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An analysis of long term complications in breast cancer patients after conservative therapy

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Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Summary

Background Breast conserving surgery followed by irradiation and subsequent systematic application of therapy has been recognized as an efficient method for the treatment of early breast cancer for many years. The results of conservative treatment show a relatively low percentage of local relapses and good cosmetic results

Aim The aim of the paper was to analyse the frequency and intensity of late complications after conservative treatment in breast carcinoma patients.

Materials/Methods A group of 67 patients with stage I and II breast carcinoma, according to the TNM classification, and who underwent conservative treatment in the Lower-Silesian Centre for Oncology between 1995 and 2001 were included in the study. All patients underwent irradiation of the breast after conservative treatment. In 93% the total dose was 50Gy and in the remaining 7% the dose amounted to 46–48Gy. The dose was around 10Gy higher at the tumour site. Irradiation of the lymph nodes was applied in 25% of cases and chemotherapy was used in 40%.

The occurrence and intensity of late complications were assessed at 3–6 monthly intervals. Complications included: lymphatic swelling of the ipsilateral upper limb, necrosis of the soft tissues, post-radiation pneumonia, lung fibrosis, post-radiation rib fractures, plexopathy, late skin reaction and telangiectasia. Intensity was assessed using our own 4 level scale.

Results Level 2 complications were observed in 22% of the patients and Level 3 complications were seen in 6%. No Level 4 complications were observed. Lymphatic swelling of the ipsilateral upper limb was the most frequent complication and occurred in 22% of the patients. Level 2 and Level 3 swelling was observed in 14.5%. Level 2 and 3 late post-radiation reactions were observed in 9% of the patients. Telangiectasia within the boost area was observed in 4.5% of the patients and outside the boost area in 9%. No local recurrence of carcinoma was observed.

Conclusions The results of conservative treatment of breast carcinoma patients show low intensification of complications.

Key words **breast carcinoma • conservative treatment • radiotherapy • complications • lymphatic swelling**

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Background

Breast conserving surgery followed by irradiation and subsequent systematic application of therapy has been recognized as an efficient method for the treatment of early breast cancer for many years. The results of conservative treatment show a relatively low percentage of local relapses and good cosmetic results [1–3]. The therapy is burdened with side effects, as are others kinds of therapy. Efficient therapy leads to a lengthening of the lives of patients, with the effect that the occurrence and intensification of late post-radiation complications becomes more probable.

Clinical research has shown that the probability of the occurrence of late post-radiation reactions depends on many factors, including the level of fraction dose, total applied dose, irradiated volume of tissues, choice of radiotherapy technique, irradiation of the post-tumour site (boost), homogeneity of the dose in the treated area, whether or not systemic therapy is combined with irradiation and on the individual characteristics of the patient [4–8].

The results of long-term clinical research allow for the selection of a group with late complications resulting from breast irradiation, the most frequently occurring being pain, swelling and breast fibrosis. These, however, subside with time. Atrophy, telangiectasias, skin and soft tissue necrosis also occur from time to time. Radiotherapy of lymph node areas may result in serious complications, such as swelling of the ipsilateral upper limb, post-radiation pulmonary fibrosis, broken ribs or defects in the shoulder plexus. Such complications are increasingly frequent, irreversible and very difficult to treat [9–11].

To assess the risk of the occurrence of these complications, it is necessary to conduct long-term observation and monitoring of late post-radiation reactions in everyday oncological treatment. The EORTC/RTOG (the European Organization for Research and Treatment of Cancer and the Radiation Therapy Oncology Group) has proposed the use of the LENT-SOMA scale to assess the occurrence and intensification of late post-radiation reactions [12,13]. The scale, as presented by Fehlauer et al. [14], may only be used for the assessment of the late effects of mammary gland irradiation while numerous other studies have concentrated only on selected complications, with the result that it is difficult to make a full assessment of the frequency and intensity of possible failures in conservative therapy. Lymphatic swelling of the ipsilateral upper limb [7,15–17] and obtained cosmetic effects [6,7,11,18] were assessed most often. There have been few studies on the occurrence and intensity of significant post-radiation complications though these are necessary to fully assess the tolerance of selected treatment methods [15,16,19].

Aim

The aim of the study was to prospectively analyse the frequency and intensity of late complications after conservative treatment of breast cancer patients according to our own 4 degree scale of complication intensity.

