Background: At present, dynamic contrast enhancement-MRI (DCE-MRI) has immense role in diagnosis and evaluation extent of breast cancer. As for diagnosis, evaluation pattern of kinetic enhancement in dynamic contrast study is performed after gadolinium injection. Since each breast cancer has internal pathophysiological variety, the kinetic enhancement patterns are supposed to be varied within each mass as well.

Objective: This study aimed to investigate characteristics and additional value of volumetric analysis of kinetic enhancement patterns on DCE-MRI in evaluating breast cancer in Thai patients.

Methods: We retrospectively studied 52 women, 67 lesions which were histologically proven breast cancer, using software of breast MRI and generating 3D volumetric voxels covered total tumor volume in DCE-MRI which performed between January 2014 and December 2017. Measurement of enhancement pattern was categorized by software into percentage of part of tumor which enhanced in each pattern. Consequently, percentages of enhancement in different types were collected which allocated in type I (persistent), type II (plateau) and type III (washout) enhancements. Analysis of the kinetic pattern was done together with subgroup analysis of each type of tumor (IDC, DCIS and other subtypes of breast cancer) as well as tumor grades.

Results: The mean percentages of enhancement pattern in kinetic assessment by 3D voxels of tumor volume showed the most common 72% type I enhancement, followed by 14.3% type III enhancement and 13.7% type II enhancement. Subgroup analysis showed similar higher type I enhancement in both IDC (68.3%) and DCIS (81.3%). However, there were slightly higher suspicious malignant pattern of enhancement (31.7% type II and 18.7% type III enhancements) in IDC more than DCIS as well as in high tumor grade (grade 3) more than low tumor grade (grade 1) (37% type II and 30.7% type III enhancements), but there were no significant differences.

Conclusion: Volumetric analysis showed heterogeneity of kinetic curve enhancement patterns inside each tumor. That means each tumor has a variety of enhancement patterns in itself and dissimilarity with others. The majority of pattern was found as type I enhancement which was not particular for malignant, whereas there was only 28% with suspicious kinetic enhancement patterns (type II and type III enhancements). The slightly higher suspicious malignant pattern of enhancement (type II and III enhancements) in IDC more than DCIS along with high tumor grade was observed, deprived of statistical significance.

Keywords: Breast MRI, breast cancer, volumetric kinetic assessment, color coded breast MRI.
Thus, DCE-MRI is now believed to be the most effective diagnostic modality correlated with the pathophysiology of the tumor confidentially.(8)

Since each breast cancer has internal pathophysiological variety, the kinetic enhancement patterns also vary within each mass.(4, 5) Therefore, if we created sampling only a part of the mass to perform kinetic time curve, it could instigate error of the result in both inter-and intraobserver reliabilities.(6, 7) Accordingly, this study aimed to find out the reliable method of kinetic assessment by using volumetric measurement of the whole lesion of breast cancer in DCE-MRI.

Material and methods

Population

This retrospective study of new or recurrent breast cancer patients examined breast DCE-MRI at affiliated educational medical centers in Thailand. Four hundred and fifty-nine examinations that underwent breast DCE-MRI examinations from January 2014 to December 2017 were reviewed. One hundred and one studies were included because of pathological-proven breast cancer by a pathologists after definitive surgery, identified by size, type and tumor grade. We excluded cases of prior received neoadjuvant chemotherapy, excisional or incisional biopsy, and surgery at the site of interesting and breast implantation. Other exclusion criteria were non-mass enhancement with faint contrast enhancement and region of interest on post-processing DCE-MRI less than 5 mm (solid portion) in minimal dimension. Fifty-two remaining patients, 67 lesions of breast cancers were included.

MRI technique and analysis

MRI examination with 1.5 tesla (Magnetom Espree, Global Seimens Healthcare, Germany) was used. Patients were in prone position and using 6-channels bilateral breast surface coils.

The pre-contrast sequences were performed by axial T1-weighted image with fat suppression, axial T2-weighted image, axial T2-weighted image with STIR and coronal T1-weighted image.

The post-contrast enhanced sequences were performed by using the protocol as follows: T1-weighted image with fat suppression, TR/TE of 4.75/1.45, flip angle of 10°, the field of view of 340 mm, matrix of 336 × 448 and 1.30 mm slice thickness. The dynamic contrast enhancement sequences were performed before and after injection of 0.1 mmol/kg gadopentetate dimeglumine (Gadovist) at 60, 120, 180, 240, 300 and 360 seconds. Our protocol was obtained by post-processing subtract images and computer-aided detection (CAD) with color coding assessment. The magnetic resonance spectroscopy (MRS) and apparent diffusion coefficient (ADC) values were performed in some patients.

