JCO 2000;18:2828), and may significantly influence systemic treatment. The objective of this study was to analyze the impact of ITL on axillary lymph node involvement, relapse, and mortality risk, in patients both with and without systemic and loco-regional treatment.

Retrospective analysis was conducted of 2,414 patients, who underwent R0 resection of the primary tumor and systematic axillary lymph node dissection (at least 5 lymph nodes resected) for UICC I-III stage breast cancer. Patients with unknown ITL, multifocal tumor spread, central ITL, or tumor location within 15° of the border between outer and inner quadrants were excluded from the study. Median observation time was 6.7 years.

The ITL was within or between the medial quadrants of the breast in 33.6% of the patients (n=810) and in the lateral hemisphere of the breast in 66.4% (n=1,604). Tumor size, histopathological grading, and estrogen receptor status were balanced between patients with lateral and medial ITL. Metastatic axillary lymph node involvement was significantly associated with a lateral tumor location (P<.0001). The mean number of axillary lymph node metastases was increased by 29% in cases with lateral ITL (2.2 vs. 1.7, P=.003). In a multivariate logistic regression analysis, allowing for ITL, estrogen receptor status, grading and tumor size, ITL was confirmed as significant risk factor (P=.02) for axillary lymph node involvement. ITL, however, did not correlate with either disease free survival (DFS) or overall survival (OS), by univariate (DFS: P=.41; OS: P=.57) or by multivariate analysis (DFS: P=.16; OS: P=.98).

In contrast to previous reports, we conclude that there is no sufficient evidence to support any independent prognostic significance of ITL in early breast cancer. However, medial tumor location may lead to underestimation of the axillary lymph node involvement, and, thus, inadequate systemic treatment.

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Potentiation of radiation-induced subcutaneous fibrosis by concomitant use of tamoxifen in adjuvant breast cancer treatment

D. Azria[1], W. Jeanneret Sozzi[2], A. Zouhair[2], P.A. Coucke[2], A. Kramar[3], R.O. Mirimanoff[2], M. Ozsahin[2]. *[1] INSERM EMI 0227 CRLC Val d'Aurelle, Radiation Oncology, Montpellier, France; [2] Centre Hospitalier Universitaire Vaudois (CHUV), Radiation Oncology, Lausanne, Switzerland; [3] CRLC Val d'Aurelle, Biostatistics, Montpellier, France*

In this study, we wanted to assess whether concomitant administration of tamoxifen (TMX) and adjuvant radiation therapy (RT) increases the risk of developing subcutaneous fibrosis after conservative or radical surgery in breast cancer patients. Therefore, we evaluated 149 women with breast cancer treated using adjuvant RT after conservative or radical surgery who took part among 399 patients with miscellaneous cancers included in the KFS 00539-9-1997/SKL 00778-2-1999 prospective study evaluating the predictive value of CD4 and CD8 T-lymphocyte apoptosis on the development of radiation-induced late effects. Median age was 57 years (range: 26-82). RT consisted of 50-Gy whole-breast or thoracic wall irradiation in 2-Gy fractions using either Co60 (n = 97) or 6-MV (n = 52) photons completed with a localized external electron boost up to 66 Gy. Adjuvant TMX concomitant with RT was prescribed at a dose of 20 mg/day for a period of five years in 91 patients (61%). All patients receiving TMX were hormonal receptor positive, and none of them received adjuvant chemotherapy. There were 20 premenopausal and 71 postmenopausal patients (median age: 60 years; range: 36-82). Acute and late toxicities were assessed according to CTC 2.0 and RTOG/EORTC grading systems, respectively. Breast volume and skin dose was estimated using physical RT parameters. In a median follow-up of 29 months (range: 23-73), 144 patients are alive with (n = 5) or without disease. Five patients died from breast cancer without any grade 3 side effects (1, 13, 33, 38, and 41 months). Acute toxicity was observed in all but 4 patients (3%). One hundred six (71%), 34 (23%), and 5 (3%) patients experienced grade 1, 2, and 3 acute side effects, respectively. No statistically significant difference was observed between the TMX and no TMX groups in terms of acute toxicity (p = 0.58). There was no significant correlation between the early and late toxicity (R^2 = 0.05). Thirty-five patients out of 91 (38%) in the TMX group and 15 out of 58 (26%) in the no TMX group experienced grade 2 or 3 late skin toxicity (p = 0.11). However, grade 2 or 3 subcutaneous fibrosis was significantly higher in patients treated with concomitant TMX (42 patients out of 91 (46%) in the TMX group vs. 10 out of 58 (17%) in the no TMX group; p = 0.0002). Breast volume and skin dose did not interfere with subcutaneous fibrosis. However, grade 3 telangiectasia incidence was more frequent but not statistically significant in patients with high breast volume irradiated with Co60 compared to 6-MV photons. We conclude that the concomitant use of TMX with RT increases significantly subcutaneous fibrosis. In patients treated with adjuvant hormonal treatment, TMX should be delayed until the completion of RT.

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The predictive value of specimen radiography to predict margins involvement in 188 breast infraclinic carcinomas.

C. Mazouni[1], R. Rouzier[1], C. Balleyguier[2], M.C. Mathieu[3], S. Delaloge[4], H. Marsiglia[5], J.-R. Garbay[1], J.-R. Garbay[1]. *[1] Institut Gustave Roussy, Surgery, Villejuif, France; [2] Institut Gustave Roussy, Radiology, Villejuif, France; [3] Institut Gustave Roussy, Pathology, Villejuif, France; [4] Institut Gustave Roussy, Oncology, Villejuif, France; [5] Institut Gustave Roussy, Radiotherapy, Villejuif, France*

Backround: This study was undertaken to evaluate the role of specimen radiography in predicting margins status for breast impalpable lesions.

