

doi: 10.3978/j.issn.2095-6959.2017.04.011

View this article at: <http://dx.doi.org/10.3978/j.issn.2095-6959.2017.04.011>

81例CT引导下经皮肺穿刺活检标本临床病理结果

王炯, 颜瑾, 徐轲, 闫雪波, 姜雪勤, 朱莹莹, 江子丰

(安徽医科大学第一附属医院老年呼吸内科, 安徽医科大学呼吸病研究所, 合肥 230022)

[摘要] 目的: 分析CT引导下经皮肺穿刺活检标本的临床病理学及免疫组织化学诊断, 结合血清肿瘤标志物检测探讨其对肺部占位性病变的诊断价值。方法: 回顾性分析81例肺部占位性病变患者CT引导下肺穿刺活检标本病理学、25例免疫组织化学诊断及73例血清肿瘤标志物癌胚抗原(carcino-embryonic antigen, CEA), 细胞角蛋白19片段(cytokeratin-19-fragment, CYFRA21-1), 神经元特异性烯醇化酶(neuron-specific enolase, NSE)检测结果。结果: 81例CT引导下肺穿刺活检标本组织病理学诊断率为96.3%, 其中恶性病变53例(腺癌29例, 鳞癌20例, 小细胞癌1例, 未明确类型的非小细胞肺癌1例, 其他类型肺癌1例, 胸腺恶性肿瘤1例); 良性病变25例(炎性包块7例, 结核5例, 肺炎7例, 硅沉着病3例, 炎性假瘤2例, 神经鞘瘤1例); 25例行免疫组织化学检查的病例中诊断恶性肿瘤24例(腺癌13例, 鳞癌8例, 小细胞癌1例, 未确定分型2例), 其中P63及CK5/6在鳞癌阳性率为87.5%, TTF-1及CK-7在腺癌阳性率为69.2%和76.9%, 差异有统计学意义($P < 0.05$); CEA, CYFRA21-1, NSE及3项联合对肺癌诊断的灵敏度分别为54.9%, 68.6%, 37.3%, 80.4%。结论: CT引导下经皮肺穿刺活检标本病理诊断阳性率高, 结合免疫组织化学及血清肿瘤标志物联合检测可为肺癌的诊断及病理分型提供辅助性参考依据。

[关键词] 肺占位; CT引导下经皮肺穿刺活检; 病理学; 免疫组织化学; 肿瘤标志物

Clinicopathological results of 81 specimens of CT guided percutaneous lung biopsy

WANG Jiong, YAN Jin, XU Ke, YAN Xuebo, JIANG Xueqin, ZHU Yingying, JIANG Zifeng

(Department of Geriatrics Pulmonary, Research Institute of Respiratory Disease, First Affiliated Hospital of Anhui Medical University, Hefei 230022, China)

Abstract **Objective:** To analyze the clinicopathological and immunohistochemical results of CT guided percutaneous lung biopsy specimens, and to investigate the diagnostic value of serum tumor markers in the diagnosis of pulmonary space occupying lesions. **Methods:** The pathological diagnosis of 81 specimens of CT guided lung biopsy, of which 25 cases of immunohistochemical results and 73 cases of the concentrations of serum tumor markers [carcino-embryonic antigen (CEA), cytokeratin-19-fragment (CYFRA21-1), neuron-specific enolase (NSE)] were analyzed retrospectively. **Results:** The diagnosis rate of 81 specimens of CT guided percutaneous lung biopsy was 96.3%, there were 53 cases of malignant lesions included 29 adenocarcinoma, 20 squamous carcinoma,

收稿日期 (Date of reception): 2017-02-08

通信作者 (Corresponding author): 王炯, Email: wangjiong7286@163.com

1 small cell carcinoma, 1 uncertain type of non-small cell lung cancer, 1 other types of lung cancer and 1 thymic carcinoma. Twenty-two cases of benign lesions included 7 inflammatory mass, 5 tuberculosis, 7 pneumonia, 3 pneumoconiosis, 2 inflammatory pseudotumor and 1 neurilemmoma. Immunohistochemical staining was used in 25 cases, 24 cases were diagnosed as malignant lesions included 13 adenocarcinoma, 8 squamous carcinoma, 1 small cell carcinoma and 2 uncertain type of lung cancer. The positive rate of P63 and CK5/6 in squamous cell carcinoma were 87.5%, TTF-1 and CK-7 were 69.2% and 76.9% in adenocarcinoma, there were significant differences between them ($P < 0.05$); the sensibility of CEA, CYFRA21-1, and NSE of diagnosis the lung cancer were 54.9%, 68.6%, and 37.3% respectively. In combined detection for three targets, the sensibility rate was 80.4%.