Materials and Methods

75 patients after conservative surgery and with histopathologically confirmed invasive breast carcinoma were treated with irradiation at the Department of Radiotherapy I, Lower Silesia Centre for Oncology, between 1995 and February 2001. Eight patients were excluded from the analysis (7 failed to attend biannual control examinations and 1 died following a myocardial infarction 18 months after completion of radiotherapy to the left breast). The remaining group of 67 patients was used as research material. The average period of observation was 49 months while the shortest and longest periods of observation were 30 and 82 months respectively. The period of observation from the end of radiotherapy to the end of the observation period (in months) is presented in Table 1.

Patients with unilateral invasive breast carcinoma were analysed. In 31 patients, carcinoma was found

Table 1. Duration of observation from the end of radiotherapy (months).

Duration of observation in months	Number of patients	Number of patients (%)
30–36	23	34
37–48	15	22
49–60	7	11
61–82	22	33

Table 2. TNM Advancement in a group of 67 patients.

Advancement acc. to TNM	Number of patients (%)
T1N0	70
T1Nx	2
T1N1	22
T2N0	3
T2N1	3

in the left breast and in the right breast of 36 patients. The youngest patient was 27 years of age at the time of surgery while the oldest was 70 years old. The average age was 49 years. In a group of 30 patients, a tumourectomy was performed and in 37 patients (i.e. 55%) a more extensive quadrantectomy was performed. In tumourectomy patients, tumours were removed with a surrounding 1cm margin of healthy tissue. In quadrantectomy patients, tumours were removed with a 2–3cm margin of tissue and the skin from over the tumour. The removal of three levels of axillary lymph nodes was performed either simultaneously or consecutively in 95% of cases (64 patients).

In most cases, i.e. in 59 patients (88%), the tumour was in the upper outer quadrant, in 4 patients (6%) it lay on the border between the upper quadrants and in 4 patients it was located in the lower quadrants. The group comprised patients in stages I (T1N0M0) and II (T1N1M0, T2N0M0 i T2N1M0) of advancement according to the TNM classification, with primary tumours not larger than 3 cm in diameter. 94% of the patients had T1 features.

The N1 feature – metastases to the axillary lymph nodes – was observed in 25% of the patients (17 patients). The characteristics of clinical advancement according to the TNM classification is presented in Table 2.

Ductal carcinoma was most frequently diagnosed in the microscopic examination of the primary tumour (in 84% of the patients). A medium level of malignancy (G2) was most frequent (48%) while low malignancy (G1) was diagnosed in 32% and high malignancy (G3) was diagnosed in 20% of the patients.

All patients after conservative surgery were irradiated. Radiotherapy was started, on average, 9 weeks after surgery. The shortest period before radiotherapy was 3 weeks and the longest was 26 weeks. All patients whose irradiation was started more than 12 weeks after the surgery were also treated chemically.

Photon irradiation was conducted under megavolt conditions, mainly 4 and 6MeV and, during the period from1995 to 1997, also with Co-60 at 1.25MeV and photons at 9MeV.

In 93% of cases the whole breast was irradiated, up to a total dose of 50Gy, and in 7% (5 patients) a total dose of 46–48Gy was used. Additionally, the dose was boosted at the tumour site using a 10Gy dose at 6, 9, 12 or 16MeV. Photon boost was used sporadically. If metastases were observed in more than one axillary lymph node, irradiation of the supraclavicular area and axilla with a total dose of 50Gy was applied. Radiotherapy of the ”nod” area was used in 17 patients.

For irradiation of the breast, an isocentric technique with tangential fields was used. The common isocentre technique was used for irradiation of the breast with supraclavicular and axillary lymph nodes. The daily fractional dose calculated at the reference point (isocentre) was 2Gy. In cases involving a large volume of breast tissue a fractional dose of 1.8Gy was used.

Patients with metastases to the axillary lymph nodes (pN1) and tumours larger than 1cm were treated by chemotherapy or hormone therapy, depending on receptor status. Chemotherapy was used in 27 patients. 25 women received CMF chemotherapy and 2 received AC chemotherapy. 12 patients received CMF chemotherapy during radiotherapy. Usually, CMF chemotherapy was applied in 1–2 courses, during which all three CMF cytostatics were administered.