Material and methods: We retrospectively reviewed clinical, pathologic data and specimens radiography from 188 patients with DCIS referred in our centre between 1997 and 2000 for microcalcifications discovered at breast screening. The lesions were preoperatively localised by using a guide-wire. Specimen radiographic findings and clinico-pathological data were correlated with margin status.

Results: A total of 188 lesions revealed pure ductal carcinoma in situ (DCIS) in 125 (66%) and mixed carcinoma in 63 (34%). On specimen radiographs, the lesions were closed (<5mm) to one edge of lumpectomy in 74 (39%) cases. Histologic margins were positive in 86 cases (46%) and close (< 5 mm) in 51 (27%) cases. The factors associated with positive margins, in the univariate analysis, were a distance less than 5 mm from the tumour to the edge of the specimen radiograph (p=0.04) and multifocality (p=0.05). In the multivariate analysis (logistic regression), a radiologic margin<5mm was the only risk factor for close histologic margins. We therefore tested radiologic margin<5 mm as a potential tool to decrease the risk of close histological margins. Sensitivity, specificity, predictive positive and negative values are reported in Table 1.

Efficacy of specimen radiographs for detecting residual tumors

	Pathologic findings	
	Margins <5mm	Free margins >5mm
Incomplete excision	82 (43.6%)	6 (3.2%)
Complete excision	60 (32%)	40 (21.2%)
Se= 58% Sp=87%	VPP= 93%	VPN= 40%

Conclusions: Specimen radiograph findings were found to be a predictive factors of margins involvement when tumor distance to the margin was less than 5 mm and may therefore lead the surgeon to perform an additional excision.

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Breast cancer: immediate breast reconstruction after radical surgery

D.D. Pak. *P.A.Herzen Cancer Research Institute, General Oncology, Moscow, Russian Federation*

Background: We reviewed the results of 11 years' experience with different techniques for immediate reconstruction in breast cancer patients.

Materials and methods: Between 1991 and 2002 a total of 611 breast cancer patients were operated. All patients were divided into 4 groups according to the type of breast reconstruction technique. Group I included 154 patients (stage IIa, IIb) who underwent qaudrantectomy and regional lymph node dissection with immediate breast reconstruction using major pectoral (32) and latissimus dorsi (LD) (122) flaps. Group II - 386 women (stage IIa, IIb, IIIa) who underwent breast resection (70-90% of breast tissue and regional lymph nodes were removed) . Breast was reconstructed using LD flaps. Group III - 46 patients (stage IIa, IIb, IIIa) who underwent modified radical mastectomy. Breast was reconstructed using LD (18) and pedicled TRAM (28) flaps. Group IV - 25 women (stage I, IIa, IIb, IIIa) who underwent skin/areola sparing mastectomy. In all cases breast was reconstructed using LD flap and silicone breast implant. Radiotherapy and drug therapy were administered depending on the stage of disease, receptor status, etc.

Results: In group I 5-year overall survival rate was 92,4% and 87,5% for stages IIa and IIb respectively. Local recurrence rate was 0% and 4,6%. Esthetic results: excellent – 21,6%, good – 49%, satisfactory – 26%, poor – 2%. In group II 5-year overall survival rates were as follows: IIa – 88,3%, IIb – 84,3%, IIIa – 72,4%. Esthetic results: excellent – 21,6%, good – 48%, satisfactory – 28,4%, poor – 2%. The rate of immediate postoperative complications was 7,3% (28 patients) : total necrosis of the flap – 3, marginal necrosis – 2, wound suppuration – 2, bleeding – 3. In group III 5-year overall survival rates were as follows: IIa – 87,9%, IIb – 83,3%, IIIa – 73,6%. Local recurrence rate was 1,9%. Esthetic results: excellent – 21,7%, good – 49,6%, satisfactory – 28,4%, poor – 1%. The rate of immediate 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.

B. Guix, I. Henriquez, J.I. Tello, J.A. Lejarcegui, G. Zanon, P. Palombo, D. Rubio, J.M. Del Campo. *Fundacio IMOR, Medical Institute for Onco-Radiotherapy, Radiation Oncology, Barcelona, Spain*

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

Z. Kahán[1], Z. Varga[1], M. Csenki[1], E. Szil[1], A. Balogh[2], Z. Gyulai[2], Y. Mándi[2], L. Thurzó[1]. [1] *Szeged University of Science, Department of Oncotherapy, Szeged, Hungary;* [2] *Szeged University of Science, Department of Microbiology and Immunobiology, Szeged, Hungary*

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), and the dose received by a 25% volume of the ipsilateral lung (D). 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.

Abstract 431 – Table

	Age (year)	MLD (Gy)	CLD (cm)	$V_{20\,Gy}$ (%)	$D_{25\%}$ (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

$p \leq 0.05$

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

T. Wells[1], R. Davies[2], E. Heath[1], H. Taylor[3], A. Thomson[1], C. Wakeley[4], E. Whipp[1]. [1] *Bristol Haematology and Oncology Centre, Oncology, Bristol, United Kingdom;* [2] *Royal Devon and Exeter Hospital, Radiology, Exeter, United Kingdom;* [3] *Bristol Royal Infirmary, Research and Development Support Unit, Bristol, United Kingdom;* [4] *Bristol Royal Infirmary, Radiology, Bristol, United Kingdom*

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 (Spearmans 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