Sunny-side-up egg sign: a characteristic appearance of breast cancer after radiofrequency ablation on MRI

Poster No.: C-1776
Congress: ECR 2013
Type: Scientific Exhibit
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Keywords: Cancer, Ablation procedures, MR, MR-Diffusion/Perfusion, Breast
DOI: 10.1594/ecr2013/C-1776

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Purpose

Breast cancer is the most common cancer worldwide in women [1]. With an implementation of mammography screening, number of patients with early stage cancer has doubled [2]. Surgical excision with or without systemic therapy is a mainstay for such patients. Paralleling with a stage migration to smaller and lower stage at presentation, local therapy for breast cancer has evolved in pursuit of less invasive techniques without compromising oncologic outcome. Thermal ablation therapy is one of a candidate for minimal invasive surgery. Radiofrequency ablation (RFA) therapy for breast cancer has been developed and studied since the first report in 1999 [3-13]. RFA therapy was followed by immediate surgical resection in most of those pilot studies with a histopathological confirmation of complete coagulation necrosis. Upon the encouraging results, recent studies evaluate RFA as a primary local therapy in limited patient population, such as medically inoperable elderly patients. Knowledge of imaging findings of therapeutic change after RFA may be of paramount importance in the future because of its unfamiliarity among radiologists and a need for surveillance, although a role of RFA in clinical practice is yet to be determined. Therefore, a purpose of the present study is to describe the imaging findings of follow up MRI in patients with breast cancer after receiving RFA therapy.
Methods and Materials

Patients

A cohort of 37 women (mean age 53.7), who participated in a feasibility study that evaluated safety and efficacy of RFA for breast cancer, was included in the present study. Written informed consent was waived by institutional review board for the retrospective nature of the study. The eligibility criteria for the feasibility study, which are described in detail in a paper by Yamamoto et al [14], includes single, invasive ductal carcinoma, diameter of 2 cm or less, and no evidence of ductal spread on imaging studies.

RFA procedure

Patients underwent sentinel node biopsy and RFA under general anesthesia. A single needle 17-gauge electrode with a 3 cm noninsulated tip (Cool-tip, Covidien, Boulder, CO, USA) was used. The needle tip was advanced into the tumor parallel to the long axis of the tumor with real time ultrasound guidance. After injecting 5% glucose solution into the retromammary space and subareolar tissue, RF delivery was started at a power of 5W, and then increased each minute until automatically stopped based on temperature.

Treatment algorithm

If sentinel node biopsy results were positive, axillary lymph node dissection was performed. Tumor viability was evaluated with nicotinamide adenine dinucleotid (NADH)-diaphorase staining of the specimen obtained with a vacuum assisted biopsy system and dynamic contrast-enhanced MRI (DCE-MRI), 3 to 4 weeks after RFA. If tumor viability was confirmed and hence RFA therapy was judged incomplete, salvage surgery was scheduled. In the case of complete RFA, whole breast radiation therapy was administered for a total dose of 50 Gy at 2 Gy per fraction, with or without boost dose of 10 Gy for tumor site. Adjuvant systemic therapy was also administered if indicated. Breast MRI examinations were obtained before, immediately after RFA (3 to 4 weeks), and at least once a year thereafter.

Breast MRI technique

Breast MRI was performed with a 1.5 Tesla clinical scanner equipped with dedicated breast coil (Avanto, Siemens, Erlangen, Germany). After placing venous catheter in the arm, patients were placed in the prone position, with both breasts hanging in the coil. Following pulse sequences were included in the examinations: Axial short-tau inversion recovery (STIR) (TR/TE = 3850/11 ms, 394 x 240 matrix, 6 mm slice thickness, 1 acquisition), diffusion-weighted imaging (DWI) using echo-planar STIR (TR/TE = 8000/65 ms, 160 x 84 matrix, 5 mm slice thickness, 6 acquisition, b-value of 0 and 1000), and
DCE-MRI using coronal 3D T1-weighted gradient echo with fat suppression (TR/TE = 4/1 ms, 394 x 230, 3 mm slice thickness, 1 acquisition), obtained every 60 seconds before and 5 minutes after administration of gadopentetate dimeglumine or gadodiamide at a dose of 0.2 ml/kg.

**Image analysis**

All MR imaging was analyzed on the clinical PACS viewer by two board certified staff radiologists (H.T and A.H, with 26 and 6 years experience respectively) on consensus base. The observers were unaware of clinical and pathological findings such as results of biopsy after RFA. Upon earlier observations, we have evaluate a pattern of contrast enhancement of ablated area by following 3 items: (1) presence or absence of ring enhancement, (2) size and completeness of ring enhancement if present, and (3) presence or absence of peripheral and internal nodule and its contrast enhancement. We coined the term "sunny-side-up egg sign", which refers to a combination of complete or incomplete ring and internal nodule on DCE-MRI or DWI. Similarly, findings on DWI were analyzed by following 3 items: (1) identification on DWI, (2) shape of high intensity on DWI, and (3) presence or absence of nodular high intensity and apparent diffusion coefficient of the nodule. Background parenchymal enhancement pattern was categorized either present or absent applying the criteria described by Hambly et al.; minimum to mild enhancement in their criteria was assigned to absent, and moderate to marked enhancement to present [15].
Results

During the mean follow-up period of 29.9 month (median 30 month), mean number of MRI examinations per patient was 3.3. Overall, 116 MRI examinations were performed. Mean size of the primary tumor was 1.16 cm. Sentinel lymph node biopsy was positive in 7 patients.

