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Fast Temporal Resolution Dynamic Contrast-Enhanced MRI: Histogram Analysis Versus Visual Analysis for Differentiating Benign and Malignant Breast Lesions

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Abstract

OBJECTIVE.—The purpose of this study was to validate a kinetic assessment based on visually identified peak enhancement, which is routinely used in clinical practice, for differentiating benign from malignant lesions during fast dynamic contrast-enhanced MRI.

MATERIALS AND METHODS.—Between January 2015 and December 2016, 90 consecutively registered patients with 105 breast lesions (40 benign, 65 malignant) underwent dynamic contrast-enhanced 1.5-T MRI that included one unenhanced and eight contrast-enhanced fast temporal resolution (10 seconds) whole-breast acquisitions. Histogram analysis was performed to measure the voxel-based enhancement of the entire lesion to obtain 90th, 75th, and 50th percentile values at each time point and to generate kinetic curves. Two observers selected visually identified peak enhancement within the lesions to generate the kinetic curves. The kinetic curves from histogram and visually identified peak enhancement analyses were fitted by means of an empiric mathematic model (EMM): $S(t) = A \times (1 - e^{-\alpha t})$, where A is the upper limit of signal intensity, e indicates the exponential function, and α (min^{-1}) is the rate of increase in signal intensity. The initial slope of the kinetic curve ($A \times \alpha$) and the initial AUC (AUC_{30}) were calculated. These parameters were compared between benign and malignant lesions, and results from visually identified peak enhancement analysis were compared with those from histogram analysis.

RESULTS.—Benign lesions were successfully differentiated from malignant lesions in both visually identified peak enhancement and histogram analyses (90th and 75th percentile values) on the basis of α , $A \times \alpha$, and AUC_{30} from the EMM. There was no significant difference in ROC AUC in these EMM parameters between visually identified peak enhancement and histogram analyses ($p = 0.21$).

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Supplemental Data

Available online at www.ajronline.org.

CONCLUSION.—Kinetic assessment with visually identified peak enhancement was acceptable for differentiating benign from malignant lesions.

Keywords

breast; cancer; fast dynamic contrast-enhanced MRI; kinetics; MRI

Semiquantitative kinetic analysis of whole-breast dynamic contrast-enhanced MRI (DCE-MRI) performed with high spatial resolution has been found useful in differentiating benign from malignant lesions, and this method has been used in the BI-RADS MRI lexicon [1–3]. In standard DCE-MRI, limited temporal resolution (generally 60–90 seconds) is used to obtain high spatial resolution images for high-quality morphologic assessment [4]. To detect differential features in tumor vasculature between benign and malignant lesions more effectively, however, higher temporal resolution images obtained during the early phases of DCE-MRI (fast temporal resolution, or fast, DCE-MRI) may be more useful than standard DCE-MRI [5, 6].

For fast DCE-MRI to date, a view-sharing method that combines the data from different partial k-space samplings [7–9] and a non-view-sharing approach that relies on conventional uniform k-space sampling have been developed [10–12]. Both methods generate images with high temporal resolution that cover the entire breast. Kinetic assessment in the very early contrast-enhanced phases of fast DCE-MRI has been found to be comparable to the standard kinetic assessment obtained from the combination of the early and delayed phases of standard DCE-MRI for differentiating benign and malignant lesions [8, 11]. Therefore, fast DCE-MRI would be advantageous because it does not require sampling of signal intensity during the delayed phase of contrast agent uptake, reducing the total acquisition time by 4 minutes at the maximum, according to published data [8, 11].

For the kinetic assessment of fast DCE-MRI, diagnostic parameters have been obtained from the kinetic curves generated for voxels displaying the greatest enhancement selected visually by radiologists [5, 6, 8, 11]. This procedure is convenient and efficient for radiologists. Although appropriate selection of voxels with the greatest enhancement within a tumor in the very early contrast-enhanced phase is critical for accurate evaluation of vascularity, selection of the representative voxels by human eyes (visual analysis) can be difficult and imprecise because the changes in signal intensity within a lesion in the very early phase are often subtle and heterogeneous, and the spatial resolution of fast DCE-MRI is limited in achieving high temporal resolution. Because radiologists in clinical practice routinely use kinetic assessment with visual analysis, it is critical to determine whether this approach has the same diagnostic accuracy as use of semi-quantitative analysis to determine which voxels have the greatest enhancement.

