Conference paper
UDC: 618.19-006:616-089.8:615.849.1

Jasmina MLADENOVIĆ
Nenad BOROJEVIĆ

INSTITUTE FOR ONCOLOGY AND RADIOLOGY OF SERBIA, BELGRADE, SERBIA AND MONTENEGRO

Postoperative radiotherapy in early breast cancer

KEYWORDS: Breast Neoplasms; Radiotherapy; Postoperative Period; Brachytherapy

INTRODUCTION

Breast radiotherapy (RT) has changed over the passed few decades mainly due to changes in locoregional treatment of the breast cancer and improvements in technology of radiotherapy equipment.
Randomized trials have established that survival rates after conservative surgery and breast irradiation are equivalent to those observed after modified radical mastectomy. Moreover, the use of screening mammography has led to a relative increase in small tumors, ideally suitable for breast conservation. As a consequence, the use of conservative surgery has risen progressively during the 1980s and 1990s, with a corresponding increase in the importance of breast irradiation (1). In addition, recent meta-analysis of randomized trials have established that breast cancer mortality could be significantly reduced by locoregional RT, and that the increased intercurrent mortality observed in older trials was caused by excess in cardiovascular deaths, associated with the old techniques. Newer trials of postmastectomy RT have demonstrated a clear survival improvement, without excess cardiac morbidity, leading to an increased confidence in the use of adjuvant locoregional RT (2,3).
The overview by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) showed that adjuvant RT reduced the annual odds of local recurrence by a factor of 3. The 68% reduction in locoregional failure (LRF) resulted in 13% reduction in the annual odds of death from breast cancer, indicating that a 4-to 1 ratio exists between the local control benefit and survival benefit associated with RT (4).

BREAST IRRADIATION FOR DUCTAL CARCINOMA *IN SITU*

Since the introduction of screening mammography, there has been an enormous increase in the detection of ductal carcinoma *in situ* (DCIS), about 20% of all breast cancers. DCIS is local disease confined to the breast without any ability to produce systemic metastases and with minimal failure after adequate local therapy. The most important risk factor for recurrence is the width of the tumor-free margin. Presence of necrosis and nuclear grade are also predictors of prognosis and they are incorporated in Van Nuys classification. Current treatment for DCIS ranges from simple tumor excision, to various forms of wider excision (quadrant resection), to mastectomy. All treatments less than mastectomy require postoperative RT. The earlier reports of breast conservation of DCIS demonstrated that the recurrence rates were high; around 20-30% at 10 years and 50% of recurrences were in the form of invasive disease (5). But two big randomized trials (EORTC and UK DCIS) showed an approximately 2-fold reduction in the risk of local recurrence with RT. Some studies observed a low recurrence risk with clear margins exceeding 10 mm, suggesting that it might be safe to omit RT in that subgroup of patients, but randomized trials indicated that RT reduces local recurrence in all subgroup of patients with DCIS. Therefore, until conclusive randomized evidence allows definition of subgroups in whom RT can be safely omitted, RT should remain part of the standard breast-conserving therapy for all patients with DCIS, as is the case for invasive cancer.

BREAST IRRADIATION AFTER CONSERVATIVE SURGERY

Today the standard conservative treatment for early invasive breast cancer consists of complete surgical resection of the primary tumor (achieving at least histologically clear margins), axillary dissection or sentinel node biopsy, and postoperative whole breast radiation therapy. Total dose to the breast is usually 50 Gy in 5 weeks delivered with tangential fields and additional boost of 10-16 Gy to the tumor bed with electrons or brachytherapy.
Randomized trials show that breast irradiation reduces the relative risk of ipsilateral breast recurrence by approximately 75% (1). Since breast recurrences are most often observed within the vicinity of the primary lesion, a localized radiation boost to the tumor bed is frequently recommended. Trials have demonstrated that boost irradiation significantly improves local control compared with whole breast irradiation alone. After 50 Gy whole breast irradiation, adding a boost of 16 Gy decreases local recurrence rates by a factor of almost 2. The absolute benefit from boost treatment is particularly marked in young patients, and is indicated for all patients less than 50 years of age (6). Choice of boost technique is likely to depend largely upon the personal preference and training of the radiation oncologist and upon the local infrastructure.
The rational for whole breast irradiation is that it will eliminate possible areas of occult multicentric *in situ* or invasive cancer in remote areas of the breast. But, approximately 80% of breast cancer recurrences after lumpectomy occur near the original tumor site whether they are treated with excision alone or followed by whole breast irradiation. In addition, a very important reduction in LRF has been observed in older patients (over 55 years), also in the group without postquadrantectomy irradiation. These observations encourage the idea of more limited treatment in order to avoided whole breast irradiation.
Partial breast irradiation (PBI) is a new approach where a single or multiple fractions are given to the excision site and the adjacent tissues in a short period of time. The main advantages of this method are the avoidance of unnecessary side effects, shortening of the overall treatment time and improving the quality of life. PBI includes interstitial brachytherapy (low dose rate or high dose rate), external beam radiotherapy and intraoperative radiotherapy.
IntraOperative Radiation Therapy (IORT) is a special irradiation technique refers to the delivery of a high single radiation dose to the tumor bed during the surgical intervention, after the removal of the tumor mass (7,8). Modern IORT is carried out with electron beams produced by a mobile linear accelerator with a spectrum of electron energy (3-12 MeV), which can be directly placed in operation room. Besides the reduction in total time of treatment, important advantages of IORT are the protection of surrounding tissues (hart, lung, skin) and avoidance of the interactions with the systemic therapy.
Another novel approach in irradiating the tissue immediately surrounding the lumpectomy cavity is the MammoSite radiation therapy system (9). This technique provides a simpler and more assured technique for performing breast brachytherapy. The system consists of balloon applicator, which is inserted into the resection cavity immediately after lumpectomy. An HDR Ir-192 source is positioned at the center of the balloon with the planned target volume (PTV) consists of a 1 cm thick spherical shell surrounding the balloon.
In spite of very promising first results of PBI in clinical trials, there is still a

