)	2013	107	TTCNB 18-G	97	100	98 [‡] (9)	≤ 1	Virtual CT scan
Takeshita (52)	2015	391*	Mixed	NA	NA	88	≤ 2	
Jiao de (58)	2014	17*	TTCNB 16-G	NA	100	94	≤ 2	
Pooled analysis				92.3		92.8		
Studies reporting data for nodules ≤ 1 cm								
Wallace (20)	2002	57*	TTNA 20 to 22-G	82	100	88	≤ 1	
Laurent (21)	2000	7*	TTCNB 20-G	67	100	86	≤ 1	
Hiraki (28)	2009	151*	TTCNB 20-G	90	100	93	≤ 1	
Hur (30)	2009	10*	TTNA 20 to 22-G	67	100	80	≤ 1	GGO
Yamauchi (31)	2011	8*	TTCNB	86	100	88	≤ 1	GGO
Ng (36)	2008	47*	TTNA 22-G	68	100	79	≤ 1	
Choi (39)	2013	268*	Mixed, all 20-G	93	99	95 [‡] (27)	< 1	Some GGO
Lee (42)	2014	70*	TTCNB 18-G	88	100	93	≤ 1	
Choo (44)	2013	107	TTCNB 18-G	97	100	98 [‡] (9)	≤ 1	Virtual CT scan
Pooled analysis				88.7		92.6		

*, subset of a larger population with smaller lesions; ‡, excludes nondiagnostic biopsies (number of biopsies excluded). CT, computed tomography; TTNA, transthoracic needle aspiration; TTCNB, transthoracic core needle biopsy; GGO, ground-glass opacities; NA, not available.

Table 3 Test characteristics for CT guided transthoracic needle biopsy for GGO lesions

Study	Year	No.	Type of biopsy	Sensitivity (%)	Specificity (%)	Diagnostic accuracy (%)	Lesion sizes (cm)	Other
Inoue (29)	2012	66*	TTCNB 20-G	95	100	95	0.5-3.5	Pure GGO
Hur (30)	2009	28	TTNA 20 to 22-G	71	100	82	0.8-2.8	GGO
Yamauchi (31)	2011	67	TTCNB	97	100	97	0.6-4.7	GGO
Yamagami (32)	2013	85	TTCNB	88	100	91	0.4-3	GGO
De Filippo (35)	2013	78*	TTNA 20-G	86	100	86	0.7-3	Some GGO
Kim (38)	2008	43*	TTCNB 18 or 20-G	92	100	91	0.9-3.1	GGO
Choi (39)	2013	268*	Mixed, all 20-G	93	99	95	<1	Some GGO
Lu (50)	2012	52*	TTCNB 20-G	94	100	94	≤3	GGO
Pooled analysis				91.4		92.5		

*, subset of a larger population with adequate follow up. CT, computed tomography; TTNA, transthoracic needle aspiration; TTCNB, transthoracic core needle biopsy; GGO, ground-glass opacities.

Electromagnetic navigational-transthoracic needle aspiration (E-TTNA)

Although CT and US guided TTNA have been proven safe and effective they do not provide mediastinal staging which is essential in providing prognostic information as well as selecting appropriate surgical and oncologic treatment. A novel thoracic navigational system recently developed by Veran Medical Technologies (St Louis, MO, USA) allows operators to perform a virtual CT guided electromagnetic navigational TTNA using a CT scan of the chest obtained prior to the procedure which is virtually paired with the patient using a tracking pad placed on the chest. This allows the operator to perform mediastinal lymph node staging with convex endobronchial ultrasound (EBUS), navigational bronchoscopy if needed and a navigational E-TTNA all in one setting.

Diagnostic accuracy

A single center safety and feasibility trial of 24 patients using the above system was recently completed showing a diagnostic yield of 83% for E-TTNA (91), which is comparable to the above cited yield using real time imaging. Of note, when EBUS TBNA of mediastinal lymph nodes as well as navigational bronchoscopy using the same system was completed in the same study the diagnostic yield was raised to 92%.

