Advances in Clinical Medicine 临床医学进展, 2023, 13(12), 20190-20196
Published Online December 2023 in Hans. https://www.hanspub.org/journal/acm
https://doi.org/10.12677/acm.2023.13122842

Lung-RADS分级在肺结节良恶性鉴别诊断中的应用价值研究

依力夏提·马木提，阿里甫·依马木*

新疆医科大学附属肿瘤医院，新疆 乌鲁木齐

收稿日期：2023年11月27日；录用日期：2023年12月21日；发布日期：2023年12月28日

摘 要

在高危人群中开展肺癌筛查有益于发现早期肺癌，提高肺癌的生存率。早期肺癌最常见的表现即为肺结节，但肺结节并非肺癌所独有，而包括各种疾病，其良恶性质的鉴别是当今研究的热点与难点。2014年，美国放射学会(ACR)创建了肺部影像报告和数据系统(Lung-RADS 1.0)。该系统于1年更新至Lung-RADS 1.2019，随着更多数据的出现，预计将进一步更新。Lung-RADS为报告肺癌筛查(LCS)低剂量CT (LDCT)胸部检查时提供了通用词典和标准化结节随访管理范式，并可作为质量保证和结果监测工具。使用Lung-RADS旨在提高LCS性能并带来更好的患者预后。本文详细的介绍了Lung-RADS的发展史、应用价值以及其面临的挑战，并提出了展望。

关键词

肺癌，肺结节，Lung-RADS，LDCT

Study on the Application Value of Lung-RADS in the Differential Diagnosis of Benign and Malignant Lung Nodules

Yilixiati Mamuti, Alifu Yimamu*

Tumor Hospital Affiliated to Xinjiang Medical University, Urumqi Xinjiang

Received: Nov. 27th, 2023; accepted: Dec. 21st, 2023; published: Dec. 28th, 2023

Abstract

Lung cancer screening in high-risk groups is beneficial to detect early lung cancer and improve the

*通讯作者。

文章引用: 依力夏提·马木提, 阿里甫·依马木. Lung-RADS 分级在肺结节良恶性鉴别诊断中的应用价值研究[J]. 临床医学进展, 2023, 13(12): 20190-20196. DOI: 10.12677/acm.2023.13122842

survival rate of lung cancer. The most common manifestation of early-stage lung cancer is lung nodules. Lung nodules are not unique to lung cancer, but include a variety of diseases, and the identification of their benign and malignant properties is a hot and difficult issue in today's research. In 2014, the American College of Radiology (ACR) created Lung-RADS 1.0, which was updated to Lung-RADS 1.2019 in 1 year, and it is expected that it will be further updated as more data become available. Lung-RADS provides a common lexicon and standardised nodal follow-up management paradigm for reporting of Lung Cancer Screening (LCS) low-dose CT (LDCT) chest examinations and can be used as a quality assurance and outcome monitoring tool. The use of Lung-RADS is intended to improve LCS performance and lead to better patient prognosis. This article provides a detailed history of the development of Lung-RADS, the value of its application, and the challenges it is facing, as well as an outlook.

Keywords

Lung Cancer, Lung Nodules, Lung-RADS, LDCT

1. 引言

肺癌(LC)是全球癌症死亡的首要原因[1]。自 2000 年以来，肺癌从 120 万例上升到 180 万例，在 2019 年十大死因中排名第六，而在我国肺癌是发病率最高的恶性肿瘤，也是癌症相关死亡的主要原因[2]。尽管肺癌的治疗水平在逐步提高，但 5 年生存率仍低于 20% [3]。能接受全切的中晚期肺癌患者的 5 年生存率为 20%~40%，而不能接受全切的晚期肺癌患者的 5 年生存率仅为 2%~3% [3] [4]。然而，早期肺癌患者手术切除后的 5 年生存率为 70%~100% [5]。因此，早期发现、早期诊断和早期治疗是提高肺癌患者生存率的关键[6]。早期肺癌通常在肺部有小结节，这被认为是判断原发性肺癌的关键特征[7]。然而，并非所有的肺部结节都是恶性病变，因此肺部结节的识别和预测是 LC 早期诊断的重要步骤[8]。

