European Journal of Radiology 83 (2014) 1771–1777

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Image and pathological changes after microwave ablation of breast cancer: A pilot study

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ARTICLE INFO

Article history:
Received 24 April 2014
Received in revised form 14 June 2014
Accepted 20 June 2014

Keywords:
Breast cancer
Microwave ablation
MR imaging

ABSTRACT

Purpose: To prospectively assess MR imaging evaluation of the ablation zone and pathological changes after microwave ablation (MWA) in breast cancer.
Materials and methods: Twelve enrolled patients, diagnosed with non-operable locally advanced breast cancer (LABC), were treated by MWA and then neoadjuvant chemotherapy, followed by surgery. MR imaging was applied to evaluate the effect of MWA. Hematoxylin-eosin (HE) staining and transmission electron microscopy (TEM) were applied to analyze the ablated area.
Results: All MWA procedures were performed successfully under local anesthesia. For a mean duration of 2.15 min, the mean largest, middle and smallest diameters in the ablated zone 24-h post-ablation in MR imaging were 2.98 cm ± 0.53, 2.51 cm ± 0.41 and 2.23 cm ± 0.41, respectively. The general shape of the ablation zone was close to a sphere. The ablated area became gradually smaller in MR imaging. No adverse effects related to MWA were noted in all 12 patients during and after MWA. HE staining could confirm the effect about 3 months after MWA, which was confirmed by TEM.
Conclusions: 2 min MWA can cause an ablation zone with three diameters larger than 2 cm in breast cancer, which may be suitable for the local treatment of breast cancer up to 2 cm in largest diameter. However, the long-term effect of MWA in the treatment of small breast cancer should be determined in the future.

1. Introduction

Image-guided nonsurgical ablative therapies, including radiofrequency, microwave, cryotherapy and laser therapy, have received increasing attention as minimally invasive treatments to destroy various solid tumors [1–4]. Microwave ablation (MWA) is a promising minimally invasive local therapy with many advantages [5–7], including large ablation zones, short ablation durations, and improved convection profile. MWA has been accepted as an effective therapy in the treatment of hepatic tumors [8–10], and has been applied to treat other solitary tumors [11–14].

Since satisfied cosmetic outcomes may be obtained by nonsurgical ablative therapies without the removal of breast tissue, ablative therapies have been evaluated in many clinical research studies [3,15–18]. Our previous phase I ablation-resection study firstly shows that MWA of small breast cancers is feasible under general anesthesia, but the extent of ablation zone may be underestimated [11]. To our knowledge, there is no study reporting the long-term evolution of microwave ablated breast cancer. For clinical use of MWA for breast cancer, the long-term evolution of ablated lesions is urgently needed.

MR imaging can be used to predict tissue damage after ablation because necrosis is typically visualized as a nonperfused volume after contrast material administration [19,20]. So it is suitable for evaluating the efficacy of MWA. Previous studies suggest MR imaging is suitable for long-term follow-up of radiofrequency ablated breast cancer [17,20]. The pathological confirmation of the efficacy is the gold standard for MWA of breast cancer. The pathological findings are only reported in few studies about radiofrequency ablation of breast cancer [15,16]. Moreover, the correlation between MR imaging and pathological findings is necessary for long-term follow-up. Up to now, the correlation is only reported in a previous study about radiofrequency [16].

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http://dx.doi.org/10.1016/j.ejrad.2014.06.015
0720-048X/

MWA has not been applied for local therapy for breast cancer patients. MR imaging and pathological changes after microwave ablation of breast cancer have not been reported. In this prospective study, we report the data about MR imaging evaluation of the ablation zone and pathological changes after MWA in breast cancer for the first time.

2. Materials and methods

2.1. Patient enrollment

The study protocol was approved by the institutional ethics committee (No. 2011-SR-106), and written informed consent was provided by all patients. From February 2012 to September 2013, patients diagnosed with LABC in our hospital were recruited in this prospective pilot study.

The inclusion criterion were as follows: (a) invasive breast cancer proved by using core-needle biopsy; (b) non-operable LABC; (c) patients who wanted to receive neoadjuvant chemotherapy; and (d) Karnofsky performance status greater than 70% [11,18]. Patient exclusion criteria included the following: (a) patients not suitable for neoadjuvant chemotherapy; (b) patients with medical contraindications to MR imaging; (c) patients with evidence of coagulopathy, chronic liver diseases, or renal failure; (d) patients taking anticoagulant drugs; and (e) patients who were pregnant or breast-feeding. Hormone receptor and human epidermal growth factor receptor 2 status were determined by using immunohistochemical analysis of tissue from core-needle biopsy specimens prior to treatment.

