

## Conservative Treatment in Breast Cancer King Faisal Specialist Hospital (KFSH) Experience

MOHAMAD EL-SENOUSSI, C.E.S. (Paris)\*; HASSAN ABDALLAH, M.D.\*;  
INAS EL-ATTAR, Dr.PH.\*\*\* and AHMAD ABDEL-WARITH, M.D.\*\*

*The Departments of Radiotherapy\*, Medical Oncology\*\* and Biostatistics\*\*\*, National Cancer Institute, Cairo University.*

### ABSTRACT

**Background:** Breast saving surgery and radiation therapy have been established as an effective therapeutic approach for early breast cancer. This method has produced local control rate equivalent to that following mastectomy with the additional benefit of breast preservation in the majority of patients. We present the experience of KFSH in the management of 98 patients in the Kingdom of Saudi Arabia.

**Methods:** Ninety-eight female patients with reasonable tumor/breast size ratio were treated by conservative surgery and radiotherapy with or without adjuvant chemo-hormonal therapy and were closely followed up.

**Results:** Between 1981 and 1990, 98 patients benefited from breast saving surgery. Forty-nine patients (50%) were below the age of 40. The group included 15 T1, 52 T2, 29 T3 and 2 Tx tumors. The 5-year overall survival and local control rates of the whole group was 79±6% and 88±4% respectively. The lymph node (LN) status, site of the primary tumor, extent of surgery, dose of radiotherapy to the tumor bed, as well as the chemo-hormonal therapy were all studied as prognostic factors. The only significant factor was the site of the primary tumor. Patients with inner quadrant tumors had a 5-year local control rate of 74±10% compared to 90±4% for outer quadrant lesions ( $p = 0.01$ ).

**Conclusion:** Conservative surgery and radiotherapy for relatively early breast cancer became an accepted therapeutic alternative in breast cancer therapy. More attention has to be given by the therapy team to recruit more patients especially those with small outer quadrant tumors to benefit from this less morbid surgery.

**Key Words:** *Conservative breast - Breast cancer - Prognostic factors - Breast cosmeses - Lactation - Saudi Arabia.*

### INTRODUCTION

Breast cancer is the most common form of malignancy in the Arabic women in the region [1,7] and is similar to what is reported in North America and Western Europe [6].

For almost a century, removal of the affected breast and the axillary lymph nodes has been the corner stone of primary treatment for these patients. Death in the majority of instances is still due to distant metastasis. The later phenomenon is essentially attributed to the biology of the disease, rather than to the extent of the local treatment. In the late fifties, sporadic data emerged indicating that conservative surgery and radiotherapy give equal local control and survival rate, compared to radical mastectomy alone. Since then, efforts have been made by different institutions and study groups over the past several decades to improve cosmeses and decrease morbidity without compromising the probability of local control. This conservative approach is now popular in North America and Western Europe; hopefully it will attain more attention in our region [8,11,14]. The aim of the present work was to review the KFSH experience in the conservative management of carcinoma of the breast.

### PATIENTS AND METHODS

Between January 1981 and December 1990, 9729 adult female patients presented to the KFSH, 1369 of them were diagnosed as breast cancer (14%). Only 98 female patients (7%) benefited from breast saving surgery.

Complete clinical examination, biochemical profile and metastatic work up were performed for all patients. The metastatic work up included chest X-ray, abdominal ultrasound and bone scan. Bilateral mammography was performed in some of the patients. The patients were staged according to the UICC TNM staging system [3].

The identified breast tumor was removed with an adequate margin. Usually for a small tumor lumpectomy was done, with an estimated 1 cm margin of the normal breast tissue around the tumor. In larger tumors, the breast segment, or quadrant harboring the tumor was removed totally, to allow for a 2 cm margin around the tumor. In all central quadrant lesions and the majority of T3 lesions, conservative surgery was resorted to, because of the patient refusal of mastectomy. Two separate incisions were made one for the breast tumor and the other for the axillary lymph node dissection. Eighty-seven patients underwent axillary dissection. In 11 patients with clinically negative axillae; axillary dissection was not performed. The number of pathologically identified axillary LN, varied between 3-23 lymph nodes, with an average of 7. In the majority of patients level 1 and 2 were dissected and in few of them level 3 was included as well.