2. 肺癌筛查

肺结节(PNs)的临床诊断多采用 X 射线胸片，90%以上的肺结节患者有明显的异常胸片。然而，X 射线胸片对早期 LC 患者的准确性有限，其诊断价值也因存在“盲区”和不利的密度分辨率而受到限制[9]。螺旋 CT 扫描因其立体、直观和连续扫描的特点，在临床上被广泛用于多种疾病的诊断。然而，由于 CT 检查的辐射剂量较高，其在肺部疾病中的应用价值一直受到质疑[10]。近年来，低剂量计算机断层扫描(LDCT)治疗 LC 成为热点。有研究指出，在检出率方面，与胸片相比，LDCT 对 PN 的检出率高 3 倍，对 LC 的检出率高 4 倍，对 I 期 LC 的检出率高 6 倍[11]。在降低总死亡率方面，美国 33 个研究点的结果显示，LDCT 组 LC 死亡人数比 X 线组减少 6.7%，LC 导致的死亡率降低约 20% [12]。因此，2013 年美国癌症协会推荐 LDCT 用于 LC 高危人群，并制定了相关筛查指南[13]。此外，目前 LDCT 筛查还可辅助诊断肺气肿、冠状动脉钙化等其他疾病，为筛查对象带来更多益处[14] [15]。

随着 CT 扫描仪空间分辨率的提高与更先进的后处理软件相结合，肺癌筛查中肺结节的患病率可能在 21%至 86%之间变化，具体取决于采集方案、纳入的人群以及 2006~2018 年期间使用的指南[16]。虽然大多数检测到的肺结节是良性的，但非钙化肺基线结节受试者的肺癌发病率为 2%~11% [17] [18]。基线时有非钙化结节的受试者中，约有 3%~4%会在接下来的 2~5 年内发展为肺癌[19]。肺癌的危险因素，

如体型、年龄和吸烟等已经确定[20]，但对肺结节的危险因素及其恶性风险知之甚少，这可能至关重要，因为肺结节是肺癌的早期表现。

3. Lung-RADS 的应用

西方国家已经制定了肺癌筛查方案。美国放射学会根据美国国家肺部筛查试验(NLST)、荷兰－比利时肺癌筛查试验(NELSON)和国际早期肺癌行动计划(I-ELCAP) [21] [22] [23] [24]公布的标题数据，于 2014 年发布了“肺部 CT 筛查报告和数据系统(Lung-RADS)”1.0 版[25]。Lung-RADS 已成为全球最广泛使用的筛查发现结节的报告和管理辅助工具之一，1.0 版在应用于 NLST 群体时，通过将阳性基线筛查的阈值尺寸从 4 毫米(最大直径)提高到 6 毫米(平均直径)，有效且显著地降低了假阳性率，但假阴性率仅略有下降[26]。此后，亚洲首个基于人群的多中心前瞻性肺癌筛查项目－韩国肺癌筛查项目(K-LUCAS)也采用了 1.0 版[27]。

2019 年发布了 Lung-RADS 1.1 版[25]。Lung-RADS 委员会由该领域的八位权威专家组成，他们根据对现有文献的审查，确定了需要澄清和改进的领域，从而发布了更新版。将非实性结节的大小阈值从 20 毫米提高到 30 毫米，是因为有证据表明，与实性结节和部分实性结节相比，这类结节的体积倍增时间(VDT)更长，病程一般也更缓慢[28]-[33]。平均直径小于 10 毫米且符合 NELSON 试验所定义的肺内淋巴结标准的硬膜外结节被重新归类为第 2 类结节(以前为第 3 类或第 4A 类) [34]-[39]。鉴于这些结节的恶性率较低，且肺-RADS 3 类结节的癌症诊断率总体较低，因此这些变化有望降低假阳性筛查率。针对 4B 结节还增加了一项新的建议，即允许进行短间隔随访 LDCT，以考虑到可能是感染性或炎症性的新结节或快速增大的结节。据报道，间隔期癌症发生率较低，考虑到中期发展为大肿瘤的可能性不大，因此支持这一建议[40]。还明确了测量和计算平均结节直径的方法，建议报告的平均结节直径精确到小数点后一位[41]。此外，正如随后所讨论的，体积测量也被纳入其中。最后，取消了之前分配给肺癌幸存者重返筛查的修饰符，以避免无病 5 年或 5 年以上患者的 LCS 和肺癌监测之间的混淆。

