

Local regional therapy

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POSTER

Lymph node metastases detection by FDG-PET and sentinel node biopsy in breast cancer patients: comparison of these different approaches

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Background: axillary dissection (ALND) for detection of metastatic involvement is used to plan adjuvant treatments for breast cancer (BC) patients. ALND is a costly procedure with various side effects. 80% or more of T1 patients are node negative and might avoid ALND. Recently, sentinel node (SN) biopsy has been suggested as reference method for the evaluation of regional nodal metastases and for the decision on the need of a ALND. SN biopsy is an invasive approach, with a not negligible risk of false negative results. Conversely, Positron Emission Tomography (FDG-PET) is a non-invasive repeatable method able to evaluate all the regional nodes in BC: our PET experience on nodal involvement in BC has given interesting data of sensitivity and negative predictive value, comparable with SN biopsy. The aim in this work is a direct comparison between the two methods in term of sensibility, accuracy and predictive value in the same series.

Methods: T1N0 BC patients were studied. FDG-PET has been performed no later than 48 hours before surgery. Lymphoscintigraphy has been performed within 6 hours before surgery. After breast surgery, radio-guided biopsy of the SN has been performed followed by a complete ALND. Metastatic involvement of the SN and the other non-SN has been evaluated on definitive sections and represented the basis of the comparison between the two methods.

Results: Until now 28 patients have been studied. The average age was 56 years (range=39-70). All patients had pT1 BC except 3 pT2 (size less than 2.5 cm). The average histological tumor size was 13 mm (range=2-23 mm). All lymph nodes detected by lymphoscintigraphy were in axilla, and detection rate was 100%. All SN were identified with intra-operative gamma probe, then biopsied. All patients underwent ALND (on the average, 17 lymph nodes surgically removed). 10 patients of 28 showed nodal metastases. The SN biopsy results showed 3 false-negative (2 partial and 1 embolic involvement detected in non-SN), whereas FDG-PET failed to detect 4 axillary nodal involvement (2 microembolic, 1 partial and 1 pluriembolic); one patient with partial nodal involvement was undetected both the methods. No false positive FDG-PET scan was registered.

Conclusions: This is the first study comparing these two different methods on the same series. The preliminary results suggest a similar sensitivity, thus giving a contribution to a further statement on validity of FDG-PET for evaluation of BC regional node involvement.

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Influence of systemic therapy on pulmonary function tests in breast cancer patients irradiated to the internal mammary and medial supraclavicular lymph node chain

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Purpose: To evaluate the changes in lung function in breast cancer patients irradiated on the internal mammary and medial supraclavicular (IM-MS) lymph nodes with the standard irradiation technique as described in EORTC protocol 22922.

Materials and methods: Between 2/1998 and 2/2000, 75 breast cancer patients with almost normal baseline lung function values have been prospectively followed with lung function tests. All were concomitantly irradiated to the IM-MS lymph nodes and the breast or thoracic wall to a dose of 50Gy/2Gy. Spirometry (FEV1 and VC), total lung capacity (TLC) and carbon monoxide transfer factor (TLCo) were measured before and 3, 6 and 12 months after the start of radiotherapy.

Results: The data after one year of follow-up have been analysed in all 75 patients. Adjuvant chemotherapy was administered in 24 patients and hormonal therapy (tamoxifen) in 30. Twenty-one patients either received no adjuvant treatment or underwent radiocastration and were analysed together.

Dunnett's one-tailed T-tests were performed to evaluate the differences at the different time points as compared to baseline. For the entire patient

population a significant decrease was found for TLC at 6 months (5,2%; p=0.016) and for TLCo at 3 and 6 months (6,8%; p=0.008 and 5,5%; p=0.033). All parameters recovered to pre-treatment values at 1 year.

A MANOVA-test showed that the lung function parameters evolved differently over time in the three adjuvant treatment groups. The levels of significance were p=0.031, p=0.017, p=0.003 and p=0.0001 for FEV1, VC, TLC and TLCo respectively. Dunnett's one-tailed T-tests performed for the different groups revealed a statistically significant decrease in TLC at 6 months (12,3%; p=0.028) and in TLCo at 3 and 6 months (9,8%; p=0.006 and 9,1%; p=0.010) in the chemotherapy group. There was a trend towards a decreased TLCo at 12 months in patients receiving hormonal treatment (7,7%; p=0.072).

Conclusion: Overall decreases in lung function after radiotherapy to the breast or thoracic wall combined with standard IM-MS lymph node chain irradiation fully recover at one year follow-up. The type of adjuvant systemic treatment has a statistically significant impact on the evolution of the parameters over time. Whether the trend in decreased TLCo at 12 months in patients having received radiotherapy and tamoxifen will translate into a persistent TLCo decrease remains to be evaluated.

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Replacing axillary dissection by irradiation in cNO postmenopausal women with breast cancer: long term results in patients treated between 1986 and 1993

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Purpose: The aim of this prospective study was to evaluate whether in breast cancer patients irradiation of the clinically uninvolved axilla (cNO) can obtain similar good local control rates, equal overall survival and less axillary morbidity as seen with axillary dissection.