Tele-cobalt post-operative radiotherapy was started 2 to 3 weeks after surgery to allow for proper wound healing and to improve arm mobility for proper positioning during radiotherapy. In all patients the treated volume included the breast, chest wall, supraclavicular fossa and the axillary apex. The axilla and internal mammary nodes (IMC) were included in patients with histologically confirmed axillary LN metastasis or if the axilla was not dissected. The IMC alone was irradiated in central and inner quadrant tumors.

The dose to the whole breast ranged between 40-56 Gy (1.8-2Gy/F, 5 F/week), only eight patients received doses lower than 46 Gy and 10 patients received doses higher than 50 Gy. The radiotherapy dose to the tumor bed ranged between 50-70 Gy, it was 60-65 Gy in 72 patients. The breast was treated by two tangential portals with or without wedges. Beam splitter was utilized and bolus was used in only 2 patients. The boost dose was given to the tumor bed using electron beam of 6-12 Mev depending on the breast size and the depth of the tumor as assessed preoperatively. The boost dose varied between 10-20 Gy (GD) with 2-2.5 Gy per fraction. In six patients, the boost was carried out by Ir192 implant. Two of them received peri-operative implant. Manual after-loading was adopted and a dose of 15-20 Gy was given.

Adjuvant chemotherapy was offered to 33

pre-menopausal patients with axially lymph node metastasis, while seven post-menopausal women were given adjuvant tamoxifen 10 mg twice daily. Fifty-eight patients did not receive any chemotherapy, either because the axillary lymph nodes were negative, or the patient refused chemotherapy. Four patients received CMF regimen (cyclophosphamide 600 mg/m<sup>2</sup>, methotrexate 40 mg/m<sup>2</sup> and 5-fluorouracil 600 mg/m<sup>2</sup> given IV day 1 of cycle every 21 days) and 29 received the FAC regimen (5-fluorouracil 500 mg/m<sup>2</sup>, Adriamycin 50 mg/m<sup>2</sup> and cyclophosphamide 500 mg/m<sup>2</sup> given IV day 1 of cycle every 21 days). The maximum total dose of Adriamycin was 300 mg/m<sup>2</sup>. Systemic chemotherapy was administered concomitantly with radiotherapy (after 2 weeks from the start of radiation) or after the end of radiotherapy, depending on the tolerance of the patients.

The cosmetic outcome was graded from excellent to poor considering the appearance, size, shape and consistency of treated breast compared to the other breast (Table 2).

The survival estimates were calculated using the Kaplan-Meier product limit method. The comparison between the survival curves of the different groups was done using the Wilcoxon test. All reported *p*-values were two sided. *p* value of < 0.05 was considered significant. Survival and local control rates are presented ( $\pm$  standard error [12]).

## RESULTS

The present work is a retrospective analysis of 98 female patients with carcinoma of the breast treated in the radiotherapy department of the KFSH between 1981-1990. Saudi nationals comprised 78 patients (79%), the remaining 20 patients (21%) were expatriates that belong to seven nationalities, eight of them were Egyptians.

The age ranged between 19-68 years with a median of 43 years, 49 patients (50%) were below the age of 40 years. The right breast was involved in 48 patients, compared to 50 patients in the left side.

The primary was located in the outer quadrants of the breast in 68 patients and the inner quadrants were involved in 20 patients. In 10 patients the tumor was located at the junction of the outer and the inner quadrants or centrally located. There were 15 T1 tumors, 52 T2, 29 T3

and in 2 patients the size of the primary was unknown (Tx).