在 Lung-RADS 1.1 框架中，根据线性二维测量的平均值将结节生长定义为>1.5 mm 的做法仍然保留。不过，结节测量有两个显著变化。首先，除二维测量外，现在还包括体积测量。其次，关于二维测量，指南现在建议测量到小数点后一位，并报告小数点后一位的平均直径。另一方面，Fleischner 协会警告说，对于肺部结节，0.1 毫米的测量值可能并不精确。事实上，他们认为小于 3 毫米的结节太小，无法准确测量。据我们所知，还没有研究评估过测量到小数点后第一位的实用性。随着 Lung-RADS 1.1 框架的采用，未来的研究将对评估这一新要求的价值有所启发。

4. 挑战与展望

从生物学角度看，肺肿瘤细胞最初沿着肺泡内壁生长，肺泡间隔的增厚程度很小。随着肿瘤细胞数量的增加，肺泡壁增厚并塌陷。由于肺泡被细胞侵袭和取代，结节变得更加致密，在 CT 图像上表现为亚实性或完全实性。引入 Lung-RADS 是为了标准化报告，并根据估计的恶性肿瘤风险指导 LCS 期间发现的肺结节的管理。回顾性应用 Lung-RADS 对 NLST 数据，结果显示性能得到改善，假阳性率显著降低[42]。然而，在常规临床实践中，关于 Lung-RADS 性能的数据有限[43]。研究显示，与根据 Lung-RADS 推荐预测的恶性肿瘤患病率相比，所有评估的 Lung-RADS 类别(3、4A、4B 和 4X)的恶性肿瘤发生率更高[44]。尽管如此，被归类为 Lung-RADS 4 类的支气管内结节绝大多数是良性的。

Lung-RADS 主要根据 2D 测量强调结节大小和生长。在指导癌症治疗决策方面，RECIST 中的 2D 测量比单直径测量更准确；每种情况都有不同程度的差异，这些差异可能是决策可以容忍的[45] [46] [47]。一些研究强调了二维测量的局限性，显示出显著的观察者内和观察者间变异性[48] [49] [50]。不同吸气程

度的扫描采集也会影响轴向结节的测量[51]。这些固有的测量误差可能导致对结节大小和尺寸变化的高估或低估。使用卡尺测量确定结节生长或生长不足可能是错误的，导致 Lung-RADS 分类不准确。研究结果显示，通过自动或半自动体积分析(包括测量部分实性结节的固体成分)可提高重现性[52] [53]。然而，结节边缘复杂性和不规则性的增加导致 3D 测量和 VDT 的变异性更大[54] [55]。不同软件程序之间的测量也显示出很大的差异，当使用相同的软件不一致时，很难进行比较。Lung-RADS 1.1 在平均直径测量旁边包括体积测量，以适应已经使用体积测量的实践，并为未来体积测量的标准化提供一条途径。

5. 小结

CT 具有方便迅速、分辨力高、图像清晰的特点。CT 扫描技术不断进步，使肺结节的检出率逐年上升，为诊断早期肺癌带来帮助，对提高平均生存率和降低经济成本有着重要意义。Lung-RADS 分级可以通过不同分级清晰分辨影像的表现为标准对肺结节进行重新分类，探讨单一病灶内部及边缘 CT 征象对肺结节良、恶性鉴别的价值以及有助于提高鉴别诊断肺结节良、恶性的效能。Lung-RADS 将随着新信息的出现而继续更新，以解决与临床实践中使用该系统相关的持续挑战，将给患者带来更好的护理和结果。

参考文献

[1] Lin, S., Gao, K., Gu, S., *et al*. (2021) Worldwide Trends in Cervical Cancer Incidence and Mortality, with Predictions for the Next 15 Years. *Cancer*, **127**, 4030-4039. https://doi.org/10.1002/cncr.33795