The region of interest (ROI) of volumetric kinetic assessment on DCE-MRI was performed on work station by two radiologists who has 10-and 30-year of experience in breast imaging. The most visible in the cut of the tumor was carefully selected and drawn in square or rectangular shape 3D voxels to include whole tumor. The background parenchymal enhancement were avoided. The CAD software generated color-coding image then analyzed the pattern of enhancement after created voxels on the tumor. Subsequently, the percentages of part of tumor which enhanced in each pattern were obtained. According to Breast Imaging-Reporting and Data System (BI-RADS) 2013 (fifth edition) from American College of Radiology (ACR), kinetic assessment has been described in early phase (within 2 minutes) and delayed phases (after 2 minutes). Types of enhancement patterns in the delayed phase are categorized into, namely: a) type I (persistent)- continuous enhancement more than 10% increase in signal over time; b) type II (plateau)- signal intensity does not change over time after its initial rise or flat; and, c) type III (washout)- signal intensity decreases more than 10% after its highest point from its initial rise (Figure 1). Type II and Type III enhancements are known as suspicious patterns for malignancy which increased much concern in Type III, while Type I is recognized as benign pattern. Finally, data of each tumor were collected and categorized percentage of enhancement in each pattern.

All patients were confirmed by definitive surgery and pathohistology with identified size, type and tumor grade. Tumor grades were classified as grade 1, 2 and 3, corresponding with low, intermediate and high, respectively.
Volumetric kinetic assessment in dynamic contrast enhanced-MRI (DCE-MRI) of breast cancer: A new method for evaluation of whole tumor enhancing pattern

Statistical analysis

The mean ± standard deviation (SD) was used in the continuous data such as age, size of the tumor, and timing between operation and breast DCE-MRI.

Our study used three different patterns of enhancement in delayed phase for analysis. The percentage of each pattern from the volumetric kinetic study was assessed by using mean (± SD) and median.

As for comparison of the 3 groups of kinetic patterns were performed with one-way ANOVA or the Kruskal-Wallis test. $P < 0.05$ was indicated the significant statistical difference. Using statistical software with SPSS, version 22 was performed for statistical analysis.

Results

Fifty-two women, 67 lesions of breast cancers were included, their mean age was 47.8 years, the range of 24 - 74 years old. The majority of malignant type was 45 lesions (67%) of invasive ductal carcinoma (IDC), followed by 12 lesions (18%) of ductal carcinoma in situ (DCIS) and 10 lesions (15%) of other subtypes of breast cancer. The other subtypes of breast cancer included, namely: 4 invasive lobular carcinomas, 2 invasive micropapillary carcinomas, 1 malignant phyllodes tumor, 1 tubular carcinoma, 1 secretory carcinoma, and 1 mucinous carcinoma. The sizes of the tumors were performed by the histologic report, 2.7 cm of mean and 1.9 cm of the median. The mean timing between breast DCE-MRI and operation was 2.1 months (range, 1 - 9 months) (Table 1).

Finally, the mean and the median percentages of the kinetic assessment using volumetric evaluation of total tumor volume showed majority of 72.0% and 72.5% type I enhancement (Figure 2), followed by 13.7% and 11.7% type II enhancement, and 14.3% and 9.1% type III enhancement (Figures 3 - 4) (Table 1).

Figure 1. CAD with color coding was performed of the delayed phase on volumetric analysis. Type I (persistent) - increase signal intensity more than 10%; Type II (plateau) - signal intensity not change more than 10%; and, Type III (washout) - decrease signal intensity more than 10%.

Figure 2. 51-year-old woman with computer-aided detection (CAD) with color coding on DCE-MRI assessment of grade 2, invasive ductal carcinoma (IDC). (A) Axial contrast-enhanced T1-weighted imaging with fat suppression at 180 seconds after contrast injection, shows a $1.5 \times 2.7 \times 1.7$ cm irregular enhancing mass at outer part of left breast (arrow); (B) Color overlay map of CAD shows a rectangular shape of region of interest (ROI). The persistent enhancement is shown in blue area, the plateau enhancement showed in green area and the washout enhancement in red area; and, (C) Calculated type of enhancement is 21.4% washout, 23.8% plateau and 54.8% persistent enhancements.
Figure 3. 62-year-old woman with computer-aided detection (CAD) with color coding on DCE-MRI assessment of grade 2, invasive ductal carcinoma (IDC): (A) Axial contrast-enhanced T1-weighted imaging with fat suppression at 120 seconds after contrast injection, shows a 1.8 × 1.2 cm enhanced mass at upper mid quadrant of the right breast; (B) Color overlay map of CAD shows a rectangular shape of region of interest (ROI). The persistent enhancement is shown in blue area, the plateau enhancement in green area and the washout enhancement in red area; and, (C) Calculated type of enhancement is 42.3% washout, 28.8% plateau and 28.9% persistent enhancements.