Address correspondence to:
Jasmina Mladenović, Institute for Oncology and Radiology of Serbia, Pasterova 14, 11000 Belgrade, Serbia and Montenegro, E-mail: mladenovicj@ncrc.ac.yu

The manuscript was received: 30.09.2005.

Accepted for publication: 15.10.2005.

considerable controversy about the optimal minimum treatment of early breast carcinoma required for adequate local control without compromising the therapeutic effect.

LOCAL RADIOTHERAPY AFTER RADICAL MASTECTOMY

Recent trial overviews establish conclusively that locoregional RT following ablative surgery not only improves tumor control, but also improves overall survival in appropriate high-risk patients (2,3). Based on these trials, post-mastectomy radiotherapy (PMRT) should be recommended to all patient who are at more than 20% risk of LRF (tumor larger than 5 cm or involving the skin or more than four positive nodes). Patients with T1-2 tumors and less than four involved axillary nodes generally have LRF rates less than 15% and for that intermediate risk group of patients there was insufficient evidence to recommend PMRT routinely. For this subgroup of patients further research will be required to determine which patients could have sufficient benefit regarding locoregional control or survival to justify PMRT.

Locoregional irradiation after modified radical mastectomy refers to RT involving the ipsilateral chest wall, as well as the ipsilateral axillary, supra- and infraclavicular and internal mammary lymph nodes. It is unclear whether all these areas need to be irradiated, but current evidence suggests that the chest wall is probably the critical target for PMRT.

For patients undergoing reconstruction after mastectomy with prostheses (implants or tissue expanders), most of the evidence suggests that complications are more frequent and cosmesis is poorer with addition of radiation (10). RT can lead to a hardening of implants by capsular contracture, and leakage or rupture of expanders may occur. RT seems to have no significant effect on the viability and relatively minor effect on the cosmetic outcome of reconstruction with myocutaneous flaps, irrespective of whether RT is given before or after surgery. In general, reconstruction with implants should be avoided where there is a high likelihood of RT being required.

CONCLUSION

Postoperative RT has a very important role in multidisciplinary treatment of early breast cancer. Future research will have to investigate the indications for more selective use of adjuvant RT, and use of newer techniques of imaging, treatment planning, and beam delivery for optimizing breast cancer treatment in order to improve target dose homogeneity and better protection of normal tissues, with corresponding reductions in breast fibrosis and other side-effects. This is very important because the overall prognosis for patients with early breast cancer is relatively good, and significant proportion may be expected to live for several decades after successful primary treatment.

REFERENCES

1. Kurtz J. the curative role of radiotherapy in the treatment of operable breast cancer. Eur J Cancer 2002; 38:1961-74.

2. Overgaard M, Hansen PS, Overgaard J, Rose C, Andersson M, Bach F, et al. Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy. N Engl J Med 1997; 337:949-55.

3. Ragaz J, Jackson SM, Le N, Plenderleith IH, Spinelli JJ, Basco VE, et al. Adjuvant radiotherapy and chemotherapy in node-positive premenopausal women with breast cancer. N Engl J Med 1997;337:956-62.

4. Early Breast Cancer Trialists' Collaborative Group. Favourable and unfavourable effects on long-term survival of radiotherapy for early breast cancer: an overview of the randomized trials. Lancet 2000;355:1757-70.

5. Mansel RE, Ductal carcinoma in situ: surgery and radiotherapy. Breast 2003;12:447-50.

6. Poortmans P, Bartelink H, Horiot JC, Struikmans H, Van der Bogaert W, Forquet A, et al. The influence of the boost technique on local control in breast conserving treatment in the EORTC "boost versus no boost" randomized trial. Radiother Oncol 2004;72:25-33.

7. Orecchia R, Ciocca M, Lazzari R, Garibaldi C, Leonardi MC, Luini A, et al. Intraoperative radiation therapy with electrons (ELIOT) in early-stage breast cancer. Breast 2003;12:483-90.

8. Veronesi U. Orecchia R. Luini A, et al. A preliminary report of intraoperative radiotherapy (IORT) in limited-stage breast cancers that are conservatively treated. Eur J Cancer 2001;37:2178-83.

9. Streter OE, Vicini FA, Keisch M, Astrahan MA, Jozef G, Silverstein M, et al. MammoSite radiation therapy system. Breast 2003;12:491-6.

10. Tallet AV, Salem N, Moutardier V, Ananian P, Braud A, Zalta R, et al. Radiotherapy and immediate two-stage breast reconstruction with a tissue expander and implant: complication and esthetic results. Int J Rad Oncol Biol Phys 2003;57:136-42.