电磁导航支气管镜系统在呼吸系统疾病诊治中的应用现状与展望

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［摘要］ 支气管镜为获取肺外周病变(peripheral pulmonary lesions，PPL)的一种微创技术。传统支气管镜引导的经支气管肺活检(transbronchial lung biopsy，TBLB)在X线透视指导下进行，诊断率相对较低。电磁导航支气管镜(electromagnetic navigation bronchoscopy，ENB)是近年来出现的一项新的微创诊断技术。其对PPL诊断率优于传统经支气管镜。多项研究已显示出ENB诊断PPL具有的可行性和安全性，并且显示出ENB在PP定位和治疗领域具有潜在的应用前景。该文就这一技术临床应用现状作一综述。

［关键词］ 支气管镜；电磁导航；诊断；肺外周病变

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Electromagnetic navigation bronchoscopy for the diagnosis and treatment of respiratory disease: current and future perspective

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［**Abstract**］ Bronchoscopy is a minimally invasive method for obtaining peripheral pulmonary lesions (PPL). Traditional bronchoscopy-guided transbronchial lung biopsy (TBLB) is performed under X-ray guidance, and diagnostic rate is relatively low. A new, real-time electromagnetic navigation bronchoscopy (ENB) is a minimally invasive diagnostic technique which appeared in recent years. Studies suggest ENB is a feasible and safe method for diagnosis of PPL which shows higher diagnostic yields than traditional TBLB, and its potential application in localization and treatment of PPL. This article reviews the clinical application of the technique.

［**Key words**］ Bronchoscopy; Electromagnetic navigation; Diagnosis; Peripheral pulmonary lesions

随着低剂量CT筛查应用普及，肺孤立性肺结节(solitary pulmonary nodule，SPN)发现率增加，但低剂量螺旋CT组发现结节经病理确诊的假阳性率为96.4%[1]。因此术前明确肺外周病变(peripheral pulmonary lesions，PPLs)的性质具有重要意义。

1　PPL常见诊断方式

目前常见PPL有创诊断方式包括支气管镜检查、经胸壁针吸活检、胸腔镜下切除活检、开胸探查等。经胸壁针吸活检在CT、B超等引导下进行，对PPL有着较高诊断率，但气胸发生率高(3.1%～41.7%)，部份病灶难以到达，并可能存在潜在肿瘤胸膜转移风险[2-3]。电磁导航支气管镜(electromagnetic navigation bronchoscopy，ENB)是2000年后开始使用于临床的PPL经支气管诊断技术，近年来临床应用日益广泛。ENB是将虚拟

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支气管镜和电磁定位技术相结合的新一代支气管镜检查和治疗手段，可以实时准确对常规支气管镜无法到达的PPL或纵隔和肺门淋巴结进行定位，又可通过活检通道行经支气管肺活检(transbronchial lung biopsy，TBLB)或经支气管针吸活检(transbronchial needle aspiration，TBNA)获取病变组织行病理检查。同时可以进行介入治疗(如局部注射药物或进行放射性粒子植入等)。与传统气管镜比较，通过术前准确定位和术中实时导航，ENB检查可以缩短检查时间和提高病变定位和活检的诊断率[4]，本文将综述ENB在呼吸系统疾病诊治中的应用。

2 技术原理、设备与操作方法

目前广泛使用的ENB系统是SuperDimension公司研制的InReach系统。该系统主要包括气管镜磁导航系统主机、磁导航电磁板、导航定位导管、气管镜工作通道延长导管和导航定位传感器(图1)。InReach系统利用胸部CT图像进行三维重建结构路线图，然后在支气管镜检查过程中携带引导导管达到病变部位。由于引导导管顶端携带有电磁定位传感器，因此可以将病变位置实时地再现到预先生成的肺脏3D路线图上。患者躺在磁性板上使得全胸处于弱磁场中，插入头端带有微传感器的特殊弯曲导管伸入支气管腔内。导管可以通过旋转准确地送达病灶所在部位进行穿刺活检。