Figure 4. 64-year-old woman with computer-aided detection (CAD) with color coding on DCE-MRI assessment of grade 1, invasive ductal carcinoma (IDC): (A) Axial contrast-enhanced T1-weighted imaging with fat suppression at 120 seconds after contrast injection, shows a 1.7 × 1.4 cm irregular enhancing mass at upper inner quadrant of the left breast (arrow); (B) Color overlay map of CAD shows a rectangular shape of region of interest (ROI). The persistent enhancement is shown in blue area, the plateau enhancement showed in green area and the washout enhancement showed in red area; and, (C) Calculated type of enhancement is 56.2% washout, 21.9% plateau and 21.8% persistent enhancements.

Table 1. Demographic data and percentages of volumetric kinetic assessment in different enhancement patterns.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 67)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>47.8 (24 - 74)</td>
</tr>
<tr>
<td>Size of tumors (cm)</td>
<td>2.7 ± 2.1 (1.9)</td>
</tr>
<tr>
<td>Timing between operation and breast DCE-MRI (months)</td>
<td>2.1 ± 1.8 (1 - 9)</td>
</tr>
<tr>
<td>Percentages of volumetric kinetic assessment in DCE-MRI (%)</td>
<td></td>
</tr>
<tr>
<td>Type I enhancement</td>
<td>72.0 ± 21.6 (72.5)</td>
</tr>
<tr>
<td>Type II enhancement</td>
<td>13.7 ± 9.9 (11.7)</td>
</tr>
<tr>
<td>Type III enhancement</td>
<td>14.3 ± 14.4 (9.1)</td>
</tr>
</tbody>
</table>
Histologic Types

Three subgroups include 67% IDC, 18% DCIS and 15% other subtypes of breast cancer. We found type I enhancement is the majority in among all types of breast cancer (Table 2). IDC shows the highest 68.3% type I enhancement, followed by 16.7% type III enhancement and 15.0% type II enhancement. In the DCIS showed the same as result of IDC, the highest 81.1% type I enhancement (9.8% type III and 8.9% type II enhancements).

Comparison between the mean percentages of different enhancement pattern and each histologic type of cancers as follows: a) type I enhancement; DCIS (n = 12) of 81.3%, other subtypes of breast cancer (n = 10) of 77.3%, and IDC (n = 45) of 68.3% ($P = 0.125$), b) type II enhancement; IDC of 15.0%, other subtypes of breast cancer of 13.6%, DCIS of 8.9% ($P = 0.166$), c) type III enhancement; IDC of 16.7%, DCIS of 9.8%, other subtypes of breast cancer of 9.1% ($P = 0.377$) (Table 2).

We found a higher percentage of suspicious enhancement patterns (Type II and Type III) in IDC group (31.7%) than DCIS group (18.7%). However, there is no significant difference.

Tumor grades

Among three tumors grades, grade 2 was the largest group (65%), followed by grade 3 (21%) and grade 1 (14%). Comparisons between the mean percentages of each enhancement pattern and tumors grades were also calculated by using volume study of kinetic assessment. The majority was type I enhancement in which was found, 69.3% in grade 1, 75.2% in grade 2 and 63.0% in grade 3 ($P = 0.224$).

Followed by type II and type III enhancements of which were respectively found 12.5% and 18.2% of grade 1, 11.6% and 13.1% of grade 2, 18.3% and 18.7% of grade 3 ($P = 0.096$ and $P = 0.713$) (Table 2).

There were higher percentage of type II enhancement and type III enhancement which are suspicious enhancement pattern for malignancy in grade 3 tumor but they did not reach statistical significance.

Discussion

Recently, we assessed both information of tumor morphology and kinetic assessment in breast MRI for diagnosis of breast cancer based on ACR BI-RADS 2013 (fifth edition). Kinetic assessment aimed to determine the uptake and washout of contrast media in tissue as the time passed. (4) There were many factors that affected the rate of contrast media uptake such as capillary permeability, blood volume, contrast media distribution volume, and other aspects of local anatomy and physiology. (4) In general, the type III enhancement in the delayed phase was preferred malignancy due to abnormal tumor vessels which have intense microvessels and high permeability. (4) For this reason, cancer seems to have vascular shunts then consequently early wash out was occurred. The type I enhancement was preferred benign lesions whereas the type II enhancement is classified as intermediate that can be both benign and malignant lesions. However, overlapping of enhancement patterns in one tumor either benign or malignant lesions were discovered.

Table 2. Different enhancement patterns of volumetric kinetic curve assessment compared with histologic type and tumor grades of the breast cancer.