As regard the lymph node status, 57 patients had clinically negative lymph node while 37 had clinically palpable lymph nodes in the axilla (N1). In 4 patients the lymph node status was undetermined (Nx). Pathologically; 46 patients were NO, 25 patients had from 1-3 positive nodes and 9 patients had more than 3 positive lymph nodes. In seven patients, the number of positive lymph nodes was not clear. Eleven patients refused axillary intervention but all had clinically negative axillae.

*Local control:* The 5-year overall local control rate was  $88\pm 4\%$  (Fig. 1). Different prognostic factors affecting the local control were studied. They included the age, LN status, site of the primary tumor and its T-stage, extent of surgical resection, the dose of radiotherapy to the whole breast and to the tumor bed (Table 2).

Patients at the age of 40 years or younger had a 5-year local control rate of  $86\pm 6\%$ , compared to  $89\pm 5\%$  for older patients ( $p = 0.8$ ). As regard, the extent of surgery 46 patients had lumpectomy, 43 segmentectomy and 9 quadrantectomy. The 5-year local control rate was  $88\pm 6\%$ ,  $83\pm 6\%$  and  $100\%$  respectively ( $p = 0.2$ ). Only 2/15 T1 patients failed at 29 and 46 months of follow-up. One of them was salvaged by mastectomy and followed for 54 months after salvage operation. T1 + T2 tumors had a 5-year local control rate of  $87\pm 5\%$  compared to  $89\pm 5\%$  for T3 lesions (Fig. 2) with no significant difference between the 2 groups ( $p = 0.9$ ). Lymph node status, also did not influence the local control rate of the group. Patients with clinically positive nodes had a 5-year local control rate of  $86\pm 6\%$  compared to  $90\pm 5\%$  for patients with negative nodes ( $p = 0.7$ ).

The 5-year local control rate of 20 patients with inner quadrant lesions was  $74.3\%$  compared to  $90.6\%$  for 68 patients with outer quadrant lesions (Fig. 3) and the difference was statistically significant ( $p = 0.01$ ). The patients who received a whole breast dose  $< 50$  Gy had a 5-year local control rate of  $88\pm 4\%$ , compared to  $92.7\pm 5\%$  for those treated with a dose  $> 50$

Gy, but the difference was not statistically significant. Those who received a dose of 60 Gy to the tumor bed had a 5-year local control rate of  $83\pm 6\%$  compared to  $92\pm 5\%$  for those who received higher dose, the difference was not significant.

*Survival rates:* The 5-year overall survival rate was  $79\pm 6\%$  (Fig. 1). The same prognostic factors that were studied for local control, were studied for the survival rates. None of them was significant. The 5-year actuarial survival for patients with T1, T2 and T3 tumors were  $87\pm 12\%$ ,  $82\pm 7\%$  and  $71\pm 11\%$  respectively ( $p = 0.8$ ). Patients with negative axillary lymph nodes had 5-year survival rate of  $89\pm 6\%$  compared to  $76\pm 9\%$  for patients with positive axillae, the difference was not statistically significant.

Only 40 patients of the group received systemic treatment. The 5-year survival rate for patients who did not receive systemic therapy was  $87\pm 6\%$  compared to  $72\pm 9\%$  for those who received systemic therapy and the difference was not significant ( $p = 0.4$ ).

The overall cosmetic outcome was good to excellent (Fig. 4), except in five patients. One of them had a bulky breast, she suffered from persistent breast edema and local discomfort due to fat necrosis. The remaining four patients developed noticeably small shrunken breasts after radiotherapy. Three of them had marked disfigurement and the fourth showed extensive telangectasia. The five patients that got pregnant afterwards experienced breast discomfort, nipple and skin hyperthetasia with moderate degree of breast engorgement. Breast feeding from the treated breasts was associated with nipple discomfort and the milk was serous in appearance and not liked by the babies.

Table (1): Grading of the cosmetic outcome after conservative breast treatment.

1- Excellent	No appreciable difference
2- Very good / Good	Mild/moderate difference
3- Fair / Poor	Marked difference

Simplified from Krishann et al., 1987 [10].