The occurrence and intensification of late complications were assessed regularly in 3–6 month

Table 3. Intensity of late complications.

Complication	Level 1	Level 2	Level 3	Level 4
Necrosis of soft tissues	Moderate	Resection required	Skin transplant required	Resection within the chest wall required
Post-radiation pneumonia	Moderate	Medium	Hospitalisation required	Life threatened
Lung fibrosis	Asymptomatic (visible changes in chest x-ray)	Effort dyspnoea	Dyspnoea in normal activity	Dyspnoea at rest
Rib fracture	One rib	Two or three ribs	Over five ribs	
Plexopathy	Subjective symptoms	Moderate objective symptoms	Weakened functioning	Paralysis
Skin reaction acc. to RTOG/EORTC	Slight atrophy, colour changes	Spotted atrophy, moderate telangiectasia	Significant atrophy and telangiectasia	Ulceration

Table 4. Intensity of telangiectasias.

Telangiectasia within the boost area	$<1cm^2$	$1–4cm^2$	$>4cm^2$
Telangiectasia outside the boost area	$<1cm^2$	$1–4cm^2$	$>4cm^2$

Table 5. Relationship between swelling and irradiation of lymph node areas.

Use of lymph node radiotherapy	Swelling (n – number of patients)	No swelling (n – number of patients)	Total
Yes	7	10	17
No	8	42	50
Total	15	52	67

periods. Occurrences of lymphatic swelling of the ipsilateral upper limb, soft tissue necrosis, post-radiation pneumonia, pulmonary fibrosis, post-radiation rib fractures, plexopathy, late skin reactions and telangiectasia were analysed. The intensification of the above symptoms was assessed according to our own 4-level scale which is presented in Table 3. Late post-radiation skin reactions were assessed using the RTOG/EORTC scale. The scale of telangiectasia intensification in the breast and boost area was based on the LENT SOMA scale, as presented in Table 4.

The frequency of the occurrence and intensification of lymphatic swellings were thoroughly analysed. The circumference of both upper limbs was measured at four levels at 6-monthly intervals.

If a circumferential difference of 2cm or more at corresponding levels was recorded, it was considered to be the result of a lymphatic swelling. The period between the end of treatment and the occurrence of the swelling was also assessed.

A 4-level scale based on the LENT SOMA system was used to determine the degree of swelling:
Level 1: minimum swelling; a 2–3cm difference in limb circumference at corresponding levels;
Level 2: medium swelling; a 3–5cm difference in limb circumference at corresponding levels;
Level 3: intensive swelling; a difference in limb circumference of more than 5cm or impaired functioning of the limb;
Level 4: loss of limb functions.

The influence of radiotherapy on the occurrence of swelling in the supraclavicular and axillary lymph node areas was assessed. Statistical analysis was performed using the statistical software Statistica 6.0 PL. The Chi-square test was used and test values *N*, *df*, and *P* were defined.

Table 6. Frequency of late complications after treatment.

Complication	Level 1 Number of patients (%)	Level 2 Number of patients (%)	Level 3 Number of patients (%)	Level 4 Number of patients (%)
Necrosis of soft tissues	0	1 (1.5)	0	0
Lung fibrosis	3 (4.5)	1 (1.5)	0	0
Post-radiation pneumonia	0	0	0	0
Rib fracture	0	1 (1.5)	0	0
Plexopathy	2 (3.0)	0	0	0
Skin reaction acc. to RTOG/EORTC	5 (7.5)	3 (4.5)	3 (4.5)	0
Lymphatic swelling	5 (7.5)	9 (13.0)	1 (1.5)	0
Total	15 (22.5)	9 (22.0)	4 (6.0)	0

Table 7. Intensity of telangiectasia.

	Level 1 Number of patients, (%)	Level 2 Number of patients, (%)	Level 3 Number of patients, (%)
Telangiectasia within the boost area	1 (1.5)	1 (1.5)	1 (1.5)
Telangiectasia outside the boost area	0	0	6 (9.0)

Results

Lymphatic swelling of the ipsilateral upper limb was the most frequently observed late complication. It was observed in 15 (22%) of the 67 analysed cases. The swelling occurred after an average of 16 months from the end of radiotherapy (ranging from immediately after therapy to 2 years after it). Level 1 swelling was observed in 5 patients, Level 2 in 9 and Level 3 in only one patient.