Conclusion: Combination of pathological and immunohistochemical detection of CT-guided percutaneous lung biopsy specimen with lung tumor makers can improve the sensitivity and accuracy rate of diagnosis of early stage lung cancer. Immunohistochemical results are useful to identify the pathologic category of lung tumor.

Keywords pulmonary space-occupying lesions; CT-guided per cutaneous lung biopsy; pathology; immunohistochemistry; tumor marker

肺内多种原因如支气管肺癌、多发性肺转移瘤、肺平滑肌瘤、肺错构瘤、肺结核球、肺炎性假瘤、球形肺炎、肺脓肿、肺包囊虫病、外伤性血肿等均可形成肺部占位性病变, 病变小者如米粒大小结节影甚或淡羽毛样、磨玻璃样高密度影, 大者可占据半个胸腔, 其中以支气管肺癌、肺结核球和肺部炎性肿块最多见^[1-2]。准确诊断病变的性质对治疗方案的选择相当重要, 自Haaga首次采用CT引导下经皮肺穿刺活检以来, 现已成为临床一项较为成熟的经皮肺微创穿刺活检获取标本病理检查以明确肺部占位性病变性质的诊断技术^[3-5]。本文回顾性分析了安徽医科大学第一附属医院老年呼吸内科81例肺部占位性病变患者行CT引导下肺穿刺活检标本病理诊断结果, 结合组织免疫组织化学及血清肿瘤标志物检测, 探讨其对肺部占位性病变的诊断价值。

1 对象与方法

1.1 对象

2014年10月至2016年6月间因肺部占位性病变性质待查在安徽医科大学第一附属医院老年呼吸内科住院行CT引导下经皮肺穿刺活检术获得病理标本的81例患者, 其中男57人, 女24人, 年龄20~82(60±13)岁, 病变位于右肺46例(右上肺9例, 右中肺4例, 右下肺12例, 多发4例), 左肺27例(左上肺12例, 左下肺11例), 双肺多发病变8例; 其中73例患者同时有完善的癌胚抗原(carcino-embryonic antigen, CEA), 细胞角蛋白19片段(cytokeratin-19-fragment, CYFRA21-1)和神经元特异性烯醇化酶(neuron-specific enolase, NSE)

检测结果。该研究获得医院伦理委员会批准。

1.2 肺穿刺活检操作

根据肺部病灶部位确定患者穿刺体位, CT扫描确定穿刺点后, 用PRECISA 16G活检针按测定的穿刺点和角度穿刺后重复扫描, 确认针尖位于病灶内, 在患者屏气状态下用活检枪取材, 标本以95%酒精固定后送检病理。

1.3 活检标本病理分析

病理结果均由我院病理科高级职称医师作出, 其中25例患者进一步行免疫组织化学检测完成分子水平上的鉴定, 免疫组织化学标志分子主要包括TTF-1, CK7, P63, CK5/6, CD56, CgA, NSE, Syn等。

1.4 血清肿瘤标志物测定

本组有73例患者空腹采集静脉血后分别测定血清CEA, CYFRA21-1和NSE三项肿瘤标志物, 由我院核医学科完成, 阳性参考值标准分别为: CEA >5.0 ng/mL, CYFRA21-1 >3.3 ng/mL, NSE >17.0 ng/mL。

1.5 统计学处理

采用SPSS19.0统计软件, 计数资料采用 χ^2 检验, 计量资料以均数±标准差($\bar{x} \pm s$)表示, $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 病理学结果

81例患者中3例未明确诊断, 明确诊断

78例,诊断率为96.3%。确诊病例中,恶性肿瘤53例,其中肺恶性肿瘤52例(腺癌29例,鳞癌20例,未明确类型的非小细胞肺癌1例,小细胞癌1例,其他类型肺癌1例),胸腺恶性肿瘤1例;肺部良性病变25例,其中炎性包块7例,结核5例,肺炎7例,硅沉着病3例,炎性假瘤2例,神经鞘瘤1例(表1,图1)。

