Various Criteria of Lung Cancer Response Evaluation: Overview

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Abstract— **Lung cancer is a widely spread disease that is really wreaking havoc these days. Therefore, clinicians should find efficient solutions to prevent the lung tumor from growing or traveling to other parts of the body. To do so, it's important to use the imaging modalities in the interest of disease evolution assessment, as time goes by. This article is concerned with an overview of the major existing anatomic criteria used over the time for response evaluation in lung tumor. In addition, this paper summarizes the concepts of RECIST, revised RECIST, and the WHO guidelines. Added to that, an examination of the correlation between the various set of criteria is presented and the shortcomings and advantages of each one are highlighted. Further, the usefulness of these guidelines for the image processing community is also studied. We aim by this paper to help the oncology community develop the treatment procedure, forecast whether a treatment has enough merit to be used by larger numbers of patients and provide a more efficient care for the patient.**

Keywords— RECIST; WHO criteria; RECIST 1.1; Lung Cancer; Advantages; Limitations; Image Processing.

I. INTRODUCTION

Imaging represents 90% of the arguments for the therapeutic choice, and indicates the therapeutic evaluation of the tumor. Assessment of the change in tumor burden is an important feature of the clinical evaluation of cancer therapeutics: both tumor shrinkage (objective response) and disease progression are useful endpoints in clinical trials. For this purpose, many definitions and assumptions of tumor response criteria have been explored over the years. In order to tell whether cancer patients improve ("respond"), stay the same ("stable") or worsen ("progression") during the treatment, different sets of published rules were defined.
Early attempts to define the objective response of a tumor to anticancer agent or drugs, were made in the early 1960's and were developed over the years. Lung cancer is the leading cause of cancer death for men and women all over the world [1]. In fact, according to the World Health Organization (WHO) rankings, lung cancer is the most commonly diagnosed cancer worldwide (1.8 million,13.0% of total) [2] and accounts for more deaths annually than breast, prostate and colon cancer combined [3]. These statics were not always so. About 150 years ago, lung cancer was a rare disease. In 1878, malignant lung tumors represented only 1% of all cancers. By 1918, the percentage has increased to almost 10% and by 1927 to more than 14% [4]. When radiation and x-ray [5] were discovered at the end of the 19th century, physicist took advantage of these discoveries to probe the human body and non-surgical cancer treatment approaches came along [6]. Surgeons and hospital radiologists started to work together. In 1968, a large amount of cancer data started to be compiled with the use of computers. Great efforts have been spent over the past 50 years.

The imaging modalities or tests that are commonly performed [7], [8] in order to determine the stage of lung cancer are: *CT scan of the chest and abdomen* [9] [10] which provides detailed pictures of lung tumor and anatomy and is important for staging and treatment planning. *PET scan* [11] [10] that uses radioactive sugar because cancer cells use sugar rapidly and is important for identifying spread to lymph nodes or other organs. *MRI scan of the brain* which is also one of the best currently available and reproducible methods to measure target lesions selected for response assessment. MRI scan of the brain may be necessary to determine if the tumor has spread to the brain.

II. QUANTITATIVE IMAGING BIOMARKERS

In order to determinate the effectiveness of new oncology drugs, a number of sets of rules and morphological criteria were developed over the years: The World Health Organization (WHO) criteria that were published since 1981 by Miller et al. [12] and continues to be used [13] even more than a decade after the introduction of Response Evaluation Criteria In Solid Tumors version 1.0 (RECIST 1.0) criteria that were published in 2000 by Therasse et al. [14] and the revised in 2009 as version 1.1 (RECIST 1.1) [15]. These sets

of criteria were developed to estimate response to cytotoxic chemotherapeutic agents [16] and to observe change in tumor size during treatment [17].

The World Health Organization (WHO) criteria are based on a two-dimensional measurement as shown in Figure 1 and the sum of the products of the longest diameters (LD) with its greatest perpendicular in the target lesion, or in other terms the surface of the rectangle that englobes the target. The objective response of a measurable disease [18] can be confirmed 4 weeks [19] after the beginning of the treatment and is depending upon the percentage of the evolution in the product of the longest diameters, four response types were identified: *Complete response (CR)-*The disappearance of all known disease [12] and all signs of cancer in response to treatment. The complete response does not always mean the cancer has been cured and is also called complete remission and that's the positive response that the treatment aims to give [20]. *Partial response (PR)-*A decrease of at least 50% from baseline (BL) in the size of a tumor [19]. *Stable disease(SD)-*Cancer that is neither decreasing nor increasing in extent or severity. According to the WHO criteria the stable disease is a decrease of lower than 50% or increase of lower than 25% with regard to the previous test [19]. *Progressive disease (PD)-*Cancer that is growing, spreading or getting worse. It is an increase of greater than 25% of one or more lesions or appearance of new lesions [19].