3 临床应用

3.1 诊断PPL

Solomon等[5]在1998年首次报道了使用ENB的动物实验结果，该研究对8只猪进行了ENB的针吸活检试验，结果表明ENB能够提高PPL的诊断率。2000年，Solomon等[6]又报道了15例临床患者，同时比较了胸壁体表定位与气管内定位的准确性，研究表明气管内定位法误差距离远低于体表定位法。2014年，呼吸杂志发表了有关ENB诊断肺内结节准确率和安全性的荟萃分析[7]。该分析入组了15个临床试验，共1 033个肺内结节[8-22](表1)。ENB整体诊断灵敏度为64.9%，准确率为73.9%；诊断肺癌的灵敏度为71.1%，阴性预测值为52.1%。气胸的发生率为3.1%，其中1.6%的患者要求胸管引流。该分析同时得出了结节位置在肺上叶或中叶，结节的大小，虚拟支气管中注册点与实际操作中注册点的注册误差，CT上是否有支气管充气征，是否与外周超声探头联合使用以及是否使用外鞘管吸引作为取样手段与ENB诊断率相关。异质性分析显示，使用全麻和快速现场细胞学可获得更好的诊断效果。

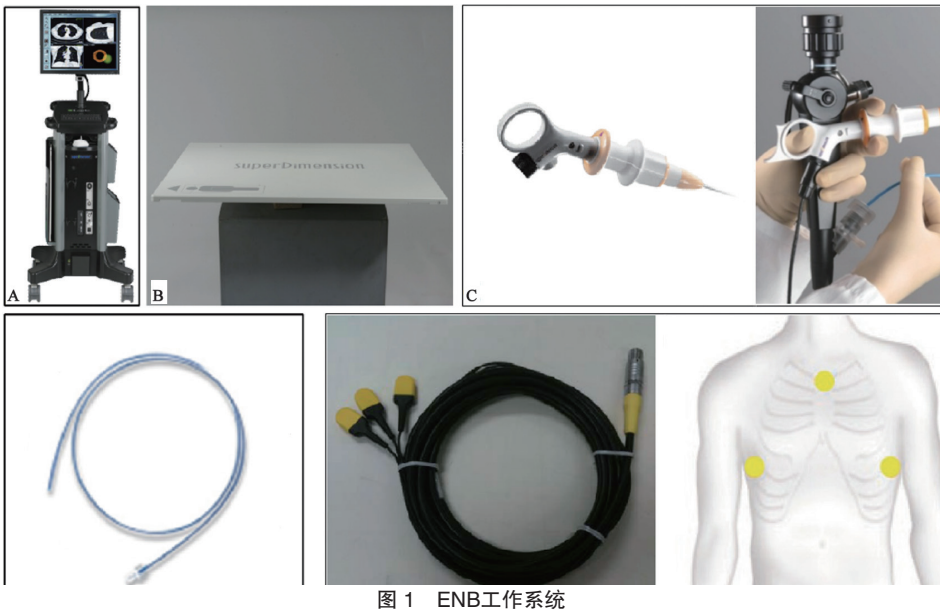

图1 ENB工作系统

Fig. 1 ENB system

A: System computer; B: Electromagnetic plate; C: Navigational locatable guide; D: Bronchoscope extended working channel; E: Navigation positioning sensor

