RESEARCH COMMUNICATION

Interoperative Radiotherapy of Seventy-two Cases of Early Breast Cancer Patients During Breast-conserving Surgery

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Abstract

Objective: To evaluate interoperative radiotherapy after breast conservative surgery in early breast cancer patients in terms of postoperative complications, cosmetic outcome and recurrence events. Methods: From June 2007 to Dec 2011, 143 early breast cancer patients received breast conservative surgery. Seventy-two (study group) received interoperative radiotherapy, compared with 71 patients (control group) given routine radiotherapy. Postoperative complications were evaluated 1 month after surgery; cosmetic outcome was evaluated 1 year postoperatively; recurrence and death events were followed up. Results: The average wound healing time was 13–22 d in the study group and 9–14 d in the control group. In the study group, 2 patients developed lymphoedema, 16 patients showed wound edema while no such side effects were found in the control group. No infection or hematomas were found in either group. In the study group (59 cases), overall cosmetic outcome in 53 patients was graded as excellent or good, and in 6 as fair or poor. Meanwhile in the control group (56 cases), 42 patients were graded as excellent or good, and 14 as fair or poor (P=0.032). After a follow-up from 3 to 54 months (median: 32 months), two patients (2.78%) in study group developed local relapses, one of them (1.39%) died, 2 patients (2.78%) developed bone metastases. In control group, one patient (1.41%) developed local relapse, 2 patients (2.82%) developed bone metastases, and no one died. Conclusion: Intraoperative radiotherapy is safe and reliable with good cosmetic outcome.

Keywords: Breast neoplasm - radiotherapy - breast conservative surgery

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Introduction

Whole breast radiotherapy after completion of chemotherapy in breast-conserving surgery (BCS) has become the standard treatment of early breast cancer (Fisher et al., 2002; Veronesi et al., 2002). In recent years, because of application of sentinel lymph node biopsy many patients are exempt from complications associated with lymph node dissection (Veronesi et al., 1997; Veronesi et al., 2001). Veronesi et al. (2001) found that 85% of recurrence after BCS occurred in the scar area and they proposed that whether the whole breast radiotherapy after BCS could be replaced by partial radiotherapy only around the tumor bed. Since the end of the last century, many researches on partial breast irradiation therapy after BCS have been reported (Veronesi et al., 2003; Luini et al., 2005; Beal et al., 2007; Sawaki et al., 2009; Abbott et al., 2011). Intraoperative radiotherapy (IORT) is to deliver sufficient quantities of single irradiation only to the tumor bed after tumor resection surgery.

From June 2007 to Dec 2011, 143 cases of patients with early breast cancer underwent breast conservative surgery in our hospital: 72 cases underwent interoperative radiotherapy in study group and 71 cases underwent routine radiotherapy in control group. The effect of treatment by intra-operative radiotherapy is more satisfactory compared with the control group. The results are reported as follows.

Materials and Methods

Patients

This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of the Fourth Peoples Hospital of Wuxi City. Written informed consent was obtained from all participants.

The patients enrolled were met on the following criteria: 1) Ages of the patients: ≥ 40 years old. The age limit can be relaxed in case of those patients with special type of cancer (such as mucinous adenocarcinoma) or tumor size (diameter: ≤ 1cm). 2) Tumor distance from the areola ≥ 2 cm, tumor size ≤ 2.5 cm. 3) Multifocal cancer was excluded by preoperative mammography films, color B- scan ultrasonoscope or MRI examination. No obvious axillary lymph node enlargement was found