WHO criteria were progressively abandoned because of its lack of standardization over time. The Response Evaluation Criteria in Solid Tumor (RECIST) [21] [14] are based on the measurement of the longest diameter of lesions as shown in Figure 1; unidimensional rather than bi-dimensional measures for evaluating the tumor burden. It introduces the notion of the measurable minimal size, and the maximal number of lesions that will be taken into account (up to 10, a maximum of 5 per organ), thus, the notion of target and non-target lesion.

CT scans presented in Figure 1 are provided by Radiology service of Salah Azaiez Institute in Tunisia. The revised RECIST guideline version 1.1 (RECIST 1.1) [22] was presented by the RECIST Working Group, based in part on investigations using a database consisting of more than 6,500 patients with about 18,000 target lesions [23]. Major changes in RECIST 1.1 included lymph node LN measurement, the maximum number of target lesions, and the definition of disease progression [24].
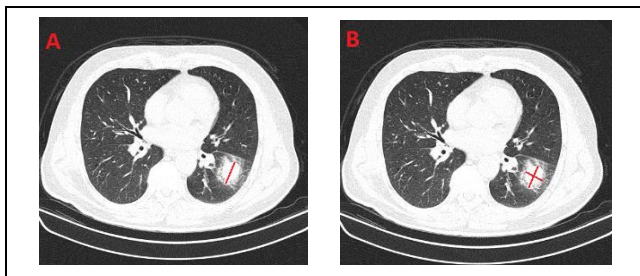

Fig. 1. A: RECIST unidimensional and B: WHO two-dimensional

The maximum number of target lesions have been reduced from ten to fine in total, and from five to two per organ.

Disease progression have been clarified [25]. RECIST 1.1 showed almost perfect agreement with RECIST 1.0 in tumor response assessment of patients with non-small cell lung cancer (NSCLC) [23].

III. RECIST 1.1

Currently, the standard metric, by which disease progression is measured, is the set of guidelines RECIST (version 1.1).

Initially, there are two types of tumor lesions: *Measurable lesions-* that can be accurately measured in at least one dimension with longest diameter ≥ 20 mm using conventional techniques or greater than 10 mm by spiral CT scan. *Non-measurable lesions-* all other lesions, including small lesions where longest diameter < 20 mm with conventional techniques or <10 mm with spiral CT scan. Only patients with measurable disease at baseline should be included in protocols where objective tumor response is the primary endpoint [26].

All measurable lesions up to a maximum of two lesions per organ and five lesions in total, representative of all involved organs should be identified as target lesions and recorded and measured at baseline [27]. Target lesions should be selected on the basis of their size (lesions with the longest diameter LD). A target lesion is a measurable lesion whose longest diameter is greater than 10 mm if it is clinically assessed or with CT, and greater than 20 mm if it is radiographically assessed. If the target lesion is a LN, the short-axis measurements should be used and recorded ≥ 15 mm.

All lesions not identified as target lesions, including pathological lymph nodes and all non-measurable lesions, should be identified as non-target lesions and be recorded at baseline [28]. Lymph nodes, if considered as a non-target lesion, should be used and recorded < 15 mm.

All lesions (or sites of disease) not identified as target lesions, including pathological lymph nodes and all non-measurable lesions, should be identified as non-target lesions and be recorded at baseline [28]. Measurement of these lesions are not required and they should be followed as 'present', 'absent' or in rare cases 'unequivocal progression'. Lymph nodes, if considered as a non-target lesion, should be used and recorded < 15 mm.

The response quantification criteria of target lesions can be: *Complete response(CR)-*Disappearance of all target lesions. *Partial Response (PR)-*At least a 30% decrease in the sum of the longest diameter of target lesions, taking as reference the baseline sum of the longest diameter. *Stable Disease (SD)-*Neither sufficient shrinkage to qualify for PD nor sufficient increase to qualify for PD, taking as reference the smallest sum LD since the treatment started. *Progressive Disease (PD)-*At least a 20% increase in the sum of the LD of target lesions, taking as reference the smallest sum LD since the treatment started or the appearance of one or more new lesions. Figure 2 below depicts the response quantification of target lesions.

