

Progress of radiotherapy after breast-conserving surgery combined with silicone prosthesis reconstruction

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Abstract. – Breast cancer is the malignant tumor with the highest incidence in women. The standard treatment for early breast cancer is radical surgery combined with radiotherapy, but many studies have shown that adjuvant radiotherapy after breast-conserving surgery combined with silicone prosthesis reconstruction is gradually expected to become the new standard treatment because this method can obtain a good local tumor control rate, and has a cosmetic effect. Compared with myocutaneous flap reconstruction, silicone prosthesis implantation has the advantages of less trauma, simple operation, beautiful appearance, and no overlap of donor areas during reconstruction. It is a safe and feasible surgical method without worrying about necrosis and atrophy of myocutaneous flap. This emerging combination therapy may become the best mode of early breast cancer treatment.

Key Words:

Breast cancer, Breast-conserving surgery, Radiotherapy, Silicone prosthesis.

ing surgery combined with silicone prosthesis reconstruction can not only achieve good local control rates, but also improve the appearance of the body, thereby significantly improving the quality of life^{2,3}. At present, implants are widely used for breast reconstruction, allogeneic implants mainly include silicone implants and saline implants, autologous implants mainly include latissimus dorsi musculocutaneous flap and transrectus abdominus musculocutaneous flap. This paper analyzes the progress of the correlation between silicone implant reconstruction and radiotherapy by summarizing the latest literature.

Breast-Conserving Surgery

At present, breast cancer surgery is divided into total resection and breast conserving surgery (BCS). Breast cancer is a systemic disease, and the breast mass is only a local manifestation of the breast. For some small breast cancer, European and American countries choose to retain mastectomy, plus axillary lymphadenectomy, and post-operative radiotherapy. A randomized controlled retrospective study of 20-year follow-up for early breast cancer by Veronesi et al⁴ showed that there was no significant difference in long-term survival rate between breast-conserving surgery and total tumor resection, and there was no statistical difference in the incidence of contralateral, distant metastasis, and second primary cancer, and the quality of life of breast-conserving patients was significantly improved. A 20-year randomized follow-up study in Denmark also showed that

Introduction

The incidence of breast cancer ranks first among female malignant tumors, and the mortality rate ranks second, only to lung cancer¹. In the past, early breast cancer mainly used radical surgery. In recent years, adjuvant radiotherapy for early invasive breast cancer or carcinoma *in situ* has gradually been included in standard treatment. Adjuvant radiotherapy after breast-conserv-

there was no statistical difference in local tumor control rate and 10-year disease-free survival rate the incidence of distant metastasis and secondary primary cancer between the two methods. A large number of long-term follow-up studies show that breast conserving surgery is the first choice for early and small breast cancer.

Radiotherapy After Breast-Conserving Surgery

Whole breast irradiation (WBI) after breast-conserving surgery is considered to be the standard treatment after breast-conserving surgery. External irradiation of 45-50 Gy can reduce the 5-year recurrence rate from 23% to 7%⁶. The survival rate of adjuvant radiotherapy after breast-conserving surgery combined with silicone prosthesis reconstruction is similar to that of total resection alone⁷. Kunkler et al⁸ show that whole breast irradiation after breast-conserving surgery can prolong the life of early patients (T0-2N0-1M0), and the recurrence rate without postoperative irradiation is less than 5.5%. Veronesi et al⁹ concluded that postoperative radiotherapy was suitable for women 55 to 65 years old with positive axillary lymph nodes or ductal infiltration, but had no significant effect on overall survival. However, many recent studies have shown that the recurrence of ipsilateral breast tumor after breast-conserving surgery is mostly located in the primary tumor. Therefore, many scholars believe that there is no need for the whole breast radiotherapy. Local breast irradiation [Partial breast irradiation (PBI)] began to rise, and most of them adopted the mode of accelerated hyperfractionation (AHF). The common used PBI techniques are: intraoperative radiotherapy, intracavitary radiotherapy, intertissue intubation radiotherapy and so on¹⁰. Vaidya et al¹¹ found that affecting overall survival and distant metastasis can be used as an alternative to total breast irradiation, but the relationship between PBI and local and axillary recurrence rates is statistically significant, and the relationship between partial irradiation and local and axillary recurrence needs to be further clarified. Intraoperative radiotherapy (IORT) is mainly used for local incremental irradiation in breast-conserving therapy, which can avoid dose-sensitive tissue and make the tumor bed exposed to higher dose. The technique avoids the damage to normal tissue and has a bright future¹². A good control rate of tumor bed recurrence can also be obtained