Table (2): Local control rate according to different prognostic factor in 98 breast cancer patient treated conservatively.

	5-year local control	Significance
Overall	87.7±4%	
< 40 y	85.9±6%	
> 40 y	88.9±5%	0.8
<i>T-stage:</i>		
T1+T2	86±5%	
T3	89±5%	0.9
<i>Extent of surgery:</i>		
Lumpectomy	88±6%	
Segmentectomy	83±6%	
Quadrectomy	100%	0.2
<i>Site of tumor:</i>		
Outer quadrant	90.6±4%	
Inner quadrant	74.3±10%	0.01
<i>Lymph node status:</i>		
Positive	86±6%	
Negative	90±5%	0.7

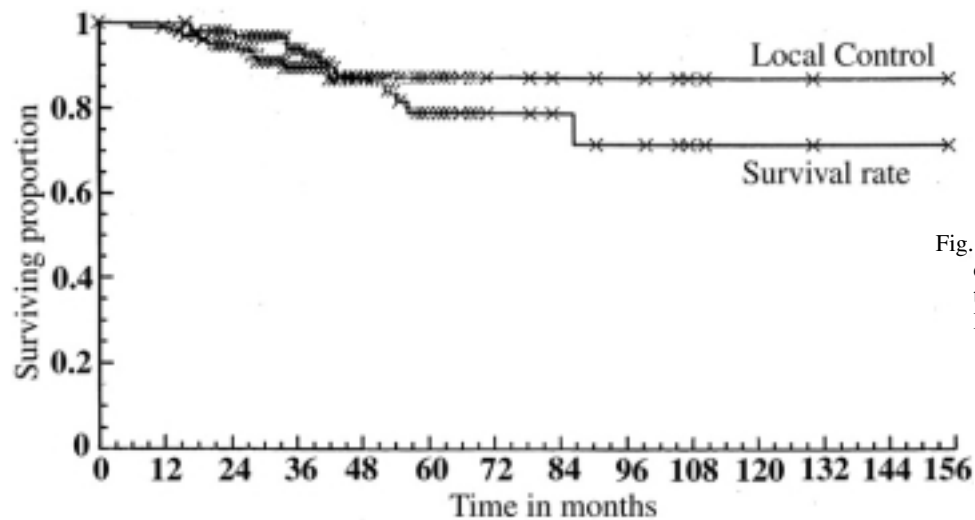


Fig. (1): Survival and local control after conservative treatment breast cancer KFSH 1981-1990.

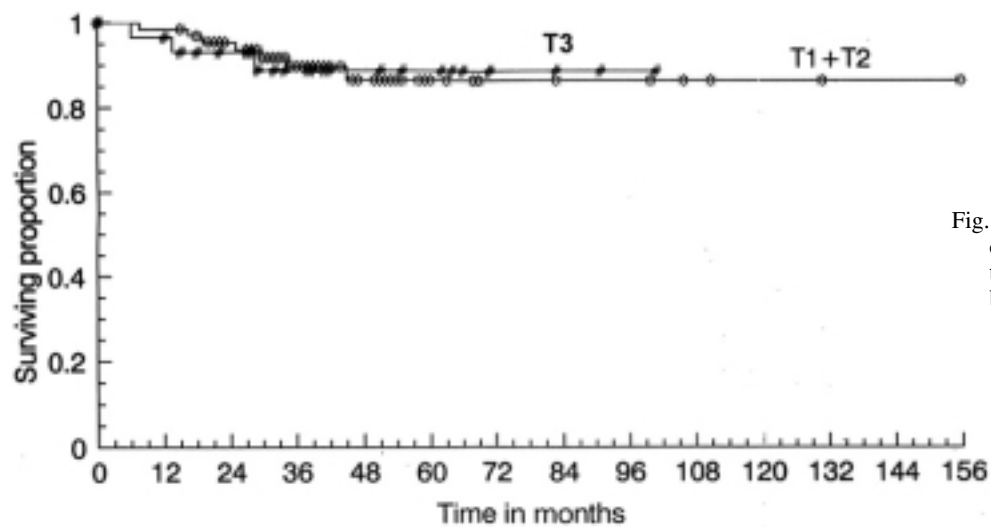


Fig. (2): Local control according to T-stage distribution conservative breast cancer KFSH 1981-1990.

