lower number of useless axillary lymphoadenectomies is mainly due to the increased operative use of sentinel lymphonode biopsy.

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Gene therapy with proangiogenic plasmids to enhance vascularity of pedicled transverse rectus abdominis myocutaneous flaps in a rat model

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Background: The vascularity of pedicled transverse rectus abdominis myocutaneous (TRAM) flaps used for breast reconstruction may be unreliable. We assess the value of gene therapy with proangiogenic plasmids encoding vascular endothelial growth factor, VEGF165 (pVEGF) and basic fibroblast growth factor, bFGF in a rat model of TRAM flap.

Material and Methods: TRAM flap island (2.5 × 6 cm) was incised over the right rectus abdominis muscle of Lewis rat, and raised to the midline from left side and to the lateral margin of rectus muscle on the right. Both left and right superior epigastric vessels, and left inferior epigastric vessels were divided, thus leaving the entire flap vascularized by the right inferior epigastric pedicle alone. The muscle was left in situ in its sheath.

Six groups of Lewis rats (7 animals in each group) were used. TRAM flap in group I was injected with pVEGF intramuscularly (i.m.), in group II – with pVEGF intradermally (i.d.). Group III received bicistronic plasmid (pVIF) encoding VEGF165 and bFGF i.m., group IV – pVIF i.d., group V – double dose of pVIF i.d., and group VI served as a control.

Rats were sacrificed on day 7. TRAM flaps were photographed and drawn on a transparent foil, with exact marking of necrotic area. The drawing was scanned, and the area of healthy (no macroscopic signs of necrosis) part of skin island was assessed in percentages by a graphic computer program.

Results: Mean area of healthy skin island in the control group was 48%. Best results were obtained by injecting pVEGF i.m. – 79% of healthy skin, and pVIF i.d. – 67.1%. Injection of pVEGF i.d and pVIF i.m. resulted in obtaining 56.6% and 56.1%, respectively. Double dose of pVIF i.d. gave no effect: 48.6%; histopathology examination showed signs of intense fibrogenesis in this group, indicating competitive stimulation of fibroblasts against epithelial cells.

Conclusions: Gene therapy is very promising in enhancing the vascularity of experimental pedicled myocutaneous island flaps. Further experiments are needed to assess it's potential value in clinical application.

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Skin sparing mastectomy with conservation of the nipple-areola-complex and autologous reconstruction is an oncological safe procedure – an extended follow-up study

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Background: The oncological safety of less radical surgical procedures like skin sparing mastectomy (SSM) and nipple sparing mastectomy (NSM) can not be evaluated by randomized trials. Therefore we investigated, if SSM and NSM with immediate autologous reconstruction are as safe in oncological terms as modified radical mastectomy (MRM) also in long lasting follow-up.

Material and Methods: Between 1994–2000 246 selected patients with an indication for MRM were treated with SSM, NSM, or MRM. Short term results were published 2003 [1]. After a mean follow-up of 101 (range 32–126) months 238 evaluable patients with SSM (N = 48), NSM (N = 60) or MRM (N = 130) were analyzed for local recurrence (LR), distant metastases (DM), breast cancer specific death (BCSD) and aesthetic results.

Results: LR occurred in 10.4% (SSM), 11.7% (NSM) and 11.5% (MRM) of all patients (p = 0.974). Also with regard to isolated DM (25.0%, 23.3%, respectively 26.2%; p = 0.916) and BCSD (20.8%, 21.7%, respectively 21.5%; p = 0.993) there were no significant differences between subgroups. There was a significant decrease of excellent aesthetic results over time (SSM after 59 months follow-up: 78.4% and after 101 months: 47.9%; p = 0.004; NSM: 73.8% to 51.7%; p = 0.025). An important risk factor for decreased cosmetic score was application of adjuvant radiotherapy.

Conclusion: Skin sparing mastectomy or nipple sparing mastectomy with immediate autologous reconstruction are oncologically safe techniques. But adjuvant radiotherapy decreases the aesthetic results even after a longer period of time.

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Local recurrence following breast conservation surgery with 5-mm target margin and 40-Gray breast radiotherapy for invasive breast cancer

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Background: The risk of ipsilateral breast tumour recurrence (IBTR) following breast conservation surgery (BCS) is dependent on treatment- and tumour-related variables. Treatment-related variables include surgical margin status and postoperative radiotherapy. Tumour-related factors include size of tumour, histological grade and tumour biology. In our unit, we have performed BCS with a target radial margin of 5-mm for invasive breast cancer (IBC) combined with fractionated 40-Gy breast radiotherapy postoperatively since 1999. The aim of the current study is to identify risk factors that are predictive of local recurrence in a cohort of patients who underwent our treatment regime for IBC.