<table>
<thead>
<tr>
<th>Histologic types</th>
<th>Type I (%)</th>
<th>P-value</th>
<th>Type II (%)</th>
<th>P-value</th>
<th>Type III (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDC (n = 45)</td>
<td>68.3±23.2 (70.5)</td>
<td>0.125</td>
<td>15.0±10.0 (11.8)</td>
<td>0.166</td>
<td>16.7±15.9 (12.7)</td>
<td>0.377</td>
</tr>
<tr>
<td>DCIS (n = 12)</td>
<td>81.3±17.0 (88.8)</td>
<td></td>
<td>8.9±8.0 (6.9)</td>
<td>0.096</td>
<td>9.8±10.9 (7.1)</td>
<td></td>
</tr>
<tr>
<td>Other* (n = 10)</td>
<td>77.3±15.1 (75.3)</td>
<td>0.244</td>
<td>13.6±10.5 (12.0)</td>
<td></td>
<td>9.1±7.5 (6.3)</td>
<td></td>
</tr>
<tr>
<td>Tumor grades</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1 (n = 8)</td>
<td>69.3±28.6 (73.7)</td>
<td>0.244</td>
<td>12.5±11.6 (7.8)</td>
<td>0.096</td>
<td>18.2±21.2 (7.3)</td>
<td>0.713</td>
</tr>
<tr>
<td>2 (n = 37)</td>
<td>75.2±19.2 (74)</td>
<td></td>
<td>11.6±8.5 (11)</td>
<td></td>
<td>13.1±12.7 (9.1)</td>
<td></td>
</tr>
<tr>
<td>3 (n = 12)</td>
<td>63.0±26.0 (59.7)</td>
<td></td>
<td>18.3±11.1 (21.0)</td>
<td></td>
<td>18.7±17.6 (14.0)</td>
<td></td>
</tr>
</tbody>
</table>

Note.- IDC= invasive ductal carcinoma; DCIS= ductal carcinoma in situ.
Other* = other subtypes of breast cancer
In our study, we confirmed that overall cancers have had heterogeneity of kinetic pattern inside each tumor as using 3D voxels covered the whole tumor volume. Therefore, each tumor has a variety of enhancement pattern in itself and dissimilarity with others. The majority of enhancement pattern of kinetic assessment was found as type I enhancement that was not particular for malignant, while only 28% of malignant have shown the suspicious kinetic assessment (type II and type III). Our findings were in concordance with the results of Leong LC, et al. (14) They reported different heterogeneous component of the mean percentages of tumor volumes on the delayed phase. They found the majority of 51% type I enhancement, followed by 28.8% type II enhancement, and 19.9% type III enhancement.

In addition, subgroup analysis of different histologic types and tumor grades also presented slight higher suspicious enhancement pattern (type II and type III enhancements) in IDC than DCIS as well as in high tumor grade (grade 3) than low tumor grade (grade 1) depriving statistical significance. This result is also in concordance with Leong LC, et al. (14) Therefore, volumetric kinetic measurement for the whole tumor volume has not provided an advantage in distinguishing tumor subtypes and tumor grades.

Few prior studies (11 - 13) found that the most common presentation of DCIS was type I enhancement, especially in non-mass DCIS. This is explained by the fact that DCIS mostly grow in the normal breast tissue without expression of vascular endothelial growth factor (VEGF), related to poor angiogenesis. (10) Thus, poor washout of contrast media was seen.

In the other subtype of breast cancer group, which comprised of 40% ILC, revealed higher percentages of type I enhancement pattern when compared with the IDC group. Similar theory is also applied to ILC due to no expression of VEGF and poor angiogenesis. (9, 10)

For our suggestion, focusing on the kinetic assessment parameter in order to diagnosis breast cancer, we could not use only kinetic enhancement patterns for diagnosis breast cancer even performing the whole tumor volume. Multiple selective sampling of the kinetic measurement at various parts of the tumor and correlation with other parameters such as tumor morphology, apparent diffusion coefficient (ADC) value, and MR spectroscopy (MRS) was recommended.

Lastly, there is a limitation of our study due to small sample size. Larger studies should be performed in the future.

**Conclusion**

For interpretation of breast cancer, the kinetic assessment of DCE-MRI with 3D voxels of whole tumor volume has not provided an advantage in distinguishing tumor histologic subtype and tumor grades. The confirmation of heterogeneity of kinetic enhancement patterns inside each tumor were obtained, which implied a variety of tumor and multifactor related to enhancement pattern. Thus, we could not use only kinetic assessment dissemination as merely the only criteria for diagnosis breast cancer. The correlation of other information is necessary including tumor morphology, ADC value and MRS.

**Conflict of interest**

The authors, hereby, declare no conflict of interest.

**References**


Volumetric kinetic assessment in dynamic contrast enhanced-MRI (DCE-MRI)
of breast cancer: A new method for evaluation of whole tumor enhancing pattern

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