

postoperative complications was 10.9% (5 patients): total necrosis – 1, marginal necrosis – 3, bleeding – 1. In group IV only 1 (4.0%) had marginal necrosis of the flap. We observed no local relapses in this group.

**Conclusion:** Different techniques of immediate breast reconstruction with autologous tissues following radical surgery must become a standard in the surgical treatment of breast cancer.

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### Second conservative treatment for early breast cancer: 12-years results from a pilot study.

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**Aim of the study:** To report the long term results obtained in a prospective group of patients treated by local excision and high-dose-rate brachytherapy for locally recurrent breast cancer.

**Methods:** Second lumpectomy followed by HDR brachytherapy implant to the tumor bed plus a 3 cm safety margin was offered to 43 patients with breast-only local recurrences after conservative treatment between 12/1990 and 04/2002. Patients were offered mastectomy, but they rejected it. Brachytherapy was given between 1 and 3 weeks after excision. Implants were done at the time of surgery in 37 cases and in the remaining 6 patients at the time of beginning treatment. The average number of implanted tubes was 7 (range 4-11) and the average volume of the reference isodose curve was 56 cc. HDR brachytherapy doses were 30 Gy in 12 fractions in 5 days. 34 patients received systemic treatment: 12 with chemotherapy; 11 with tamoxifen and 1 both. No patient was lost for follow-up. Special attention to local, regional or distant recurrence, survival, fibrosis, late effects and cosmesis was done during the follow-up period.

**Results:** All patients completed treatment. During the 12-year, 1-year minimum follow-up, there were 8 patients who had regional (2 cases) or distant metastases (6 cases) as their first site of failure. Three of them experienced a differed local recurrence and 1 of them died from the disease. Actuarial results at 12-year were: local control 84.2%; disease free survival 65.4%; and survival 90.7%. Cosmetic results were satisfactory in 89.4%. No patient experienced arm edema or grade 3-4 early or late complications. Between the 12 patients that were followed-up for at least 10-years, 10 of them were with their breast still in place at 10-year.

**Conclusions:** HDR brachytherapy was a safe and effective method of treatment for small-size, low-risk, local recurrence after local excision in conservatively treated patients. The dose of 30 Gy of HDR brachytherapy given in 12 fractions along 5 days at 2.5 Gy/fraction, 2-3 times every day was safe in patients previously treated. The good results achieved justifies the initiation of randomized trials exploring its use as standard treatment in selected patients with low-risk recurrent breast tumors.

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### Radiation pneumonitis in early breast cancer patients: effects of systemic treatments

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The development of radiation pneumonitis in breast cancer depends mainly on the characteristics of the radiotherapy (RT) and the patient, but chemotherapy or hormone therapy (HT) may also influence its occurrence. Radiation-induced lung changes were investigated in 65 patients given RT after curative surgery for breast cancer. Twenty-five patients completed a taxane-based perioperative chemotherapy regimen \*4 weeks prior to RT. Thirty-five patients received adjuvant HT (tamoxifen, n=27, anastrozole, n=8) \*2 weeks before and during RT. Another 5 patients (controls) received no medication. Conformal RT was carried out according to CT-based 3D radiation treatment planning (Helax TMS) with a linear accelerator. The following RT parameters were analysed: the ipsilateral mean lung dose

(MLD), the central lung distance (CLD), the lung volume receiving 20 Gy (V<sub>20</sub>), and the dose received by a 25% volume of the ipsilateral lung (D<sub>25</sub>). CT scans were performed prior to and 3-6 months after the completion of RT. In addition, plasma TGF-β levels were determined before and during HT, and also in the controls, as follows: before RT, at the completion of RT, and 3 months later. All the chemotherapy patients and 42-50% of the HT patients, and 20% of the controls received locoregional irradiation, while in the other cases only the operated breast was treated with RT. The irradiated lung volume was significantly larger in the patients who received chemotherapy than in the HT or control patients (table).

Radiogenic changes only rarely were detected in the patients after taxane chemotherapy, and no clinical symptom of pneumonitis occurred. Pneumonitis grade I was diagnosed in 3 cases in the tamoxifen group, and in 1 patient in the anastrozole group. However, minor radiogen changes were detected on CT in one-third of both groups. No radiogenic damage was seen in the controls. Radiation-induced lung changes well correlated with older age. The TGF-β levels were significantly higher after tamoxifen treatment, whereas no such effect was observed after anastrozole therapy (Table). Radiogenic pneumonitis is a rare event after postoperative treatment in breast cancer if conformal RT is carried out. The effect of tamoxifen in elevating the TGF-β level may play a role in the development of radiogen lung damage.

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### Breast scar and tumour cavity visualisation using MR imaging in the conventional radiotherapy treatment position

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**Background:** Scar and tumour cavity visualisation is essential for planning adequately targeted adjuvant breast external beam radiotherapy and boost dose treatment. This study investigated the role of MR imaging in visualising scar and tumour cavity.