[2] Zheng, R., Zeng, H., Zuo, T., *et al*. (2016) Lung Cancer Incidence and Mortality in China, 2011. *Thoracic Cancer*, **7**, 94-99. https://doi.org/10.1111/1759-7714.12286

[3] Yang, D., Liu, Y., Bai, C., *et al*. (2020) Epidemiology of Lung Cancer and Lung Cancer Screening Programs in China and the United States. *Cancer Letters*, **468**, 82-87. https://doi.org/10.1016/j.canlet.2019.10.009

[4] Ni, Y., Huang G., Yang, X., *et al*. (2022) Microwave Ablation Treatment for Medically Inoperable Stage I Non-Small Cell Lung Cancers: Long-Term Results. *European Radiology*, **32**, 5616-5622. https://doi.org/10.1007/s00330-022-08615-8

[5] Goldstraw, P., Chansky, K., Crowley, J., *et al*. (2016) The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. *Journal of Thoracic Oncology*, **11**, 39-51. https://doi.org/10.1016/j.jtho.2015.09.009

[6] Osarogiagbon, R.U., Liao, W., Faris, N.R., *et al*. (2022) Lung Cancer Diagnosed through Screening, Lung Nodule, and Neither Program: A Prospective Observational Study of the Detecting Early Lung Cancer (DELUGE) in the Mississippi Delta Cohort. *Journal of Clinical Oncology*, **40**, 2094-2105. https://doi.org/10.1200/JCO.21.02496

[7] Bhende, M., Thakare, A., Saravanan, V., *et al*. (2022) Attention Layer-Based Multidimensional Feature Extraction for Diagnosis of Lung Cancer. *BioMed Research International*, **2022**, Article ID: 3947434. https://doi.org/10.1155/2022/3947434

[8] Gu, Y., Lu, X., Yang, L., *et al*. (2018) Automatic Lung Nodule Detection Using a 3D Deep Convolutional Neural Network Combined with a Multi-Scale Prediction Strategy in Chest CTs. *Computers in Biology and Medicine*, **103**, 220-231. https://doi.org/10.1016/j.compbiomed.2018.10.011

[9] Sathyakumar, K., Munoz, M., Singh, J., *et al*. (2020) Automated Lung Cancer Detection Using Artificial Intelligence (AI) Deep Convolutional Neural Networks: A Narrative Literature Review. *Cureus*, **12**, e10017. https://doi.org/10.7759/cureus.10017

[10] Kim, S.H., Choi, Y.H., Cho, H.H., *et al*. (2016) Comparison of Image Quality and Radiation Dose between High-Pitch Mode and Low-Pitch Mode Spiral Chest CT in Small Uncooperative Children: The Effect of Respiratory Rate. *European Radiology*, **26**, 1149-1158. https://doi.org/10.1007/s00330-015-3930-x

[11] Balata, H., Evison, M., Sharman, A., *et al*. (2019) CT Screening for Lung Cancer: Are We Ready to Implement in Europe? *Lung Cancer*, **134**, 25-33. https://doi.org/10.1016/j.lungcan.2019.05.028

[12] Prosper, A.E., Inoue, K., Brown, K., *et al*. (2021) Association of Inclusion of More Black Individuals in Lung Cancer Screening with Reduced Mortality. *JAMA Network Open*, **4**, e2119629. https://doi.org/10.1001/jamanetworkopen.2021.19629

[13] Roberts, H., Walker-Dilks, C., Sivjee, K., *et al*. (2013) Screening High-Risk Populations for Lung Cancer: Guideline Recommendations. *Journal of Thoracic Oncology*, **8**, 1232-1237. https://doi.org/10.1097/JTO.0b013e31829fd3d5

[14] Lee, J.W., Kim, H.Y., Goo, J.M., *et al*. (2018) Radiological Report of Pilot Study for the Korean Lung Cancer Screening (K-LUCAS) Project: Feasibility of Implementing Lung Imaging Reporting and Data System. *Korean Journal of Radiology*, **19**, 803-808. https://doi.org/10.3348/kjr.2018.19.4.803