Methods and Results: Between 1999 and 2004, 563 patients who underwent BCS for IBC were identified. Women received adjuvant chemotherapy or hormonal therapy as clinically indicated. After a median follow-up of 58 months, 5 of the 563 (0.9%) patients developed IBTR. The 5-year actuarial IBTR rate was 1.1%. In terms of distant disease recurrence (DDR), 29 of the 563 (5.20%) had DDR during follow-up, giving a 5-year actuarial DDR rate of 5.4%. Multivariate analyses identified Nottingham prognostic index (NPI) as the only significant independent prognostic factor for IBTR (p = 0.018).

Conclusion: The 5-year IBTR rate after BCS with 5-mm target margin and fractionated 40-Gy breast radiotherapy is low at 1.1%. NPI may be useful in stratifying patients who are at greater risk of IBTR.

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Predictive factors of nipple areolar complex invasion in breast cancer patients with mastectomy

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Background: Skin-sparing mastectomy with nipple areolar complex (NAC) preservation improves aesthetic outcome for breast cancer patients. This study was performed to investigate predictive factors of NAC-base neoplastic involvement to define the indications for NAC preservation.

Materials and Methods: A retrospective analysis of 198 mastectomy patients was conducted to determine the frequency of malignant NAC invasion. The association between NAC involvement and predictive factors, including tumor size, axillary nodal status, nuclear grade, hormone receptor status, tumor multiplicity, tumor location, tumor nipple distance (TND), and lymphovascular invasion (LVI), was evaluated.

Results: The overall frequency of malignant nipple involvement was 19 of 198 (9.6%). Significant differences were found in tumor size, axillary nodal status, tumor nipple distance, TND, and LVI. According to this study, clinical contraindications for NAC preservation include tumors >2.4 cm, positive axillary lymph node, TND < 4 cm, and positive LVI.

Conclusions: NAC preservation can be possible in selected patients if we consider the possibility of pre or intraoperative measurement, tumor size, axillary nodal status, TND, and LVI evaluation.

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Breast conserving surgery in locally advanced breast cancer treated with primary chemotherapy: experience at Istituto Nazionale Tumori

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Background: The aim of present report is to evaluate the applicability of breast conserving surgery (BCS) after primary systemic chemotherapy (PSC) in women with locally advanced breast cancer (LABC) and to assess the sufficiency of the a priori criteria adopted to select tumors amenable to BCS.

Material and Methods: In this retrospective analysis patients with LABC consecutively treated at the Istituto Nazionale Tumori in Milan from February 1986 to September 2007 were considered. The therapeutic program consisted of PSC (single agent anthracycline or high dose chemotherapy [HDS] or taxanes-containing regimens) followed by surgery and radiotherapy (chest wall or residual breast ± homolateral

supraclavicular area). Conservative surgery was considered only when the following criteria were met: limited disease size after PSC, no edema, erythema or extensive direct skin infiltration, expected good cosmesis, patient request. Full axillary dissection was performed in all patients.

Results: Main pretreatment characteristics, response to PSC and absence of invasive breast cancer in the breast (pCR) are reported in the table according to the surgical procedure (radical mastectomy or RM vs BCS).

	Total	RM	BCS
No. of patients	471	408	63 (13%)
% cli	12	13	5
% T4d	24	28	6
% T size >5 cm	57	63	22
% ORR	79	78	82
% pCR	3	3	1.5
% pN0	26	24	36

After a median follow-up of 58 months (1–205) local-regional recurrences were documented in a similar percentage of patients, regardless of the type of surgery adopted (local recurrence: RM 5% vs BCS 6%; regional $\pm$ local recurrence: RM 5% vs BCS 5%), while distant metastases were the first site of disease relapse in 36% of patients after RM and in 22% after BCS.

Conclusions: The analysis suggests that in selected patients with LABC treated with PSC, breast conserving surgery plus radiotherapy is feasible, safe and is not exposing patients to a sub-optimal local-regional control. Administered drug therapy, selection criteria and factors predicting the feasibility of BCS will be presented in detail.

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Should we follow western guidelines for axillary clearance in breast cancer in developing countries?

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Introduction: The standard guidelines recommend level I and II clearance for operable breast cancer. A majority of patients (more than 65%) treated in the west are node negative. In developing countries, we see larger tumours in operable breast cancers, with a possibility of leaving behind disease in level III, if these recommended guidelines are adhered to.

Methods: We retrospectively evaluated 1175 operable breast cancer patients in the period 2003–2005. The level III axillary nodes were dissected separately during axillary clearance. All operable breast cancer patients who underwent breast conservation surgery and mastectomy, including those who received neoadjuvant chemotherapy, were included in the study. We correlated level III nodal metastasis with the tumor quadrant, tumor size, metastasis in level I and II nodes in the axilla, tumor type, tumor grade and presence of lymphovascular emboli.

