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Irradiation of lymphatic drainage (LDI) in the treatment of breast carcinoma (BC): clinical indications and technical problems. Volumes analysis (VA) and local control (LC). Results of a mono institutional study

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Purpose: LDI is beneficial in BC radiotherapy but it presents several technical problems due to the anatomic complexity of the involved volumes. We present data from a mono institution study to evaluate technical problems, VA and homogeneity, medium term LC.

Method and Materials: 850 consecutive patients (pts) with BC, observed between January 2002 and December 2002, entered in a house protocol in which pts with either one of the following: a) >4 positive nodes (PN), massive or extra capsular node invasion (MI), <13 nodes in the surgical specimen, were scheduled to receive LDI at the time of tangential fields. Total mastectomy accounted for 170 cases (20%), while 680 (80%) received a conservative surgical approach. LDI was done in 154 cases (18.1%) because one of the following: 4 to 5 PN 46 pts (30% of 154), 6 to 10 PN 62 pts (40%), more than 10 PN 23 pts (15%), MI 23pts(15%); MI was also present in 92 pts (69%) as a concomitant feature. LDI was carried out either with 4 isocentric fields technique (4F), (131 cases, 85%), or through a modified extended tangential fields technique (MT) (23 cases, 15%). A cumulative analysis on the dose distribution was done utilizing DVH and biological evaluation (TCP and NTCP). Local control data are projected at 5 years.

Results: We observed differences in VA in favour of 4F technique, when evaluated through DVH analysis. 4F technique allowed a better PTV coverage (17%) than MT. Humeral head V50 was smaller for 4F technique (30% to 60%) than MT; dose-homogeneity index showed a 10% dose variation inside PTV for 4F with a minimum dose to supraclavicular nodes (SN) >45 Gy as compared to a dose variation of 30% or more with MT with a minimum dose to SN ranging 25 to 30 Gy. As far as LC we had 2 SN failures in MT group, TCP and NTCP were also in favour of 4F while no patient did yet relapse in FT group.

Conclusions: LDI in BC represents a technical challenge for radiation oncologists. Dosimetric analysis shows that 4F technique represents a feasible and effective method of treatment. Even if other techniques may be used, volumes coverage and dose homogeneity support the superiority of 4F technique, pending statistically significant data on clinical and results.

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The use of the BCT in the population included in the EORTC22922/10925 investigating elective lymph node irradiation comparing with 22881/10882 investigating the role of a boost in early breast cancer

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Purpose: To compare the treatment given, in relation to the tumour and patient characteristics in two consecutive, large prospective phase III trials conducted by the EORTC RT and Breast Cancer Groups in the past 15 years.

Methods: During 1989–1996, EORTC 22881/10882 trial (BOOST) included 5318 pts with unilateral pT1-T2 pN0-N1 M0 breast cancer. During 1996–2004, EORTC 22922/10925 trial (IM-MS) included 4004 pts with unilateral, operable breast cancer, with positive axillary nodes and/or location in the medial or central quadrants.

Results: See the table. Due to the inclusion criteria for these trials, the tumour characteristics in the IM-MS trial are less than in the BOOST trial. Stage distribution (UICC 6th TNM) in the BCT group of IM-MS trial was: 42% St I, 34% St IIA, 15% St IIB and 8% St IIIA compared to 63% St I, 26% St IIA, 5% St IIB and 4% St IIIA in the BOOST trial. Nevertheless, in the IM-MS trial the BCT was used in 76% of pts of which 85% received a mean of 14 Gy radiotherapy boost dose. The percent of pts receiving the boost by age decade was: 97% < 35 years, 92% in 36–50 years, 84% in 51–60 years and 78% in the pts older than 60 years. According to the tumour stage and actual guidelines many more pts have also received adjuvant systemic treatment in the IM-MS than in the BOOST trial.

Conclusion: Results of the IM-MS trial may more accurately reflect the use of the BCT in the current daily practice. The BOOST trial results, proving the effectiveness of a boost dose in improving local control in the BCT was largely incorporated in the IM-MS trial without a significant correlation between the boost dose and age decade or stage.

Pathology	22881/10882	22922/10925
pT1	78%	70%
pT2	19%	29%
pT3	0%	1%
1–3 positive nodes	17%	39%
> 4 positive nodes	4%	8%
Loco regional/adjuvant treatment		
Boost delivery	50%	85%
Boost dose	16/6–29	14/1–26
Chemotherapy	14%	50%
Hormonal therapy	20%	58%

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Improving equity of access to treatment for breast cancer patients in south east Scotland: an audit of time from final surgery to radiotherapy

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Summary: A review of prospective cancer audit data in S E Scotland highlighted significant differences in time from final surgery to start of adjuvant radiotherapy between the five breast service hospitals, despite all patients being treated with radiotherapy in the regional centre. Further audit was undertaken to analyse these differences at each stage of the patient journey, pin-pointing particular problem areas, and measures were subsequently introduced to streamline the process.