Findings of DCE-MRI

Incomplete/complete ring enhancement was observed at the first MRI after RFA in 29 (78%) and 6 (16%) patients, respectively (Fig. 1-5). Ring enhancement was not observed in 2 (5%). Among patients with incomplete ring enhancement at the first MRI, complete ring enhancement was observed in 23 out of 29 patients (79%) at the following MRI. Sunny-side-up egg sign was positive in 27 patients (73%) at any point during the follow-up period. Size of ring enhancement tended to decline relatively rapidly within the first year and gradually thereafter (Fig. 6).

Peripheral nodular enhancement was observed in 8 patients (22%) (Fig. 7-9). Peripheral nodular enhancement disappeared in 4 patients and was stable in 4 patients at the following MRI. Among the patients with or without peripheral nodular enhancement, background parenchymal enhancement was positive at 2 and negative at 12, and positive at 28 and negative at 74 examinations, respectively.

Findings of DWI

At 64 examinations in 30 patients (81%), the following 5 patterns were observed on DWI: (a) sunny-side-up egg (n = 26, 41%), (b) inhomogeneous (n = 21, 33%), (c) homogeneous (n = 11, 17%), (d) ring (n = 3, 5%), and e) void (n = 3, 5%) (Fig. 10-14). Among the 64 examinations in which any aforementioned patterns were observed, ADC value was measurable in 57 (89%). Mean ADC value was 1.65±0.59 m²/s. The time course of ADC values was inconsistent among the patients (Fig. 15).
Fig. 1: A 78-year-old woman with invasive ductal carcinoma of the left breast. (a) Pretreatment DCE-MRI shows a 2 cm enhancing mass in the upper inner quadrant.

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Fig. 2: (b) One month after RFA. Coronal precontrast T1-weighted image (T1WI) of the dynamic series. Ablated tumor shows faint hyperintensity (arrow).

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**Fig. 3:** (c) The first phase of coronal T1WI of the DCE-MRI after contrast injection. Tumor (arrow) is surrounded by incomplete ring (arrowhead), which represents sunny-Side-up egg sign.

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**Fig. 4:** (d) Subtraction image of the first phase. Tumor shows no enhancement.

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Fig. 5: (e) DCE-MRI obtained 2 years after RFA. Thin and smooth ring enhancement is seen at the ablated area.

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Fig. 6: Graph shows time course of maximum diameter of ring enhancement in each patients.

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Fig. 7: A 45-year-old woman with invasive ductal carcinoma of the right breast. (a) The first phase of coronal T1WI of DCE-MRI shows markedly enhancing mass in the lower inner quadrant of her breast.

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**Fig. 8:** Subtraction image of DCR-MRI at 6 month after RFA reveals the complete ring enhancement and a peripheral nodule in a 6-o'clock position (arrow).

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Fig. 9: Subtraction image of DCR-MRI at 1 year after RFA reveals the complete ring enhancement and a peripheral nodule in a 6-o'clock position (arrow). The nodule remains stable in size. The ablated area and overlying skin had become swollen and erythematous. The patient underwent a resection of the affected area for cosmetic reason. Histopathological examination of the resected tissue revealed fat necrosis and surrounding fibrosis with no evidence of malignancy.

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Fig. 10: Representative patterns of ablated area on axial DWI (b = 1000). Ablated area is indicated in the red circle. Sunny-side-up egg type.

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Fig. 11: Inhomogeneous type.

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Fig. 12: Homogeneous type.

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**Fig. 13:** Ring type.

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Fig. 14: Void type.

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Fig. 15: Graph shows time course of ADC values.

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Conclusion

Coagulation necrosis of tumor and adjacent normal tissue, induced by delivery of radiofrequency energy, elicits tumor devasculization and inflammatory response and hyperemia around the ablated area. This combination is likely to be represented in the most typical finding shown in our study, sunny-side-up egg sign. Previous studies elucidated imaging findings after RFA of liver tumor. [16,17] Typically, ablated area shows no vascularity and hyperintensity on T1WI, with or without surrounding enhancement, which is assumed to represent hyperemia. The similar findings were observed in our study. Time course of the ring enhancement was in agreement with the study reported by Nagashima et al, which had shown gradual diminishment of the ring enhancement [18]. Peripheral nodular enhancement raises the suspicion of residual or recurrent tumor in liver imaging after RFA. However, peripheral nodular enhancement was either stable or resolved in our study. The etiology of the peripheral nodular enhancement is unknown for retrospective nature of our study. Pathologic correlation was available in only one case. Ablated breast tissue was removed in a woman, in whom inflammatory mass developed. Peripheral nodule was observed in her breast MRI 4 month prior to the surgery (same patient as illustrated in Fig. 8, 9). Histopathological examination of the resected tissue had shown fat necrosis and infiltration of inflammatory cells, with no evidence of malignancy. Peripheral nodular enhancement seen in our study may be a unique inflammatory response.

In conclusion, non-enhancing central hyperintensity within ring-shaped enhancement was typical finding after ablation. Peripheral nodular enhancement can be occasionally observed.