In this study, we performed histogram analysis of the signal-intensity enhancement of all voxels in a lesion and obtained the percentile values of the enhancement. We compared these results of histogram analysis with those of visual analysis to investigate whether visual analysis is reliable.

Materials and Methods

Patients

Institutional review board approval was obtained for this retrospective study, and the informed consent requirement was waived. We retrospectively reviewed breast MRI studies performed at the University of Chicago between January 2015 and December 2016. Among 546 consecutively registered patients who underwent 1.5-T breast MRI, 152 patients had biopsy-proven benign or malignant lesions or clinically confirmed benign lesions. Patients were excluded from the study for the following reasons: fast DCE-MRI had not been performed because of a flaw in the equipment ($n = 11$); MRI was performed to evaluate the effectiveness of neoadjuvant chemotherapy ($n = 42$); and MRI was performed only for postoperative evaluation ($n = 9$). Thus, 90 patients with 105 lesions (40 benign, 65 malignant) were included in this retrospective study. For 30 patients, MRI was performed for screening because of high risk of breast cancer. For the other 60 patients, MRI was used for diagnostic staging of known breast cancer. All patients were women (mean age, 51 years; range, 16–77 years).

The number of malignant lesions was 65, consisting of 46 invasive ductal carcinomas, six invasive lobular carcinomas, 11 ductal carcinomas in situ, one papillary carcinoma, and one poorly differentiated carcinoma. The number of benign lesions was 40, consisting of 21 fibroadenomas, one case of usual ductal hyperplasia, one papilloma, 12 cases of benign breast parenchyma, one case of focal columnar change, one case of proliferative fibrocystic change, and three inflammatory lymph nodes. Pathologic proof was obtained by percutaneous core needle biopsy for all but 11 benign lesions (all presumed fibroadenomas), which had been clinically diagnosed before this study by means of mammography or ultrasound follow-up lasting more than 2 years.

Among the 65 malignant lesions, 9- to 14-gauge core needle biopsies were performed in all cases (58 under ultrasound guidance, five under stereo-tactic guidance, and two under MRI guidance). Among the 29 benign lesions, 21-gauge fine-needle aspiration under ultrasound guidance was performed in 12 cases. In the other 17 cases, 9- to 14-gauge core needle biopsies (13 under ultrasound guidance, four under MRI guidance) were performed. All biopsy procedures were performed by breast radiologists at the University of Chicago.

Patient background factors—age, menopausal status, lesion diameter, and lesion type (mass or nonmass)—were compared between benign and malignant lesions to confirm whether background factors influenced differentiation of benign from malignant lesions.

MRI Acquisition

A 1.5-T MRI system (Intera Achieva, Philips Healthcare) with single-source radiofrequency transmission was used for all imaging. All patients were imaged in the prone position with both breasts placed in a 16-channel bilateral breast coil. Protocols included fast and standard DCE-MRI with a 3D fat-suppressed T1-weighted gradient-echo sequence. The parameters for fast DCE-MRI were as follows: TR/TE, 4.7/2.3; voxel size, $1.5 \times 1.5 \times 3.5$; sensitivity-encoded (SENSE) acceleration factor (right-left), 4; SENSE acceleration factor (foot to head), 2; half-scan factor, 0.7 (k_1), 0.85 (k_2); temporal resolution, 10 seconds; number of

sections, 110; flip angle, 12°; FOV, 360 × 360 mm; fat suppression method, spectral attenuated inversion recovery (SPAIR). For standard DCE-MRI the parameters were as follows: TR/TE, 5.5/2.7.; voxel size, 0.8 × 0.8 × 2; SENSE acceleration factor (right-left), 3; SENSE acceleration factor (foot to head), 2; half-scan factor, 1 (k_y), 1 (k_z); temporal resolution, 60 seconds; number of sections, 200; flip angle, 12°; FOV, 360 × 360 mm; fat suppression method, SPAIR). Contrast administration was IV infusion of 0.1 mmol/kg gadobenate dimeglumine (MultiHance, Bracco International) followed by a 20-mL saline flush at a rate of 2 mL/s. The DCE series included an unenhanced acquisition for both standard and fast DCE-MRI.