Fig. 2. Schematic representation of response quantification
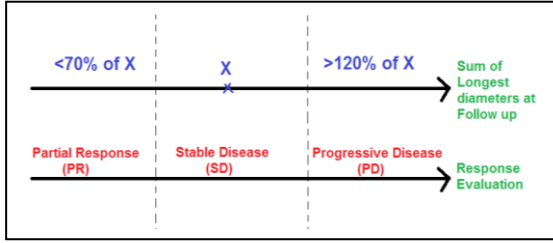
The response quantification criteria of non-target lesions can be: *Complete response (CR)*-Disappearance of all non-target lesions [29] and normalization of tumor marker level. *Incomplete response/ Stable Disease (SD)*-Persistence of one or more non-target lesion(s) or/and maintenance of tumor marker level above the normal limits**.** *Progressive Disease (PD)*-Appearance of one or more new lesions and/or unequivocal progression of existing non-target lesions.

IV. CRITICS

The table 1 summarizes the advantages and the drawbacks that WHO criteria, RECIST criteria and RECIST 1.1 criteria present in the evaluation of the tumor response to treatment of patients with lung cancer.

V. IMAGE PROCESSING COMMUNITY AND RECIST CRITERIA

RECIST criteria have been of use for the image processing community in terms of tumor measurement and growth rate computation. Levine et al. [30] used geometrical considerations from synthetic tumor data embedded in CT data to prove that RECIST criteria give relatively better results for union of ellipsoids than realistic lung tumors. Bevilacqua et al. [31] proposed a technique for measuring and classifying lung nodules. Starting with a framework that fully and automatically segment the respiratory system and semi-automatically segment pulmonary nodules using a set of synthetic data [32]. These first two steps have been established for accurate assessment of tumor progression and its classification according to its malignancy. Prescott et al. [33] emphasizes in their study that WHO and RECIST criteria are the only two quantitative imaging biomarkers for solid tumor and discuss their challenges. Emaminjad et al. [34] used chest CT scans of NSCLC patients for lung tumor segmentation, tumor-related image features measurement and cancer recurrence risk prediction. Their study highlights the difficulty faced by radiologists in interpreting a large number of CT scans and subjectively measuring tumors longest diameter and the unreliability of RECIST criteria due to the inter-reader variability. Diciotti et al. [35] proposed an estimation on nodule size that doesn't need tumor segmentation. Their method comprises a scale-space representation where lung nodules are analyzed by Laplacian of Gaussian kernels. Using a set of CT scans, RECIST criteria where utilized to prove the high correlation between the characteristic scale computed in the Laplacian of Gaussian scale-space and the diameter of the sphere that have the same volume. Brown et at. [36] presented

a Computer Aided lung nodule Detection system, with a law false positive rate and a measurement system that generates RECIST criteria reports. Paskin et al. [37] modeled a set of clinical tumors that cover various geometries and locations within the lung. The set of tumor models are meant to be used as ground truth data for volumetric methods comparison and volumetric RECIST application. Beaumont et al. [38] proposed a method to predict the reliability of assessment of lung tumor volume changes on CT scans using RECIST criteria.

CONCLUSION

We provide in this paper an exhaustive summary of lung cancer and the imaging modalities that are commonly used for its diagnosis. An overview of the various morphological criteria used for cancer response evaluation is presented followed by a comparative study between them. We described then the existing works of the literature that are concerned with the usefulness of the guideline for the image processing community. One can foresee the role of quantitative imaging biomarkers will not only continue to grow, but will also benefit significantly, in terms of accuracy, from the future advancements in medical image processing techniques.

REFERENCES

[1] E. Bullitt MD, "the web site of the american association of physics in medecine," [Online]. [Accessed 2016].

[2] C. G. Zubrod, M. Schneiderman, E. Frei, C. Brindley, B. Shnider, R. Oviedo, R. Jones, U. Jonsson, J. Colsky, T. Chalmers, B. Ferguson, M. Dederick, J. Holland, O. Selawry, W. Regelson, L. Lasagna and A. H. Owens, "APPRAISAL OF METHODS FOR THE STUDY OF CHEMOTHERAPY OF CANCER IN MAN: COMPARATIVE THERAPEUTIC TRIAL OF NITROGEN MUSTARD AND TRIETHYLENE THIOPHOSPHORAMIDE," *the Eastern Cooperative Group in Solid Tumor Chemotherapy,* vol. 11, no. 1, p. 33, 1959.