2.2. Treatment procedure

Breast MR imaging was performed before treatment by two radiologists with more than 1500 interpretations experience in breast MR imaging. Then, MWA was performed by two surgeons with 17 and 5 years of experience in breast surgery, respectively. Second breast MR imaging evaluation was performed about 24 h after MWA. Patients received prescheduled neoadjuvant chemotherapy after second MR imaging evaluation. Breast MR imaging was performed before every subsequent cycle of neoadjuvant chemotherapy and surgery. Modified radical mastectomy (mastectomy and axillary lymph node dissection) was scheduled to these patients when the disease became operable. Patients were monitored during the MWA, the following chemotherapy and surgery for any MWA-induced complications by the surgeons and radiologists.

2.3. MWA protocols

The patient was placed in the supine position. Ultrasonography (US) was applied to guide MWA. Local anesthesia was induced with 1% lidocaine. Lidocaine was injected around the lesion and into retromammary space. With US guidance, the antenna was placed into the tumor. MWA was started for 2–3 min after testing the cold-water cycling system. When the patient could not tolerate the pain, the procedure was interrupted. The microwave system used in this study was the same as previous studies [7,11]. The microwave irradiation frequency was 2450 MHz, and an output power of 40 W was chosen. After ablation, patients were monitored in our hospital for at least 24 h for immediate complications.

2.4. Neoadjuvant chemotherapy

Patients received at least three 21-day cycles of neoadjuvant chemotherapy before surgery. Chemotherapy regimens were determined based on guidelines in our country and included: (1) TEC: docetaxel, epirubicin, and cyclophosphamide; (2) FEC: 5-fluorouracil, epirubicin, and cyclophosphamide; (3) NP: navelbine and cisplatin; (4) TP: docetaxel and cisplatin. After two cycles of neoadjuvant chemotherapy, clinical response was assessed by physical examination or US. When the disease progressed, the primary regimen was replaced by a new regimen.

2.5. MR imaging protocols

MR imaging was performed with a 3.0 T system (MAGNETOM Trio, Siemens, Germany) using a bilateral 8 channel phased-array breast coil with women in the prone position. Axial and sagittal T1-weighted and T2-weighted images were obtained.

The dynamic series consisted of a three-dimensional transverse fast low angle shot T1-weighted sequence (TR/TE, 4.23 ms/1.57 ms; matrix 448×296; slice thickness 0.9 mm, no gap; pixel resolution 1.1 mm $\times$ 0.8 $\times$ mm 0.9 mm) with fat suppression. A total of six dynamic acquisitions, with a temporal resolution of 60 s for a single dynamic acquisition, were performed. Contrast agent bolus injection consisted of 0.1 mmol gadopentetate dimeglumine (Magnevist, BayerSchering, Germany) per kilogram of body weight was administered at an injection rate of 3.0 ml/s, which was followed by a 20 ml saline solution.

The ablated tumor was defined as a nonperfused volume after contrast material administration [19,20]. Ablation extent was calculated on a voxel-by-voxel basis. The projections were made in the axial, sagittal and coronal directions and allowed the ablation zone to be identified in all dimensions. Two diameters in largest cross section and the largest height in coronal plane of ablated volumes in MR imaging were defined as largest, middle, and smallest diameters according to their length. The shapes of the ablated volumes were classified according to the ellipticity index calculated by using largest, middle, and smallest diameters in MR imaging. Accordingly, the fraction of the largest and smallest diameters was defined as Dl, and the fraction of the middle and smallest diameters was defined as Dm [16]. According to the previous study [16], a lesion was called spherical when both Dl and Dm were 1.5 or less.

2.6. Pathologic evaluation

After surgery, the coagulation zones were dissected and sectioned along the antenna track. The tissue sections were incubated for cell viability in the incubation medium with 2% 2,3,5-triphenyl tetrazolium chloride (Sigma) [7,21]. The largest diameter (along the antenna) was assessed macroscopically with calipers. After incubation, the tissues were fixed in formalin, embedded in paraffin, sectioned into 4-μm slices and stained with hematoxylin-eosin (HE). The pathology evaluation was performed by two pathologists (with more than 10 years of experience in breast pathologic examination).

Ultrastructure analyses with transmission electron microscopy (TEM) of the ablative zone and normal zone were performed. The ablative samples were collected from the center of the ablative zone, while the normal ones from peripheral normal breast tissues at least 3 cm away from the ablative zone. The electron microscope samples were prepared according to the guidelines. Ultrathin sections (50–80 nm) were cut and examined and micrographed with a transmission electron microscope (JEM-1010, Japan).

2.7. Data and statistical analysis

Mean $\pm$ standard deviation (SD), percentiles, and range were analyzed for each continuous variable. The volume of coagulation was calculated by using the three-dimensional axis in MR imaging with the equation $V = 4\pi(a/2)(b/2)(c/2)/3$. The association between the largest diameter in pathology and MR imaging was evaluated