The contrast-enhanced fast DCE-MRI acquisition was begun 10 seconds after the beginning of contrast injection. Eight contrast-enhanced series of fast DCE-MR images were repeatedly acquired until 90 seconds after the beginning of contrast injection was reached and were followed immediately by standard DCE-MRI (each acquisition time, 60 seconds) for four contrast-enhanced acquisitions (Fig. 1).

Image Interpretation

Two readers (9 and 14 years of experience in breast MRI) initially evaluated the longest tumor diameter and lesion type (mass or nonmass) using standard DCE-MRI. The readers were blinded to the clinical and pathologic information according to the BI-RADS MRI criteria [3].

We standardized a time of arrival of contrast agent in fast DCE-MRI according to the initial enhancement in the descending aorta at the level of the nipple. The largest oval or round ROI was placed inside the enhancing lumen of the aorta. We labeled as F1 the fast acquisition phase in which enhancement of the aorta started and labeled the subsequent 10-second phases as F2 through F8 (Fig. 2). F1 was defined as the phase when the signal intensity within an ROI in the aorta measured twice or more the mean signal intensity within the same ROI on the unenhanced images. F2 was defined as the phase occurring 10 seconds after F1.

Histogram analysis of whole-lesion enhancement—All processes (3D registration, image subtraction, 3D segmentation, and histogram analysis) were performed at a commercial software workstation (Quant 1.0, Quantitative Insights).

First, unenhanced and contrast-enhanced fast DCE-MR images were transferred to the workstation, and 3D registration and image subtraction were automatically performed. The two readers, who were blinded to the histopathologic diagnosis, performed 3D segmentation of lesions on MR images to produce a histogram of voxel-based contrast enhancement over the whole volume of lesions (whole-lesion enhancement). In this process, a deformable registration algorithm was used to generate subtraction images with gaussian-based regularization [13] for the unenhanced and contrast-enhanced images. The registration was monitored by the readers, who checked whether the registration was being properly processed (i.e., without motion artifacts).

The last phase of fast DCE-MRI was used to evaluate tumor contours by use of a 3D segmentation algorithm that involved a fuzzy c-means approach [14]. In this technique, 3D

segmentations for mass lesions were automatically performed when a pixel inside the lesion was initially selected (Fig. 3A). For nonmass lesions or lesions separate from the main tumor, individual 3D segmentations were performed for the fragments of the lesions, which were subsequently summed (Fig. 3B). Results of 3D segmentation for each lesion were reviewed by the readers, and the segmentation contour was manually modified to include the area that seemed to be part of the lesion if necessary. The contour was manually modified in 52 cases by reader 1 and in 59 cases by reader 2.

Voxel-based contrast enhancement as percentage was calculated for the segmented lesions in each phase of fast DCE-MRI [15]. It was calculated for each voxel as follows:

$$(SI_{post} - SI_{pre})/SI_{pre} \times 100,$$

where SI_{pre} and SI_{post} indicate the signal intensity of each voxel obtained before and after injection of the contrast agent [15]. A histogram of the voxel-based enhancement (Fig. 4A) and the cumulative frequency distributions of the enhancement with the cumulative frequency percentage on the y -axis (Fig. 4B) of the segmented lesion was obtained for each phase [15]. The percentile values (90th, 75th, 50th) of each lesion in each phase were obtained from the graph (Fig. 4B). Kinetic curves were then obtained from the percentile value at each time point, for example, a plot of 90th percentile enhancement versus time (Fig. 4C).

Quantitative evaluation of enhancement in a visually identified voxel——

Unenhanced and contrast-enhanced fast DCE-MR images were transferred to a clinical workstation (Dynacad, version 2.1.7, Philips Healthcare) for analysis of the signal intensity changes in representative voxels [16] performed on the subtraction images. When a reader placed a cursor over a voxel, the system displayed the voxel's enhancement obtained with the same formula [1] used in the histogram analysis. The two readers visually identified the 105 lesions and moved the cursor around to verify the value of the enhancing voxel and selected a single voxel that was presumed to have the greatest increase in signal intensity in the last phase of fast DCE-MRI in the same manner as published previously [11]. We labeled the signal intensity of the voxel selected through this process as visually identified peak enhancement.

