

# ASSESSMENT OF DYNAMIC RANGE IN DYNAMIC CONTRAST-ENHANCED BREAST EXAMINATIONS

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## Introduction

In dynamic contrast-enhanced (DCE) breast examinations, reliable classification of contrast uptake curves requires rapid T1-weighted pulse sequences to be designed to provide image intensity directly proportional to contrast agent (CA) concentration. Test objects containing a range of T1 values may be used to verify the dependency of image intensity on T1, but this process can be hindered by spatial variations of B1 [1] and incorrect determination of flip angles, not necessarily reproduced with test objects. In this work we propose to evaluate the dynamic range of breast DCE examinations retrospectively by considering the enhancement of the arteries that supply the breast. This method is validated by considering different pulse sequences, and comparing the calculated expected dynamic range to the measured dynamic range in groups of patients undergoing breast MRI.

## Method

**MRI Protocols:** Routine clinical breast examinations were undertaken at 1.5T (Philips, Best, Netherlands) at three separate hospital sites in the same institution. The DCE breast examinations were performed with 3D fat-suppressed spoiled gradient-echo sequences (Philips Thrive), with a standardized procedure for administration of a single dose of DOTAREM (Guerbet, France) at 3 mL/s (MedRad, USA). Each dynamic series consisted of one pre-contrast and eight post-contrast axial images, each acquired in approximately 1 minute. Over a period of 2 years, several protocol changes were associated with changes in clinical practice, as detailed in Table 1. For each of the 5 different protocols used, 7-10 patient examinations were selected at random and anonymised for further analysis (45 patients in total). Following the guidance of the Ethics Research Committee, this retrospective analysis is a service evaluation and does not require informed consent.

**Calculation of relative enhancement:** Signal intensity was calculated using the Bloch equations and in-house software (IDL 7.1 ITTVIS, Boulder, USA). For each protocol, the maximum relative enhancement,  $E_{max}$ , (percentage increase of signal intensity:  $[SI_{max} - SI_{pre-contrast}] / SI_{pre-contrast} \times 100$ ) [2] was calculated for blood, assuming that blood T1 varies from 1200 ms (unenhanced) to 100 ms (peak enhancement). This estimate of the range of T1 values is in agreement with the data from the MARIBS breast screening trial [3].

**Measurement of arterial relative enhancement:** For each examination, the right internal mammary artery was located (perpendicular to the axial acquisition plane) and a slice selected in a standardized position just below the first branch of this artery to the breast (Figure 1). Even at our lowest resolution, artery size was always greater than 5 pixels. In order to minimize partial volume effects, only the brightest pixel, considered the vessel centre, was chosen as the region of interest (ROI) in each dynamic frame and used to construct a nine-point signal intensity curve as a function of time. In addition to the maximum relative enhancement ( $E_{max}$ ), the time to peak enhancement ( $T_{max}$ ) was also measured for each examination, and defined as the position in the dynamic series corresponding to maximum contrast uptake.

**Data analysis:** Values of  $E_{max}$  and  $T_{max}$  were compared across protocols using either the Student's *t*-test (equal/unequal sample size and equal variance) or Welch's *t*-test (equal/unequal sample size and unequal variance) where applicable. A two tailed *p*-value <0.05 was taken to be significant. Measured values of  $E_{max}$  were also compared with calculated values.

## Results and Discussion

**Calculated relative enhancement:** Values in Table 2 confirm that  $E_{max}$  is approximately proportional to flip angle. Differences in TR, number of echoes and type of k-space coverage cause relatively minor variations across the rapid high-resolution protocols used. An increase in flip angle from 14° to 18°, or from 10° to 18°, increased relative enhancement by factors of 1.4 and 2.2 respectively.

**Measured relative enhancement:** Overall the vessel position was observed to drift as much as 6 mm in any direction across the dynamic series, justifying the methodology used to reduce partial volume effects. Means and corresponding standard deviations of measured  $E_{max}$  and  $T_{max}$  across the varying protocols are displayed in Table 2. Calculated coefficient of variation ranged from 0.16 to 0.32 suggesting good intra-group reproducibility. Measured  $E_{max}$  values are consistently lower than calculated  $E_{max}$  values (36-58% decrease). Even the maximum values of  $E_{max}$  within each patient group still fell at least 15% short of the calculated value, indicating that the shortest blood T1 achieved for peak contrast-agent concentration is longer than 100 ms.

