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Revisiting the relationship between tumour volume and diameter in advanced NSCLC patients: An exercise to maximize the utility of each measure to assess response to therapy

M. Nishino^{a,*}, D.M. Jackman^b, P.J. DiPiro^a, H. Hatabu^a, P.A. Jänne^b, and B.E. Johnson^b

^aDepartment of Radiology, Dana-Farber Cancer Institute and Brigham and Women's Hospital, 450 Brookline Ave., 75 Francis St., Boston, MA 02215, USA

^bDepartment of Medical Oncology and Department of Medicine, Dana-Farber Cancer Institute and Brigham and Women's Hospital, 450 Brookline Ave., Boston, MA 02215, USA

Abstract

AIM—To revisit the presumed relationship between tumour diameter and volume in advanced non-small-cell lung cancer (NSCLC) patients, and determine whether the measured volume using volume-analysis software and its proportional changes during therapy matches with the calculated volume obtained from the presumed relationship and results in concordant response assessment.

MATERIALS AND METHODS—Twenty-three patients with stage IIIB/IV NSCLC with a total of 53 measurable lung lesions, treated in a phase II trial of erlotinib, were studied with institutional review board approval. Tumour volume and diameter were measured at baseline and at the first follow-up computed tomography (CT) examination using volume-analysis software. Using the measured diameter ($2r$) and the equation, calculated volume was obtained as $(4/3) \pi r^3$ at baseline and at the follow-up. Percent volume change was obtained by comparing to baseline for measured and calculated volumes, and response assessment was assigned.

RESULTS—The measured volume was significantly smaller than the calculated volume at baseline (median 11,488.9 mm³ versus 17,148.6 mm³; $p < 0.0001$), with a concordance correlation coefficient (CCC) of 0.7022. At follow-up, the measured volume was once again significantly smaller than the calculated volume (median 6573.5 mm³ versus 9198.1 mm³; $p = 0.0022$), with a CCC of 0.7408. Response assessment by calculated versus measured volume changes had only moderate agreement (weighted $\kappa = 0.545$), with discordant assessment results in 20% (8/40) of lesions.

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*Guarantor and correspondent: M. Nishino, Department of Radiology, Dana-Farber Cancer Institute and Brigham and Women's Hospital, 450 Brookline Ave., Boston, MA 02215, USA. Tel.: +1 617 582 7163; fax: +1 617 582 8574. Mizuki_Nishino@dfci.harvard.edu (M. Nishino).

Conflicts of interest

Mizuki Nishino, Pamela J. DiPiro: Nothing to disclose.

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CONCLUSION—Calculated volume based on the presumed relationship significantly differed from the measured volume in advanced NSCLC patients, with only moderate concordance in response assessment, indicating the limitations of presumed relationship.

Introduction

Since described in the original Response Evaluation Criteria In Solid Tumors (RECIST; version 1.0, Appendix II) back in 2000, the relationship between change in diameter and volume of the tumours is based on the assumption that tumours are spherical.¹ Based on the assumption, when the diameter is $2r$, the volume is $(4/3)\pi r^3$.¹ The calculations are based on the assumption that proportional changes of tumour volume and product correspond to changes in tumour diameter, and vice versa. For example, a 30% decrease in diameter ($2r$) is presumed to correspond to a 65% decrease of volume; a 20% increase in diameter ($2r$) is presumed to correspond to a 73% increase of volume if the tumours are spherical.¹ This presumed relationship and the corresponding values between volume and diameter have been widely recognized among radiologists and oncologists, and cited and utilized in multiple studies of tumour measurements in lung cancer and other solid tumours.^{2–8} However, this presumed relationship will likely overestimate the volume, as the longest diameter is used to represent size and tumours are often not spherical. Therefore, it is also likely that the presumed percent changes of volume corresponding to size change are overestimated.