Obtaining the diagnostic parameters by use of an empiric mathematic model

——The original EMM was developed to fit multiple time data points of the entire period covering both early and delayed phases (full EMM) to obtain parameters showing the uptake and washout behavior [17–19]. In this study, the kinetic curves obtained from histogram analysis and visual analysis of fast temporal resolution images in the very early phase were analyzed quantitatively by fitting of the curves to the truncated (early phase only) EMM as follows [10]:

$$\Delta S(t) = A \times (1 - e^{-\alpha t}),$$

where S is the relative enhancement, t is time, A is the upper limit of signal intensity, and α (min^{-1}) is the rate of increase in signal intensity.

The goodness of fit of parameter R^2 was calculated for each lesion. The fitting process was performed for kinetic curves of each percentile value (90th, 75th, 50th) from histogram analysis and visually identified peak enhancement from visual analysis, starting from phase F1. We obtained the following secondary derivations for diagnostic parameters.

The initial slope of the kinetic curve ($\text{slope}_{\text{ini}}$) was calculated as the product of the uptake rate α and the amplitude of enhancement A :

$$\text{slope}_{\text{ini}} = A \times \alpha.$$

The initial AUC (AUC_{γ}) was calculated by integration of the kinetic curve as follows:

$$\text{AUC}_{\gamma} = A \times [\gamma - (1 - e^{-\gamma\alpha})/\alpha],$$

where γ is the time over which signal intensity was integrated. In this study, γ was 30 seconds, in accordance with the method of Jansen et al. [20]. Reproducibility of the diagnostic parameters from histogram and visual analyses obtained by each reader was evaluated by interclass correlation coefficient (ICC). The parameters were then compared between benign and malignant lesions.

Statistical Analysis

The Mann-Whitney U test was used for comparing patient age, lesion diameter, A , α , $A \times \alpha$, and AUC_{30} of EMM for the 90th, 75th, and 50th percentile values of histogram analysis and visually identified peak enhancement analysis. The Fisher exact test was used for comparing menopausal status and lesion type. Interobserver reliability of results of A , α , $A \times \alpha$, and AUC_{30} of EMM for the 90th, 75th, 50th percentile values in histogram and visually identified peak enhancement analyses was assessed by ICC. An r of 1.0 was deemed to indicate perfect agreement; 0.81–0.99, almost perfect agreement; 0.61–0.80, substantial agreement; 0.41–0.60, moderate agreement; 0.21–0.40, fair agreement; and 0.20 or less, slight agreement [21]. The performance of the fitting parameters from histogram analysis and visual analysis in differentiating benign and malignant lesions was evaluated by ROC analysis and AUC. AUCs were compared by use of the DeLong method [22]. Statistical analyses were performed with commercial software (JMP Pro 13, SAS). A value of $p < 0.05$ was considered significant. After Bonferroni correction of 16 multiple comparisons, the critical value became $p < 0.003$ ($0.05/16$).

Results

No statistically significant differences were found between the benign and malignant groups with respect to age, menopausal status, or lesion type (Table 1). The malignant group had significantly larger lesion diameter than the benign group ($p < 0.001$).

For fast DCE-MRI, the earliest contrast enhancement of the aorta was seen during the first contrast-enhanced phase in 70 lesions, the second contrast-enhanced phase in 32 lesions, and the third contrast-enhanced phase in three lesions out of the total of 105 lesions in 90 patients (Fig. 2). Motion during the examination was minimal, resulting in fine registration, and therefore no datasets were excluded from analysis.

Enhancement rate measured from histogram and visual analyses in each phase is shown in Table S1. (Table S1 can be viewed in the *AJR* electronic supplement to this article, available at www.ajronline.org.) The mathematic model was successfully fitted to the curves of fast DCE-MRI with a goodness of fit parameter R^2 greater than 0.90 for all lesions studied.

For the 90th and 75th percentile values in histogram analysis, α , $A \times \alpha$, and AUC_{30} of malignant lesions were significantly higher than those of benign lesions (all $p < 0.001$ for 90th percentile values; all $p < 0.001$ for 75th percentile values) (Table 2), but A was not (90th percentile, $p = 0.13$; 75th percentile, $p = 0.025$). For 50th percentile values, the AUC_{30} values of malignant lesions were significantly higher than those of benign lesions ($p < 0.01$), but there was no significant difference in A ($p = 0.2$), α ($p = 0.015$), or $A \times \alpha$ ($p = 0.005$) between benign and malignant lesions (Table 2).

