Correlation of MRI findings of estrogen receptor-positive breast cancer with histopathological response in postmenopausal women undergoing neoadjuvant endocrine therapy

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Purpose

Neoadjuvant chemotherapy has become the standard treatment for patients with locally advanced breast cancer [1]. This therapy aims either at a pathological complete response or at tumor reduction, allowing more frequent use of breast-conserving surgery. Although different clinical and pathological staging parameters are in use, and biologic tumor markers have been identified to predict tumor response to neoadjuvant chemotherapy [2], the evaluation of post-neoadjuvant endocrine therapy and the subsequent identification of tumors that are responsive to treatment have not been studied in detail. Fewer trials of neoadjuvant endocrine therapy, especially spanning several months before surgery, have been conducted than those for neoadjuvant chemotherapy. [3, 4] We retrospectively reviewed the magnetic resonance imaging (MRI) findings of invasive estrogen receptor-positive breast cancer in postmenopausal women undergoing neoadjuvant endocrine therapy, and correlated them with the histopathological response.
Methods and Materials

Patients

All patients provided written informed consent before undergoing the neoadjuvant endocrine therapy with an aromatase inhibitor (Exemestane) for 6 months. This study was independently approved by the institutional review board. We evaluated the MRI findings of 15 invasive estrogen receptor-positive breast cancers in 13 postmenopausal women (mean age, 63 years; range, 58-70 years) before and after neoadjuvant endocrine therapy.

Magnetic resonance imaging

This study was performed using commercially available 1.5-T MRI devices. All patients were imaged in the supine position with the arm elevated above the head. Images were obtained in the coronal plane by using the conventional surface coil on the entire affected breast, as this was prior to the introduction of the breast-surface coil at our institute. We prevented respiration-induced motion artifacts by instructing patients to take small and uniform breaths.

We performed a fast short-tau inversion-recovery (STIR) sequence using the following parameters: repetition time (TR)/time to echo (TE)/inversion time (TI), 3800 ms/70 ms/170 ms; field of view (FOV), 180 mm; matrix size 224 × 336; and slice thickness, 4 mm with a 0.4-mm gap, NEX 2. We obtained a three-dimensional (3D) fat-suppressed T1-weighted fast field-echo sequence (FST1FFE) for a dynamic study before and after a bolus 0.2 mmol/kg body weight injection of gadopentetate dimeglumine, administered using an automatic injector at 3 ml/s, followed by a 40-ml saline flush. Images were taken at 30, 60, 90, and 180 s after the beginning of the injection without subtraction. The MRI parameters for the 3D FST1FFE sequence were as follows: TR/TE, 13 ms/5.4 ms; field of view, 200 mm; flip angle, 25; matrix, 208 × 208 ; mean partition thickness, 2 mm; and time of acquisition, 35 s. Subsequently, to achieve a higher spatial resolution, a 3D FST1FFE sequence was performed with the following parameters: TR/TE, 13 ms/5.5 ms; flip angle, 30°; matrix, 224 × 224; and mean partition thickness, 1.5 mm, NEX 2. Acquisition time was 2 min 14 s.

Image interpretation

All 15 MR images of estrogen receptor-positive invasive breast cancers in 13 postmenopausal women taken before and after neoadjuvant endocrine therapy, were reviewed independently by 2 radiologists blinded to the clinicopathological findings. Both used the BI-RADS MR lexicon[5] to describe morphology and kinetics. If BI-RADS assessment categories differed between the 2 radiologists, a consensus was reached after discussion. Any contrast enhancement contiguous with the primary tumor was considered positive. Multifocal contrast enhancement in the same or neighboring
quadrant of the index tumor was considered positive even if not contiguous with the primary tumor. The parameters measured were the longest diameter of the sum of mass and non-mass-like enhancement, the longest diameter of the enhanced mass alone, the maximum area of the mass in the dynamic slices, and the intensity of each phase.

The signal-increase rate of each phase, the reduction ratios of the diameter, and the area of the lesion were also calculated. The indices were correlated with response as judged by histopathology of the surgical specimen. The response was classified based on histopathology as complete, marked, slight, and no response.

Pathological examination

Serial 5-mm slices from specimens obtained after breast-conserving surgery were used for histopathological examination. The effect of therapy on the tumor was determined histologically according to the criteria established by the Committee for Production of Histopathological Criteria for Assessment of Therapeutic Response of the Japanese Breast Cancer Society (2004 version) [6, 7]. The specimens were classified into 4 grades: Grade 0, no response, almost no change in cancer cells after treatment; grade 1, slight response, mild changes in cancer cells regardless of the extent, and/or marked changes in less than one-third of cancer cells (1a) or marked changes in one-third or more but less than two-thirds of cancer cells (1b); grade 2, marked response, marked changes in two-thirds or more of tumor cells with apparent remaining cancer cells or marked changes approaching a complete response, necrosis and/or disappearance of all tumor cells; grade 3, complete response, necrosis and/or the disappearance of all tumor cells, and/or the replacement of cancer cells by granulation and/or fibrosis.

Specimens obtained by core needle biopsy before endocrine therapy were immunohistochemically analyzed for ER (SP1, Ventana Benchmark XT; Ventana Medical Systems, Tucson, AZ, USA) and PR (1E2, Ventana Benchmark XT) using the Ventana Benchmark XT autostainer (Ventana Medical Systems, Tucson, AZ, USA). The status of the tumor for either receptor was considered to be negative if the expression was less than 10%, and positive if the expression was 10% or greater.
Results

Before neoadjuvant endocrine therapy, all 15 tumor masses could be visualized; 10 of them showed irregular margins and 5 showed spiculated margins. After the therapy, 9 distinct tumor masses were detected (Fig.1); they included 5 with irregular margins and 4 with spiculated margins. Five cases showed non-mass-like enhancement; of these, 3 showed segmental enhancement, and 2 ductal enhancement. In one case, no enhancement was seen.

All masses observed after neoadjuvant endocrine therapy were classified as showing slight or no response (9/9), whereas non-mass-like enhancements were classified as showing complete or marked response (3/6), and slight response (3/6), based on histopathology.

Furthermore, the signal-increase rate in the dynamic early phase of residual lesions correlated well with the histopathologically diagnosed response of the surgical specimen \( (r = 0.663) \) (Fig.2) and reduction ratio of the areas \( (r = 0.645) \). Weaker correlations were obtained between histopathological results and the reduction ratio of the longest diameter of the sum of mass enhancement and non-mass-like enhancement \( (r = 0.429) \), signal-increase rate in the dynamic early phase of residual lesions of mass enhancement \( (r = 0.386) \), and residual area of mass enhancement \( (r = 0.238) \).
Images for this section:

**Fig. 0:** Fig.1A. MR images from a 58-year-old woman before neoadjuvant endocrine therapy. Dynamic early-phase image before initiation of neoadjuvant endocrine therapy demonstrates a 48.5-mm enhanced mass including the long spiculae.

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**Fig. 0:** Fig.1B. MR images from a 58-year-old woman after neoadjuvant endocrine therapy. Dynamic early-phase image after neoadjuvant endocrine therapy demonstrates a 47.4-mm (including the long spiculae) enhanced mass with central necrosis.

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**Fig. 0:** Fig. 2. Scatterspots showing the correlation between the signal-increase rate (intensity/s) in the dynamic early phase of residual lesions and the histopathological response (n = 15).

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Conclusion

Our study shows that the signal-increase rate in the early phase of residual lesions in dynamic breast MRI can be used to predict histopathological response to neoadjuvant endocrine therapy.
References


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