With advances in multidetector computed tomography (MDCT) technology in the past decades, tumour volume measurements from contiguous CT data have been made possible and are under active investigation to characterize tumour response, especially in patients with lung cancer.^{2–4} A method for CT tumour volume measurements of advanced non-small-cell lung cancer (NSCLC) patients using clinical chest CT and Food and Drug Administration (FDA)-approved software has previously been established. In a study of reproducibility of the method, volume measurements were more reproducible than uni-dimensional and bi-dimensional size measurements.⁴ The results are consistent with other reports studying similar topics in lung cancer.^{2,3,9,10} Using the volume measurement technique, the present authors demonstrated the association between proportional tumour volume decrease at 8 weeks and overall survival in advanced NSCLC patients treated with a first-line epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI); patients with greater proportional volume decrease had longer survival, indicating that tumour volume can serve as an early marker for survival.⁸

Given that it has become practical to obtain tumour volume using volumetrically acquired MDCT data in lung cancer patients to assess response to anti-cancer therapy and predict survival, it is worthwhile revisiting the relationship between tumour diameter and volume in patients with lung cancer whose tumours were assessed by volume and diameter measurements, to investigate whether the volume and its proportional changes during therapy obtained by tumour volume measurements using volume analysis software matches with the calculated values obtained by the equation described in RECIST1.0.

It was hypothesized that the tumour volume obtained by actual measurement was different from the calculated value and likely to be smaller as the diameter used in RECIST is the longest diameter of the tumour. It was also hypothesized that the difference between the measured and calculated volumes were larger for larger tumours. To investigate these hypotheses the percent changes of measured and calculated values for volume and diameter at follow-up CT during therapy in reference to baseline were compared, and the concordance of response assessment by measured versus calculated values was investigated.

Materials and methods

Patients

The study population consisted of 23 patients with histologically or cytologically confirmed stage IIIB/IV NSCLC with at least one measurable lung lesion (≥ 1 cm in the longest diameter as defined by RECIST), with a total of 53 lesions (one to seven lesions per patient, average 2.3 lesions), treated in a phase II trial of first-line erlotinib at the Dana-Farber Cancer Institute with the approval of the Institutional Review Board.^{4,11} In this cohort, the inter- and intra-observer variability of the measurements using CT tumour volume measurements by commercially available, FDA-approved volume analysis software and clinical chest CT was previously assessed.⁴ The location of the lesions was intraparenchymal in 25, pleura/fissure attached in 18, and juxtavascular in 10 lesions; adjacent atelectasis was present in 17 lesions, as described previously.⁴

Chest CT examinations

CT examinations of the chest were performed at baseline and after every 8 weeks of therapy to determine response to erlotinib.^{4,11} As described previously, the clinical chest CT protocol using a four-row MDCT machine (Volume Zoom; Siemens Medical Solutions, Forchheim, Germany) was used with the following parameters: 120 kVp, 165 mAs, 2.5 mm scanning thickness, and 0.5 s exposure time.⁴ Patients were scanned in the supine position at end-inspiration, after administration of 100 ml iopromide (300 mg iodine/ml; Ultravist 300, Bayer HealthCare Pharmaceuticals, Wayne, NJ, USA) unless medically contraindicated. The axial images (5 or 7 mm thickness) were reconstructed and were transferred to a workstation with three-dimensional medical visualization and analysis software (Vitrea 2, version 4.0, Vital Images, Minnetonka, MN, USA) for analysis.⁴

Tumour volume and diameter measurements

Tumour volume measurements were performed by a board-certified radiologist with expertise in thoracic and oncologic imaging (M.N.), and the longest diameter and volume of each tumour were measured using the volume analysis software (Vitrea 2), as previously described.⁴ The reader also manually measured the longest diameter and the longest perpendicular diameter of the target lesion on a CT image that demonstrated the longest diameter of the lesion, using a calliper-type measurement tool on the Vitrea Workstation.⁴ Fifteen patients (with a total of 40 lesions) had the first follow-up CT during the trial. In these 15 patients, the reader also performed diameter and volume measurements on the first follow-up CT performed at 8 weeks of erlotinib therapy, to assess volume and diameter changes during therapy.