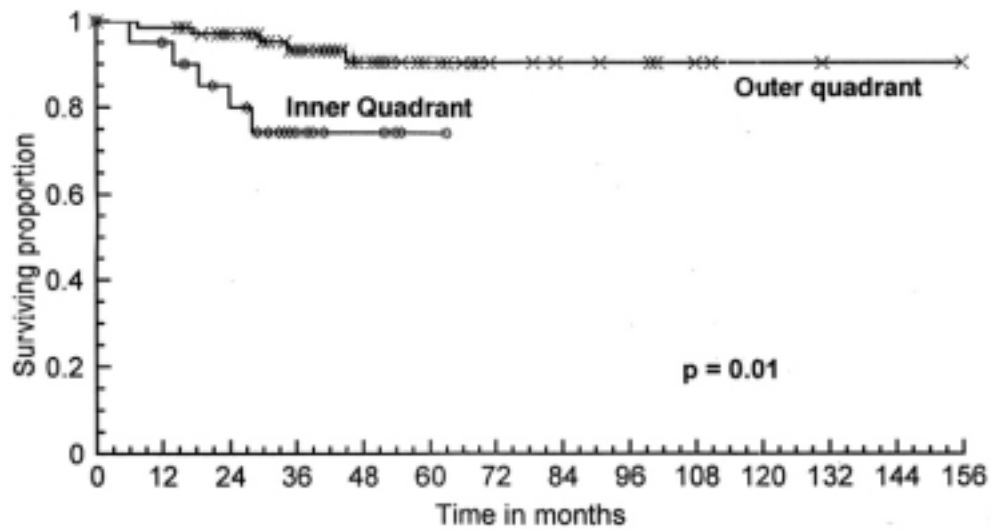


Fig. (3): Local control according to the site of the primary tumor conservative breast cancer KFSH 1981-1990.

Fig. (4): Score of the cosmetic outcome.



Fig. (4,A): Excellent with minimal changes 30 months after treatment.

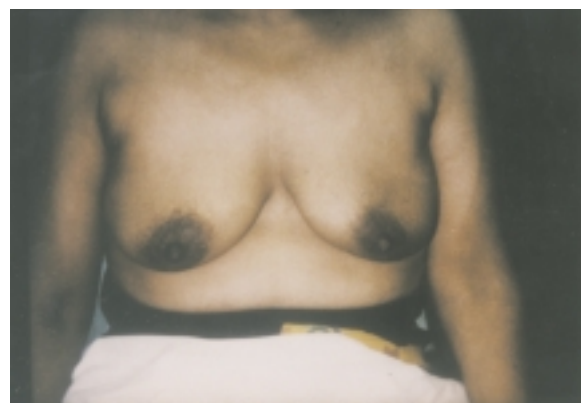


Fig. (4,B): Very good with mild changes 19 months after treatment.



Fig. (4,C): Good with moderate changes 20 months after treatment.

## DISCUSSION

The present study is a retrospective analysis of 98 women with breast cancer treated conservatively, in the radiotherapy department of the KFSH, Riyadh, Saudi Arabia. The limited number of patients treated conservatively in this study, only 7% of the total number of breast cancer in KFSH, reflects a physician bias rather than a patient's choice. A good number of patients are usually referred to KFSH after mastectomy. In USA only around 50% of eligible patients with stage I or II breast cancer were treated conservatively [8,11,14].