The influence of irradiation on lymphatic swellings of the lymph nodes of the supraclavicular – axillary area in the ipsilateral upper limb was analysed. The number of patients in groups is presented in Table 5. The data indicated that irradiation of lymph nodes influences the occurrence of swelling. It occurred more often when the axillary area was irradiated (7/10) than when it was not (8/42). The dependency is close to being statistically significant (Chi-square =3.29, df=1, P=0.069).

Table 6 shows an assessment of the frequency of late complications after conservative treatment. Post-radiation skin reaction was the second most commonly observed complication after lymphatic swelling. Level 2 and 3 post-radiation skin reactions occurred in 9 patients (13.5%). 3 patients had Level 2 post-radiation skin reactions with moderate telangiectasias in the skin of the breast. Level 3 complications occurred as skin reactions with intensified telangiectasias in the skin of the breast. Necrosis of the soft tissues occurred in one patient after irradiation of an area close to a post-operative scar which was proving difficult to heal and required resection. Necrosis developed in the vicinity of Spence's tail – the irradiated site of the tumour. Post-radiation fractures of three ribs and effort dyspnoea occurred in one patient.

Level 2 complications occurred in 22% of patients and Level 3 in 6%. None of the patients had Level 4 complications. Lymphatic swelling of the ipsilateral upper limb was the most frequent complication. The results of the analysis are shown in Table 6.

Intensification of telangiectasia is presented in Table 7.

No local recurrence of carcinoma was observed in any of the patients.

Discussion

Conservative surgery with irradiation of the breast is an alternative to mastectomy, with respect to local control and to long-term results, which allows for preservation of the organ. The purpose of conservative treatment is to provide, apart from the positive effect of breast preservation, the best possible local control and the lowest number of complications. A lot of attention has been paid to factors which influence the cosmetic and undesirable effects of conservative treatment. As possibilities for treating late results are limited, the risk of severe late complications must be kept at the lowest possible level.

Meric et al. examined the frequency and intensity of complications after breast conserving therapy in 294 patients with an average observation time of 89 months. In axillary lymphadenectomy, the lymph nodes of the first and second axillary levels were removed. The scale of the intensification of symptoms, including the occurrence of lymphatic swelling, the degree of immobilisation of the limb, breast fibrosis, axillary fibrosis, soft tissue necrosis, post-radiation pneumonia, rib fracture and plexopathy were investigated in the study. The results show that surgical conservative treatment with radiotherapy resulted in Level 2 and Level 3 late complications in only 9.9% of the patients. Lymphatic swellings of the ipsilateral upper limb were the most frequent complications. The average time to its occurrence was 17 months after surgical treatment. Non-pathological Level 2 rib fractures (of two or three ribs) occurred in one patient (0.3%). In two patients (0.7%), neurological symptoms arose, resulting from injuries to the shoulder plexus, which required the use of narcotic analgesics. In one of these two patients, pain caused a reduction in mobility of the upper limb. In two patients (0.7%), symptomatic post-radiation pneumonia occurred. Asymptomatic lung fibrosis was observed in six patients (2%) [15].

Wazer indicated that among 9% of 234 patients treated with BCT, late complications such as swelling of the arm, post-radiation pneumonia and local skin reactions occurred. Symptomatic, i.e. post-radiation pneumonia, requiring pharmacological intervention (corticosteroids or bronchodilators) was observed in 1.6% of the patients. No dependency between the frequency of complications and the extent of the surgery, number of radiotherapy fields or the use of systematic treatment was observed. However, the authors suggested that the frequency of the complication may be reduced through elimination of methotrexate during radiotherapy and by irradiating the smallest possible portion of the lungs [16].

In their study, Fowble et al. assessed complications after BCT, the most frequent of which was lymphatic swelling of the arm. Average and severe swelling of the arm was observed in 5% of patients, whereas symptomatic pneumonia, rib fractures, pericarditis and plexopathy were observed in less than 3% of the patients [19].

Chua et al. performed a retrospective assessment of 1158 patients who were conservatively treated with surgery and irradiated in the I and II stage of breast cancer. It was observed that by adding the node area to breast irradiation a significantly increased occurrence of symptomatic post-radiation pneumonia occurred. This symptom was observed in 4% of the patients whose node areas were irradiated, as compared to 1% of patients whose nodes were not irradiated ($p<0.001$) [20].