Calculating volume and diameters from the measured values

The calculated volume at baseline, $V_c(0)$, was obtained for the 53 lesions, using the measured baseline longest diameter, $D_m(0)$, and the equation described in the Appendix of RECIST1.0¹:

$$V_c(0) = (4/3)\pi r^3 = (4/3)\pi(D_m(0)/2)^3 = D_m(0)^3\pi/6$$

Similarly, the calculated volume at the first follow-up, $V_c(1)$, was obtained for the 40 lesions, using the equation and the measured longest diameter at follow-up, $D_m(1)$:

$$V_c(1) = D_m(1)^3\pi/6$$

The percent changes of measured and calculated volume [% $V_m(1)$ and % $V_c(1)$] at the first follow-up CT were obtained in reference to the baseline.

$$\%V_m(1) = [V_m(1) - V_m(0)]/V_m(0)$$

$$\%V_c(1) = [V_c(1) - V_c(0)]/V_c(0)$$

In addition, using the same equation, the calculated diameters at baseline, $D_c(0)$, and at the first follow-up, $D_c(1)$, were obtained from the measured volumes at baseline, $V_m(0)$, and at the first follow-up, $V_m(1)$, as follows:

$$D_c(0) = 2(3V_m(0)/4\pi)^{1/3}$$

$$D_c(1) = 2(3V_m(1)/4\pi)^{1/3}$$

The percent changes of measured and calculated diameter [% $D_m(1)$ and % $D_c(1)$] at the first follow-up CT were obtained in reference to the baseline.

$$\%D_m(1) = [D_m(1) - D_m(0)]/D_m(0)$$

$$\%D_c(1) = [D_c(1) - D_c(0)]/D_c(0)$$

Response assessment using measured and calculated values at the first follow-up

Response assessment was assigned based on the percent change of the diameter using measured and calculated values obtained above [% $D_m(1)$ and % $D_c(1)$], according to the cut-off values defined in the RECIST guideline [30% decrease for partial response (PR), 20% increase for progressive disease (PD)]. Response assessment was also assigned based on the percent change of volume using measured and calculated values [% $V_m(1)$ and % $V_c(1)$], according to the scaled cut-off values described in RECIST (65% decrease for PR, 73% increase for PD).¹

Statistical analysis

Agreement between measured and calculated values for diameter and volume were assessed using concordance correlation coefficients (CCCs).^{3,4} Assuming two measurements have mean u_1 and u_2 , with variance σ_1^2 , σ_2^2 , and covariance σ_{12} ,

$CCC = (2\sigma_{12}) / [\sigma_1^2 + \sigma_2^2 + (u_1 - u_2)^2]$. CCCs are composed of a measure of precision (how far each pair of measurements deviates from the best-fit line through the data) and a measure of accuracy (the distance between the best-fit line and the 45 line through the origin). A value of 1 indicates perfect agreement and -1 indicates perfect reversed agreement.^{3,4}

The percentage changes at the first follow-up between measured and calculated values were also compared using Spearman's correlation. A weighted kappa analysis was performed to assess the level of agreement between responses by measured and calculated changes. Agreement between the two assessments was categorized as poor ($\kappa_w < 0$), slight ($\kappa_w = 0-0.20$), fair ($\kappa_w = 0.21-0.40$), moderate ($\kappa_w = 0.41-0.60$), substantial ($\kappa_w = 0.61-0.80$), and almost perfect ($\kappa_w > 0.80$). All p -values were based on a two-sided hypothesis. A p -value of <0.05 was considered to be significant.