The importance of local control in breast cancer and its reflection on survival was addressed in a number of reports. About 25% of

breast cancer are cured without any systemic therapy, which reflect that not all cases of breast cancer starts as systemic disease. Improving local control should improve survival in the subset of patients that are not metastatic from the start. Overgaard et al., 1997 [15] reported in the Danish Breast Cancer Cooperative Group (DBCG) Trial, the trial included 1708 post-mastectomy pre-menopausal patients with stage II and III breast cancer. The patients were randomized between systemic therapy  $\pm$  post-operative radiotherapy. The 10-year overall survival rate was 54% for the radiotherapy + chemotherapy arm compared to 45% for the chemotherapy alone arm ( $p < 0.001$ ). In 1999 the group reported their experience in 1355 post-menopausal patients with stage II and III breast cancer. The patients were randomly allocated to tamoxifen  $\pm$  postoperative radiotherapy (RT). The 10-year overall survival rate was 45% for the RT + tamoxifen arm compared to 36% for the tamoxifen alone arm ( $p = 0.03$ ) [16]. A Canadian group reviewed 18 randomized trials and reported also the beneficial role of radiotherapy in node positive patients [20]. The important issue in post-operative radiotherapy of the breast is to avoid radiation induced cardiac complications by adopting modern techniques and to use electrons in internal mammary irradiation.

The 5-year local control rate in this study was 88%. The 12% local failure is comparable with the reports coming from Europe and North America with a local failure rate ranging between 4-20% [9,18,22]. Surgery and radiotherapy play an important role in the local control of breast cancer. The extent of surgery was studied in some reports. Tumeorectomy (TART) and quadrantectomy (QUART) was compared in a non-randomized study and both groups had the same local control and survival rates with no significant difference (Arcangeli, 1998) [2]. This in contrast to the report by Mariani et al., 1998 on a randomized trial comparing (QUART) and (TART). The local recurrence rate at 10-year was 7.4 and 18.6% for the QUART and TART respectively ( $p > 0.0001$ ) but the survival rates were not significantly different [13]. In the KFSH series the extent of resection did not significantly influence the survival or local control of the patients. The site of the primary tumor was the only factor affecting the local control. Chauvet et al., 1990 reported no significant effect for the site [4].

The dose to the whole breast and the importance of the boost dose and whether interstitial implant, cobalt 60 or electrons should be used for the boost treatment is still controversial. In our opinion, the dose to the whole breast should be in the range 45-50 Gy and that to the tumor bed should not exceed 55-60 Gy. All the patients included in the present study received a boost dose of 10-14 Gy. Romestaing et al., 1997 reported the importance of 10 Gy boost in 1024 patients randomized between boost and no boost after wide local excision +50 Gy to the whole breast. The 5-year local recurrence rate in the boost group was 3.6% compared to 4.5% for the no boost ( $p = 0.04$ ) [17]. In contrast a report by van Tienhoven et al., 1999 included 1807 patients from the EORTC and DBCG. They studied the loco-regionally relapsed patients after breast conserving treatment (BCT) or modified radical mastectomy (MRM). The 5-year survival rate after salvage treatment for both groups were 59% and 58% respectively, while the 5-year local control was 62% and 63%. The type of local treatment offered initially (MRM or BCT before relapse) for the relapsed patients did not significantly influence the relapse rate. So, they concluded that recurrence after BCT or MRM reflects the biology of the tumor rather than the intensity of local treatment [21].

Some investigators studied the relevance of the boost dose to the cosmetic result. Vrieling et al., 1999 reported on 5569 patients included in EORTC trial studying the impact of boost on the cosmetic appearance of the treated breast. At 3 years a boost dose of 16 Gy had a significant adverse cosmetic effect [23]. In a study from EORTC the extent of excision appeared to be the most important predictive factor for the cosmetic result of the treated breast [22]. Only five patients in the present study had fair to poor scale of breast cosmetic appearance. All of them were more satisfied with their body image after conservative treatment than if mastectomy had been performed for them. EORTC conducted a trial to compare MRM versus BCT and the main end point was survival. However, assessment of the quality of life was performed for some of the patients. Significant benefit in body image and satisfaction with treatment was observed in BCT patients. No significant difference was observed in the fear of recurrence between MRM and BCT group [5].