Markiewicz et al. examined a group of 1053 patients and observed that pneumonia and rib fractures were rare complications. The use of chemotherapy does not significantly increase the occurrence of symptomatic pneumonia which was noted in 1.3% of the patients treated with chemotherapy and in 0.3% of the patients who were not. The frequency of symptomatic post-radiation pneumonia in patients who received chemical treatment and whose nodes were irradiated was very low, 1.4% [7].

No cases of post-radiation pneumonia were observed in the studied group. In 3 patients (4.5%), whose node areas were irradiated, asymptomatic fibrosis was observed in the apex of the lung and one patient (1.5%) developed effort dyspnoea as a symptom of Level 2 lung fibrosis.

Soft tissue necrosis is a rarely described complication. Meric et al. observed Level 2 necrosis of the soft tissues of the breast in one out of 249 patients [15]. Wazer indicated soft tissue necrosis in 2% of patients [16]. In the present study, necrosis of the soft tissues in the boost area was observed in one patient (1.5%). It occurred in an area of a long standing scar tissue (from lymphadenectomy) which was proving difficult to heal.

The risk of post-radiation damage to the brachial plexus after post-surgical radiotherapy increases

relative to the extent of axillary lymphadenectomy, increasing fractional dose and the use of cytostatic drugs. At present, it is a rare complication [21–23]. The total dose of radiotherapy is extremely relevant. It is supposed that an increased risk of plexopathy arises when the biological equivalent of the total dose applied to brachial plexus is higher than 57Gy at fractional dose of 2Gy. The risk of post-radiation complications in the peripheral nervous system decreases as the use of three dimensional radiotherapy planning, after conservative surgical treatment of breast carcinoma, and estimations of the applied dose to the brachial plexus are more and more widely used [23]. There are few reports concerning the occurrence of post-radiation injuries of the brachial plexus in patients after conservative treatment. Pierce et al. observed medium degree post-radiation plexopathy in 20 out of 1117 (1.8%) patients who were conservatively treated and whose supraclavicular – axillary lymph nodes were irradiated with a fractional dose of 2Gy up to a total of 50Gy [24]. Chua et al. reported temporary neuropathy of the brachial plexus in 5 out of 380 patients (1%) [20].

No cases of significant injury to the brachial plexus were observed in the present study. Subjective symptoms were observed in two patients and did not bring about any considerable decrease in patients' standard of living after treatment.

Lymphatic swelling of the arm was the most frequent undesirable symptom in the group of patients used in the study.

Larson et al. examined the risk of lymphatic swelling of the arm. The main risk factor, for the occurrence of swelling, is the extent of the removal of axillary lymph nodes. After irradiation of the axillary area after full lymphadenectomy of the axilla, the 6-year risk of swelling is 36%, which is significantly higher than the 6% risk observed in patients after removal of only the lower layer of the axilla and irradiation of the axillary area (P=0.0002). Information about the extent of axillary surgery is very important for radiotherapists. After limited lymphadenectomy, irradiation of the armpit may be required to secure local control, especially when metastases to the lymph nodes is observed. The authors suggested that radiotherapy does not significantly increase the risk of swelling in such cases. However, after removal of a large part of the axilla, from the area of axillary vein, additional irradiation to the area does not improve local control and significantly increases the risk of swelling. The authors indicated that the probability of lymphatic swelling is related more to the extent of lymphadenectomy than to the number of removed lymph nodes [25].

Pezner et al. observed a more frequent occurrence of swelling in patients over 60 years of age than in younger patients ($P<0.02$). In total, swelling was observed in 14% of patients. Owing to low numbers of tested patients, no statistically relevant occurrences of swelling were observed after the use of chemotherapy or radiotherapy [26].

In Meek's study, the frequency of lymphatic swelling after surgical conservative treatment without radiotherapy was 7%, and after irradiation of the breast only, the frequency was 10% [27].

Tengrup et al. analysed the occurrence of lymphatic swellings of the upper limb after conservative treatment. The complete group amounted to 110 patients, 75 of whom were after breast irradiation and after tumourectomy, while 35 were not irradiated. The observation period lasted for 5 years, during which lymphatic swelling occurred in 21 patients (19%). Swelling was twice as frequent in the group of irradiated patients as in the group without irradiation therapy (22% and 12%, respectively). Although breast irradiation after conservative treatment does not require irradiation of the axilla, the lymph nodes of the lower level of the axilla are usually within the area to be irradiated. Swelling occurred in two or three patients within the first two years of observation [28].