Methods: Between 1986 and 1993 a total of 660 women with breast cancer after breast conserving surgery (BCS) have been irradiated in our institution, 294 of them were postmenopausal and had a clinically negative axilla at the time of diagnosis. 166 women had been referred from other hospitals after BCS including axillary dissection of level I and II, they got radiotherapy to the breast only (AxS-group) and were compared to the 128 patients treated in our hospital with BCS alone followed by radiation to the breast, axillary and supraclavicular nodes (AxRT-group).

Results: Patients characteristics of both groups were comparable, although slightly in favor of the AxS-group with regard to age, tumor size, multicentricity and receptor status. At 10 years treatment results were nearly identical and statistically not different: the incidence of local axillary relapses was 3% in the surgically treated, 5% in the irradiated axillae, local tumor control in the breast was 90% vs. 94% in AxS and AxRT-group, respectively; disease free survival 81 vs. 75% and overall survival 66 and 68%. No disadvantage was seen for the irradiated patients. In contrast, the treatment induced severe morbidity like permanent lymph edema of the breast or arm, pain or shoulder problems were significant higher in the surgically treated group than in the irradiated pts. (26% vs. 1%, including minor sequelae 45 vs. 4%, p < 0.0001).

Conclusion: In cNO postmenopausal breast cancer patients axillary dissection can safely be replaced by irradiation without impairment of tumor control. Treatment induced morbidity is significantly lower after irradiation than after surgery.

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The early treatment of radiation pneumonitis in patients after adjuvant radiotherapy for breast cancer

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We aimed to investigate the incidence rate and treatment results of radiation pneumonitis (RP) in patients treated with adjuvant radiotherapy (RT) for breast cancer.

Between 3/97-7/00 180 patients were treated with postoperative RT with Linac after computerised treatment planning. 103 (57%) patients received postmastectomy (PM) RT, while 77 (43%) received breast RT as part of their breast conserving treatment (BCT). RT of the breast after BCT was performed with tangential 6MV photons. PM RT to the chest wall was given by 2 or 3 electron fields in 72 (69.9%), tangential photon fields in 22 (21.4%) and by combination in 9 (8.7%) patients. Patients with axillary metastases

were treated with axillary+supraclavicular (A+S) fields in 95(92.2%) PM patients and in 37(48.1%) patients with BCT. Internal mammary field was added in 14(13.6%) PM patients and in 11(14.3%) BCT patients. Routine chest x-ray was performed 6 weeks after the completion of RT. Patients with abnormal chest x-ray findings or clinically diagnosed RP had spiral CT of the chest with 40 mAs. Alveolar consolidation, pleural effusion, glassy appearance and BOOP syndrome was accepted as RP in CT. 6 months later CT was repeated. All scans were evaluated by the same radiologist without knowing the clinical status. Patients with clinical symptoms received steroids and antibiotics for 15 days and the treatment results were reported.

Early pulmonary changes (within 6 months after the end of RT) was observed in 20(11.1%) out of 180 patients. 16 patients had clinical symptoms and 11 of them were correlated with radiological findings. 4 patients had radiological findings without clinical symptoms. 11 patients out of 16 with clinical symptoms received steroid and antibiotic treatment. Clinical response to treatment was 15 days in 8, 20 days in 2 and 30 days in 1 patient. Radiological complete response was observed in all treated patients. 5 patients without treatment had late clinical response and all these patients had signs of pulmonary fibrosis on their CT scans. Observed RP was calculated to be more in PM patients compared to BCT patients ($p=0.029$) with chi-square test. Electron or photon fields in chest wall RT and A+S field addition was not found to be significant for occurrence of RP.

Early treatment of RP detected by clinical and radiological signs provided faster response with less chronic changes in lung, after adjuvant RT for breast cancer patients. RP occurred more in PM than in BCT patients in our study group.

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Prognosis of chest wall recurrence compared to mammary recurrence: long-term follow-up of a matched pair analysis

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Background: Local recurrence remains a major concern after primary treatment of breast cancer and has a major impact on subsequent survival. While most studies report a poorer survival rate in patients with a local recurrence after mastectomy than after breast conservation, it remains controversial, whether different risk profiles at the time of primary diagnosis may account for this difference.

Methods: Matched pair analysis of 134 patients with newly diagnosed locoregional recurrence of breast cancer without evidence of systemic disease. Matching criteria included the primary surgical treatment, tumor size, nodal status, and age. The significance of various prognostic parameters at the time of primary diagnosis and at the time of recurrence were evaluated, by univariate and multivariate analyses, with respect to survival after recurrence. The median follow-up was 8.4 years.