In the KFSH study the addition of systemic treatment did not influence the survival or local control rates of the patients. Also, Schwegler and Gurber, 1999 in a retrospective analysis of 491 patients treated conservatively, reported no improvement of survival with chemotherapy [19]. We think that this is most probably attributable to the small number of patients included in both studies and their retrospective nature.

No doubt, breast amputation is a violation of the feminine integrity at any age, race, or color, regardless of their marital status. Unless indicated by experienced team, mastectomy should be avoided and the conservative policy has to be enforced. Both procedures yield comparable local control rate with the non-deniable psychosocial benefit of breast saving.

### REFERENCES

- 1- Annual report of the tumor registry, King Faisal Specialist Hospital and Research Center, Riyadh, Kingdom of Saudi Arabia, 1990.
- 2- Arcangeli G., Micheli A., D'Angelo L., Giovannazzo G., Arcangeli G., Tersigni R., Comandini E., Scala T., Lopez M., Mauri M. and D'Aprile M.: Conservative surgery and radiotherapy in early stage breast cancer: comparison between tumourectomy and quadrantectomy. *Radiation Oncology*, 46 (1): 39-45, 1998.
- 3- Beahers O.H., Henson D.E., Hutter R.V.P. and Kennedy B.J.: Hand book for staging of cancer. The manual for staging of cancer. American Joint Committee on Cancer and TNM committee of the International Union Against Cancer. Publisher: Philadelphia, Lippincott Company, 1993.
- 4- Chauvet B., Reynaud-Bougnoux A., Calias G., Panel N., Lansac J., Bougnoux P. and Le Floch O.: Prognostic significance of breast relapse after conservative treatment in node-negative early breast cancer. *Int. J. Radiat. Oncol. Biol. Phys.*, 19: 1125-1130, 1990.
- 5- Curran D., Van Dongen J.P., Aaronson N.K., Kiebert G., Fentiman I.S., Mignolet F. and Bartelink H.: Quality of life of early-stage breast cancer patients treated with radical mastectomy or breast-conserving procedures results of EORTC Trial 10801. The European Organization for Research and Treatment of Cancer (EORTC), Breast Cancer Co-operative Group (ECCG). *Eur. J. Cancer*, 34 (3): 307-314, 1998.
- 6- Dickson R. and Lippman M.: Cancer of the breast. In: Devita V., Hellman S., Rosenberg S. eds. *Cancer principles and practice of oncology*. Philadelphia, Lippincott-Raven Co., 1541-1616, 1997.
- 7- El-Bolkainy N., *General Pathology of Cancer*, first edition, 1991.
- 8- Farrow D.C., Hunt W.C. and Samet J.M.: Geographic variation in the treatment of localized breast cancer. *N. Eng. J. Med.*, 326 (17): 1097-1101, 1992.
- 9- Fisher B., Anderson S., Redmond C., Wolmark N., Wickerham L. and Cronin W.M.: Re-analysis 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. Eng. J. Med.*, 333: 1456-1461, 1995.
- 10- Krishnan L., Jewell W.R., Mansfield C.M., Reddy E.K. and James H.: Thomas and Krishnan E.C.: Perioperative interstitial irradiation in the conservative management of early breast cancer *Int. J. Radiat. Oncol. Biol. Phys.*, 13: 1661-1665, 1987.
- 11- Lazovich D., White E., Thomas D. and Moe R.E.: Underutilization of breast conserving surgery and radiation therapy among women stage I or II breast cancer. *JAMA*, 266: 3433-3438, 1991.
- 12- Lee E.T.: *Statistical methods for survival data analysis* publisher: John Wiley and Sons N.Y., 1992.
- 13- Mariani L., Salvadori B., Marubini E., Conti A.R., Rovini D., Cusumano F., Rosolin T., Andreola S., Zucali R. and Rilke F.: Veronesi Ten year results of a randomised trial comparing two conservative treatment strategies for small size breast cancer. *Eur. J. Cancer*, 34 (8): 1156-1162, 1998.
- 14- Natinger A., Gottlieb M., Veum T., Yahnke D. and Goodwin J.S.: Geographic variation in the use of breast conserving treatment for breast cancer. *N. Eng. J. Med.*, 326 (17): 1102-1107, 1992.
- 15- Overgaard M., Hansen P.S., Overgaard J., Rose C., Andersson M., Bach F., Kjaer M., Gadeberg C.C., Mouridsen H.T., Jensen M.B. and Zedeler K.: Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy. Danish Breast Cancer Cooperative Group 82b Trial. *N. Engl. J. Med.*, 2; 37 (14): 949-955, 1997.
- 16- Overgaard M., Jensen M.B., Overgaard J., Hansen P.S., Rose C., Andersson M., Kamby C., Kjaer M., Gadeberg C.C., Rasmussen B.B., Blichert-Toft M. and Mouridsen H.T.: Postoperative radiotherapy in high-risk postmenopausal