表1 肺占位性病变的CT引导下经皮肺穿刺活检确诊结果

Table 1 Results of CT guided per cutaneous lung biopsy of pulmonary space occupying lesions

病理结果	例数	构成比/%
恶性肿瘤	53	65.4
腺癌	29	35.8
鳞癌	20	24.7
小细胞癌	1	1.2
未分型非小细胞肺癌	1	1.2
其他类型肺癌	1	1.2
胸腺恶性肿瘤	1	1.2
良性病变	25	30.9
炎性包块	7	8.6
肺结核	5	6.2
肺炎	7	8.6
硅沉着病	3	3.7
炎性假瘤	2	2.5
神经鞘瘤	1	1.2
未明确病变	3	3.7
合计	81	100.0

2.2 免疫组织化学

本组有25例患者因肿瘤分化程度低不能明确诊断病理类型进一步行组织免疫组织化学标志,最终明确为良性病变1例,恶性肿瘤24例,13例腺癌中9例TTF-1阳性,10例CK7阳性,8例鳞癌中7例P63阳性,7例CK5/6阳性,1例小细胞肺癌CD56阳性,CgA,NSE,Syn均阴性。不同免疫组织化学相关抗体的表达在肺鳞癌与腺癌间差异有统计学意义($P<0.05$,表2)。

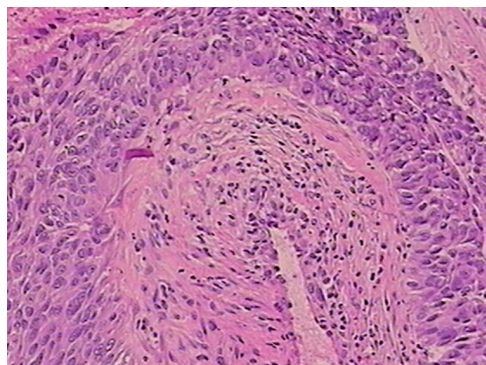


图1 经皮肺穿刺活检标本HE染色显微镜下所见(鳞癌,×400)
Figure 1 Percutaneous lung biopsy specimens were stained with HE staining and observed under microscope (Squamous cell carcinoma, ×400)

表2 不同免疫组织化学相关抗体在肺鳞癌与腺癌的表达差异

Table 2 Different expression of different immunohistochemical antibodies in lung squamous cell carcinoma and adenocarcinoma

组别	TTF-1	CK-7	P63	CK5/6	CD56
鳞癌					
+	0	4	7	7	0
-	8	4	1	1	8
阳性率/%	0	50	87.5*	87.5*	0
腺癌					
+	9	10	1	0	0
-	4	3	12	13	13
阳性率/%	69.2*	76.9*	7.6	0	0

与其他抗体比较,* $P<0.05$ 。

Compared with other antibodies,* $P<0.05$.

2.3 肿瘤标志物

73例患者同时有完善的CEA,CYFRA21-1和NSE检测结果,其中鳞癌19例,腺癌29例,其他类型肺癌3例,良性病变22例。以病理学诊断结果为“金标准”,肿瘤标志物CEA,CYFRA21-1在肺癌组中的阳性率分别为54.9%,68.6%,明显高于良性病变组,差异有统计学意义($P<0.05$);NSE阳性率在两组中阳性率分别为37.3%,27.3%,差异无统计学意义($P>0.05$,表3)。

3种标志物联合诊断阳性率明显提高(80.4%),CEA在肺癌诊断中的特异度最高(90.9%),CYFRA21-1在肺癌诊断中灵敏度最高(68.6%),3种标志物联合诊断灵敏度提高,特异度降低(表4),各种肿瘤标志物在鳞癌及腺癌诊断中灵敏度也不同(表5)。

表3 肿瘤标志物在肺良性疾病中阳性率差异

Table 3 Different positive rate of tumor markers in benign and malignant lung diseases

组别	n	CEA			CYFRA21-1			NSE			CEA+CYFRA21-1+NSE		
		+	-	阳性率/%	+	-	阳性率/%	+	-	阳性率/%	+	-	阳性率/%
肺癌	51	28	23	54.9	35	16	68.6	19	32	37.3	41	10	80.4
良性病变	22	2	20	9.1	4	18	18.2	6	16	27.3	10	12	45.5
χ^2				13.33			15.72			0.68			8.91
P				<0.001			<0.001			0.410			0.003