**Material and Methods:** 0.2 T Siemens open MR scanner with image distortion correction and loop coil, treatment wedge, positional lasers and custom-made arm pole was used to scan in the conventional treatment position [1] women with early breast cancer treated by breast-conserving surgery. 28 cases were randomly selected. Blinded to pathology and surgery details, tumour cavity dimensions and scar position were measured on hard copy MR images by two middle grade oncologists and an experienced radiologist. Intra-person agreement (for oncologists) and inter-person agreement (between oncologists and radiologist) were calculated. Analysis was only performed where there were 10 or more pairs of results.

**Results:** Tumour cavity measurements

Intra-person correlation coefficient (intraclass correlation)

	oncologist 1 - oncologist 1	oncologist 2 - oncologist 2
Axial plane	r=0.47, n=26, p=0.0069	n=8
Coronal plane	r=0.71, n=12, p=0.0042	n=1
Sagittal plane	r=0.83, n=23, p<0.001	n=7

Inter-person correlation coefficient (Pearsons correlation)

	oncologist 1 - radiologist	oncologist 2 - radiologist
Axial plane	r=0.58, n=24, p=0.003	r=0.83, n=21, p<0.001
Coronal plane	r=0.73, n=11, p=0.011	n=8
Sagittal plane	r=0.39, n=21, p=0.077	r=0.83, n=15, p<0.001

Scar measurements

Intra-person correlation coefficient (Spearman's correlation)

	oncologist 1 - oncologist 1	oncologist 2 - oncologist 2
Axial plane	r=0.27, n=23, p=0.213	n=4
Coronal plane	n=8	n=1
Sagittal plane	r=0.78, n=18, p<0.001	n=4

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	Age (year)	MLD (Gy)	CLD (cm)	V <sub>20</sub> Gy (%)	D <sub>25%</sub> (Gy)	TGF-β before HT (ng/ml)	TGF-β after HT (ng/ml)
Taxane	52.9 ± 8.7	17.9 ± 2.17*	2.9 ± 0.5	38.7 ± 7.2*	36.6 ± 5.2*	–	–
Tamoxifen	56.4 ± 11.9	13.8 ± 5.6	3.0 ± 0.9	28.4 ± 14.2	23.1 ± 16.8	24.04 ± 10.6	30.1 ± 10.7*
Anastrozole	65.5 ± 7.3	13.5 ± 4.8	3.1 ± 0.7	27.1 ± 11.8	21.5 ± 17.7	28.8 ± 6.9	20.5 ± 15.2
Control	59.4 ± 8.2	11.1 ± 6.6	2.7 ± 1.4	20.1 ± 14.9	12.0 ± 16.1	29.2 ± 5.1	36.0 ± 16.0

p<0.05

Inter-person correlation coefficient (Spearman's correlation)

	oncologist 1 - radiologist	oncologist 2 - radiologist
Axial plane	r=0.23, n=19, p=0.337	r=0.15, n=12, p=0.636
Coronal plane	n=8	n=5
Sagittal plane	r=0.47, n=16, p=0.065	r=0.44, n=13, p=0.131

**Conclusions:** MRI of the postoperative breast with the patient in the conventional treatment position demonstrated a quantifiable tumour cavity in all three planes with generally good agreement for measurements made. Scar was more difficult to visualise; it was best seen in the sagittal plane, almost certainly because skin incisions were perpendicular with this plane. Application of oil-filled markers to the scar would facilitate its measurement. MRI can be used to visualise the target volume when planning three-dimensional adjuvant breast radiotherapy.

## References

- [1] UKCCCR Breast Cancer Subcommittee START protocol: a randomised comparison of fractionation regimens after local excision or mastectomy in women with early stage breast cancer; 1998.

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## Breast morbidity after breast conserving treatment and sentinel node biopsy

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**Background:** Sentinel node biopsy (SNB) is associated with less arm morbidity compared to axillary clearance. Little is known if also the risk of breast morbidity is diminished after breast conserving therapy with more limited axillary surgery. Therefore we aimed to evaluate breast morbidity after breast conserving therapy and SNB or axillary clearance (AC).

**Patients and methods:** Altogether 161 consecutive breast cancer patient who underwent breast conserving surgery and SNB only (57), AC node negative (57) and AC node positive (46) were enrolled to the study. The clinical status and the breast ultrasonography were examined a year after the surgical treatment.

**Results:** In the clinical examination breast oedema was most common (48%) in patient in AC node positive group compared to 36% in AC node negative group and to 25% in SNB group ( $p < 0.05$  between SNB and AC node positive). Accordingly, the operated breast was smaller than the contralateral breast most often, in 46% of patients in the SNB group compared to 20% in the AC node positive group ( $p < 0.01$ ). In the breast ultrasonography subcutaneous oedema in the operated breast was more common (68-70%) in the AC groups compared to 25% in the SNB group ( $p = 0.0001$  between SNB vs AC node negative,  $p = 0.001$  between SNB vs AC node positive). Also the skin in the operated breast was the thickest, a median of 3.05 mm in the AC node positive group and thinnest in the SNB group, a median 1.8 mm, measured by ultrasonography. There were no statistical significant differences in the pigmentation of the skin and in the tenderness of the breast between the groups.