[3] S. Khokher, M. U. Qureshi and N. A. Chaudhry, "Comparison of WHO and RECIST Criteria for Evaluation of Clinical Response to Chemotherapy in Patients with Advanced Breast Cancer," *Asian Pacific Journal of Cancer Prevention,* vol. 13, pp. 3213-3218, 2012.

[4] R. L. Wahl, H. Jacene, Y. Kasamon and M. A. Lodge, "From RECIST to PERCIST: Evolving Considerations for PET Response Criteria in Solid Tumors," *The Journal of Nuclear Medecine,* vol. 50, 2009.

[5] E. Bullitt, Writer, *Strengths and Limitations of Brain Tumor Volumetric Assessment when Evaluating Tumor Treatment Response.* [Performance]. University of North Carolina-CH.

[6] P. Therasse, S. G. Arbuck, E. A. Eisenhauer, J. Wanders, R. S. Kaplan, L. Rubinstein, J. Verweij, M. V. Glabbeke, A. T. v. Oosterom, M. C. Christian and S. G. Gwyther, "new guidelines to evaluate the response to treatment in solid tumors," *Journal of the National Cancer Institute,* vol. 92, pp. 206-2016, 2 february 2000.

[7] H. Kang, H. Y. Lee, K. S. Lee and J.-H. Kim, "Imaging-Based Tumor Treatment Response Evaluation: Review of Conventional, New, and Emerging Concepts," *Korean J Radiol,* vol. 13, pp. 371-390, 2012.

[8] M. Nishino, H. Hatabu, B. E. Johnson and T. C. McLoud, "State of the Art: Response Assessment in Lung Cancer in the Era of Genomic Medecine," *Radiological Society of North America,* vol. 271, no. 11, p. 27, 2014.

[9] G. j. Gil-Su Jang et al., "Comparison of RECIST version 1.0 and 1.1 in assessment of tumor response by computed tomography in advanced gastric cancer," *Chinese Journal of Cancer Research,* p. 6, 2013.

[10] T. Berghmans, F. Pasleau, M. Paesmans, Y. Bonduele, J. Cadranel, I. C. Toth, C. Garcia, V. Giner, S. Holbrechts, J. J. Lafitte, J. Lecomte, I.

Louviaux, E. Markiewicz, A. P. Meert, M. Richez, M. Roelandts, A. Scherpereel, C. Tulippe, P. van Houtte, P. Van Schil, C. Wachters, V. Westeel and J. P. Sculier, "Surrogate markers predicting overall survival for lung cancer: ELCWP recommendations," *EUROPEAN RESPIRATORY JOURNAL,* vol. 39, no. 1, pp. 9-28, 2012.

[11] J. Cortes, J. Rodriguez, J. Diaz-Gonzalez, C. Garzon, A. Gurpide, L. Arbea, I. Gil-Bazo, V. Navarro, M. Cambeiro, A. Nicolas, S. Martin-Algarra, J. Garcia-Foncillas and E. Calvo, "Comparison of unidimensional and bidimensional measurements in metastatic non-small cell lung cancer," *British Journal of Cancer,* vol. 87, p. 158 – 160, 2002.

[12] L. Seymour and . J. Bogaerts, Interviewees, *RECIST under pressure.* [Interview]. June 2015.

[13] M. Nishino, D. M. Jackman, H. Hatabu, B. Y. Yeap, L.-A. Cioffredi, J. T. Yap, P. A. Janne, B. E. Johnson and A. D. van den Abbeele, "New Response Evaluation Criteria in Solid Tumors (RECIST)Guidelines for Advanced Non–Small Cell Lung Cancer:Comparison With Original RECIST and Impact on Assessment of Tumor Response to Targeted Therapy," *National Institutes of Health,* vol. 195(3), pp. W221-W228, 2010.

[14] H. C. Choi, J. H. Kim, H. S. Kim, S. G. Jung, S. M. Hwang, S. B. Ju and I. Yang, "Comparison of the RECIST 1.0 and RECIST 1.1 in Non-Small Cell Lung Cancer Treated with Cytotoxic Chemotherapy," *Journal of Cancer,* vol. 6, pp. 652-657, 2015.