- breast-cancer patients given adjuvant tamoxifen: Danish Breast Cancer Cooperative Group DBCG 82c randomised trial. *Lancet*, 15: 353 (9165): 1641-1648, 1999.
- 17- Romestaing P., Lehingue Y., Carrie C., Coquard R., Montbarbon X., Ardiet J.M., Mamelle N. and Gerard J.P.: Role of a 10-Gy boost in the conservative treatment of early breast cancer: results of a randomized clinical trial in Lyon, France. *J. Clin. Oncol.*, 15 (3): 963-968, 1997.
- 18- Sarrazin D., Le M., Arrigada R., Conteso G., Fontaine E., Spielmann M., Rochard F., Le Chevalier T. and Lacaure J.: Ten year results of a randomized trial comparing a conservative treatment to mastectomy in early breast cancer. *Radiation Oncol.*, 14: 177-184, 1989.
- 19- Schwegler N. and Gruber G.: Breast-preserving therapy: 19 years of monoinstitutional experience and results. *Schweiz Rundsch Med. Prax.*, 8; 88: (15): 653-662, 1999.
- 20- Timothy J., Whelan, Jim Julian, Jim Wright, Alejandro R. Jadad and Mark L. Levine: Does locoregional radiation therapy improve survival in breast cancer? a Meta Analysis: *Journal of Clinical Oncology*, 18 (6): 1220-1229, 2000.
- 21- Van Tienhoven G., Voogd A.C., Peterse J.L., Nielsen M., Andersen K.W., Mignolet F., Sylvestre R., Fentiman I.S., Van der Schueren E., van Zijl K., Blichert-Toft M., Bartelink H. and van Dongen J.A.: Prognosis after treatment for loco-regional recurrence after mastectomy or breast conserving therapy in two randomised trials (EORTC 10801 and DBCG-82TM). EORTC Breast Cancer Cooperative group and the Danish breast cancer cooperative group. *Euro. J. Cancer*, 35 (1): 32-38, 1999.
- 22- Veronesi U., Sanfi A., Savadori B., Luini A., Scozzi R., Zukali R., Marubini E., Del Vecchio M., Borracchi P. and Marchini S.: Breast conservation is the treatment of choice in small breast cancer: Long-term results of a randomized clinical trial. *Euro. J. Cancer*, 26: 668-670, 1990.
- 23- Vrieling C., Collette L., Fourquet A., Hoogenraad W.J., Horiot J.C., Jager J.J., Pierart M., Poortmans P.M., Struikmans H., Van der Hulst M., Van der Schueren E. and Bartelink H.: The influence of the boost in breast-conserving therapy on cosmetic outcome in the EORTIC "boost versus no boost" trial. EORTC radiotherapy and breast cancer cooperative groups. European Organization for Research and Treatment of Cancer. *Int. J. Radiat. Oncol. Biol. Phys.*, 1; 45 (3): 677-685, 1999.