表4 肿瘤标志物诊断肺癌的灵敏度及特异度

Table 4 Sensitivity and specificity of tumor markers in diagnosis of lung cancer

肿瘤标志物	灵敏度/%	特异度/%
CEA	54.9	90.9
CYFRA21-1	68.6	81.8
NSE	37.3	72.7
CEA+CYFRA21-1+NSE	80.4	54.5

表5 肿瘤标志物在各型肺癌中的灵敏度

Table 5 Sensitivity of tumor markers in different types of lung cancer

肿瘤标志物	灵敏度/[例(%)]	
	腺癌(n=29)	鳞癌(n=19)
NSE	11 (37.9)	7 (36.8)
CEA	21 (72.4)	8 (42.1)
CYFRA21-1	19 (65.5)	12 (63.2)
CEA+CYFRA21-1+NSE	24 (82.8)	15 (78.9)

3 讨论

尽早明确肺部占位性病变的性质对治疗方案的选择至关重要,常用的胸部影像学技术如普通X线检查、普通CT、螺旋CT三维成像技术、病变部位靶目标CT放大扫描以及正电子发射电子计算机断层扫描(PET-CT)等检查可以发现一些很有价值的信息,帮助临床医生做出诊断和正确治疗方案,但诊断的“金标准”仍是病变组织的病理学检查^[6-7]。CT引导下经皮肺穿刺活检术成为临床上广泛应用的一种微创获取病理标本的重要方法,定位准确,并发症少,与手术所获病理对肺癌

诊断有较高符合率。本组穿刺活检标本诊断率为96.3%,与既往文献[8-9]报道相符合。3例患者因取材影响未能明确诊断,考虑与以下几点因素有关^[10-11]:1)病灶过少,大病灶能多点取材获得足够的标本而小病灶则成功取材相对困难;2)病灶部位,穿刺取材处受周围炎性反应灶干扰,易误诊为炎性病变;3)穿刺水平,术者的进针角度在体表的变化会在深处造成偏差,影响取材;4)患者的配合,术中患者的密切配合也是获得满意标本的重要保证。

CT引导下肺穿刺取材标本病理组织相对较少,易受挤压破坏,加之肿瘤分化程度等因素均可影响肺癌分型的确定,可进一步行免疫组织化学检测行分子水平上的鉴定,免疫组织化学检测对确定细胞类型、协助恶性肿瘤的诊断与鉴别诊断、对肿瘤进行进一步病理分型提供依据并可为临床提供治疗方案的选择^[12-13]。本组有25例病例进行了免疫组织化学标记。TTF-1主要存在于甲状腺及Ⅱ型肺泡细胞,对以上来源的恶性肿瘤具有高选择性,CK7主要标记上皮来源细胞,本组腺癌中69.2%TTF-1阳性,76.9%CK7阳性,69.2%两者均阳性者。P63表达正常组织所有鳞状上皮,CK5/6广泛表达于乳腺肌上皮和肺支气管上皮基底细胞。本组数据显示,不同免疫组织化学相关抗体的表达在肺鳞癌与腺癌间有显著性差异,鳞癌患者P63和CK5/6阳性率较高,TTF-1和CK-7在腺癌阳性率较高,通过免疫组织化学抗体联合检测可以提高肺癌的阳性检出率和分型的准确性,与既往研究^[14-15]结果一致。CD56主要存在于胎儿及肿瘤组织的神经内分泌细胞中,有文献[16]显示:CD56高表达于SCLC,且显著高于CgA,NSE,Syn在SCLC中的表达。本组1例小细胞肺癌CD56阳性,CgA,NSE,Syn均为阴性。小细胞肺癌大多为中央型肺癌,周围型少见,多经支气管镜检查即可明确诊断,故本组病例仅纳入1例小细胞癌,