Flip angle was found to have a significant effect on maximum relative enhancement,  $E_{max}$  (Figure 2). For the radial k-space coverage, lower values of  $E_{max}$  were found for the protocols with 10° and 14° flip angle (Groups 1 and 2, respectively), in comparison with a flip angle of 18° ( $p = 0.00002$ ,  $p = 0.0003$  respectively). Although Group 1 exhibited lower  $E_{max}$  than Group 2, this difference was not found to be statistically significant ( $p = 0.08$ ). Considering linear k-space coverage, the measured  $E_{max}$  at a flip angle of 14° was significantly lower than at 18° ( $p = 0.02$ ). Relative enhancement increased by a factor of 1.5 (radial protocols) and 1.6 (linear protocols) between flip angles of 14° and 18° and 1.9 between flip angles of 10° and 18° (radial protocols), comparing favourably with simulated values. There were no statistically significant differences in  $T_{max}$  due to changes in flip angle.

On comparing protocols with the same flip angle but different types of k-space coverage, lower values of  $E_{max}$  were found for the radial k-space coverage. A significant difference was found for the 18° protocols (Groups 3 and 5,  $p = 0.02$ ), but not for the 14° protocols (Groups 2 and 4,  $p = 0.09$ ). Radial protocols reached peak enhancement at a later time than linear protocols at flip angles of both 14° ( $p = 0.008$ ) and 18° ( $p = 0.0002$ ). Radial k-space sampling involves repeated sampling of central k-space area over the duration of data acquisition, which leads to smoothed enhancement curves of reduced amplitude, accounting for the lower  $E_{max}$  and longer  $T_{max}$ .

**Conclusion:** Measurement of relative enhancement in arteries supplying the breast provides a reliable method to evaluate the dynamic range of DCE protocols, revealing significant variations produced by only small alterations in protocol. The reproducibility of results suggests a robust method, transferable across patient groups, regardless of individual differences in physiology. This demonstrates the validity of retrospective analysis in evaluating breast DCE protocols.

**References:** [1] Azlan *et al.*; Magn. Reson. Med.; 2011; doi: 10.1002/mrm.23021, [2] Kuhl *et al.*; Radiology; 1999; 211; 101-110, [3] MARIBS Trial; Lancet; 2005; 365(9473); 1769-1778.

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Table 1: Summary of MRI protocols across the five patient groups

Group	1	2	3	4	5
Sample size	8	10	10	7	10
Flip angle [°]	10	14	18	14	18
K-space sampling	Radial	Radial	Radial	Linear	Linear
TR / TE [ms]	5.10 / 2.39	5.10 / 2.35	3.94 / 1.81	4.58 / 2.27	4.10 / 1.97
Echo Train Length	100	100	60	100	100
Slice Thickness [mm]	2.5	2.5	2	2	2
In-plane resolution [mm]	0.63	0.63	1.25	1.25	1.25

Figure 1: Axial DCE breast image identifying position of right artery & enlarged images of the artery across the dynamic series (below).

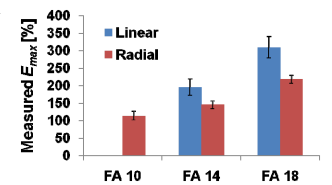
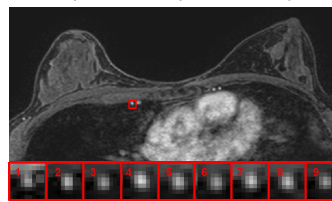


Figure 2: Mean values of  $E_{max}$  [%] across the five protocols. Error bars indicate standard error.

Table 2: Calculated  $E_{max}$  together with means & standard deviations of measured  $E_{max}$  and  $T_{max}$  across the five patient groups

Group	1	2	3	4	5
Calculated $E_{max}$ [%]	220	348	484	367	486
Measured $E_{max}$ [%]	114 ± 36	145 ± 34	218 ± 38	196 ± 63	310 ± 98
Measured $T_{max}$ [dynamic]	3.5 ± 1.2	3.0 ± 0.4	3.6 ± 0.8	2.3 ± 0.5	2.0 ± 0.0