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Selection, placement of applicator used for IORT and Implementation of IORT
gland and was touched to the lead plate to measure the plate during operation. A pin was inserted into the target plastic film wrapped in lead plate to avoid moving of lead within the gland. The first and last stitches were sewn on irradiation target and to receive the best dose distribution thickness sutures of the galactophore in front of the lead tissue. (3) Suture of galactophore: the interrupted full
The lead disc should be bigger than the size of the target placed between the free galactophore and chest muscle. a round or oval-shaped lead sheet (thickness: 3 mm, quantities of irradiation to the target of galactophore, reduce expoure to the thoracic wall and ensure sufficient necrosis. (2) Protection of thoracic wall: In order to be carefully retained to avoid postoperative flap ischemic the superficial surface of galactophore was separated from the subcutaneous fat layer, the flap blood supply should (Intra et al., 2006) . When the tumor bed outside about 3-5 cm (Intra et al., 2006). When the tumor was as the center and the skin incision was curved or radial. If the breast tumor is close to skin, the skin surface and subcutaneous adipose tissue of the tumor should be removed. If the tumor is close to chest fascia, the skin should be reserved. The tumor boundary was marked by methylene blue. Outside from the margin (about 1 cm), loop excision of the tumor was operated deeply to the pectoralis major fascia. The resection specimens were labeled with “up, down, left, right and the skin lateral edge”. Rapid histological examination of the specimen was done to determine whether the tumor was the invasive carcinoma and the cutting edge was clear. If the cutting edge was not clear, the patient had to be withdrawn from the study. Subsequently, curved incision had been done under the armpit for biopsy of sentinel lymph node or dissection of lymph node.
(1) Free of galactophore: In order to exposure the target tissue for irradiation, after the tumor was excised in experimental group, the galactophore was further free to target tissue for irradition, after the tumor was excised in (1, 5 and 15 cm) (Veronesi et al., 2001; 2003). The curve was drawn according to the obtained values of percent depth dose (PDD) of electronic accelerator after application of the cylinder (Figure 1). In order to ensure more than 90% of irradiation dose reach to the target area of breast surface and deep sides, saline gauze with 2-5mm of thickness as a tissue equivalent filler was placed on the irradiated target area of breast surface. According to the determined thickness of the breast target, 9 or 12 MeV of electronic line was selected and the prescription dose of target area was 21 Gy (the biological effect is equivalent to 58-60 Gy of conventional fractionated irradiation) by a single irradiation for about 3-5 min of duration.
After radiotherapy, withdraw the applicator from the incision, remove the breast sutures and the lead sheet, set the Pan’s drainage and suture breast and skin finnally. Antibiotics were used for prevention of postoperative infections.
Dose monitoring: IVD Solution micro-probe was placed for determination of radiation dose. Placement sites: (1) Front and back (front of lead plate) of the center and edge of the target breast; (2) Back of lead plate (front of pectoralis major muscle); (3) Outside of the applicator (1, 5 and 15 cm) (Veronesi et al., 2001; 2003).

Study items
1) The actual target dose. Whether the doses of pectoral surface and outside of the applicator (1, 5 and 15 cm) were safe. 2) Postoperative complications of IORT: Whether incision dehiscence, edema effusion, infection, hematoma, fat necrosis and liquefaction may occur after operation for a month. 3) Cosmetic evaluation of breast appearance by JCRT standard (Dubois et al., 1997). The evaluators include the surgery group, plastic surgery and radiation oncology doctors. 4) Tumor recurrence or death events.

Statistical analysis
The Software SPSS 13.0 was used for statistical analysis with the Student’s t-test. Data with a P value of less than 0.05 were considered significant.

Results
Clinical data
The detailed clinical data are shown in Table 1.

Irradiation doses
The doses in 66 cases of targeted breast with thickness from 1.4 to 3.0 cm were 20-21 Gy. The doses in 6 cases of
targeted breast with thickness above 3.0 cm were 19-20 Gy. The doses of pectoral surface and outside of the applicator with different distances were lower than 0.1 cGy.

Wound healing time
The average wound healing time in study group is 13-22 d and 9-14 d in control group. In the study group, fat deliquescence occurred in 2 patients and wound edema occurred in 16 patients but no lyponecrosis and wound edema were found in control group. No infection or hematomas were found in the two groups.

Cosmetic evaluation of postoperative breast appearance
Overall cosmetic outcome was rated after post operation for 1 year. 53 of 59 cases in the study group were graded as excellent or good, 6 patients were as fair or poor. Meanwhile in the control group (56 cases), 42 patients were graded as excellent or good, 14 patients were as fair or poor (P=0.032).

Follow-up
In the present study, after a follow-up from 3 to 54 months (median, 32 months), three cases of patients underwent sugery again in study group. According to the patient’s firm demand one case of patient underwent total mastectomy and no carcinogenesis was found in the resection specimen. Two patients (2.78%) in study group developed local relapses. No armpit lymph node was found in one case of patient through preoperative physical examination, ultrasonography and mammography. However, four pieces of lymph node metastasis were found through postoperative pathologic examination. Therefore, this patient was informed the pathway withdrawn from the study and continued to be treated with modified radical cure and postoperative radiotherapy. Unfortunately, due to the patient’s uncooperation, total mastectomy and radiotherapy had been performed until local recurrence occurred 10 months after postoperation. At present, lung metastasis was found. Tumor immunohistochemical HER2 in one case of patient was showed (++++) and the patient was further diagnosed by FISH as HER-2 positive breast cancer. The patient did not cooperate to do chemotherapy and was unwilling to be treated with targeted therapy. The patient underwent modified radical cure as local recurrence happened 12 months after postoperation and died of systemic metastases 26 months later. In study group, bone metastasis was found in 2 cases of patients (2.78%) 24 and 31 months after operation. In control group, one patient (1.41%) developed local relapse, 2 patients (2.82%) developed bone metastases, and no death occurred.