The combination of axillary lymphadenectomy with irradiation of the supraclavicular – axillary area causes significantly more frequent swelling of the arm in comparison to the group without irradiation. Swelling was observed in 9.5% of patients after axillary surgery, as compared to 6.1% of patients treated with irradiation of the supraclavicular – axillary area and in 31% of patients after axillary lymphadenectomy in combination with irradiation of the area [20]. Research conducted in Norway showed that irradiation of the axilla and supraclavicular area after axillary surgery results in a 3.5 fold increase in the risk of axillary swelling as compared to the group without irradiation. The authors were of the opinion that the increased risk of this complication indicates that less invasive methods for the treatment of the axillary area should be applied [29].

In the group assessed in the present study, lymphatic swellings of the upper limb were observed

in 15 patients (22%), after an average of 16 months had elapsed from the end of radiotherapy (ranging from immediately after the end of the treatment to 2 years after its completion). In 5 patients the difference in diameter was 2–3cm, in 9 patients 3–5cm and in one patient the difference was 7cm. The patients had lymph nodes removed from three levels of the axilla. An assessment of the frequency of swelling of the arm after radical axillary lymphadenectomy (removal of lymph nodes from three layers of the axilla) indicated no significant intensification of the complication). As the majority of the patients (80%) with swelling underwent rehabilitation (including hand or pneumatic lymph drainage, physical exercise and positioning), the swelling did not intensify and, at the final control visit, was observed in 12 patients, (18%). Seven patients with swellings underwent axillary irradiation. A relationship, close to being statistically significant (P=0.069), was found between the occurrence of lymphatic swelling and irradiation of lymph node areas.

Conclusions

The risk of late post-radiation complications after conservative breast carcinoma treatment is generally low and justifies the use of radiotherapy as a supplement to surgical treatment. This confirms the positive effects of conservative breast treatment. However, in clinical situations when irradiation of lymph node areas is necessary, the risk of lymphatic swelling in the ipsilateral upper limb may increase by 2 to 3 times. In such cases, proper rehabilitation, to counter swelling, is extremely important.

References:

1. Early Breast Cancer Trialists Collaborative Group: Favourable and unfavourable effects on long-term survival of radiotherapy for early breast cancer: an overview of the randomised trials. Lancet, 2000; 355: 1757–70
2. Fisher B, Anderson S, Redmond CK et al: Reanalysis and results after 12 years of follow-up in a randomized clinical trial comparing total mastectomy with lumpectomy with or without irradiation in the treatment of breast cancer. N Engl J Med, 1995; 335: 1456–61
3. Fisher B, Redmond C, Poisson R et al: Eight-year results of a randomized clinical trial comparing total mastectomy and lumpectomy with or without irradiation in the treatment of breast cancer. N Engl J Med, 1989; 320: 822–8
4. Barendsen GW: Dose fractionation, dose rate and iso – efect relationships for normal tissue responses. Int J Radiat Oncol Biol Phys, 1982; 8: 1981–97
5. Borger JH, Kemperman H, Smitt HS et al: Dose and volume effects on fibrosis after breast conservation therapy. Int J Radiat Oncol Biol Phys, 1994; 30: 1073–81
6. De La Rochefordiere A, Abner AL, Silver B et al: Are cosmetic results following conservative surgery and radiation therapy for early breast cancer dependent on technique?. Int J Radiat Oncol Biol Phys, 1992; 23: 925–31
7. Markiewicz DA, Schultz DJ, Haas JA et al: The effects of sequence and type of chemotherapy and radiation therapy on cosmesis and complications after breast conservation therapy ? Int J Radiat Oncol Biol Phys, 1996; 35(4): 661–8
8. Pehr AR, Marks LB, Hardenbergh P et al: Technical factors associated with radiation pneumonitis after local +– regional radiation therapy for breast cancer. Int J Radiat Oncol Biol Phys, 2002; 52(1): 137–43
9. Bosompra K, Ashikaga T, O'Brien PJ et al: Swelling, Numbness, Pain, and their relationship to arm function among breast cancer survivors: a disablement process model perspective. Breast J, 2002; 8(6): 338–48
10. Kurtz J for the EUSOMA Working Party: The curative role of radiotherapy in the treatment of operable breast cancer. Eur J Cancer, 2002; 38: 1961–74
11. Abner AL, Recht A, Vicini FA et al: Cosmetic results after surgery, chemotherapy, and radiation therapy for early breast cancer. Int J Radiat Oncol Biol Phys, 1991; 21: 331–8
12. Pavy JJ, Denecamp J, Letszert J et al: for the EORTC Late Effects Working group. Late effects toxicity scoring: The SOMA scale. Radiother Oncol, 1995; 35: 11–60
13. LENT SOMA scales for all anatomic sides. Int J Radiat Oncol Biol Phys, 1995; 31: 1049–91
14. Fehlauer F, Tribius S, Holler U et al: Long-term radiation sequelae after breast-conserving therapy in women with early-stage breast cancer: an observational study using the LENT-SOMA scoring system. Int J Radiat Oncol Biol Phys, 2003; 55(3): 651–8
15. Meric F, Buchholtz TA, Mirza NQ et al: Long term complications associated with breast –conservation surgery and radiotherapy. Ann Surg Oncol, 2002; 9: 543–9
16. Wazer DE, DiPetrillo T, Schmidt-Ullrich R et al: Factors influencing cosmetic outcome and complication risk after conservative surgery and radiotherapy for early- stage breast carcinoma. J Clin Oncol, 1992; 10(3): 356–63