For visually identified peak enhancement in visual analysis, the α , $A \times \alpha$, and AUC_{30} values of malignant lesions were significantly higher than those of benign lesions (all, $p < 0.001$) (Table 2), but A was not ($p = 0.037$).

The ICC for α , $A \times \alpha$, and AUC_{30} from the 90th and 75th percentile values was > 0.8 , indicating almost perfect agreement. The ICC for α and $A \times \alpha$ from visually identified peak enhancement was > 0.8 , indicating almost perfect agreement. The ICC for AUC_{30} from visually identified peak enhancement was 0.78, indicating substantial agreement.

ROC analysis revealed that all of the AUCs for α , $A \times \alpha$, and AUC_{30} of EMM from the 90th and 75th percentile values and those of visually identified peak enhancement were 0.70 or greater (Table 2). There was no significant difference in ROC AUC among α , $A \times \alpha$, and AUC_{30} of EMM from the 90th and 75th percentile values and those of visually identified peak enhancement ($p = 0.21$).

Discussion

We compared the diagnostic parameters from analysis of visually identified peak enhancement with those from histogram analysis. We recognize the difference between the kinetic curves of visually identified peak enhancement and those of histogram analysis. For analysis of visually identified peak enhancement, the kinetic curve was based on enhancement as a function of time in a single visually identified voxel selected as the most enhancing voxel during the last contrast-enhanced phase. In histogram analysis, however, the curve was obtained from the enhancement at a specific percentile, such as the 90th percentile, at each time point. Therefore, the voxels that contributed to the kinetic curve may not have been the same at each time point. Thus, the diagnostic parameters from histogram analysis (especially from 90th and 75th percentile values) represent the uptake behavior of the greatest enhancement in the lesion.

Buadu et al. [23] made a kinetic curve by placing an ROI on the area of maximum enhancement within a tumor and found that the steepest slope of the curve correlated with microvessel count. More recently, Mann et al. [8] reported that the most enhancing voxel from kinetic analysis of a very early phase of fast DCE-MRI was useful in discriminating benign from malignant tumors. In all of these studies, the visually identified most enhancing voxel was used because it was intuitively considered the most prominent representative of the lesion. In this study, the diagnostic accuracy of visually identified peak enhancement was comparable to that of the 90th and 75th percentile values from histogram analysis, having high interobserver reproducibility. Although there may be selection bias in selecting the voxel with greatest enhancement by moving the cursor around to select the single voxel presumed to have the greatest increase in signal intensity, the interobserver reproducibility of parameters from visually identified peak enhancement was substantial to almost perfect agreement, and the diagnostic performance was comparable to that of histogram analysis. Thus, we believe that parameters from visually identified peak enhancement, which is routinely used by radiologists in clinical practice, would be sufficient for differentiating benign and malignant lesions.

Fitting of DCE-MRI data to the EMM was originally applied to the entire contrast enhancement period, covering both the early and delayed phases (full EMM) [17–20]. Pineda et al. [10] found the truncated EMM feasible for fitting the fast DCE-MRI data with results that included 18 malignant and 15 benign lesions. The truncated EMM is a model modified to fit the data points only from the early phase exclusively for fast DCE-MRI, thus providing parameters that represent the uptake behavior of contrast material. In this study, the truncated EMM was successfully fitted to the curves of fast DCE-MRI, having a goodness-of-fit parameter R^2 greater than 0.90 for all lesions. Parameters from the model (α , $A \times \alpha$, AUC_{30}) were found effective for discriminating benign from malignant lesions.