**Conclusions:** Breast lymphoedema was more common one year after the breast conserving surgery in patients who underwent axillary clearance than in those who underwent SNB only.

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## Change of cosmetic results in time, evaluation of parameters influencing cosmetic results after breast conserving therapy (BCT) in patients with breast cancer.

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**Purpose:** Cosmetic results of breast conserving therapy in patients with breast cancer are influenced by effects of surgical treatment, radiotherapy (RT) and chemotherapy. Surgery may cause breast asymmetry, disturbing scar or nipple displacement. RT, due to fibrosis, may cause intensification of breast and nipple asymmetry, changes in breast skin pigmentation as well as intensify edema of treated breast and ipsilateral upper limb.

The aim of the paper is to define to which extent radiotherapy may influence the change of cosmetic result after BCT and how the result changes in time.

**Material and method:** Clinical material included 43 patients with breast cancer stage I and II. Mean observation time was 4.7 years (3-7 years). 37% of patients were treated with tumorectomy, 63% with quadrantectomy. Later, all patients received external radiotherapy. Measurements of breast

asymmetry, and photographs were made before radiotherapy and during follow up every 6 months. The evaluated effects were nipple displacement in medio-lateral sense, upward nipple retraction, upward retraction of the interior breast contour, difference in oblique distances between the inguilar fossa and nipple. Cosmetic result was evaluated annually using Four Point Scoring System defining the result as excellent, good, fair or poor. The amount and extent of teleangiectasia were analysed and also intensification of late radiation skin damage according to EORTC. Circumference of upper limbs was measured too.

**Results:** Qualitative and quantitative evaluation of cosmesis before radiotherapy and 3 years after was compared. Before RT, in 88% of patients cosmetic result was excellent and good. In 12% of patients it was fair and poor. 3 years after radiotherapy the results were assessed respectively in 70% and 30%. Moderate edema of arm was observed in 18% of patients. Breast edema remained until 2 years after treatment causing pain assessed according to Visual Analogue Scale of Pain. 3 years after radiotherapy, in 32% of patients late radiation damage to the skin stage I was observed (according to EORTC) and in 7% the damage was in stage II. Teleangiectasia in areas bigger than 4 square cm was observed in 18% of patients.

**Conclusions:** Essential intensification of breast asymmetry caused by RT after 3 years of observation was not observed irrespective of received cosmetic result of surgery. Fibrotic retraction of breast, nipple and breast contour displacement in lateral sense slightly lower the cosmetic effect. Late radiation skin damage, changes in pigmentation of breast skin, teleangiectasia, breast and arm edema slightly influence the decrease of cosmetic result. The main factor responsible for low cosmetic effect was the kind of surgery and the amount of removed breast tissue.

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## Prognostic factors of breast-conserving treatment for early-stage breast cancer

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**Background:** The incidence of breast cancer in Spain range between 40 and 55/100.000 habitants and it is the 20% of total dying, by cancer, in female population. It is one of the most frequent causes of dying for women in the developed countries.

**Material and Methods:** We analysed 603 patients diagnosed of breast cancer and treated with breast conserving therapy consisting of wide excision of the primary tumor, and axillary dissection in all cases except on 14 (caused for medical reasons). All the patients were treated with radiotherapy in University Hospital "12 de Octubre" in Madrid.

**Results:** The median follow-up period was 63 months (range 5-242) A total of 109 patients (18.08%) were diagnosed were included in a screening program. Histopathologic examination revealed a diagnosis of infiltrating ductal carcinoma in 510 patients (84.6%). A total of 82.9% (490 patients) presented negative margins. The incidence of local recurrence was 6.8% (41 patients) at the moment that we closed the study. Five-year disease-free survival for stage I stage II were 88%, and 80% respectively. Five year overall survival rates for stage I was 95%. The overall survival at 5, 10 and 15 years for stage II were 90%, 82% and 69% respectively. We analysed also the disease free survival and the overall survival in function of age, and regional nodal involvement. Radiation therapy was administered to the breast through two opposing tangential fields giving a dose of 45 Gy in 36.6% of patients and 50 Gy in 62.5% of patients respectively. In the analysis of multiple logistic multivariate regression, the patients with histologically positive margins, younger than 50 years or with undifferentiated histological grade developed statistically significantly more local recurrences. The administration of adjuvant endocrine therapy was essential in the reduction of the possibility of local recurrences. The presence of positive margins, the nodal involvement, the size of the tumor, and the undifferentiated histological grade were factors statistically significant in the risk of develop distant metastases. In the analysis of multiple logistic dicotomic regression demonstrated that the presence of affected margins, the presence of carcinoma in situ, the age younger than 50 years, to avoid the administration of adjuvant endocrine therapy, and if the patients had been diagnosed outside a screening program, they had more risk of develop a local recurrence.

**Conclusion:** Breast conserving therapy is an effective treatment for a selection group of patients diagnosed of breast cancer in stage I or II. The presence of positive margins, carcinoma in situ, and age younger than 50 years are adverse prognostic factor with an increased of risk of local