表 1　ENB在PPL的诊断有效性

Tab. 1　Diagnostic yield of ENB for PPL

Study	Patient selection	Number of patients/ Number of lesions	Mean diameter *d*/ mm	Type of anesthesia	Assistant techniques	The sampling techniques	Mean exam duration *t*/min	Diagnostic yield/%
Becker,2005 [8]	PPL can't be reached by routine FB, no matter the PPL size	30/30	39.8	GA	Fluoroscopy, RP-EBUS	Biopsy forcep, Brush, Curette	ND	60.0
Hautmann,2005[9]	PPL can't be reached by FB	16/16	ND	CS	Fluoroscopy	Biopsy forcep	ND	68.8
Gildea, 2006[10]	PPL can't be reached by routine FB	49/56	22.8	CS	Fluoroscopy	Biopsy forcep, Brush, BAL, NA	51	57.1
Schwarz,2006[11]	PPL can't be reached by routine FB, no matter the PPL size	13/13	33.5	CS	Fluoroscopy	Biopsy forcep, Brush	46	69.2
Makris,2007[12]	PPL can't be reached by routine FB, suspected to malignant lesion, FB,TTNA or TBNA failed to diagnose it, and had high risks for surgery operation	40/40	23.5	GA	0	Biopsy forcep●	ND	62.5
Eberhardt, 2007[13]	PPL can't be reached by routine FB	89/93	24	GA/CS	0	Biopsy forcep Brush,BAL△,NA	26.9	55.9
Eberhardt, 2007[14]	PPL can't be reached by routine FB	39/39	28	GA/CS	0	Biopsy forcep	ND	59.0
Eberhardt,2007[14]	PPL can't be reached by routine FB	40/40	24	GA/CS	RP-EBUS	Biopsy forcep	ND	87.5
Wilson,2007[15]	PPL can't be reached by routine FB	222/271	21	CS	Fluoroscopy , ROSE	Biopsy forcep, NA	ND	55.7
Bertoletti,2009[16]	PPL can't be reached by routine FB, and PET was positive for the lesion, and had high risks for surgery operation	54/54	31.2	CS*	0	Biopsy forcep, Brush	29.5	61.1
Eberhardt,2009[17]	Small PPL,and suspected to malignant lesion	54/55	23.3	GA	RP-EBUS	Biopsy forcep, Suction▲	25.7	69.1
Lamprecht, 2009[18]	PPL can't be reached by routine FB,and/or the PPL can't be found by the fluoroscopy	13/13	30	GA	ROSE	Biopsy forcep, Brush, NA	60	76.9
Seijo,2010[19]	PPL, surgery operation or TTNA was regarded as the secondary methods	51/51	25	CS	ROSE	Biopsy forcep, NA	56	66.7
Mahajan,2011[20]	PPL can't be reached by routine FB,and had high risks for surgery operation	48/49	20	CS	Fluoroscopy	Biopsy forcep, Brush, BAL	ND	49.0
Lamprecht,2012[21]	PPL can't be reached by routine FB	112/112	27.1	GA	ROSE	Biopsy forcep, Brush, NA	45.2	83.9
Pearlstein,2012[22]	PPL was suspected to malignant lesion by CT or PET, and was not fit for TTNA, had high risks for surgery operation, and no other part for biopsy	101/101	28	GA	ROSE	Biopsy forcep, Brush, NA	70	66.3

FB: Flexible bronchoscopy; PPL: Peripheral pulmonary lesion; TTNA: Transthoracic needle aspiration; PET: Positron emission tomography; GA: General anesthesia; CS: Conscious sedation; ND: No data; RP-EBUS: Radial probe-endobronchial ultrasound; BAL: Bronchoalveolar lavage; *: 50%/50% Nitrous oxide/oxygen mixture; ●: Nine attempts for biopsies, instead of mostly 3-5 in other studies; △: Do BAL through extended working channel; ▲: Suction through the guide sheath back and forth

值得注意的是，Eberhardt等[14]的研究表明在使用ENB诊断PPL时，联合应用径向扫描的支气管内超声探头(RP-EBUS)及ENB，比两者单独应用更为有效。单独应用EBUS诊断率为69%，ENB为59%，但两者结合后诊断率提高至88%，且与病灶大小无关。

由于经ENB获取组织量较少，有担心其是否足以进行病理学分析，而Ha等[23]研究对65例肺癌患者回顾性分析显示：其中3例小细胞肺癌通过形态学确认，余下的62例非小细胞肺癌中51例(78.5%)通过形态学即可确认，而11例(21.5%)需经免疫组化确认。16例经手术治疗，其中14例(87.5%)与ENB获取的组织学分型相符，1例ENB分型为非小细胞肺癌倾向腺癌的经手术证实为大细胞肺癌，1例ENB分型为鳞癌的经手术证实为腺鳞癌。腺癌15例中的14例标本量足以进行EGFR突变分析。2例患者进行*EML4-ALK*基因重排评价，标本量也已足够。这提示ENB获得的标本足够行组织学分型及驱动基因检测。