[15] 樊荣荣, 刘凯, 夏晨, 等. AI 对非门控胸部 LDCT 平扫冠状动脉钙化积分危险分层的预测价值[J]. 国际医学放射学杂志, 2022, 45(1): 21-26. https://doi.org/10.19300/j.2022.L18690

[16] Pedersen, J.H., Ashraf, H., Dirksen, A., *et al*. (2009) The Danish Randomized Lung Cancer CT Screening Trial—Overall Design and Results of the Prevalence Round. *Journal of Thoracic Oncology*, **4**, 608-614. https://doi.org/10.1097/JTO.0b013e3181a0d98f

[17] Walter, J.E., Heuvelmans, M.A. and Oudkerk, M. (2017) Small Pulmonary Nodules in Baseline and Incidence Screening Rounds of Low-Dose CT Lung Cancer Screening. *Translational Lung Cancer Research*, **6**, 42-51. https://doi.org/10.21037/tlcr.2016.11.05

[18] Liu, Y., Luo, H., Qing, H., *et al*. (2019) Screening Baseline Characteristics of Early Lung Cancer on Low-Dose Computed Tomography with Computer-Aided Detection in a Chinese Population. *Cancer Epidemiology*, **62**, Article ID: 101567. https://doi.org/10.1016/j.canep.2019.101567

[19] Wilson, D.O., Weissfeld, J.L., Fuhrman, C.R., *et al*. (2008) The Pittsburgh Lung Screening Study (PLuSS): Outcomes within 3 Years of a First Computed Tomography Scan. *American Journal of Respiratory and Critical Care Medicine*, **178**, 956-961. https://doi.org/10.1164/rccm.200802-336OC

[20] Zhou, L., Zhou, Z., Liu, F., *et al*. (2022) Establishment and Validation of a Clinical Model for Diagnosing Solitary Pulmonary Nodules. *Journal of Surgical Oncology*, **126**, 1316-1329. https://doi.org/10.1002/jso.27041

[21] Horeweg, N., Nackaerts, K., Oudkerk, M., *et al*. (2013) Low-Dose Computed Tomography Screening for Lung Cancer: Results of the First Screening Round. *Journal of Comparative Effectiveness Research*, **2**, 433-436. https://doi.org/10.2217/cer.13.57

[22] De Koning, H.J., Van Der Aalst, C.M., De Jong, P.A., *et al*. (2020) Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial. *The New England Journal of Medicine*, **382**, 503-513. https://doi.org/10.1056/NEJMoa1911793

[23] Horeweg, N., Scholten, E.T., De Jong, P.A., *et al*. (2014) Detection of Lung Cancer through Low-Dose CT Screening (NELSON): A Prespecified Analysis of Screening Test Performance and Interval Cancers. *The Lancet Oncology*, **15**, 1342-1350. https://doi.org/10.1016/S1470-2045(14)70387-0

[24] Henschke, C.I., Yip, R., Yankelevitz, D.F., *et al*. (2013) Definition of a Positive Test Result in Computed Tomography Screening for Lung Cancer: A Cohort Study. *Annals of Internal Medicine*, **158**, 246-252. https://doi.org/10.7326/0003-4819-158-4-201302190-00004

[25] Kastner, J., Hossain, R., Jeudy, J., *et al*. (2021) Lung-RADS Version 1.0 versus Lung-RADS Version 1.1: Comparison of Categories Using Nodules from the National Lung Screening Trial. *Radiology*, **300**, 199-206. https://doi.org/10.1148/radiol.2021203704

[26] Pinsky, P.F., Gierada, D.S., Black, W., *et al*. (2015) Performance of Lung-RADS in the National Lung Screening Trial: A Retrospective Assessment. *Annals of Internal Medicine*, **162**, 485-491. https://doi.org/10.7326/M14-2086

[27] Lee, J., Lim, J., Kim, Y., *et al*. (2019) Development of Protocol for Korean Lung Cancer Screening Project (K-LUCAS) to Evaluate Effectiveness and Feasibility to Implement National Cancer Screening Program. *Cancer Research and Treatment*, **51**, 1285-1294. https://doi.org/10.4143/crt.2018.464

[28] Obayashi, K., Shimizu, K., Nakazawa, S., *et al*. (2018) The Impact of Histology and Ground-Glass Opacity Component on Volume Doubling Time in Primary Lung Cancer. *Journal of Thoracic Disease*, **10**, 5428-5434. https://doi.org/10.21037/jtd.2018.08.118

[29] Lee, C.T. (2015) What Do We Know about Ground-Glass Opacity Nodules in the Lung? *Translational Lung Cancer Research*, **4**, 656-659.