by external irradiation with Targit Technology (targeted intraoperative radiotherapy; Tampa, FL, USA). It can accurately locate, treat immediately, and act directly on the tumor microenvironment. The 5-year follow-up study by Willett et al¹² on standard risk patients showed that Targit Technology (Tampa, FL, USA) is superior to traditional external irradiation technology. Randomized controlled studies between Targit Technology (Tampa, FL, USA) and traditional technology are also ongoing. Holmes et al¹³ reported an international multicenter clinical randomized controlled study showing single segmentation intermediate radiotherapy uses 50 kVx-ray to complete at the edge of the tumor bed at 20 Gy. This method avoids repeated radiotherapy and does not need to place a radioactive source. Polgár et al¹⁴ reported a 5-year randomized controlled study in 2007, which showed that high-dose rate brachytherapy (HDR) between multi-channel tissues, with a prescription of 5.2 Gy/7 and 50 Gy/25 for total breast irradiation (94.6% vs. 91.8%), cancer-specific survival (98.3% vs. 96.0%), and disease-free survival rate are not statistically different from traditional whole breast irradiation, and it has better cosmetic effects. The whole breast irradiation takes a long time, therefore, the local control rate may be affected. The partial breast irradiation takes a shorter time, which can shorten the total treatment time and waiting time. Johansson et al¹⁵ reported the first follow-up study of 51 patients with T1-T2 breast cancer who received pulsed dose rate (PDR) brachytherapy for 5 years and completed 50 Gy within 5 days. The average followed up was 86 months. The recurrence rate of this specific breast accelerated radiotherapy is similar to that of other APBI studies, and it is well tolerated, with less time and cost of treatment. In the aspect of intracavitary radiotherapy, Benitez et al¹⁶ were followed up for 5 years, and 43 of the 70 patients were treated with MammoSite device. MammoSite radiotherapy on tumor bed alone can obtain a relatively satisfactory local vacancy rate. It has the advantages of low toxic and good cosmetic effect, which is comparable to traditional whole breast irradiation and tissue implantation radiotherapy. Intraluminal consistency and inappropriate skin distance are the main factors limiting the use of MammoSite devices and long-term follow-up is needed. Vicini et al¹⁷ studied the use of MammoSite in 87 research institutions. The results showed that

a total of 1237 patients with early breast cancer received APBI treatment with MammoSite device after breast-conserving surgery. 92% of them had good cosmetic results after 92 months of treatment, which was similar to that of WBI.

Silicone Prosthesis Implantation and Radiotherapy

Compared with musculocutaneous flap reconstruction, silicone prosthesis implantation has the advantages of less trauma, simple operation, beautiful appearance, no donor site complications, and no muscular skin flap necrosis and atrophy. It is a safe and feasible surgical method. Silicone breast implants are widely used in breast augmentation, and have become a very important material for breast cancer reconstruction after resection. At the same time, pectoral muscle implantation also has better tumor screening function¹⁹. Currently, there is a large amount of evidence that silicone implants will not cause tumors, and even the incidence of breast cancer is lower than non-prostheses²⁰. Vincent et al²¹ have shown that after the implantation of silicone, with the increase of hormone levels, the rats will have temperature disturbances under the skin, and silicone acts as a neutralizer. Macadam et al²² used BREAST-Q and EORTC QLQC30 (Br23) [the BREAST-Q and the European Organization for A comparative study of Research and Treatment of Cancer Quality of Life Questionnaire C30 (Br23)] scale to investigate the satisfaction of 75 silicone implants and 68 saline implants 1 year after implantation. There is no difference in the overall physical condition of the two [EORTC QLQC30 (Br23)]. There is no conclusive evidence that silicone prosthesis can cause immune diseases. Bai et al²³ found that silicone prostheses were used after early breast cancer. Implantable breast reconstruction is similar to autoimmune tissue transplantation and has not significant effect on the patient's immune system. Some scholars²⁴ have shown that radiotherapy can increase the incidence of complications after prosthetic implantation. A comparative study of Whitfield et al²⁵ included 41 patients undergoing radiotherapy after autologous breast cancer implantation and 69 patients without radiotherapy, it showed that eight patients in the radiotherapy group developed severe capsular contracture, requiring a second operation, with a total incidence of 19.5%, and none in the non-radiotherapy groups. Radiotherapy can cause capsular contracture after implantation, which is important, especially when explaining the risks of treatment

