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Articles selected and commented on by: Fumihiko Asano, *Department of Pulmonary Medicine, Gifu Prefectural General Medical Center. Japan*



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Radial endobronchial ultrasound for the diagnosis of peripheral pulmonary lesions: A systematic review and meta-analysis.

Authors: Ali, M. S., et al.

Reference: *Respirology*. 2017 Apr;22(3):443-453.

URL: <http://onlinelibrary.wiley.com/doi/10.1111/resp.12980/full>

Comments: The bronchoscopic diagnostic yield of peripheral pulmonary lesions (PPLs) is insufficient, because the lesions are located beyond the segmental bronchus and are undetectable by bronchoscopy. This has led to the development of new bronchoscopic modalities such as radial endobronchial ultrasound (R-EBUS), electromagnetic navigation bronchoscopy (ENB) and virtual bronchoscopy (VB). This article was a systematic review and meta-analysis of radial endobronchial ultrasound for diagnosing peripheral pulmonary lesions. 57 studies with a total of 7872 lesions were included in the meta-analysis. Overall weighted diagnostic yield for R-EBUS was 70.6% (95% CI: 68-73.1%). The diagnostic yield was significantly higher for lesions >2 cm in size, malignant in nature and those associated with a bronchus sign on computerized tomography (CT) scan. Diagnostic yield was also higher when R-EBUS probe was within the lesion as opposed to being adjacent to it. Overall complication rate was 2.8%. The diagnostic yield of R-EBUS is high, and its complication rate is low. I consider that R-EBUS should be actively used for the bronchoscopic diagnosis of peripheral lesions, particularly small lesions.

Usefulness of endobronchial ultrasonography with a guide sheath and virtual bronchoscopic navigation for ground-glass opacity lesions.

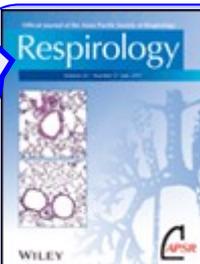
Authors: Ikezawa, Y., et al.

Reference: *Ann Thorac Surg*. 2017 Feb;103(2):470-475.

URL: <https://doi.org/10.1016/j.athoracsur.2016.09.001>

Comments: Virtual bronchoscopic navigation is a method to guide a bronchoscope to peripheral lesions under direct vision using virtual bronchoscopic images of the bronchial route. This article was a retrospective analysis of endobronchial ultrasonography with a guide sheath and virtual bronchoscopic navigation for diagnosing ground-glass opacity lesions. Endobronchial ultrasonography images could be obtained for 156 (92%) of 169 GGO predominant-type lesions, and 116 (69%) were successfully diagnosed by this method (20 of 31 pure GGO lesions [65%]; 96 of 138 mixed GGO predominant-type lesions [70%]). Regarding diagnostic yield based on computed tomography sign, cases with presence of a bronchus leading directly to a lesion had significantly higher diagnostic yield the other lesions ($p < 0.01$). In general, the diagnostic yield of bronchoscopy is low for GGO-lesions. However, even for GGO lesions, VBN combined with EBUS-GS is worth performing when these lesions involve the bronchi.

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Combination of virtual bronchoscopic navigation with conventional transbronchial needle aspiration in the diagnosis of peribronchial pulmonary lesions located in the middle third of the lungs.

Authors: Yasuo, M., et al.

Reference: Respir Investig. 2016 Sep;54(5):355-63.

URL: <https://doi.org/10.1016/j.resinv.2016.04.003>

Comments: This article reported the retrospective analysis of VBN combined with conventional TBNA for small peribronchial pulmonary lesions in Middle third zone. Diagnostic bronchoscopy was performed for 201 lesions < 20 mm, of which 16 were peribronchial lesions located in the middle third. In 15 of the 16 lesions, VBN with conventional TBNA was performed. The lesions were traced using the VBN system, and then the VBN was operated and guided by the vision of actual bronchoscopy. The TBNA site was determined by VBN, and the specimens were obtained using conventional TBNA under X-ray fluoroscopy. The diagnosis was made based on the cytological findings of the specimens. Adequate specimens were obtained in 12 (80.0%) of the cases through the novel technique of combining TBNA with VBN in bronchoscopic examinations. Seven out of the ten malignant cases (70.0%) were diagnosed by this procedure. No adverse effects were experienced, except for an acceptable amount of bleeding. Using VBN, both bronchoscopic guidance and marking of the puncture site are possible. VBN with TBNA is a promising method for small peribronchial lesions located in the middle third. In the future, prospective studies will be necessary.

Electromagnetic navigation bronchoscopy to access lung lesions in 1,000 subjects: first results of the prospective, multicenter NAVIGATE study.

Authors: Khandhar, S. J., et al.

Reference: BMC Pulm Med. 2017 Apr 11;17(1):59.