In DCE-MRI, the concentration of contrast agent in cancerous tissue depends on perfusion, leakage from capillaries, backflux from tissue to efferent vessels, and the volume of the interstitial space [24–26]. In the very early phase immediately after injection of the contrast agent, there is very little back-flux, and dependence on interstitial volume is reduced. Therefore, contrast agent uptake more directly reflects perfusion and leakage [10, 27, 28]. The contrast agent reaches abnormal afferent vessels and leaks into tissue in malignancies more quickly than in benign tumors during the earlier phase [28–30]. The parameters from the EMM, such as α (uptake rate), $A \times \alpha$ (initial slope), and AUC_{30} (integration of the kinetic curve immediately after enhancement in the descending aorta), reflect perfusion and the speed of leakage of contrast agent into tissue. This is why these parameters were significantly different between benign and malignant lesions.

In this study, the EMM fitting method was used to mathematically calculate $A \times \alpha$, or the initial slope, as the slope of a tangent of the kinetic curve at initial time 0. Mann et al. [8] used the maximum slope of the relative enhancement versus time curve and stated that the greatest slope usually was present in the first part of the curve. The maximum slope, if obtained from the first part of the curve without fitting the curve, is almost identical to the $A \times \alpha$ obtained by the fitting method. Meanwhile, the enhancement rate that Abe et al. [11] used is the slope of the curve measured without fitting at each time point after enhancement

of the aorta. This slope approximates the initial slope ($A \times \alpha$) obtained with the fitting method. Therefore, the result of $A \times \alpha$ from the EMM shows a significant difference between benign and malignant lesions that is consistent with the diagnostic effectiveness of the maximum slope reported by Mann et al. and the enhancement rate reported by Abe et al. Thus, our results and previous results show that $A \times \alpha$, or initial slope, is a diagnostically useful parameter.

This study had several limitations. First, the sample size was small. Second, there was a significant difference in diameter between benign and malignant lesions. When the lesion is small or thin, voxel selection may affect visual analysis. Further evaluation of smaller malignant lesions may be necessary to confirm our results. Third, we used a single 1.5-T MRI system, and the utility of our method has not been confirmed with other systems. Fourth, we investigated only a few parameters for differentiating benign and malignant breast lesions, although several parameters have been used to analyze signal intensity in the very early phase [31], including the model-based method [10, 18, 20], maximum slope [8], and relative enhancement rate [11]. Further evaluation of these parameters with various MRI systems is needed to identify the most robust and practical parameters for routine clinical use. Fifth, the potential for selection bias was present in this study. At the University of Chicago, most breast MRI studies are performed for one of two clinical indications: preoperative staging for patients with known malignant lesions and screening for patients at high risk. Therefore, the ratio between malignant and benign breast lesions is uneven in our archive, because most of the malignant breast lesions are obtained at staging MRI, which is one of the frequent clinical indications, whereas most of the benign lesions are infrequently detected as incidental findings. To reduce selection bias, further study with only MRI-detected malignant and benign lesions is needed.

Conclusion

Visually identified peak enhancement—the most enhancing voxel visually selected within a tumor—was effective for evaluating breast lesions with fast DCE-MRI. Diagnostic parameters obtained from EMM to voxels identified with visually identified peak enhancement are effective for differentiating benign from malignant lesions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1—
Chart shows protocols for fast temporal resolution imaging. Dynamic contrast-enhanced MRI (DCE-MRI) series includes unenhanced acquisitions for standard DCE-MRI and fast DCE-MRI acquisitions. Contrast-enhanced fast DCE-MRI starts 10 seconds after beginning of contrast injection; eight fast DCE-MRI acquisitions (each, 10 seconds) and four standard DCE-MRI acquisitions (each, 60 seconds) follow.

Fig. 2—

Chart shows methods of correction for person-to-person differences in time of arrival of contrast agent in very early phase after contrast injection. To correct for person-to-person differences in assessing time of arrival of contrast agent, phases in fast dynamic contrast-enhanced MRI (DCE-MRI) are reordered according to initial enhancement in descending aorta at level of nipple. Fast-acquisition DCE-MRI phase when aorta starts to become enhanced is F1 (*arrowhead*). Subsequent phases are F2, F3, and so on.

Fig. 3—. Methods of 3D segmentation.

A, 45-year-old woman with right breast cancer. Dynamic contrast-enhanced MR image shows mass lesion (*outline*) automatically segmented when pixel inside lesion (*pink dot*) is initially selected.

B, 41-year-old woman with right breast cancer. Dynamic contrast-enhanced MR image shows that for nonmass lesions or lesions separate from main tumor, 3D segmentations are performed for each component (*outlines*) of lesions, and then all components are combined.