to patients. Although experimental studies have shown that silicone implants will not affect the effect of radiotherapy, radiation therapy will affect silicone prostheses, especially in terms of complications and cosmetic effects, because radiation therapy can cause fibrosis and cystic contracture. It can significantly reduce the cosmetic effect, but there is no need to remove the silicone prosthesis before radiotherapy¹⁹. Whitfield et al²⁶ conducted a prospective study of the cosmetic effect of radiotherapy after LD reconstruction (n = 73) using objective breast retraction analysis (BRA), and patient reported scale [patient reported cosmetic outcomes (PRCO)]. The results showed that radiotherapy can reduce the cosmetic effect of LD reconstruction, but the patients do not think so, that is, the analysis results of the PRCO scale indicate that degree of satisfaction with cosmetic results is not related to radiotherapy or surgical methods. Therefore, it is necessary to reflect on the difference between physicians' objective data based on image and geometric measurements and the patient's own PRCO self-evaluation. This also requires the development of a more effective standard evaluation model to comprehensively evaluate the effect of postoperative radiotherapy on the cosmetic effects. The study also shows that the impact of radiotherapy on aesthetics has nothing to do with reconstructive surgery. Postoperative reconstructive radiotherapy is traditionally considered to be suitable only for tumors with a large tumor burden or poor prognosis and evidence²⁷ shows that radiotherapy can be applied to various stage of tumor treatment and has synergy with other treatments, bringing survival benefits. Disa et al²⁸ reported that postoperative reconstruction of LD combined with prostheses achieved good cosmetic results and acceptable capsular contracture rate. Currently, there is no large-scale clinical randomized controlled trial of radiotherapy after breast-conserving surgery combined with silicone prosthesis reconstruction.

Conclusions

The treatment of breast cancer is currently the most in-depth research area, and new technologies and methods continue to emerge (Table I). The two major goals of treatment are good tumor control and high quality of life (aesthetic requirements). According to the current literature, due to the short follow-up time, the optimal standard treatment plan has not yet been determined, and

Table I. QRT-PCR primer sequences.

| Researcher | Time | Groups | The main results |
|-------------------------------|------|--|--|
| Veronesi et al ⁴ | 2002 | Breast-conserving surgery VS total tumor resection | -: ong-term survival rate, incidence of contralateral, distant metastasis, second primary cancer +: quality of life |
| Clarke et al ⁷ | 2005 | Breast-conserving surgery VS total tumor resection | -: local tumor control rate, 10-year DFS rate, incidence of distant metastasis, secondary primary cancer |
| Kunkler et al ⁸ | 2009 | With postoperative irradiation VS without | +: overall survival |
| Veronesi et al ⁹ | 2001 | Postoperative radiotherapy | -: overall survival +: women 55 to 65 years old with positive axillary lymph nodes or ductal infiltration |
| Willett et al ¹² | 2007 | Targit VS traditional technology | +: Targit technology is better |
| Johansson et al ¹⁵ | 2009 | 50 Gy within 5 days VS APBI | -: recurrence rate +: tolerance, economic cost |
| Benitez et al ¹⁵ | 2007 | MammoSite radiotherapy VS traditional radiotherapy | -: local vacancy rate +: toxicity, cosmetic effect |
| Vicini et al ¹⁷ | 2005 | APBI treatment with MammoSite device VS WBI | -: cosmetic effect |
| Macadam et al ²² | 2010 | Silicone implants VS saline implants | -: overall physical condition |
| Bai et al ²³ | 2008 | Ailicone implants VS autoimmune tissue | -: implantable breast reconstruction |
| Whitfield et al ²⁵ | 2009 | Autologous implantation with radiotherapy VS without | +: severe capsular contracture |
| Whitfield et al ²⁶ | 2008 | With radiotherapy after LD reconstruction vs without | -: patient self-evaluation of cosmetic effect. +: image and geometric measurements of cosmetic effect. |

many problems need to be solved, such as prosthesis implantation after breast-conservation surgery, radiation dose after reconstruction, field standard establishment, and so on. For early breast tumors, breast-conservation surgery silicone implantation followed by radiotherapy can achieve the two major goals of early breast cancer treatment, but it still requires a large number of rigorous clinical trials and long-term follow-up are still needed to determine a more detailed treatment model.

Conflict of Interest

This project is funded by the research and data on the evaluation method of stereotactic radiotherapy equipment (subject No.: 2017YFC0113701). Research and Development of tumor real-time monitoring molecular diagnostic products based on liquid biopsy -- a major Science and Technology Project of Guangdong Province 2019B020232003. Dalian Municipal Science and Technology Innovation Projects (2018 j12sn063): a new method for the detection optical flow control chip peripheral blood tumor cells research. Science and Technology Innovation Project of Dalian City (No: 2018 j12sn063). Liaoning Provincial Key Research and Development Plan Project Name: construction project no. 2018225050 fat stem cell storage and application platform

no. 2018020143-301 Project Name of Natural Science Foundation of Liaoning Province: basic research on the regulation effect of Gegen-qinlian decoction based on 16S rRNA gene on intestinal flora of mice with radioactive enteritis project No. 20180550798; Contract No. 2018011225-301 Nature Foundation Guidance Program Ph.D Initiation Fund Project Name: the relation-ship between fluoxetine in inhibitingastrocytoma growth and TRPC1 research project No. 20180551182 Contract No. 2018011575-301.

The protocol of this study was approved by the medical Ethics Committee of West China Hospital of Sichuan university. The written informed consent of all participants was obtained.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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