Results

Measured versus calculated tumour diameter and volume at baseline

The measured volume was significantly smaller than the calculated volume (median 11,488.9 mm³ versus 17,148.6 mm³, respectively; $p < 0.0001$, Wilcoxon's sign rank test). Fig. 1 represents the relationship between the measured and calculated values for tumour diameter (Fig. 1a) and volume (Fig. 1b). The CCC for the measured and calculated diameters was 0.8871 (95%CI: 0.8359–0.9231). The CCC for the measured and calculated volumes was 0.7022 (95%CI: 0.6155–0.7722). When the measured and calculated volumes were plotted against the measured diameter (Fig. 2), the difference was larger for larger diameter tumours.

Measured and calculated tumour diameter and volume at the first follow-up

There were statistically significant differences between measured and calculated tumour diameter, as well as between measured and calculated tumour volume on the first follow-up CT examinations in 40 eligible lesions ($p = 0.0027$, 0.0022 , respectively, Wilcoxon's sign rank test). The measured volume was significantly smaller than the calculated volume (median 6573.5 mm³ versus 9198.1 mm³, respectively). The CCC was 0.9007 (95%CI: 0.8368–0.9404) for the measured and calculated tumour diameters (Fig. 3a), and was 0.7408 (95%CI: 0.587–0.8431) for the measured and calculated tumour volumes (Fig. 3b).

Response assessment at the first follow-up using measured versus calculated values

The percent changes on the first follow-up CT examinations in reference to baseline were plotted for tumour diameter (Fig. 4a) using the measured diameter and the diameter calculated from measured volume, and for tumour volume (Fig. 4b) using the measured volume and the volume calculated from the measured diameter. The concordance of response assessment using measured and calculated values was assessed. The waterfall plots of the measured and calculated percent changes of each lesion are shown in Fig. 5, for tumour diameter (Fig. 5a) and for tumour volume (Fig. 5b). Of the 40 lesions, eight lesions (20%) had discordant response assessments between the measured and calculated changes (Figs. 4 and 5, Tables 1 and 2). In the weighted κ analysis, the weighted κ -value was 0.545, indicating moderate agreement between the responses using the measured versus calculated percent changes. As the calculation between the diameter and the volume was based on the same equation, $V = (4/3)\pi r^3$, Tables 1 and 2 are mirror images of each other and yield the same weighted κ -value for response assessment results.

Discussion

Although investigations of tumour volume measurements to date often cite the relationship between changes in diameter and volume described in RECIST1.0, there has been no systematic study comparing the measured and calculated values for tumour volume and diameter in advanced NSCLC patients. The present study demonstrated that there are significant differences between measured and calculated values for both tumour diameter and volume, and that the response assessment using measured versus calculated values can be discrepant, with only moderate agreement. The results delineate the limitations of the assumed relationship between tumour volume and diameter, which was published more than a decade ago, and emphasize the importance of obtaining and evaluating the actual measured values rather than the calculated values for tumour measurements and response assessment. Awareness of such limitations is particularly important in evaluating advanced tumours, as tumours tend to become heterogeneous as they grow and likely become less spherical. The present study also suggests that the discussions of tumour volume and diameter changes to assess tumour response and progression during therapy may not necessarily have to depend on the presumed relationship, especially investigating the relevant cut-off values for the proportional changes of tumour volume and diameter.

Measured versus calculated values were significantly different at baseline as well as at the first follow-up, both for tumour diameter and volume, with the measured volume being significantly smaller than the calculated volume. The results were as expected, as the relationship between diameter and volume assume that tumours are spherical and that the half of the longest diameter used in RECIST represents the radius of the sphere.¹ Although not surprising, the results clearly demonstrate the discrepancy between the measured and calculated values, which arose from the discrepancy between the assumption and the reality; tumours are often not spherical, rather, they have an irregular and heterogeneous shape. The difference between the measured and calculated volume was larger for larger-diameter tumours, indicating that the discrepancy is more important in larger, advanced-stage tumours.