3.2 淋巴结活检与肺癌分期

肺癌的准确分期对于治疗方案的选择以及预后的判断具有十分重要的意义。ENB对淋巴结转移和肺癌分期上的诊断价值和安全性鲜有报道。2006年Gildea等[10]对60例患者经ENB定位活检。肺部病灶与淋巴结大小分别为(22.8 ± 12.6) mm及(28.1 ± 12.8) mm，总体成功率为率为80%，其中肺部病灶的取样成功率为74%(40/54)，纵隔淋巴结取样成功率为100%(31/31)；恶性病变的准确率为74%(32/43)。该项研究结果提示使用ENB诊断淋巴结阳性率要高于PPL。最近一项研究比较了传统TBNA与ENB引导下的TBNA在纵隔和肺门淋巴结肿大的诊断价值和安全性。研究入组了44例患者共88组淋巴结进行ENB-TBNA诊断，50例患者共64组淋巴结进行C-TBNA诊断[24]。根据病理结果，ENB-TBNA的诊断率为72.8%，C-TBNA的诊断率为42.4%。亚组分析结果显示ENB-TBNA和传统TBNA诊断率跟淋巴结大小相关。

3.3 治疗中的应用

3.3.1 放疗基准标记的放置

立体定向放疗(stereotactic body radiation therapy，SBRT)主要用于不适合或者不愿意进行手术切除的肺实质病变患者。ENB还能够用在SRBT时基准标记的放置，提高安置放疗标记准确性。研究显示通过ENB安置放疗基准标记，9例病变有8例准确定位，1周后标记保存率为90%[25]。在另外的研究中，对患者实施射波刀前，215/217(99%)患者螺旋弹簧基准标记通过ENB准确安置，相对于常规方法安置线性基准标记8/17(58%)优势明显，且气胸发生率仅为5.8%[26]。Kupelian等[27]在SBRT中应用ENB引导放置定位参考标志物，并与传统方法经CT定位或X线定位进行比较：23例PPL且不适宜手术治疗的肺癌患者，病灶平均直径为2.6 cm，其中15例在CT定位或X线定位下通过经皮肺穿刺完成，8例通过ENB引导下经支气管镜放置方法完成，23例均成功放置标志物，通过CT或X线定位的15例中8例气胸(53%)，而经ENB定位患者未出现气胸等并发症。Harley等[28]在研究中对43例患者放置定位参考标志物，对于中央型肿物应用EBUS微探头定位，对于PPL采用ENB联合EBUS微探头定位。结果表明放置2周后30例患者的标志物没有出现移位或丢失，其余13例仍至少有1个以上标志物保留，对放疗定位没有影响。值得一提的是，入选的43例患者中平均年龄为74.4岁，其中31例伴有严重慢性阻塞性肺疾病，14例伴有冠心病，这些患者均因不能耐受传统经皮肺穿刺操作并发症而选择经ENB引导经支气管镜放置的方法完成。

3.3.2 胸腔镜手术胸膜表面投放染色标记

胸腔镜手术(video-assisted thoracic surgery，VATS)是常见治疗微小PPL的有效方法。但是对于小于1 cm微小病变，胸腔镜切除最大难点是病灶太小难以发现。微小PPL的ENB定位和染色标记相当于给胸腔镜安装上了一个“路标”，外科医师能够在胸腔镜下看到靶点进行病灶切除。Krimsky等[29]报道了通过ENB引导下在

21个微小PPL(平均13.4 mm，范围7～29 mm)中，17个病变成功放置染色标记物，成功标记的染料在病变附近脏层胸膜标记，均成功行楔形切除。通过对微小PPL的定位，解决了以往对于微小PPL手术定位困难的问题。

3.3.3 引导PPL后装放疗

已有学者通过在ENB下寻找病灶，然后用支气管内超声确认病变部位，并沿活检通道插入放疗导管。引入IR192放射源的总剂量为15～30 Gy，3次/周。对18例无法手术治疗的周围型肺癌患者实施ENB引导气道内近距离放疗，结果表明，其中50%(9/18)患者肿瘤疗效达到完全缓解，50%(9/18)患者取得部分缓解，未出现明显不良反应[30]。ENB引导的近距离放疗对不可切除的周围型肺癌是安全、有效方法，可减少对周围正常组织的损伤。