Safety

Using the pilot study cited above, safety of E-TTNA appears to be equivalent to conventional CT guided TTNA.

There were five pneumothoraces (20%) after the combined procedure with only two patients requiring pigtail chest tube catheters and admission. There was no other incidence of bleeding, hemoptysis, prolonged intubation or other complications reported.

Although this data is promising, the above pilot data only involves a single center with 24 patients. Further multi-centered, randomized trials with larger enrollment need to be completed before drawing conclusions about the diagnostic accuracy and safety of E-TTNA alone and in comparison to conventional image guided TTNA.

Conclusions

Image guided TTNA remains an important modality in the diagnosis of thoracic diseases, particularly malignancies. This review has shown a high overall diagnostic yield, sensitivity and specificity for pulmonary nodules using CT and US guided imaging after analysis of 75 published articles. E-TTNA was also examined using data from a recent single center pilot study that showed similar diagnostic yield to the two previously mentioned imaging modalities. However, as this is a small, single center study, this data must be taken in context, with further large multi-center trials needed before this modality can be accepted as an alternative to CT or US guided TTNA.

Regarding safety, both CT and US guidance were extremely safe with the two most common complications reported being PTX, a large proportion of which can be managed conservatively with observation rather than tube

Table 4 Safety profile of CT guided transthoracic needle biopsy

Study	Year	Number	PTX rate (95% CI if available) (%)	PTX with chest tube (95% CI if available) (%)	Hemorrhage (95% CI if available)* (%)
Wiener (59)	2011	15,865	15.0 (14.0-16.0)	6.6 (6.0-7.2)	1.0 (0.9-1.2)
Geraghty (13)	2003	846	26.7	8.7	NA
Kazerooni (60)	1996	121	44.6	14.9	NA
Nakamura (61)	2011	156	59.6	7.7	NA
Laurent (62)	1999	307	19.9	2.0	NA
Saji (63)	2002	289	26.6	14.2	NA
Yamagami (64)	2002	134	34.4	2.2	NA
Yeow (65)	2001	117	12	0	3
Yeow (66)	2004	660	23.4	1.4	3.9
Yildirim (67)	2009	225	26.2	7.6	12.9
Khan (68)	2008	135	17	2.2	6.7
Nour-Eldin (69)	2015	650	25	4.3	NA
Dennie (70)	2001	506	22.9	6.5	NA
Haramati (71)	1991	131	27.4	4.6	3.8
Kuban (72)	2015	4,262	30.3	15	NA
Chami (73)	2015	163	36.2	5.5	NA
Schulze (74)	2015	664	21.7	6	NA
Kim (75)	2015	1,227	21.4	2.9	NA
Larscheid (11)	1998	130	43	18.5	NA
Lopez Hänninen (12)	2001	79	24	5.1	0
Yankelevitz (14)	1997	114	20.2	5.3	0
Charig (15)	2000	183	26.2	2.2	7.1
Hirose (16)	2000	50	42	12	NA
Arslan (17)	2002	294	8.2	1	3.1
Lucidarme (18)	1998	91	34	3.3	9.9
García Río (19)	1994	84	14.3	4.8	1.2
Wallace (20)	2002	61	62.2	31.1	NA
Ohno (22)	2003	162	28.4	2.5	NA
Heyer (23)	2008	172	26.2	NA	NA
Yeow (25)	2003	631	23.5	NA	NA
Bladt (27)	2006	72	9.7	NA	1.7
Hur (30)	2009	28	17.9	7.1	10.7
Yamauchi (31)	2011	90	15.6	NA	14.4
Yamagami (33)	2004	22	31.8	4.5	4.5
Yang (34)	2015	311	17.7	0.9	11.6
Ng (36)	2008	55	52.7	9.1	NA
Zhuang (37)	2013	102	8.8	NA	14.7
Kim (38)	2008	55	18.2	1.8	12.7
Li (41)	2013	169	14.8	1.8	6.5
Lee (42)	2014	1,153	17	NA	6.9