As tumour response assessment is based on the percent change of measurements, the percent changes of measured versus calculated diameters, as well as measured and calculated volumes, at the first follow-up in reference to baseline were further investigated, as an exercise to assess the impact of the discrepancy of measured versus calculated values in response assessment. The response assessment by measured versus calculated values had only moderate agreement (weighted $\kappa = 0.545$). The agreement was much lower compared to other studies assessing the agreement of response assessment between two different response assessment criteria, RECIST1.0 and 1.1, in advanced NSCLC patients, where the agreement was almost perfect, with weighted κ -values of 0.905,¹² and 0.970.¹³ Given the results, calculated values, either the volume calculated from the diameter or the diameter calculated from the volume, should not be used for response assessment.

There has been increasing attempts to utilize tumour volume measurements in response assessment in solid tumours including lung cancer, and multiple reports have been published on this topic, in terms of reproducibility,^{3,4,9,10} association of tumour genotype,¹⁴ and

association with clinical outcome.^{5–8,15–17} Many reports describing tumour volume measurements based their discussions on the relationship between diameter and volume described in RECIST1.0 in 2000, on comparison of the size and volume of the tumour, and comparing the threshold of response and progression for changes during therapy.^{2–8} In the present authors' experience of presenting tumour volume measurement data in advanced NSCLC patients, one of the most frequently asked question was how the tumour volume data compared with tumour size (diameter), when converted to an uni-dimensional measure using the equation described in RECIST1.0. The question made us realize the impact of the relationship described in 2000 that remains to date, and provided the motivation to revisit the relationship using the measured volume data.

Given the increasing availability of advanced MDCT technology and volume-analysis software with high reproducibility, it is expected that tumour volume measurements will be performed more widely in clinical practice.^{3–5} Given the discrepancy of measured and calculated data in response assessment, caution should be applied in converting the percent changes in volume into the percent change in size and vice versa. Based on the present data, a 65% decrease in volume is not necessarily a 30% decrease in diameter, and a 73% increase in volume is not necessarily a 20% increase in diameter. Rather than converting the values using the equation, it is time to interpret volume as volume, and diameter as diameter; although volume and diameter are related to each other, each of the measures has unique advantages and disadvantages, and should be applied appropriately in various settings of oncological imaging and response assessment.^{4,18} For example, tumour diameters can be measured easily without advanced equipment and, therefore, can be applied widely with ease, whereas measuring one dimension on one axial plane of the irregular tumour with heterogeneous growth may not be able to detect changes of tumour burden during therapy.¹⁸ Tumour volume, on the other hand, has an advantage of incorporating the volume of the entire lesion; however, this requires software and equipment specifically designed for the task. The important discussion going forward is not whether volume is better than diameter, but which of the measures should be used when and how, in order to maximize the contribution of imaging and response assessment to the cancer patient care.

Another important issue in applying tumour volume and diameter measurements in response assessment is measurement variability. As demonstrated by multiple investigations, variability of tumour volume measurements is smaller than that of diameter measurements,^{3,4,9,10} and is much smaller than the range, –65% and +73%, which were presumed to correspond to –30% and +20% diameter changes. As changes beyond measurement variability can be considered to represent true change in tumour burden, it is important to be aware of the range of variability of each technique to accurately interpret the data. It is also important to note the variability may be cohort specific, and depend of types and stages of tumour.¹⁸ In addition, it is ultimately necessary to identify a reliable threshold for volume or size changes that is associated with clinical outcome, including progression-free survival and overall survival.

Limitations of the present study include a retrospective design and a small number of patients treated at a single institution. The study is based on measurements from one radiologist, because intra- and interobserver measurement variability has already been

studied and published using the same technique.⁴ Although thinner section thickness is preferred for volume measurements in general, the study utilized the clinical chest CT with 5 or 7 mm section thickness, which is another limitation of the study. The results of the study should be interpreted in the context of the study design.