URL: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5387322/>

Comments: As navigational bronchoscopy, there are VBN and EMN. EMN is based on not only CT but also electromagnetic information, and the sensor is guided to the lesion. This article reported a prespecified 1-month interim analysis of the first 1,000 primary cohort subjects in a prospective, multicenter study of the superDimension™ navigation system. ENB index procedures were conducted for lung lesion biopsy (n = 964), fiducial marker placement (n = 210), pleural dye marking (n = 17), and/or lymph node biopsy (n = 334; primarily endobronchial ultrasound-guided). Lesions were in the peripheral/middle lung thirds in 92.7%, 49.7% were <20 mm, and 48.4% had a bronchus sign. Radial EBUS was used in 54.3% and general anesthesia in 79.7%. Among the 964 subjects (1,129 lesions) undergoing lung lesion biopsy, navigation was completed and tissue was obtained in 94.4% (910/964). The ENB-related pneumothorax rate was 4.9% overall and 3.2% CTCAE Grade ≥2 (primary endpoint). The ENB-related Grade ≥2 bronchopulmonary hemorrhage and Grade ≥4 respiratory failure rates were 1.0 and 0.6%, respectively.

This study demonstrated low adverse event rates in a generalizable population across diverse practice settings.

With additional cases and follow-up observation, high diagnostic yields of EMN are expected in not only expert institutions but also general hospitals. In addition, since the cost of EMN is higher than that of VBN, it may be important to identify the group for whom EMN is useful.

Electromagnetic navigation bronchoscopy for Identifying lung nodules for thoracoscopically resection.

Authors: Marino, K. A. et al.

Reference: Ann Thora Surg. 2016 Aug;102(2):454-7.

URL: <https://doi.org/10.1016/j.athoracsur.2016.03.010>

Comments: This article was a retrospective analysis of identifying lung nodules for thoracoscopic resection using electromagnetic navigation. Seventy patients underwent electromagnetic navigation bronchoscopy marking with methylene blue followed by minimally invasive resection. The median nodule size was 8 mm (range, 4-17 mm). The median distance from the pleural surface was 6 mm (range, 1-19 mm). There were no conversions to thoracotomy. Nodule marking was successful in 70 of 72 attempts (97.2%). There were no adverse events related to electromagnetic navigation bronchoscopy-guided marking or wedge resection.

Localizing and marking small pulmonary nodules using electromagnetic navigation bronchoscopy is safe and effective for nodule identification before minimally invasive resection. EMN is useful for the bronchoscopic diagnosis of small peripheral lesions but not treatment.

Sequential multimodality bronchoscopic investigation of peripheral pulmonary lesions.

Authors: Steinfert, D. P., et al.

Reference: Eur Respir J. 2016 Feb;47(2):607-14.

URL: <http://erj.ersjournals.com/content/47/2/607>

Comments: To increase the diagnostic rate, the method of how new bronchoscopic modalities are combined with routine bronchoscopy is important. This article was a prospective, nonrandomized observational single-centre cohort study examining consecutive patients undergoing investigation of peripheral pulmonary lesions (PPLs). Authors routinely performed Endobronchial ultrasound (EBUS) with virtual bronchoscopy (VB), and only utilised electromagnetic navigation (EMN) where EBUS was unable to locate PPLs or where the probe was adjacent to the lesion and on-site cytologic examination was nondiagnostic. 236 consecutive patients with 245 PPLs had lesion size 22.8+/-12.4 mm (mean+/-sd). PPLs were localised using EBUS+VB alone in 188 (77%) and was diagnostic in 134 of these (71.3%). EMN in 57 patients achieved EBUS localisation in a further 17 patients (30.9%), improving overall visualisation yield to 85%. Nine of these 57 procedures achieved a definitive diagnosis (16%), improving overall diagnostic yield to 58.4%. Sensitivity for diagnosis of lung cancer was 70% (131/188; 95% CI 63-76%). There have been no studies comparing VBN and EMN. However, the localization rate and diagnostic sensitivity of radial probe EBUS + VB alone for the diagnosis of PPLs is high. This article indicates that the EBUS localization rate and procedural yield are improved only modestly (by 8 and 4%, respectively) with the addition of EMN. Considering that the cost of EMN is higher than that of VBN, it may be practical at present for EMN to be performed in patients for whom diagnosis is difficult using EBUS with VBN.

Complications of convex-probe endobronchial ultrasound-guided transbronchial needle aspiration: a multi-center retrospective study.

Authors: Caglayan, B, et al.

Reference: Respir Care. 2016 Feb;61(2):243-8.

