Original Study

Breast-Conservative Surgery Followed by Radiofrequency Ablation of Margins Decreases the Need for a Second Surgical Procedure for Close or Positive Margins

Isabel T. Rubio,[1] Stefania Landolfi,[2] Meritxell Molla,[3] Javier Cortes,[4] Jordi Xercavins[1]

Abstract

Excision of breast cancer followed by radiofrequency ablation is a feasible technique that is used to decrease the need for a second surgical procedure for close or positive margins, and in the long-term, the technique may reduce the incidence of local recurrences.

Background: Excision of breast cancer followed by radiofrequency ablation (eRFA) is a technique designed to increase negative margins in breast-conservative surgical procedures. The objective of this study is to analyze the impact of eRFA in avoiding a second surgical procedure for close or positive margins after a breast-conservative surgical procedure. **Material and Methods:** From February 2008 to May 2010, 20 patients were included. After lumpectomy, the eRFA was performed in the lumpectomy cavity, and biopsies from each margin from the radial ablated cavity walls were obtained. Biopsy samples were assessed for tumor viability. **Results:** eRFA was successful in 19 of 20 patients. In all patients, the devitalized tissue extended beyond a 5- to 10-mm radial depth of the biopsy sample. Overall, 6 patients (31%) had margins < 2 mm, 4 of them with < 1 mm margin. All 6 of these patients had no tumor viability according to analysis of biopsy samples stained with 2,3,5-triphenyltetrazolium chloride. At a median follow-up of 46 months, no local recurrence had been found. **Conclusion:** This study supports the feasibility of eRFA treatment. In our study, the eRFA method has spared 31% of patients from undergoing a re-excision surgical procedure, and it may, in the long-term, reduce local recurrences.

Clinical Breast Cancer, Vol. 14, No. 5, 346-51
Keywords: Breast cancer, Lumpectomy cavity, Radiofrequency ablation, Recurrences, Reoperation

Introduction

Breast-conservative surgery (BCS) has largely replaced mastectomy in patients with early breast cancer, as survival differences between the 2 options have note been shown.[1,2] The objective of BCS is to remove a tumor with negative margins to decrease the chance of local recurrences (LRs). The disadvantage of BCS is the risk of LR, which has been reported to be between 6% and 16%.[3] Obtaining negative margins at the time of surgery decreases the incidence of LR.[4-7] Even with these data, studies have shown that positive margins are found in 20% to 40% of patients.[8] Margin status is considered a predictive factor of LR, and positive margins are related to high rates of residual tumor.[9] In addition, 75% to 90% of LRs occurred at the lumpectomy bed.[10]

Radiofrequency ablation (RFA) is obtained by heat generated from high-frequency alternating currents. As the friction-generated heat from ion movement in the tissues rises the temperature, it causes damage to the cells. The first use of RFA in breast cancer was reported in 1999, and since then, RFA has gained acceptance as a technique for percutaneous ablation of breast cancer. Several reports of percutaneous RFA in patients with breast cancer have shown complete coagulative necrosis of intact tumors in 86% to 100% of

Presented at the 8th European Breast Cancer Conference (EBCC-8), March 21-24, 2012; Vienna, Austria

[1]Breast Surgical Unit, Breast Cancer Center
[2]Department of Pathology
[3]Department of Radiation Oncology
[4]Department of Medical Oncology, Breast Cancer Center
Vall d'Hebron Instituto de Oncología. Hospital Universitario Vall d'Hebron. Universitat Autònoma de Barcelona, Barcelona, Spain

Submitted: Oct 27, 2013; Revised: Feb 7, 2014; Accepted: Feb 12, 2014; Epub: Feb 21, 2014

Address for correspondence: Isabel T. Rubio, MD, Breast Surgical Unit, Breast Cancer Center, Hospital Universitario Vall d'Hebron, Paseo Vall d'Hebron 119-129, 08035 Barcelona,Spain
E-mail contact: irubio@vhebron.net

1526-8209/$ - see frontmatter
http://dx.doi.org/10.1016/j.clbc.2014.02.002

patients.[11-17] Among the problems of percutaneous RFA use is incomplete ablation that has been attributed to technical reasons or underestimation of tumor size by imaging. The increased use of magnetic resonance imaging (MRI) for preoperative assessment of breast cancer has increased the detection of residual tumor after RFA in patients with infiltrating ductal carcinoma.[16,18,19] Excision of breast cancer followed by radiofrequency ablation (eRFA) is a technique that has been developed to ensure negative margins at the time of surgery in patients with early breast cancer. Klimberg et al.,[20] in a pilot trial, showed the feasibility of this technique and the decrease in the need for re-excision of inadequate margins in 41 patient who underwent lumpectomy followed by intraoperative RFA. Of 41 patients, 11 had inadequate margins, but only 1 required re-excision for a grossly positive margin.

The objective of our study was to evaluate the accuracy and effectiveness of RFA on margins to reduce the number of patients requiring second surgeries for close (< 3 mm) or positive margins and to accurately ablate a margin of ≥ 1 cm margin around the tumor bed.