对CD56诊断小细胞癌的价值不具有参考性, 需在今后进一步收集更多病例加以探讨。

肿瘤标志物是恶性肿瘤细胞中存在或异常产生, 或机体对肿瘤细胞刺激所产生的特征性物质, 对于恶性肿瘤的早期诊断, 分期, 预后及疗效具有参考价值^[17-18]。我院常规用于肺癌筛查的肿瘤标志物包括CEA, CYFRA21-1和NSE等3项指标。CEA可在多种恶性肿瘤中过度表达, 在肺癌的表达中以肺腺癌显著升高。CYFRA21-1是存在于上皮细胞胞质中的单克隆抗体, 当肿瘤细胞坏死裂解时, 可在血清中检测。NSE参与糖酵解过程, 以神经源性或神经内分泌细胞改变明显, 因此认为对小细胞癌具有诊断意义。本组71例患者3项肺癌标志物检测结果表明: CEA及CYFRA21-1在恶性疾病中阳性率显著高于良性疾病, CYFRA21-1敏感性最高, 而CEA特异性最高, 3项肿瘤标志物联合检测可以提高肺癌诊断的阳性率及灵敏度, CEA灵敏度为54.9%, 与文献^[19]报道中35%~70%相符, 在腺癌组灵敏度达72.4%, 显著高于鳞癌组, 我们认为CEA对腺癌分型有指导意义。CYFRA21-1在鳞癌及腺癌中灵敏度相当, 未表现出显著差异。本组病例中NSE对肺癌诊断的灵敏度较低, 与文献NSE对小细胞肺癌有较高的灵敏度不符, 可能与本组病例小细胞肺癌例数过少导致NSE阳性例数降低, 从而影响其诊断的灵敏度有关。

综上所述, CT引导下经皮肺穿刺活检标本病理学诊断阳性率高, 免疫组织化学及血清肿瘤标志物检测可为肺癌的诊断及病理分型提供辅助性参考依据。

参考文献

- 王蓓, 王晓伟, 张红雷, 等. 活检在肺部占位性病变诊断中的意义[J]. 诊断病理学杂志, 2015, 22(9): 548-553.
WANG Bei, WANG Xiaowei, ZHANG Honglei, et al. Significance of biopsy for pathological diagnosis of lung cancer in pulmonary lesions[J]. Chinese Journal of Diagnostic Pathology, 2015, 22(9): 548-553.
- Ocak S, Duplaquet F, Jamart J, et al. Diagnostic accuracy and safety of CT-guided percutaneous transthoracic needle biopsies: 14-gauge versus 22-gauge needles[J]. J Vasc Interv Radiol, 2016, 27(5): 674-681.
- Haaga JR, Alfidri RJ. Precise biopsy localization by computer tomography[J]. Radiology, 1976, 118(3): 603-607.
- Matsui Y, Hiraki T, Mimura H, et al. Role of computed tomography fluoroscopy-guided cutting needle biopsy of lung lesions after transbronchial examination resulting in negative diagnosis[J]. Clin Lung Cancer, 2011, 12(1): 51-55.
- 黄水北, 简继红, 伍竞. CT引导下经皮肺穿刺活检对肺部外周占位性病变诊断的临床价值[J]. 实用中西医结合临床, 2015, 15(8): 62-63.
HUANG Suibei, JIAN Jihong, WU Jing. Clinical value of CT guided percutaneous lung biopsy in the diagnosis of peripheral pulmonary space-occupying lesions[J]. Practical Clinical Journal of Integrated Traditional Chinese and Western Medicine, 2015, 15(8): 62-63.
- Galea A, Adlan T, Gay D, et al. Comparison of digital tomosynthesis and chest radiography for the detection of noncalcified pulmonary and hilar lesions[J]. J Thorac Imaging, 2015, 30(5): 328-335.
- Suzuki K, Watanabe S, Mizusawa J, et al. Predictors of non-neoplastic lesions in lung tumours showing ground-glass opacity on thin-section computed tomography based on a multi-institutional prospective study[J]. Interact Cardiovasc Thorac Surg, 2015, 21(2): 218-223.
- 刘亚芳, 邢旸, 宋勇. 不同途径获取肺癌组织对病理类型诊断的差异性分析[J]. 医学研究生学报, 2016, 29(5): 500-503.
LIU Yafang, XING Ze, SONG Yong. CT-guided percutaneous needle lung biopsy versus surgical specimens in the diagnosis of different pathological types of lung cancer[J]. Journal of Medical Postgraduates, 2016, 29(5): 500-503.
- Cardoso LV, Souza Júnior AS. Clinical application of CT and CT-guided percutaneous transthoracic needle biopsy in patients with indeterminate pulmonary nodules[J]. J Bras Pneumol, 2014, 40(4): 380-388.
- 刘强, 赵建龙, 杨丽, 等. 肺部占位性病变患者CT引导下经皮肺穿刺活检术穿刺次数及并发症的影响因素研究[J]. 实用心脑血管病杂志, 2015, 23(11): 25-28.
LIU Qiang, ZHAO Jianlong, YANG Li, et al. Influencing factors of puncture times and postoperative complications of lung space-occupying lesions patients undergoing CT guided percutaneous pulmonary puncture biopsy[J]. Practical Journal of Cardiac Cerebral Pneumal and Vascular Disease, 2015, 23(11): 25-28.
- Kim YD, Lee BY, Min KO, et al. Intrapulmonary recurrence after computed tomography-guided percutaneous needle biopsy of stage I lung cancer[J]. J Thorac Dis, 2014, 6(7): 1004-1006.
- Roy S, Nandi A, Das I, et al. Comparative study of cytology and immunocytochemistry with trucut biopsy and immunohistochemistry in diagnosis of localized lung lesions: A prospective study[J]. J Cytol, 2015, 32(2): 90-95.
- 张鹏, 韩一平, 黄玲, 等. TTF-1和p63在NSCLC组织中的表达及临床意义[J]. 中国肺癌杂志, 2009, 12(9): 995-999.
ZHANG Peng, HAN Yiping, HUANG Ling, et al. Expression and clinical significance of TTF-1 and p63 in NSCLC[J]. Chinese Journal of Lung Cancer, 2009, 12(9): 995-999.