Fig. 4—. Example of histogram analysis of whole lesion in one case.

A, Voxel-based enhancement. Histogram shows enhancement on *x*-axis and number of voxels on *y*-axis.

B, Cumulative frequency distributions. Graph shows curve representing relative cumulative frequency of voxels (i.e., percentage of number of cumulative voxels at each enhancement in total number of voxels analyzed). Percentile values (90th, 75th, and 50th) (*blue*) of each lesion in every phase are obtained from curve.

C, Percentile value at each time point. Graph shows kinetic curves obtained from percentile value at each time point for percentile enhancement versus time (*squares*). Kinetic curves obtained from each percentile value are fitted to truncated empirical mathematic model for percentile enhancement versus time (*circles*).

TABLE 1:

Patient Characteristics

Variable	Benign (<i>n</i> = 40)	Malignant (<i>n</i> = 65)	<i>P</i>
Age (y)			0.01 ^{<i>a</i>}
Median	47	52	
Range	16–69	28–77	
Menopausal status (no. of patients)			0.53 ^{<i>b</i>}
Premenopausal	26 (65)	37 (57)	
Postmenopausal	14 (35)	28 (43)	
Diameter (mm)			< 0.001 ^{<i>a</i>}
Median	10	22	
Range	4–36	2–137	
Lesion type (no. of patients)			0.22 ^{<i>b</i>}
Mass	34 (85)	48 (74)	
Nonmass	6 (15)	17 (26)	

Note—Values in parentheses are percentages.

^{*a*}Mann-Whitney *U* test.

^{*b*}Fisher exact test.

TABLE 2:

Comparison of Fitting Parameters From Histogram and Visual Analyses Between Benign and Malignant Lesions

Parameter	Benign (<i>n</i> = 40) ^a	Malignant (<i>n</i> = 65) ^a	<i>P</i>	AUC	ICC
90th Percentile					
A	195 ± 234	167 ± 87	0.13	0.41	0.75 (0.64, 0.83)
α	0.06 ± 0.04	0.11 ± 0.11	< 0.001 ^b	0.77	0.93 (0.89, 0.95)
A × α	10 ± 13	17 ± 15	< 0.001 ^b	0.74	0.90 (0.85, 0.93)
AUC ₃₀	2167 ± 1645	2918 ± 1186	< 0.001 ^b	0.70	0.92 (0.89, 0.95)
75th Percentile					
A	114 ± 93	138 ± 156	0.025	0.63	0.69 (0.52, 0.80)
α	0.07 ± 0.08	0.11 ± 0.11	< 0.001 ^b	0.75	0.84 (0.77, 0.90)
A × α	7.9 ± 11	14 ± 15	< 0.001 ^b	0.74	0.87 (0.81, 0.91)
AUC ₃₀	1632 ± 1234	2298 ± 985	< 0.001 ^b	0.71	0.91 (0.87, 0.94)
50th Percentile					
A	99 ± 145	86 ± 31	0.2	0.43	0.81 (0.71, 0.87)
α	0.10 ± 0.17	0.09 ± 0.07	0.015	0.36	0.57 (0.37, 0.71)
A × α	5.4 ± 4.6	8.5 ± 6.2	0.005	0.66	0.73 (0.60, 0.82)
AUC ₃₀	1156 ± 839	1616 ± 853	0.0029 ^b	0.67	0.89 (0.85, 0.93)
Visually identified peak enhancement					
A	137 ± 171	126 ± 42	0.037	0.37	0.66 (0.50, 0.77)
α	0.09 ± 0.12	0.19 ± 0.2	< 0.001 ^b	0.73	0.94 (0.90, 0.96)
A × α	8.3 ± 7.3	25 ± 28	< 0.001 ^b	0.75	0.89 (0.84, 0.93)
AUC ₃₀	1711 ± 1142	2727 ± 1219	< 0.001 ^b	0.74	0.78 (0.68, 0.86)

Note—After Bonferroni correction of 16 multiple comparisons, the critical value became $p < 0.003$ (0.05/16). Values in parentheses are 95% confidence limits. ICC = interclass correlation coefficient.

^aValues are mean ± SD.

^bStatistically significant.