[30] De Hoop, B., Gietema, H., Van De Vorst, S., *et al*. (2010) Pulmonary Ground-Glass Nodules: Increase in Mass as an Early Indicator of Growth. *Radiology*, **255**, 199-206. https://doi.org/10.1148/radiol.09090571

[31] Gulati, C.M., Schreiner, A.M., Libby, D.M., *et al*. (2014) Outcomes of Unresected Ground-Glass Nodules with Cytology Suspicious for Adenocarcinoma. *Journal of Thoracic Oncology*, **9**, 685-691. https://doi.org/10.1097/JTO.0000000000000143

[32] Yankelevitz, D.F., Yip, R., Smith, J.P., *et al*. (2015) CT Screening for Lung Cancer: Nonsolid Nodules in Baseline and Annual Repeat Rounds. *Radiology*, **277**, 555-564. https://doi.org/10.1148/radiol.2015142554

[33] Veronesi, G., Travaini, L.L., Maisonneuve, P., *et al*. (2015) Positron Emission Tomography in the Diagnostic Work-Up of Screening-Detected Lung Nodules. *European Respiratory Journal*, **45**, 501-510. https://doi.org/10.1183/09031936.00066514

[34] Ahn, M.I., Gleeson, T.G., Chan, I.H., *et al*. (2010) Perifissural Nodules Seen at CT Screening for Lung Cancer. *Radiology*, **254**, 949-956. https://doi.org/10.1148/radiol.09090031

[35] De Hoop, B., Van Ginneken, B., Gietema, H. and Prokop, M. (2012) Pulmonary Perifissural Nodules on CT Scans: Rapid Growth Is Not a Predictor of Malignancy. *Radiology*, **265**, 611-616. https://doi.org/10.1148/radiol.12112351

[36] Schreuder, A., Van Ginneken, B., Scholten, E.T., *et al*. (2018) Classification of CT Pulmonary Opacities as Perifissural Nodules: Reader Variability. *Radiology*, **288**, 867-875. https://doi.org/10.1148/radiol.2018172771

[37] Macmahon, H., Naidich, D.P., Goo, J.M., *et al*. (2017) Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017. *Radiology*, **284**, 228-243. https://doi.org/10.1148/radiol.2017161659

[38] Xu, D.M., Gietema, H., De Koning, H., *et al*. (2006) Nodule Management Protocol of the NELSON Randomised Lung Cancer Screening Trial. *Lung Cancer*, **54**, 177-184. https://doi.org/10.1016/j.lungcan.2006.08.006

[39] Mcwilliams, A., Tammemagi, M.C., Mayo, J.R., *et al*. (2013) Probability of Cancer in Pulmonary Nodules Detected on First Screening CT. *The New England Journal of Medicine*, **369**, 910-919. https://doi.org/10.1056/NEJMoa1214726

[40] Shlomi, D., Ben-Avi, R., Balmor, G.R., *et al*. (2014) Screening for Lung Cancer: Time for Large-Scale Screening by Chest Computed Tomography. *European Respiratory Journal*, **44**, 217-238. https://doi.org/10.1183/09031936.00164513

[41] Li, K., Yip, R., Avila, R., *et al*. (2017) Size and Growth Assessment of Pulmonary Nodules: Consequences of the Rounding. *Journal of Thoracic Oncology*, **12**, 657-662. https://doi.org/10.1016/j.jtho.2016.12.010

[42] Chung, K., Jacobs, C., Scholten, E.T., *et al*. (2017) Malignancy Estimation of Lung-RADS Criteria for Subsolid Nodules on CT: Accuracy of Low and High Risk Spectrum When Using NLST Nodules. *European Radiology*, **27**, 4672-4679. https://doi.org/10.1007/s00330-017-4842-8