14. 徐晓艳, 杜华, 宝鲁日, 等. 非小细胞肺癌活检标本中CK7、TTF-1、NapsinA、CK5/6及p63的表达及其意义[J]. 诊断病理学杂志, 2015, 22(11): 688-691.
XU Xiaoyan, DU Hua, BAO Luri, et al. Expression and significance of CK7, TTF-1, NapsinA, CK5/6 and p63 in biopsy specimen of non-small cell lung cancer[J]. Chinese Journal of diagnostic Pathology, 2015, 22(11): 688-691.
15. Mukhopadhyay S, Katzenstein AL. Subclassification of non-small cell lung carcinomas lacking morphologic differentiation on biopsy specimens: Utility of an immunohistochemical panel containing TTF-1, napsin A, p63, and CK5/6[J]. Am J Surg Pathol, 2011, 35(1): 15-25.
16. 张雯雯, 孔庆暖, 韩增磊, 等. 小细胞肺癌组织CD56、CgA、Syn及TTF-1表达及联合诊断意义[J]. 齐鲁医学杂志, 2013, 28(2): 109-111.
ZHANG Wenwen, KONG Qingnuan, HAN Zenglei, et al. Expression of CD56, CgA, Syn, and TTF-1 in small cell lung cancer and their significance in combined diagnosis[J]. Medical Journal of Qilu, 2013, 28(2): 109-111.
17. Okamura K, Takayama K, Izumi M, et al. Diagnostic value of CEA and CYFRA 21-1 tumor markers in primary lung cancer[J]. Lung Cancer, 2013, 80(1): 45-49.
18. Wang B, He YJ, Tian YX, et al. Clinical utility of haptoglobin in combination with CEA, NSE and CYFRA21-1 for diagnosis of lung cancer[J]. Asian Pac J Cancer Prev, 2014, 15(22): 9611-9614.
19. Ramshankar V, Krishnamurthy A. Lung cancer detection by screening - presenting circulating miRNAs as a promising next generation biomarker breakthrough[J]. Asian Pac J Cancer Prev, 2013, 14(4): 2167-2172.

本文引用: 王炯, 颜瑾, 徐轲, 闫雪波, 姜雪勤, 朱莹莹, 江子丰. 81例CT引导下经皮肺穿刺活检标本临床病理结果[J]. 临床与病理杂志, 2017, 37(4): 713-718. doi: 10.3978/j.issn.2095-6959.2017.04.011

Cite this article as: WANG Jiong, YAN Jin, XU Ke, YAN Xuebo, JIANG Xueqin, ZHU Yingying, JIANG Zifeng. Clinicopathological results of 81 specimens of CT guided percutaneous lung biopsy[J]. Journal of Clinical and Pathological Research, 2017, 37(4): 713-718. doi: 10.3978/j.issn.2095-6959.2017.04.011