[15] R. J. Hicks, "Role of F-FDG PET in Assessment of Response in Non–Small Cell Lung Cancer," *THE JOURNAL OF NUCLEAR MEDICINE,* vol. 50, no. 5, pp. 31S-42S, 2009.

[16] E. Ness, "RECIST: Applying the Rules," [Online].
Available: https://ccrod.cancer.gov/confluence/download/attachments/ 71041052/RECIST6.pdf. [Accessed 25 February 2016].

[17] J. Schuijf, J. Bax and E. van der Wall, "Anatomical and functional imaging techniques: basically similar or fundamentally different?," *Netherlands Heart Journal,* vol. 15, 2007.

[18] S. N. Histed, M. L. Lindenberg, E. Mena, B. Turkbey, P. L. Choyke and K. A. Kurdziel, "Review of Functional/ Anatomic Imaging in Oncology," *National Institute of Health,* vol. 33, pp. 349-361, 2013.

[19] H. S.A, P. M.C, O. D., Z. J., M. C.S, K. M.G. and G. M.S., "Comparison of CT volumetric measurement with RECIST response in patients with lung cancer," *European Journal of Rdiology,* vol. 85, pp. 524-533, 2016.

[20] Q. Ding, X. Cheng, L. Yang, Q. Zhang, J. Chen, T. Li and H. Shi, "PET/CT evaluation of response to chemotherapy in non-small cell lung cancer: PET response criteria in solid tumors (PERCIST) versus response evaluation criteria in solid tumors (RECIST)," *Journal of Thoracic Disease,* vol. 6, 2014.

[21] Y. Liu, S. Litière, E. GE de Vries, D. Sargent, L. Shankar, J. Bogaerts and L. Seymour, "The role of response evaluation criteria in solid tumour in anticancer treatment evaluation: Results of a survey in the oncology community," *European Journal of Cancer,* vol. 50, pp. 260-266, 2014.

[22] E. L. van Persijn van Meerten, H. Gelderblom and J. L. Bloem, "RECIST revised: implications for the radiologist. A review article on the modified RECIST guideline," *Eur Radiol,* vol. 20, p. 1456–1467, 2010.

[23] J. H. Kim, S. J. Min, H. J. Jang, J. W. Cho, S. H. Kim and H. S. Kim, "Comparison of RECIST 1.0 and RECIST 1.1 in Patients with Metastatic Cancer: A Pooled Analysis," *Journal of Cancer,* vol. 6, no. 4, pp. 387-393, 2015.

[24] A.-C. Toffart, D. Moro-Sibilot, S. Couraud, P. Merle, M. Perol, N. Girard, P.-J. Souquet, B. Mastroianni, G. R. Ferretti, P. Romand, P. Chatellain, A. Vesin, E. Brambilla, C. Brambilla and J.-F. Timsit, "Evaluation of RECIST in chemotherapy-treated lung cancer: the Pharmacogenoscan Study," *Toffart et al. BMC Cancer,* vol. 14, p. 989, 2014.

[25] S. R. Prasad , Writer, *Limitations of RECIST guidelines.* [Performance]. University of Texas Health Science Center at San Antonio.

[26] E. Coche, "RECIST and Beyond," *JBR - BTR,* vol. 96, pp. 167-171, 2013.

[27] D. Colombi, E. Di Lauro, M. Silva, C. Manna, C. Rossi, M. De Filippo, M. Zompatori, L. Ruffini and N. Sverzellati, "Non-small cell lung cancer after surgery and chemoradiotherapy: follow-up and response assessment," *Diagn Interv Radiol,* vol. 19, p. 447–456, 2013.

[28] M. Lin, N. Bhagat, O. Pellerin, R. Rao, R. Loffroy, R. Ardon, B. Mory, D. K. Reyes, J.-F. Geschwind and B. Manor, "Volumetric RECIST: an improved way to assess tumor response after transcatheter arterial chemoembolization (TACE)," *European Society of Radiology,* 2012.

[29] "Gefitinib," Wikipedia, the free encyclopedia, 02 April 2016. [Online]. Available: https://en.wikipedia.org/wiki/Gefitinib. [Accessed 13 April 2016].

[30] M. Tatsumi, T. Watabe, H. Kato, M. Imaizumi, E. Shimosegwa and J. Hatazawa, "PERCIST and RECIST in evaluating treatment response in lung cancer receiving gefitinib therapy," *The Journal of Nuclear Medicine,* vol. 53, p. 234, 2012.