URL: <https://doi.org/10.4187/respcare.03838>

Comments: EBUS-TBNA is widely used as a gold standard for the stage diagnosis of lung cancer. This article was a multi-center retrospective questionnaire survey to assess serious complications related to convex-probe EBUS-TBNA and to determine the complication rate in a large group of subjects. Only complications requiring further treatment/intervention were considered serious. In a total of 3,123 cases within a 5-y period, EBUS-TBNA was performed for staging lung cancer in 15.8%, diagnosis in 67.5%, and diagnosis and staging in 16.3%. EBUS-TBNA was performed 11,753 times (3.76/case) at 6,115 lymph node stations and lesions (1.92/station or lesion). Five serious complications were recorded (0.16%): fever lasting >24 h, infection of bronchogenic cyst, mediastinal abscess, pericarditis, and pneumomediastinitis with empyema, each in one case. EBUS-TBNA is a generally safe examination method, but attention should be paid to the possible development of severe complications.

Endobronchial ultrasound-guided cautery-assisted transbronchial forceps biopsies: safety and sensitivity relative to transbronchial needle aspiration.

Authors: Bramley, K., et al.

Reference: Ann Thorac Surg. 2016 May;101(5):1870-6.

URL: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4861078/>

Comments: For the bio-diagnosis prior to lung cancer treatment, larger adequate tissue samples are also necessary for TBNA. This article evaluated safety and sensitivity of the sequential use of TBNA and a novel technique called cautery-assisted transbronchial forceps biopsy (ca-TBFB). The study prospectively enrolled 50 unselected patients undergoing convex-probe EBUS. All lymph nodes exceeding 1 cm were sequentially biopsied under EBUS guidance using TBNA and ca-TBFB. There were no significant adverse events. In nodes determined to be malignant, TBNA provided higher sensitivity (100%) than ca-TBFB (78%). However, among nodes with granulomatous inflammation, ca-TBFB exhibited higher sensitivity (90%) than TBNA (33%). The larger samples obtained from ca-TBFB increased its sensitivity to detect granulomatous disease and provided adequate specimens for clinical trials of malignancy when specimens from needle biopsies were insufficient. The sequential use of TBNA and ca-TBFB is considered to be safe and it allows larger sample collection. This method is worth attempting in selected cases.

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Diagnostic yield and safety of cryoprobe transbronchial lung biopsy in diffuse parenchymal lung diseases: systematic review and meta-analysis.

Authors: Dhooria, S, et al.

Reference: Respir Care. 2016 May;61(5):700-12.

URL: <https://doi.org/10.4187/respcare.04488>

Comments: Transbronchial lung biopsy is insufficient for diagnosing diffuse parenchymal lung diseases because obtained samples are small. This article was a systematic review and meta-analysis describing the efficacy and safety of cryo-transbronchial lung biopsy in diagnosis of diseases diffusely involving the lung parenchyma. The pooled diagnostic yield of cryo-transbronchial lung biopsy of 14 studies (1,183 subjects) was 76.9% if only definitive diagnoses were considered. Four studies (321 subjects) the performance of flexible forceps biopsy and cryo-transbronchial lung biopsy. The diagnostic yield of cryo-transbronchial lung biopsy (86.3%) was significantly higher than that of flexible forceps biopsy (56.5%) with an odds ratio of 6.7 and a number needed to treat of 4. The size of samples obtained with cryo-transbronchial lung biopsy was significantly bigger compared with flexible forceps biopsy (20.4 vs 4.3 mm, $P = .005$). The complications of cryo-transbronchial lung biopsy included pneumothorax (6.8%), severe bleeding (0.3%), and death (0.1%). Cryo-transbronchial lung biopsy is a relatively safe procedure with good diagnostic yield in diffuse parenchymal lung diseases. This method is effective because it is less invasive than thoracoscopic biopsy, but requires adequate training in manipulation and measures against complications.

Effect of endobronchial coils vs usual care on exercise tolerance in patients with severe emphysema: The RENEW randomized clinical trial.

Authors: Sciruba, F. C., et al.

Reference: JAMA. 2016 May 24-31;315(20):2178-89.

URL: <http://jamanetwork.com/journals/jama/fullarticle/2522517>

Comments: Bronchoscopic lung volume reduction is less invasive compared with Lung volume reduction surgery. This article reported a multi-center randomized clinical trial conducted among 315 patients with emphysema and severe hyperinflation to assess 1-year effectiveness and safety of endobronchial coil treatment. Participants were randomly assigned to continue usual care alone ($n = 157$) vs usual care plus bilateral coil treatment ($n = 158$). Median change in 6-minute walk distance at 12 months was 10.3 m with coil treatment vs -7.6 m with usual care ($P = 0.02$). Improvement of at least 25 m occurred in 40.0% of patients in the coil group vs 26.9% with usual care (odds ratio, 1.8; $P = 0.01$). Major complications occurred in 34.8% of coil participants vs 19.1% of usual care ($P = 0.002$). Other serious adverse events including pneumonia (20% coil vs 4.5% usual care) and pneumothorax (9.7% vs 0.6%, respectively) occurred more frequently in the coil group. The use of endobronchial coils compared with usual care resulted in a 1-year improvement in median exercise tolerance. However, further evaluation of the long-term effects is necessary, and since severe complications often develop, indications should be carefully considered at present.



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