Patients and Methods

Patient Eligibility

For this prospective, nonrandomized trial, patients with a diagnosis of T1-2 N0, unicentric, and unilateral infiltrating ductal carcinoma of the breast who presented in our clinic and required a lumpectomy were included. Patients were recruited from February 2008 to May 2010. Exclusion criteria were neoadjuvant chemotherapy, pregnancy, breast implants, extensive microcalcifications, and tumors located < 1 cm from the skin or the pectoralis muscle. The study was approved by the institutional review board, and patients signed an informed consent form. Breast imaging was performed with mammography and breast ultrasonography. MRI was not performed prior to surgery. Patients completed a subjective cosmetic result survey at baseline and at 6 months. Cosmetic results were recorded on scale of 1 to 6, 1 being not at all satisfied and 6 being extremely satisfied. Assessments based on the Radiation Therapy Oncology Group (RTOG) scale, which records acute radiation morbidity, were performed at 6 and 12 months after the radiation therapy (XRT) and as part of postoperative assessment of the affected breast.

After surgery, all patients received whole-breast irradiation as part of the standard treatment at our institution. Patients were required to come to the clinic for follow-up visits for a minimum of 2 years after the procedure. The first visit was a postoperative follow-up visit occurring within 2 weeks of the surgery. Afterward, patients returned every 6 months for a mammogram, for 2 years. After that, patients returned to the clinic for the standard follow-up protocols. Immediate and late complications from the procedure were recorded.

eRFA Procedure

Once they were in the operating room, patients underwent the standard procedures for a sentinel lymph node biopsy[21] and for a lumpectomy; tissue specimens were sent fresh for tissue banking and for routine processing and margin-width assessment. The lumpectomy was immediately followed by the RFA procedure. The target temperature was set to 100°C for 15 minutes for ablating the tissue cavity. A purse-string suture was performed in the lumpectomy cavity to approach the tissue, and the RFA device (StarBurst XL Semi-Flex, AngioDynamics, Queensbury, NY) was inserted into the lumpectomy cavity.[20] The arrays were deployed into the cavity, and the eRFA was started. Once the procedure was finished, the device was removed from the cavity. Next, 4 perpendicular incisional biopsies of the radial ablated cavity walls (medial, cranial, lateral, and caudal walls) were obtained. These biopsies were obtained to provide anterior to posterior radial tissue slices, approximately 2 cm in radial depth and 0.5 cm in width. With minimal drying and tissue distortion, these 4 biopsy slices were submitted fresh (without fixation) and sent to the pathology department for 2,3,5-triphenyltetrazolium chloride (TTC) viability staining to document the radial depth of the cavity. Careful hemostasis was obtained and all the oil aspirated, and then the cavity was closed according to standard procedure following a lumpectomy.

Pathologic Assessment

The 4 incisional biopsies from the ablated cavity wall were labeled with the patient's name and identifiers, including the cavity wall from which each sample was obtained and immediately sent fresh from the operating room to the pathology department. Care was taken to not dry, wash or rinse with water, crush, or distort the tissue biopsies during handling. A delicate suture marked the lumpectomy cavity edge of each biopsied tissue sample for orientation. The unstained incisional wall biopsies were digitally photographed and then immediately placed in a TTC vitality stain for 1 hour in a 37°C water bath. (TTC staining allows for regions of thermal necrosis to be highlighted and identified using a dehydrogenase enzyme—and cofactor-based reaction that converts the tetrazolium salt to a formazan pigment within viable tissues. This results in a cytochemical color change from colorless to red-orange in tissues with preserved enzymatic activity, in other words, viable tissues.) Following staining, the tissue samples were digitally photographed again. Later, they were fixed in 10% neutral buffered formalin and embedded in paraffin for further hematoxylin—eosin (H&E) standard staining and histological evaluation of the biopsies.

Results

The eRFA technique was successful in 19 patients out of 20. The mean patient age was 66.9 years (range, 46-76 y). The mean pathologic tumor size was 14.7 mm (range, 4-28 mm). Tumor and patient characteristics are shown in Table 1.

In all patients, the devitalized tissue extended beyond the 5- to 10-mm radial depth of the biopsy sample (range, 4-16 mm). Of the 20 patients, 12 of the 19 patients (63%) had negative margins (> 3mm) at the time of the final pathologic assessment. Furthermore, 6 patients (31%) had margins < 2 mm in the final pathologic assessment. All 6 of these patients had incisional biopsies from the cavity wall with no tumor viability detectable after staining with TTC. (Fig. 1) In 1 patient, an invasive carcinoma was found at the edge of the punch biopsy, > 1 cm away from the coagulative necrosis (Fig. 2). This patient underwent a mastectomy.

Intraoperative-margin status was assessed by macroscopic visualization, and frozen section was performed if any margin was considered suspicious. There was no reported positive margin intraoperatively, and reported close margins were taken care of with