[31] X. Ling, S. Jinglie, Y. Tang, Z. Xiao and H. Xu, "Comparing response rates using RECIST, EORTC and PERCIST criteria for response evaluation in patients with non-small-cell lung cancer," *The Journal of Nuclear Medecine,* vol. 55, p. 512, 2014.

[32] A. Sudhakar, "History of Cancer, Ancient and Modern Treatment Methods," *Journal of Cancer Science & Therapy,* vol. 1(2), pp. 1-4, 2009.

[33] I. A. f. R. o. Cancer, "Latest world cancer statitics," World Health Organization, Lyon,France, 12 December 2013.

[34] H. A. Schaitberger, T. H. Miller, R. M. Duffy, J. E. Brinkley, A. Berman , D. Prezant, A. Abdu, T. K. Adrich, D. W. Appel, M. P. Bars, A. Chandra, N. Chirakalwasan and A. Devereaux, Respiratory Diseases and the Fire Service, New York: FEMA , U.S. Fire Administration.

[35] . W. Hanspeter, "PROFILES IN TOXICOLOGY :A Short History of Lung Cancer," *TOXICOLOGICAL SCIENCES,* vol. 64, pp. 4-6, 2001.

[36] A. Assmus, Early History of X Rays, 1995.

[37] "The History of Cancer," Amercican Cancer Society, 2014.

[38] R. Rivera-Garcia, C. S. White and P. A. Templeton, "Lung Cancer: Value of Various Imaging Modalities," *Clinical Lung Cancer,* vol. 1, no. 2, pp. 130-136, 1999.

[39] "CT Scans," National Cancer Institute, [Online]. Available: http://imaging.cancer.gov/patientsandproviders/cancerimaging/ctscans. [Accessed 19 April 2016].

[40] R. L. Wahl, H. Jacene, Y. Kasamon and M. A. Lodge, "From RECIST to PERCIST: Evolving Considerations for PET Response Criteria in Solid Tumors," *The Journal of Nuclear Medecine,* vol. 50, no. 5, pp. 122S-150S, 2009.

[41] A. Miller, B. Hoogstraten, M. Staquet and A. Winkler, "Reporting Results of Cancer Treatment," *Cancer,* vol. 47, p. 211, 1981.

[42] S. Khokher, M. U. Qureshi and N. A. Chaudhry, "Comparison of WHO and RECIST Criteria for Evaluation of Clinical Response to Chemotherapy in Patients with Advanced Breast Cancer," *Asian Pacific J Cancer Prev,* vol. 13, pp. 3213-3218, 2012.

[43] "22," PAREXEL International Coporation , 2016. [Online]. Available: http://www.irrecist.com/recist/index.html. [Accessed 10 February 2016].

[44] F. D. Gonzalez-Guindalini, M. P. Botelho, C. B. Harmath, K. Sandrasegaran, F. H. Miller, R. Salem and V. Yaghmai, "Assessment of Liver Tumor Response to Therapy: Role of Quantitative Imaging," *Radiological Society of North America,* vol. 33, no. 6, pp. 1781-800, 2013.

[45] T. Temel, M. A. Hollar, M. Tann, M. D. Kohli, F. Akisik and . S. Kumaresan, "Response Criteria in Oncologic Imaging: Review of Traditional and New Criteria," *Radiological Society of North America,* vol. 33, p. 1323–1341, 2013.

[46] E. A. Gehan and M. C. Tefft, "Will There Be Resistance to the RECIST (Response Evaluation Criteria in Solid Tumors)?," *Journal of the National Cancer Institute,* vol. 92, no. 3, pp. 179-181, 2000.

[47] k. James, E. Eisenhauer, M. Christian, M. Terenziani, D. Vena, A. Muldal and P. Therasse, "Measuring Response in Solid Tumors: Unidimensional Versus Bidimensional Measurement," *Journal of the National Cancer Institute,* vol. 91, 1999.

[48] A. S. Behnaz, J. Snider, C. Eneh, G. Esposito, E. Wilson, Z. Yaniv, E.

Cohen and K. Cleary, "Quantitative CT for Volumetric Analysis of Medical Images: Initial Results for Liver Tumors," in *Medical Imaging 2010: Image Processing,*, 2010.

[49] E. EIisenhauer, P. Therasse, J. Bogaerts, L. Schwartz, D. Sargent, R. Ford, J. Dancey, S. Gwyther, M. Mooney, L. Rubinstein, L. Shankar, L. Dodd, K. Kaplan, D. Lacombe and J. Verweij, "New response evaluation criteria in solid tumours:Revised RECIST guideline (version 1.1)," *EUROPEAN JOURNAL OF CANCER,* vol. 45, p. 228 –247, 2009.