17. Pezner RD, Patterson MP, Hill RL et al: Arm lymphedema in patients treated conservatively for breast cancer: relationship to patient age and axillary node dissection technique. Int J Radiat Oncol Biol Phys, 1986; 12: 2079–83

18. Taylor ME, Perez CA, Halverson KJ et al: Factors influencing cosmetic results after conservation therapy for breast cancer. Int J Radiat Oncol Biol Phys, 1995; 31(4): 753–64

19. Fowble B: Interaction of chemotherapy and radiation in the treatment of nonmetastatic breast cancer. In: Meyr JL, Veath JM. Radiotherapy/chemotherapy interactions in cancer therapy. Front Radiat Ther Oncol, Basel, Karger, 1992; 95–114

20. Chua B, Ung U, Boyages J: Compiting considerations in regional nodal treatment for early breast cancer. The Breast Journal, 2002; 8(1): 15–22

21. Olsen NK, Pfeiffer P, Johannsen L et al: Radiation induced brachial plexopathy: neurological follow-up in 161 recurrenc – free breast cancer patients. Int J Radiat Oncol Biol Phys, 1993; 26: 43–9

22. Powell S, Cooke J, Parsons C: Radiation – induces brachial plexus injury: follow-up of two different fractionation schedules. Radiother Oncol, 1990; 18: 213–20

23. Hicer-Grzenkowicz J, Gałecki J, Grudzień-Kowalska M et al: Popromienne uszkodzenia splotu ramiennego u chorych na raka piersi. Nowotwory, 2001; 4: 411–9

24. Pierce SM, Recht A, Lingos TI et al: Long term radiation complication following conservative surgery and radiation therapy in patients with early stage breast cancer. Int J Radiat Oncol Biol Phys, 1992; 23: 915–23

25. Larson D, Weinstein M, Goldberg I et al: Edema of the arm as a function of the extent of axillary surgery in patients with stage I–II carcinoma of the breast treated with primary radiotherapy. Int J Radiat Oncol Biol Phys, 1986; 12: 1575–82

26. Pezner RD, Patterson MP, Hill LR et al: Breast retraction assesment: an objective evaluation of cosmetic results of patients treated conservatively for breast cancer. Int J Radiat Oncol Biol Phys, 1985; 11: 575–8

27. Meek AG: Breast radiotherapy and lymphedema. Cancer, 1998; Suppl. 83/12: 2788–97

28. Tengrup I, Tennvall-Nittby L, Christiansson I: Arm morbidity after breast- conserving therapy for breast cancer. Acta Oncol, 2000; 39(3): 393–97

29. Ververs JMMA, Roumen RMH, Vingerhoets AJ et al: Risk, severity and predictors of physicial and psychological morbidity after axillary lymph node dissection for breast cancer. Eur J Cancer, 2001; 37: 991–9