[43] Barbosa Jr., E.J.M., Yang, R. and Hershman, M. (2021) Real-World Lung Cancer CT Screening Performance, Smoking Behavior, and Adherence to Recommendations: Lung-RADS Category and Smoking Status Predict Adherence. *American Journal of Roentgenology*, **216**, 919-926. https://doi.org/10.2214/AJR.20.23637

[44] Dyer, S.C., Bartholmai, B.J. and Koo, C.W. (2020) Implications of the Updated Lung CT Screening Reporting and Data System (Lung-RADS version 1.1) for Lung Cancer Screening. *Journal of Thoracic Disease*, **12**, 6966-6977. https://doi.org/10.21037/jtd-2019-cptn-02

[45] Choi, J.H., Ahn, M.J., Rhim, H.C., *et al*. (2005) Comparison of WHO and RECIST Criteria for Response in Metastatic Colorectal Carcinoma. *Cancer Research and Treatment*, **37**, 290-293. https://doi.org/10.4143/crt.2005.37.5.290

[46] Van Persijn Van Meerten, E.L., Gelderblom, H. and Bloem, J.L. (2010) RECIST Revised: Implications for the Radiologist. A Review Article on the Modified RECIST Guideline. *European Radiology*, **20**, 1456-1467. https://doi.org/10.1007/s00330-009-1685-y

[47] Nishino, M., Jagannathan, J.P., Ramaiya, N.H., *et al*. (2010) Revised RECIST Guideline Version 1.1: What Oncologists Want to Know and What Radiologists Need to Know. *American Journal of Roentgenology*, **195**, 281-289. https://doi.org/10.2214/AJR.09.4110

[48] Revel, M.P., Bissery, A., Bienvenu, M., *et al*. (2004) Are Two-Dimensional CT Measurements of Small Noncalcified Pulmonary Nodules Reliable? *Radiology*, **231**, 453-458. https://doi.org/10.1148/radiol.2312030167

[49] Heuvelmans, M.A., Walter, J.E., Vliegenthart, R., *et al*. (2018) Disagreement of Diameter and Volume Measurements for Pulmonary Nodule Size Estimation in CT Lung Cancer Screening. *Thorax*, **73**, 779-781. https://doi.org/10.1136/thoraxjnl-2017-210770

[50] Van Riel, S.J., Sanchez, C.I., Bankier, A.A., *et al*. (2015) Observer Variability for Classification of Pulmonary Nodules on Low-Dose CT Images and Its Effect on Nodule Management. *Radiology*, **277**, 863-871. https://doi.org/10.1148/radiol.2015142700

[51] Oxnard, G.R., Zhao, B., Sima, C.S., *et al*. (2011) Variability of Lung Tumor Measurements on Repeat Computed Tomography Scans Taken within 15 Minutes. *Journal of Clinical Oncology*, **29**, 3114-3119. https://doi.org/10.1200/JCO.2010.33.7071

[52] Petrick, N., Kim, H.J., Clunie, D., *et al*. (2014) Comparison of 1D, 2D, and 3D Nodule Sizing Methods by Radiologists for Spherical and Complex Nodules on Thoracic CT Phantom Images. *Academic Radiology*, **21**, 30-40. https://doi.org/10.1016/j.acra.2013.09.020

[53] Bankier, A.A., Macmahon, H., Goo, J.M., *et al*. (2017) Recommendations for Measuring Pulmonary Nodules at CT: A Statement from the Fleischner Society. *Radiology*, **285**, 584-600. https://doi.org/10.1148/radiol.2017162894

[54] Wang, Y., Van Klaveren, R.J., Van Der Zaag-Loonen, H.J., *et al*. (2008) Effect of Nodule Characteristics on Variability of Semiautomated Volume Measurements in Pulmonary Nodules Detected in a Lung Cancer Screening Program. *Radiology*, **248**, 625-631. https://doi.org/10.1148/radiol.2482070957

[55] Gietema, H.A., Wang, Y., Xu, D., *et al*. (2006) Pulmonary Nodules Detected at Lung Cancer Screening: Interobserver Variability of Semiautomated Volume Measurements. *Radiology*, **241**, 251-257. https://doi.org/10.1148/radiol.2411050860