Value of RECIST (Unidimensional), WHO (Bidimensional) and Volumetric Measures of Breast Tumor Response on MRI for Predicting Recurrence Free Survival in Patients Undergoing Preoperative Chemotherapy

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Introduction

Assessment of response to preoperative chemotherapy has traditionally relied on bidimensional tumor measurement guidelines proposed by the World Health Organization (WHO) in their 1979 Handbook For Reporting Results of Cancer Treatment. In primary breast cancer, these measurements are typically based on palpation at physical exam, a technique that is susceptible to clinician variability, breast size and composition, and factors such as post-biopsy swelling. In 2000, Therasse et al. introduced a unidimensional technique termed Response Evaluation Criteria in Solid Tumors, or RECIST. RECIST adopted a simplified measurement method using the sum of longest diameters of target lesions, whereas previous WHO criteria used the sum of the products of the two longest diameters in perpendicular dimensions. Studies in the metastatic setting indicate good agreement between response classification by WHO and RECIST criteria, and a CT phantom study demonstrated 100% agreement between RECIST and volume measures [1-3]. MRI allows volumetric assessment of tumor size, and previous studies have shown that tumor volume is a promising indicator of treatment response and overall patient outcome [4]. The purpose of this study was to compare the value of RECIST (unidimensional), WHO (bidimensional), and volumetric measures of breast tumor response for predicting recurrence free survival (RFS) in patients undergoing preoperative chemotherapy.

Methods

Patients: Sixty-one patients undergoing preoperative treatment for locally advanced breast cancer were imaged with MRI before, after one cycle, and after four cycles of chemotherapy. Patients with inflammatory cancer, deemed non-measurable by RECIST, were excluded. Clinical measurements of tumor longest diameter at physical exam were recorded before and after treatment. Twenty-one patients recurred after surgery, with a mean time to recurrence of 108 weeks. The mean follow up time in the non-recurrent group was 190 weeks.

MR Imaging: Patients were imaged on a 1.5T Signa system (General Electric Medical Systems, Milwaukee, WI) using a bilateral phased-array breast coil. A fat suppressed, contrast-enhanced, T1-weighted 3DFGRE sequence was acquired sagittally, and the following imaging parameters were used: TR = 8 ms, TE = 4.2 ms, 20° flip angle, 2 NEX, FOV 18-20 cm, 2 mm slice thickness, and 256 × 192 acquisition matrix.

Post-Processing: Longest dimension (LD) of tumor was manually measured on the sagittal slice demonstrating maximum tumor extent. For bidimensional measurements, a second in-plane diameter was measured perpendicular to the longest diameter. Multiple, distinct lesions were measured separately, and tumor extent was recorded based on RECIST and WHO guidelines. A second, independent user repeated all longest diameter measurements to test reproducibility. Volume was calculated using a semi-automated tumor segmentation algorithm that adds all pixels meeting previously determined enhancement criteria [4]. Figure 1 shows a tumor with corresponding RECIST, WHO, and volume measurements.

Statistics: Univariate Cox proportional hazards analysis was used to assess the value of RECIST, WHO, and volume measurements for predicting RFS. Statistically significant variables were then combined in a multivariate model to determine which size measures yielded the greatest predictive value.

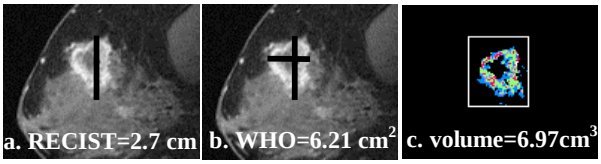

Figure 1 shows a tumor with size measurements in a. one, b. two, and c. three dimensions.

Results

Reproducibility of longest dimension (LD) measurements was good, with 89% concordance between readers. Univariate Cox proportional hazards analysis showed that final tumor volume on MRI was most predictive of recurrence free survival (p=.0002). Other significant univariate predictors of recurrence free survival are shown in Table 1.

	Univariate		Multivariate	
Variable	P-value	HR	P-value	HR
Final volume (cm3)	.0002	1.043		
Final % Δ volume	.0026	1.023	**.0026**	1.021
Initial volume (cm3)	.0033	1.023	**.0033**	1.025
Final WHO LD (cm2)	.0037	1.055		
Final RECIST LD (cm)	.0042	1.385		
Final % Δ WHO	.0174	1.017		
Final % Δ RECIST	.039	1.017		
Final clinical LD (cm)	.042	1.181		

Table 1 shows variables that were predictive of RFS in univariate and multivariate analyses. P-values and hazard ratios (HR) are given.

The statistically significant variables were then combined, and in the resulting multivariate proportional hazards model, initial tumor volume (p=.0033) and final change in tumor volume on MRI (p=.0026) were the only independently significant variables, more significant than longest dimension measured by RECIST, WHO, or clinical exam.

Discussion

In this study, RECIST (unidimensional) guidelines, WHO (bidimensional) criteria, and volumetric assessment of tumor size were compared to determine which technique was most valuable for predicting recurrence free survival in patients undergoing preoperative chemotherapy. The results indicated that semi-automated analysis of tumor volume was a better predictor of RFS than longest dimension measured manually by RECIST or WHO guidelines, and that a model containing initial tumor volume and final change in volume on MRI provided the most predictive value. The results support previous work demonstrating the value of MRI tumor volume for predicting patient outcome [4].

References

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