[50] H. Chalian, H. G. Tore, J. M. Horowitz, R. Salem, F. H. Miller and V. Yaghmai, "Radiologic Assessment of Response to Therapy: Comparison of RECIST Versions 1.1 and 1.0," *Radiological Society of North America,* vol. 31, no. 7, p. 2093–2105, 2011.

[51] E. L. van Persijn van Meerten, H. Gelderblom and J. L. Bloem, "RECIST revised: implications for the radiologist. A review article on the modified RECIST guideline," *Eur Radiol,* vol. 20, pp. 1456-1467, 2010.

[52] "Response Evaluation Criteria in Solid Tumors," Wikipedia, the free encyclopedia, 07 January 2016. [Online]. Available: https://en.wikipedia.org/wiki/Response_Evaluation_Criteria_in_Solid_ Tumors. [Accessed 15 January 2016].

[53] P. I. corporation, in *RECIST 1.1 Fanbook*, Federal Street Billerica, USA, PAREXEL International corporation, 2014, p. 30.

[54] "Response Evaluation Criteria in Solid Tumors (RECIST)," The Chemoth.com Website, [Online]. Available: http://chemoth.com/recist. [Accessed 03 february 2016].

[55] M. Nishino, J. P. Jagannathan, N. H. Ramaiya and A. Van den Abbeele, "Revised RECIST Guideline Version 1.1: What Oncologists Want to Know and What Radiologists Need to Know," *American Journal of Roentgenology (AJR),* vol. 195, pp. 281-289, 2010.

[56] Z. H. Levine, B. R. Galloway and A. P. Peskin, "RECIST Applied to Realistic Tumor Models," *Journal of Research of the National Institute of Standards and Technology,* vol. 116, no. 3, pp. 685-688, 2011.

[57] V. Bevilacqua, D. Ranieri, G. Nacci, G. Brunetti, P. Larizza and F. Marino, "An Innovative Soft Computing Framework to Measure and Classify Solid Pulmonary Tumors from CT Images," *Journal of Bioinformatics and Biological Engineering ,* vol. 2, no. 1, pp. 45-62, 2014.

[58] A. P. Peskin, K. Kafadar, A. Dima, J. Bernal and D. Gilsinn, "Synthetic Lung Tumor Data Sets for Comparison of Volumetric Algorithms," in *CSREA Press*, Las Vegas, Nevada, USA, 2009.

[59] P. W. Jeffrey , "Quantitative Imaging Biomarkers: The Application of Advanced Image Processing and Analysis to Clinical and Preclinical Decision Making," *Journal of Digital Imaging,* vol. 26, pp. 97-108, 2013.

[60] N. Emaminejad, W. Qian, Y. Guan, M. Tan, Y. Qiu, H. Liu and B. Zheng, "Fusion of Quantitative Image and Genomic Biomarkers to Improve Prognosis Assessment of Early Stage Lung Cancer Patients," *IEEE Transactions on Biomedical Engineering ,* vol. 65, no. 5, pp. 1034-1043, 2016.

[61] S. Diciotti, S. Lombardo, G. Coppini, L. Grassi, M. Falchini and M. Mascalchi, "The LoG Characteristic Scale: A Consistent Measurement of Lung Nodule Size in CT Imaging," *IEEE TRANSACTIONS ON MEDICAL IMAGING,* vol. 29, no. 2, pp. 397- 409, 2010.

[62] M. S. Brown, P. Lo, J. G. Goldin, E. Barnoy, G. H. J. Kim, M. F. McNitt-Gray and D. R. Aberle, "Toward clinically usable CAD for lung cancer screening with computed tomography," *European Radiology,* vol. 24, pp. 2719-2728, 2014.

[63] A. P. P. A. Dima, "Modeling Clinical Tumors to Create Reference Data for Tumor Volume Measurement," in *ISVC*, Las Vegas, NV, USA, 2010.

[64] H. Beaumont, S. Souchet, J. M. Labatte, A. Iannessi and A. W. Tolcher, "Changes of lung tumour volume on CT -prediction of the reliability of assessments," *Cancer Imaging ,* vol. 15, no. 17, 2015.