4 安全性

其气胸发生率与传统支气管镜检查气胸发生率相同，无其他不良反应及并发症。其他并发症及注意事项与传统支气管镜发生率相同[4]。

5 展望

ENB应用通过微创获得PPL病理诊断已经成为可能，将来应侧重通过电磁导航技术，精确定位病灶后，进一步对病灶进行标记，以便外科医师术中快速确定病变的位置与精准切除的范围；或结合射频消融等消融技术，在ENB的引导下，直接对病灶进行消融治疗。

[参 考 文 献]

[1] NATIONAL LUNG SCREENING TRIAL RESEARCH TEAM, ABERLE D R, ADAMS A M, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening [J]. N Engl J Med, 2011, 365(5): 395-409.

[2] TOMIYAMA N, YASUHARA Y, NAKAJIMA Y, et al. CT-guided needle biopsy of lung lesions: a survey of severe complication based on 9783 biopsies in Japan [J]. Eur J Radiol, 2006, 59(1): 60-64.

[3] SCHREINER A M, JONES J G, SWISTEL A J, et al. Transthoracic fine needle aspiration resulting in implantation metastasis in the superficial tissues of the breast [J]. Cytopathology, 2013, 24(1): 58-60.

[4] LEONG S, JU H, MARSHALL H, et al. Electromagnetic navigation bronchoscopy: A descriptive analysis [J]. J Thorac Dis, 2012, 4(2): 173-185.

[5] SOLOMON S B, WHITE P J, ACKER D E, et al. Real-time bronchoscope tip localization enables three-dimensional CT image guidance for transbronchial needle aspiration in swine [J]. Chest, 1998, 114(5): 1405-1410.

[6] SOLOMON S B, WHITE P J, WIENER C M, et al. Three-dimensional CT-guided bronchoscopy with a real-time electromagnetic position sensor: a comparison of two image registration methods [J]. Chest, 2000, 118(6): 1783-1787.

[7] GEX G, PRALONG J A, COMBESCURE C, et al. Diagnostic yield and safety of electromagnetic navigation bronchoscopy for lung nodules: a systematic review and meta-analysis [J]. Respiration, 2014, 87(2): 165-176.

[8] BECKER H D, HERTH F, ERNST A, et al. Bronchoscopic biopsy of peripheral lung lesions under electromagnetic guidance: a pilot study [J]. J Bronchol Interv Pulmonol, 2005, 12: 9.

[9] HAUTMANN H, SCHNEIDER A, PINKAU T, et al. Electromagnetic catheter navigation during bronchoscopy: validation of a novel method by conventional fluoroscopy [J]. Chest, 2005, 128(1): 382-387.

[10] GILDEA T R, MAZZONE P J, KARNAK D, et al. Electromagnetic navigation diagnostic bronchoscopy: a prospective study [J]. Am J Respir Crit Care Med, 2006, 174(9): 982-989.

[11] SCHWARZ Y, GREIF J, BECKER H D, et al. Real-time electromagnetic navigation bronchoscopy to peripheral lung lesions using overlaid CT images: the first human study [J]. Chest, 2006, 129(4): 988-994.

[12] MAKRIS D, SCHERPEREEL A, LEROY S, et al. Electromagnetic navigation diagnostic bronchoscopy for small peripheral lung lesions [J]. Eur Respir J, 2007, 29(6): 1187-1192.

[13] EBERHARDT R, ANANTHAM D, HERTH F, et al. Electromagnetic navigation diagnostic bronchoscopy in peripheral lung lesions [J]. Chest, 2007, 131(6): 1800-1805.

[14] EBERHARDT R, ANANTHAM D, ERNST A, et al. Multimodality bronchoscopic diagnosis of peripheral lung lesions: a randomized controlled trial [J]. Am J Respir Crit Care Med, 2007, 176(1): 36-41.

[15] WILSON D S, BARTLETT R J. Improved diagnostic yield of bronchoscopy in a community practice: combination of electromagnetic navigation system and rapid on-site evaluation [J]. J Bronchol Interv Pulmonol, 2007, 14: 227.