Table 4 (continued)

Table 4 (continued)

Study	Year	Number	PTX rate (95% CI if available) (%)	PTX with chest tube (95% CI if available) (%)	Hemorrhage (95% CI if available)* (%)
Choi (43)	2012	173	31.8	1.7	14.5
Choo (44)	2013	107	6.5	NA	5.6
Lima (45)	2011	97	27.8	12.4	2
Yu (48)	2002	52	11.5	0	5.8
Floridi (49)	2014	95	21.1	0	NA
Lu (50)	2012	55	47.3	NA	20
Lasparas (51)	2008	409	4.2	0.2	0.2
Takeshita (52)	2015	750	36.8	NA	12.1
Usköl (53)	2009	134	16.4	NA	NA
Niu (54)	2015	84	16.7	2.4	NA
Loh (55)	2013	399	34.8	3	3.8
Lee (56)	2012	94	25.5	1	NA
Yaffe (57)	2015	181	26.5	1.1	9.4
Jiao de (58)	2014	110	12	NA	6.5
Pooled analysis			20.5	7.3	2.8

*, includes the subset of clinically apparent bleeding only: hemoptysis, hemothorax, hemorrhagic shock, chest wall hematoma, or symptoms prompting imaging. CT, computed tomography; PTX, pneumothorax; CI, confidence interval; NA, not available.

Table 5 Test characteristics for US guided transthoracic needle aspirations for pulmonary lesions

Study	Year	No.	Sensitivity (%)	Specificity (%)	Diagnostic accuracy (%)	Pleural based lesion	Other	PTX (%)
Knudsen (80)	1996	134	100 [†] (15)	94 [†] (15)	98 [†] (15)	Y		3.7
Targhetta (81)	1993	64	91	100	86	Y		3.1
Yuan (82)	1992	30	92	100	90	Y	Lesions <3 cm	3.3
Yang (83)	1985	25	100	100	84	Y		8
Chen (84)	1995	40	97	100	88	Y		5
Chen (85)	1996	34*	96	100	88	Y	≤3 cm	2.5
Dallari (86)	1999	45	92	100	80	Y		0
Khosla (87)	2009	21	90	100	95	Y		0
Hsu (88)	1993	16	94	100	94	Y	Apical lesions	0
Meena (89)	2015	109	80	90	83	Y	6.4% hemoptysis	8.3
Pooled analysis			91.5		88.7			4.4

*, subset of a larger population with adequate follow up; †, excludes nondiagnostic biopsies (number of biopsies excluded). US, ultrasound; TTNA, transthoracic needle aspiration; TTCNB, transthoracic core needle biopsy; Y, yes; N, no; PTX, pneumothorax.

thoracostomy, as well as hemorrhage. Serious complications including hemothorax, air embolism, or cardiopulmonary arrest have been reported, but are extremely rare. There is a higher reported PTX rate using CT guided imaging as compared to US guidance. This is likely secondary to the

fact that US guided biopsies are only performed on nodules and masses that are directly abutting the pleura. E-TTNA also appears to have an equivalent safety profile compared to CT guided TTNA, but again this data must be taken in context as discussed above.

One disadvantage with percutaneous biopsy of potential lung malignancies is the inability to simultaneously stage the mediastinum as is possible with bronchoscopic lung biopsy with simultaneous convex EBUS trans-bronchial needle aspiration of mediastinal lymph nodes. However, as diagnostic yield for bronchoscopic biopsies of peripheral lung nodules remains significantly lower than with CT guided TTNA even under navigational guidance (92), a combined modality of performing EBUS staging, attempted bronchoscopic biopsy and if unsuccessful E-TTNA biopsy of the suspected nodule may provide an efficient and convenient pathway to lung cancer diagnosis and staging for patients in the near future.

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Footnote

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