TABLE I. SUMMARIZATION OF ADVANTAGES AND DRAWBACKS OF TUMOR RESPONSE EVALUATION CRITERIA TO LUNG CANCER TREATMENT.

Method	Ref.	Advantages	Ref.	Limitations
WHO	[39]	-Relatively easy and fast to do (4 mouseclicks, one multiplication).	[14]	-The integration of the change in size of measurable lesions into response assessment vary among research groups.
	[20]	-It's possible to determine the quantity of the effect the treatment upon the tumor.	[14]	-The minimum lesion size and number of lesions per organ to be measured differ from a research group to another.
	[39]	-The distance calculation between two points is generally available.	[14]	- The progressive disease is defined as the considerable variation in only one lesion by some researcher groups and defined as the considerable variation of overall tumor load by others.
	[39]	-Better detection of the change in tumor than RECIST.	[14]	- The integration of three-dimensional measures into response assessment became confusing since the arrival of new imaging modalities like computed tomography CT and magnetic resonance imaging MRI.
	[20] [40]	-It's possible to compare drugs occording to their effectivity.		
		-Even though the WHO criteria are old, they are still beeing practiced and are effective in many clinical response evaluation.	[43]	-The volume measurements are not included in the WHO criteria partly because of the limitation of the imaging techniques as well as the restriction of available measurement methods.
	[41]	-WHO criteria shows progression of tumor more rapidly than RECIST.	[7]	-Instable results when acquisition of slice angle and assessment of tumor cavitation.
	[42]	-WHO criteria are more sensitive then other sets of criteria to changes in tumor volume.	[20]	-The planning of such studies required too much time.
RECIST 1.0	[23]	-RECIST 1.0 has been widely accepted as a standardized measure of tumor response, particularly in oncologic clinical trials with objective response or time to progression as primary endpoints.	[49]	-The issues that were raises on RECIST 1.0 includes the total number of lesions to be assessed, the assessment of LNs and the utility of newer imaging technologies such as multi-detector computed tomography (MDCT) and positron emission tomography (PET).
	[40]	-The application of RECIST criteria is simpler and more convenient than the WHO criteria as well as its calculation.	[43]	-The number of target lesions to be treated is quite big.
	[44]		[50]	-The step of confirmation can waste a lot of time.
	[45]		[51]	-Lymph nodes are not adquatly assessed.
	[40]	-The response evaluation is standardized.	[10]	-The imaging guidance is missing (ei .what imaging modalities should be uses? Functional imaging such as PET, SPECT,etc .. or anatomical imaging such as CT, MRI,etc ..)
	[46]	-There is no major discrepancy with the WHO criteria (especially for NSCLC patients) which makes it easier for clinicians in the application of response evaluation criteria.	[52]	-Uni-dimensional RECIST criteria does not help predict overall survival as accurately as volumetric measurements.
	[47]		[53]	-RECIST is not the most sensitive set criteria to detect complete remission (e.g. PERCIST is a better detector of complete response).
	[48]	-It's an earlier endpoint than survival. So it's really a surrogate.	[54]	-Non applicability of RECIST in certain disease types (e.g. brain tumor, lymphoma, bone lesions).
RECIST 1.1	[46]	-Its major advantage over earlier methods of response was simplifying the number of lesions that had to be measured and types of measurement she took: one measurement instead of two measurements and two lesions in each organ instead of up to ten. In brief, RECIST 1.1 were published to simplify, optimize and standardize the original criteria.	[58]	-One of the several weaknesses that RECIST has is that it's only for solid tumors. As a matter of fact, there is no criteria for non-solid tumors, especially that, in some cancers, tumors can change from solid to non-solid.
	[55]		[59]	- RECIST also does not treat the case where the tumor growth is non-spherical or asymmetric.
	[41]		[46]	-RECIST 1.1 can be misleading in some cases
			[60]	
	[56]	-Since RECIST 1.1 assess a maximum of 5 tumors (vs. 10 in RECIST), they result in a higher complete response rate than the original RECIST criteria (at least in lymph nodes).	[46] [61]	-RECIST 1.1 can generate a mixed response (i.e. some lesions become bigger and others become smaller and sometimes there is a new lesion) especially when immune treatments are being used. However, if you wait long enough, the tumor may disappear and thus the response may even be complete.
	[57] [48]	-RECIST 1.1 relatively performs the best prediction of overall survival	[62] [63] [64]	-RECIST criteria use single 2D slice plane, ignoring the fact that tumors are non-homogenous and are 3D structures.