In conclusion, calculated tumour volume and diameter based on the equation of presumed relationship were significantly different from the measured values in advanced NSCLC patients. Response assessment using calculated values were only moderately concordant with that using measured values, indicating the limitations of the presumed relationship of volume and diameter to assess response to therapy. Going forward, the emphasis should be placed on how to maximize the utility of tumour volume and diameter measurements, making use of advantages and complementing disadvantages of each measure.

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References

1. Therasse P, Arbuck SG, Eisenhauer EA, et al. New guidelines to evaluate the response to treatment in solid tumors: European Organization for Research and Treatment of Cancer, National Cancer Institute of the United States, National Cancer Institute of Canada. *J Natl Cancer Inst.* 2000; 92:205–216. [PubMed: 10655437]
2. Zhao B, Schwartz LH, Moskowitz CS, et al. Lung cancer: computerized quantification of tumor response—initial results. *Radiology.* 2006; 241:892–898. [PubMed: 17114630]
3. Zhao B, James LP, Moskowitz CS, et al. Evaluating variability in tumor measurements from same-day repeat CT scans of patients with non-small cell lung cancer. *Radiology.* 2009; 252:263–272. [PubMed: 19561260]
4. Nishino M, Guo M, Jackman DM, et al. CT tumor volume measurement in advanced non-small-cell lung cancer: performance characteristics of emerging clinical tool. *Acad Radiol.* 2011; 18:54–62. [PubMed: 21036632]
5. Rothe JH, Grieser C, Lehmkuhl L, et al. Size determination and response assessment of liver metastases with computed tomography-comparison of RECIST and volumetric algorithms. *Eur J Radiol.* 2013; 82:1831–1839. [PubMed: 22717124]
6. Warren KE, Patronas N, Aikin AA, et al. Comparison of one- two-, and three-dimensional measurements of childhood brain tumors. *J Natl Cancer Inst.* 2001; 93:1401–1405. [PubMed: 11562391]
7. Shah GD, Kesari S, Xu R, et al. Comparison of linear and volumetric criteria in assessing tumor response in adult high-grade gliomas. *Neuro Oncol.* 2006; 8:38–46. [PubMed: 16443946]
8. Nishino M, Dahlberg SE, Cardarella S, et al. Tumor volume decrease at 8 weeks predicts survival in EGFR-mutant advanced non-small-cell lung cancer patients treated with EGFR tyrosine kinase inhibitor. *J Thorac Oncol.* 2013; 8:1059–1068. [PubMed: 23787800]
9. Mozley PD, Schwartz LH, Bendtsen C, et al. Change in lung tumor volume as a biomarker of treatment response: a critical review of the evidence. *Ann Oncol.* 2010; 21:1751–1755. [PubMed: 20332135]
10. Mozley PD, Bendtsen C, Zhao B, et al. Measurement of tumor volumes improves RECIST-based response assessments in advanced lung cancer. *Transl Oncol.* 2012; 5:19–25. [PubMed: 22348172]