Results: Risk factors at the time of presentation, such as tumor size and lymph node status, were comparable between both groups. Local recurrence occurred on an average 9 months earlier in patients after mastectomy ($P=0.08$). Univariate analysis showed that lymph node status ($P=0.0001$) and disease free interval from primary treatment to local recurrence ($P=0.0002$) were the most significant single prognostic factors for survival after local recurrence. Breast conservation alone was shown to be of marginal statistical influence (only $P=0.05$). However, multivariate analysis demonstrated that the combination of disease free interval and the primary surgical treatment modality is the most significant independent risk factor for cancer related death ($P=0.0001$).

Conclusion: Local recurrence after mastectomy seems to be associated with worse survival than after breast conserving therapy. Early onset of chest wall recurrence, moreover, represents the highest independent risk for cancer associated death.

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Breast cancer: locoregional relapse after mastectomy without postoperative radiotherapy

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Purpose: To analyse the pattern of relapse and survival in patients (pts) with breast cancer operated on with radical surgery and not irradiated postoperatively.

Materials: From 1970 to 1998, 2384 pT1-4 breast cancer patients (pts) underwent mastectomy without postoperative radiotherapy (RT). Median

age was 55 years (yrs). Premenopausal pts were 909. Distribution by pTNM was the following: T1 690, T2 1294, T3 177, T4 223; N0 1144, N1 1098, N2 60, N3 1. 625 pts had 1-3 positive axillary lymph nodes (N+), 303 4-9 N+, and 235 10+ N+. There was lymphovascular invasion (LVI) in 88 out of 186 pts. Margins were positive in 250 out of 2270 pts. 397 pts were ER and/or PgR positive, 187 pts were ER and PgR negative. 520 pts received chemotherapy, 677 pts were given endocrine therapy.

Results: 517 pts (21.6%) developed a locoregional relapse (LRR). The pattern of first LRR by site was the following: isolated chest wall 227; supraclavicular nodes 139; internal mammary chains 32; axillary nodes only 18; multiple sites 101 (51/101 with involvement of supraclavicular regions). Risk of supraclavicular relapse increased with number of involved axillary nodes (N0: 3%; 1-3 N+: 6%; 4-9 N+: 14%, 10+ N+: 24%). 914 pts developed distant metastases (38%) and 231 had second tumors (including 135 breast cancers). The 10-year actuarial risk of LRR was: pT1 15% vs pT2 25% vs pT3 35% vs pT4 35% (statistically significant: ss); pN0 16% vs pN+ 31% (ss); pT1N0 14% vs pT1N+ 19% (not significant: ns); pT2N0 18% vs pT2N+ 32% (ss); pT3N0 25% vs pT3N+ 37% (ss); pT4N0 9%, vs pT4N+ 42% (ss); N0 (14%) vs 1-3 (N+ 20%) vs 4-9 (N+ 38%) vs 10+ N+ (58%); age: < 35 yrs 39% vs 36-49 yrs 25% vs 50-69 yrs 23% vs 70+ yrs 18% (ss); positive margins 44% vs negative margins 21% (ss); negative receptors 36% vs positive receptors 24% (ss); presence vs absence of LVI (50% vs 30%: ss). The Cox regression analysis confirmed pT, number of N+, pN and age as major independent prognostic factors for LRR; receptors status was also significant.

Conclusions: According to the current analysis, pts with pT2-4 and N+ lesions or with 4+ N+ or < 35 year old or with positive margins or negative ER and PgR or with LVI have got a > 30% 10 year actuarial risk of LRR that should be taken into account when planning postoperative RT. The minimal volume of postmastectomy RT should include the whole chest wall but the addition of the supraclavicular/axillary apex region merits consideration, especially for pts with 10+ N+.

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Sentinel node dissection in breast cancer: the Gustave-Roussy institute experience

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Purpose: Sentinel node biopsy (SNB) accurately predicts axillary status, thus avoiding axillary dissection if the sentinel node (SN) is negative. We used this technique during two phases: during the first period, all patients were submitted to axillary dissection; in the second period, among patients with a tumor size below 15mm, only those with positive SN had axillary dissection.

Methods: During the learning phase (1997-1999) localization of SN was achieved with radio-colloid only. Since 1999, we used both radio-colloid with pre-operative lympho-scintigraphy, and per-operative staining with patent blue, with subdermal injections.

Results: In the first series (65 patients) the mean tumor size was 22 mm, the detection rate was 66% with a positive SN in 40% of patients. There was no false negative and the SN was the only metastatic node in 76% of patients. In the second series (109 patients) mean tumor size was 14 mm, the detection rate was 96%. 39% of the SN were metastatic, the SN being the only positive node in 50% of these cases, and bearing micro-metastasis in 10 cases. Per-operative frozen section examination of the SN was used if it was macroscopically suspicious and completion axillary dissection performed only in patients with positive SN.

Conclusion: Our experience confirms that SN mapping using both the radio-colloid and the dye techniques is the procedure of choice for axillary nodes staging in patients with small size (< 15 mm) breast cancer, without palpable axillary node.

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Internal mammary (IM) sentinel lymph node (SN) detection and excision in breast cancer

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Purpose: Identification and dissection of SN can replace axillary dissection in trained centers, in patients where the tumour is less than 3 cm and