Results: The median tumour size was 3 cm and the median number of nodes positive for metastasis was three. Overall, 9.4% of the patients with operable breast cancer had metastasis in the level III axillary lymph nodes. There was a proportional correlation of level III node positivity to number of positive LN in level I and II – node negative had 0.2% skip metastasis in level III; 1−3 positive nodes in level I & II had 4.3% level III node positive rate; 4−9 positive nodes had 32% level III metastasis, and >9 nodes positive had 61% level III nodal metastasis. Incidence of metastasis was similar in tumors from inner and outer quadrants. Level III node metastasis was significantly higher in patients with larger tumours.

Conclusions: We believe leaving behind disease in the axillary apex in nearly 1 in 3 patients is unlikely to satisfy the curative intent of surgery in early breast cancer.

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Merits and demerits of parasternal lymph nodes dissection

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Introduction: Based on the results of a randomized controlled study, Milan trial conducted by Veronesi et al., the role of parasternal node (PS) dissection has been considered questionable. However, PS metastasis and recurrence are occasionally encountered and are believed to have a poor prognosis. In our department, PS dissection was actively performed until 2000 in patients with breast cancer measuring $\geqslant$3 cm and located medially (or bilateral disease). We report the merits and demerits of PS dissection.

Subjects and Methods: The subjects were 171 patients with breast cancer who underwent PS dissection before December 2000. Patients who had PS metastases were reviewed, and the outcome was compared with that in patients without metastases.

Results: Of the 171 patients, 33 (19.3%) were PS-positive. They were aged from 39 to 80 years (mean: 56.7 years) and consisted of 31 patients with Invasive ductal carcinoma, 1 with Mucinous carcinoma, and one with Medullary carcinoma histologically. Seven patients had PS metastases alone (no axillary node involvement). Of the 171 patients undergoing PS dissection, 96 had nodal metastases, comprising 28 PS-positive patients (group A) and 68 PS-negative patients (group B). In group A, 13 patients suffered from recurrence and 15 patients did not. In group B, 16 patients had recurrence and 52 did not. Thus, recurrence was significantly more common in patients who had PS involvement than in those without it.

Conclusion: Although the effect of PS dissection was unclear, the presence or absence of PS metastasis seems to be an important prognostic factor.

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Have young women undergone excessive radical surgery without improving survival?

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Introduction: Two percent of all breast cancer appear in young women. In women 35 and under, the diagnostic role of mammograms is debatable. It is also unclear of the necessity of performing mastectomy and that if the overall prognosis worsens. Hormone therapy and ovarian ablation must be considered important therapeutic tools.

The goal of this study was to evaluate the result and survival of the therapeutic strategy in these patients diagnosed and treated for breast cancer in our hospital with a 5 year minimum follow-up and to identify which treatment is the most suitable.

Methods: A retrospective study was carried out on 71 women 35 years old and younger diagnosed with breast cancer in our hospital between 1983–2000. Statistic analysis was carried out with SPSS 13. A survival study was designed with Kaplan–Meier method.

Results: Conservative surgery was performed on approximately half of the patients.

Mastectomized patients presented a significantly higher number of locoregional relapses than conservative surgery ($p = 0.031$). Global survival was similar in patients who underwent conservative and radical surgery. Adjuvant treatment with chemotherapy ($p = 0.61$) did not influence the number of locoregional relapses, but it did influence in distant metastasis. In the group who underwent chemotherapy, a smaller proportion of disease free patients were seen in a 5 year follow-up (44.7% vs 78.3%) ($p = 0.077$). Global survival was similar in both groups.

After having performed a multivariate analysis (ANOVA) considering the tumour size as a confounding factor, it is observed that neither the type of surgery or undergoing chemotherapy influence the prognosis.

Radiotherapy did not influence the global survival rate nor did it influence disease free survival. Patients who were prescribed adjuvant hormone therapy presented a significantly higher number of relapses ($p = 0.011$).

Conclusions: In univariate analysis, patients who underwent mastectomy and those who received chemotherapy experimented the highest number of locoregional relapses and distant metastasis.

With ANOVA the tumour size was the confounding factor and it was shown that neither the type of surgery or chemotherapy influenced in the prognosis.

The 5 year survival of patients who underwent hormone therapy was less favourable. More than 50% patients lived more than 15 years after treatment.

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Subcutaneous mastectomy including conservation of the nipple areolar complex: broadening the indications

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Background: Numerous authors consider multiple predictive factors to decide whether the nipple areola complex (NAC) can be preserved or not during mastectomy. These are: tumor-nipple distance, tumor size, axillary lymph-node status and lymphovascular invasion. Thus, only a very limited