Discussion
After a BCS, patient with early breast cancer often undergo chemotherapy and whole breast radiotherapy for 5-7 weeks. However, there always exist atrophy of the irradiated breast, rough skin and pigmentation in some patients treated by whole breast radiotherapy. Appearance of the conserving breast is often less than desirable. Thus these results triggered researches whether it is necessary to undergo the whole breast radiotherapy after BCS. The results of follow-up of 12 years after BCS reported by Veronesi et al showed that 85% of local recurrence occurred in the surgical area and the remaining 15% in the different quadrants out of the surgical area. The results of a small-scale radiation research performed by Ribeiro et al. (1993) indicated that the rate of local recurrence after small range of radiotherapy slightly increased. The main local recurrence was invasive lobular carcinoma. There were no differences on survival rate. Results of other
studies (Perera et al., 1997; Vicini et al., 1999) also showed that the local control rate of local radiotherapy after BCS was 92-100%. Therefore, research on IORT after BCS increased gradually in recent years. The advantages are listed as follows: (1) Accurate location of the targeted radiotherapy region and direct irradiation to the high risk of recurrence of breast; (2) To avoid the vital organs (lung, heart, etc.) to be irradiated, and to reduce radiation injury and occurrence of the secondary primary induced by radiation; (3) Application of single high dose of irradiation may improve the radiation biological effects. 21GY of a single dose of irradiation in surgery has equivalent effect to 58-60 GY of conventional radiotherapy; (4) Shortening the interval of surgery and radiotherapy. (5) To effectively resolve the patients’ problems of round trip to the radiotherapy center; (6) Because of irradiation by IORT only to small partial breast some adverse effects including atrophy of the irradiated breast, rough skin and pigmentation can be avoided after the whole breast radiotherapy. Further more, it has good cosmetic effect which is also the original intention of BCS.

IORT has been carried out in our center since June 2007. The linear accelerator we used in the present study was Varian Clinic 23EX. The percent depth dose (PDD) of the electron accelerator will change when the applicator was used. Therefore, we determined the PDD values of 9Mev and 12Mev using different types of applicators. According to the determined values and the thickness of the breast target, 9 or 12 MeV of electronic line was selected. Saline gauze with 2-5mm of thickness as a tissue equivalent filler was placed on the irradiated target area. According to the optimal parameters, the determined values of doses after irradiation were: The doses in 66 cases of targeted breast with thickness from 1.4 to 3.0 cm were 20-21 Gy. The doses in 6 cases of targeted breast with thickness above 3.0 cm were19-20 Gy. The doses in 6 cases of targeted breast with thickness above 3.0 cm were19-20 Gy. The doses of pectoral surface and outside of the applicator with different distances were lower than 0.1 cGy. The results demonstrated that application of IORT carried out in our center is center safe and reliable not needing to worry about the irradiation injury to lung, heart, skin and the counter side of breast.

IORT has fewer complications. According to the results reported by Veronesi et al. (2005), complications were found only in 38 (6.3%) of 590 cases of patients, which included: severe fibrosis in 1 case (0.2%), mild fibrosis in 18 cases (3%), fat necrosis in 15 cases (2.5%), hematoma in 2 cases (0.3%), shrinking skins in 2 cases (0.3%). In the present study, of the 72 cases of patients, two cases have been told to quit IORT. Recurrence may be related to the patients’ uncooperation with the treatment, but not to IORT itself. Sixty-nine cases of the follow-up patients met the inclusion criteria have not been found local recurrence so far. Therefore, as long as strict indications are applied, satisfactory rate of local control can be guaranteed.

In summary, we carried out IORT after BCS of breast cancer in 72 cases of patients. The preliminary results of 54-month follow up suggested that IORT is safe, reliable with good cosmetic outcome and satisfactory tumor local control, which is worthy of further investigation.

References


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