11. Jackman DM, Yeap BY, Lindeman NI, et al. Phase II clinical trial of chemotherapy-naïve patients > or $\frac{1}{4}$ 70 years of age treated with erlotinib for advanced non-small-cell lung cancer. *J Clin Oncol*. 2007; 25:760–766. [PubMed: 17228019]
12. Nishino M, Jackman DM, Hatabu H, et al. 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. *AJR Am J Roentgenol*. 2010; 195:W221–W228. [PubMed: 20729419]
13. Nishino M, Cardarella S, Jackman DM, et al. RECIST 1.1 in NSCLC patients with EGFR mutations treated with EGFR tyrosine kinase inhibitors: comparison with RECIST 1.0. *AJR Am J Roentgenol*. 2013; 201:W64–W71. [PubMed: 23789698]
14. Zhao B, Oxnard GR, Moskowitz CS, et al. A pilot study of volume measurement as a method of tumor response evaluation to aid biomarker development. *Clin Cancer Res*. 2010; 16:4647–4653. [PubMed: 20534736]
15. Dehing-Oberije C, De Ruyscher D, van der Weide H, et al. Tumor volume combined with number of positive lymph node stations is a more important prognostic factor than TNM stage for survival of non-small-cell lung cancer patients treated with (chemo)radiotherapy. *Int J Radiat Oncol Biol Phys*. 2008; 70:1039–1044. [PubMed: 17889446]
16. Alexander BM, Othus M, Caglar HB, et al. Tumor volume is a prognostic factor in non-small-cell lung cancer treated with chemoradiotherapy. *Int J Radiat Oncol Biol Phys*. 2011; 79:1381–1387. [PubMed: 20605346]
17. Kozak MM, Murphy JD, Schipper ML, et al. Tumor volume as a potential imaging-based risk-stratification factor in trimodality therapy for locally advanced non-small cell lung cancer. *J Thorac Oncol*. 2011; 6:920–926. [PubMed: 21774104]
18. Nishino M, Jagannathan JP, Krajewski KM, et al. Personalized tumor response assessment in the era of molecular medicine: cancer-specific and therapy-specific response criteria to complement pitfalls of RECIST. *AJR Am J Roentgenol*. 2012; 198:737–745. [PubMed: 22451534]

Figure 1.

The relationship between the measured and calculated values for tumour diameter (Fig. 1a) and volume (Fig. 1b) at baseline. The measured volume was significantly smaller than the calculated volume (median 11,488.9 mm³ versus 17,148.6 mm³, respectively; $p < 0.0001$, Wilcoxon's sign rank test). The CCC for the measured and calculated diameter was 0.8871 (95% CI: 0.8359–0.9231). The CCC for the measured and calculated volume was 0.7022 (95% CI: 0.6155–0.7722).

Figure 2.

The measured volumes (triangle) and the calculated volumes (square) were plotted against the measured diameter. The difference between the measured and calculated values was larger for larger diameter tumours.

Figure 3.

The relationship between the measured and calculated values for tumour diameter (a) and volume (b) at the first follow-up. The measured volume was significantly smaller than the calculated volume (median 6573.5 mm³ versus 9198.1 mm³, respectively; $p < 0.0022$, Wilcoxon's sign rank test). The CCC was 0.9007 (95%CI: 0.8368–0.9404) for the measured and calculated tumour diameters (a), and was 0.7408 (95%CI: 0.587–0.8431) for the measured and calculated tumour volumes (b).

Figure 4.

Scatter plot of the measured and calculated percent changes for tumour diameter (a) and for tumour volume (b) on the first follow-up images in reference to baseline. The eight observations (8/40, 20%) highlighted by circles represent discordant results between the response assessments using the measured and calculated values (the weighted $\kappa = 0.545$).

Figure 5.

The waterfall plots of the measured and calculated percent changes of the 40 lesions, for tumour diameter (a) and for tumour volume (b). Eight lesions (20%) with discordant response assessment between the measured and calculated changes are indicated by the asterisks.

Table 1

Concordance between responses by the percent changes of measured diameter versus calculated diameter.

Response using calculated diameter from measured volume	Response by measured diameter		
	PR	SD	PD
PR	2	0	0
SD	2	27	3
PD	0	3	3

Weighted kappa: 0.545.

The number in each cell represents the number of lesions with corresponding response assessment (PR, SD, or PD) on the follow-up scan based on measured versus calculated diameters.

PR, partial response; SD, stable disease; PD, progressive disease.

Table 2

Concordance between responses by the percent changes of measured volume versus calculated volume.

Response using calculated volume from measured diameter	Response by measured volume		
	PR	SD	PD
PR	2	2	0
SD	0	27	3
PD	0	3	3

Weighted kappa: 0.545.

The number in each cell represents the number of lesions with corresponding response assessment (PR, SD, or PD) on the follow-up scan based on measured versus calculated volume.

PR, partial response; SD, stable disease; PD, progressive disease.