[16] BERTOLETTI L, ROBERT A, COTTIER M, et al. Accuracy and feasibility of electromagnetic navigated bronchoscopy under nitrous oxide sedation for pulmonary peripheral opacities: an outpatient study [J]. Respiration, 2009, 78(3): 293-300.

[17] EBERHARDT R, MORGAN RK, ERNST A, et al. Comparison

of suction catheter versus forceps biopsy for sampling of solitary pulmonary nodules guided by electromagnetic navigational bronchoscopy [J]. Respiration, 2010, 79(1): 54–60.

[18] LAMPRECHT B, PORSCH P, PIRICH C, et al. Electromagnetic navigation bronchoscopy in combination with PET–CT and rapid on–site cytopathologic examination for diagnosis of peripheral lung lesions [J]. Lung, 2009, 187(1): 55–59.

[19] SEIJO L M, DE TORRES J P, LOZANO M D, et al. Diagnostic yield of electromagnetic navigation bronchoscopy is highly dependent on the presence of a bronchus sign on CT imaging: results from a prospective study [J]. Chest, 2010, 138(6): 1316–1321.

[20] MAHAJAN A K, PATEL S, HOGARTH D K, et al. Electromagnetic navigational bronchoscopy: an effective and safe approach to diagnose peripheral lung lesions unreachable by conventional bronchoscopy in high–risk patients [J]. J Bronchology Interv Pulmonol, 2011, 18(2): 133–137.

[21] LAMPRECHT B, PORSCH P, WEGLEITNER B, et al. Electromagnetic navigation bronchoscopy (ENB): Increasing diagnostic yield [J]. Respir Med, 2012, 106(5): 710–715.

[22] PEARLSTEIN D P, QUINN C C, BURTIS C C, et al. Electromagnetic navigation bronchoscopy performed by thoracic surgeons: one center's early success [J]. Ann Thorac Surg, 2012, 93(3): 944–949, discussion 949–950.

[23] HA D, CHOI H, ALMEIDA F A, et al. Histologic and molecular characterization of lung cancer with tissue obtained by electromagnetic navigation bronchoscopy [J]. J Bronchology Interv Pulmonol, 2013, 20(1): 10–15.

[24] DIKEN ÖE1, KARNAK D, ÇILEDAĞ A, et al. Electromagnetic navigation–guided TBNA vs conventional TBNA in the diagnosis of mediastinal lymphadenopathy [J]. Clin Respir J, 2015, 9(2): 214–220.

[25] ANANTHAM D, FELLER–KOPMAN D, SHANMUGHAM L N, et al. Electromagnetic navigation bronchoscopy–guided fiducial placement for robotic stereotactic radiosurgery of lung tumors: a feasibility study [J]. Chest, 2007, 132(3): 930–935.

[26] SCHROEDER C, HEJAL R, LINDEN P A. Coil spring fiducial markers placed safely using navigation bronchoscopy in inoperable patients allows accurate delivery of CyberKnife stereotactic radiosurgery [J]. J Thorac Cardiovasc Surg, 2010, 140(5): 1137–1142.

[27] KUPELIAN PA, FORBES A, WILLOUGHBY TR, et al. Implantation and stability of metallic fiducials within pulmonary lesions [J]. Int J Radiat Oncol Biol Phys, 2007, 69(3): 777–785.

[28] HARLEY D P, KRIMSKY W S, SARKAR S, et al. Fiducial marker placement using endobronchial ultrasound and navigational bronchoscopy for stereotactic radiosurgery: an alternative strategy [J]. Ann Thorac Surg, 2010, 89(2): 368–373, discussion 373–374.

[29] KRIMSKY WS, MINNICH DJ, CATTANEO SM, et al. Thoracoscopic detection of occult indeterminate pulmonary nodules using bronchoscopic pleural dye marking [J]. J Community Hosp Intern Med Perspect, 2014, 4: 23084.

[30] HARMS W, KREMPIEN R, GREHN C, et al. Electromagnetically navigated brachytherapy as a new treatment option for peripheral pulmonary tumors [J]. Strahlenther Onkol, 2006, 182(2): 108–111.

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