Background: S E Scotland Cancer Network (SCAN) (www.scan.scot.nhs.uk) aims to improve care, treatment and equity of access for cancer patients across the region. The SCAN Breast Group, comprising clinical and non-clinical staff from the five hospital breast services, and from the regional oncology service at the Edinburgh Cancer Centre (ECC), ensures coordination and consistency through defined pathways and protocols of care. There is evidence that delay in initiating radiotherapy (RT) after surgery compromises local control.

Availability of reliable performance data is key to the network's ability to monitor and improve the quality of cancer care. A core evidence-based and defined dataset for Breast Cancer is collected by all three managed clinical networks in Scotland.

Outline of problem: The Scottish national clinical standard states: 70% of patients to start RT within 28 days of final surgery (excluding those requiring adjuvant chemotherapy first).

Data review of patients diagnosed 2001–2 and 2002–3 identified (a) that no hospitals came close to meeting the standard and (b) that there was variation between the five hospital services, although all patients are treated at the ECC.

Issues of RT capacity were already being addressed at national level through planned expansion of the RT services. However, a more detailed review of data was needed to assess the reasons for the variance between hospitals and to find ways to improve on these.

Method: The detailed steps in the patient pathway from surgery to post-operative RT were identified and additional data was collected from casenotes and the RT booking system to supplement the prospective audit data. Analysis was undertaken using MS Excel.

Analysis and Interpretation: Median waits in each hospital ranged from 39–75 days (2001–2) and 40–60 days (2002–3), with the relative ranking of each hospital remaining constant throughout the period of analysis. The main area of variability was the period from initiating booking of RT to the start of treatment planning. Accumulated waits depended on timing of appointments, pathology reporting, and processes for delivering RT booking forms.

Strategy for change: First appointment with clinical oncologist arranged at pathology Multidisciplinary Meeting (MDM) and provisional RT booking form completed.

The process for delivery of forms to ECC was streamlined.

A specialist radiographer was appointed to coordinate the patient's journey and act as a contact (in addition to Breast Care Nurses).

Expansion of RT capacity in ECC: more machine time and radiographer/physics staffing. Rapid reporting of pathology in all five breast services.

Effects of change: Shortened time from MDM decision to start of post-operative treatment.

Avoidance of unplanned delays

Next steps: Increased frequency of pathology MDMs is under consideration, to shorten the time to discussion about adjuvant therapy.

Appointment of MDM coordinator to implement systematic tracking of patient's progress, and assist the specialist radiographer to avoid unscheduled delays in treatment.

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Expression of inducible heat shock protein 70 in breast cancer cells correlates with their radioresistance

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It is of importance to elucidate molecular determinants of enhanced radioresistance that many human tumors exhibit in vivo; such an approach would enable to artificially strengthen the anti-tumor action of clinical radiotherapy. The aim of the present study was to investigate how different patterns of the stress-inducible 70 kD heat shock protein (Hsp70) expression in human breast cancer cells correlate with their radioresistance.

A breast cancer-derived cell line MCF-7 and cancer breast biopsies were here studied. The cell and biopsy samples were analyzed in Western blotting and immunofluorescence staining with an antibody specific to an inducible form of Hsp70. Up- or down-regulations of inducible Hsp70 in the cultured cells were achieved by infection with virus-based vectors expressing either inducible Hsp70 or its RNAi, respectively. After gamma-radiation exposure, the death and survival of the irradiated cells were evaluated in TUNEL and clonogenic assays.

It was found that MCF-7 cells constitutively expressed the inducible form of Hsp70. The additional (Hsp70-vector-induced) increase in the intracellular Hsp70 content rendered these cells considerably more radioresistant. Conversely, the RNAi-vector-induced down-regulation of the basal level of inducible Hsp70 in MCF-7 cells significantly decreased their radioresistance. These in vitro data correlated well with results of studying of the breast cancer biopsies: the same tumors exhibited both the enhanced resistance to radiotherapy (clinical data) and the high levels of expression of inducible Hsp70 (data of in situ analyses of the biopsies).

Taken together these findings allow to conclude that the inducible form of Hsp70, when accumulated in human breast cancer cells, contributes to their enhanced radioresistance. Consequently, artificial suppression of the expression of inducible Hsp70 in the tumors could render them more sensitive to radiotherapy; the latter conclusion gives additional motivation for development of clinically applicable ways to manipulate the in vivo expression of Hsp70.

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The importance of patient's position in CT-scan based localization of the Internal Mammary Chain (IMC) and Supra Clavicular Nodes (SCN) for breast cancer (BC) radiation therapy planning

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Purpose: To evaluate the importance of treatment position in the evaluation of the exact localization of SCN and IMC and their variability among patients in order to improve treatment planning in BC patients.

Material and Methods: A total of 46 CT scans of the chest were examined. All patients were female with breast conserving treatments. The study was divided into two phases. The first consisted in the measurements on the diagnostic CT scan. This scan was performed in the supine position with both arms over the head for diagnostic reasons. All diagnostic CT scans – patients were injected for the procedure. When the injection was done on the left side, measurements were performed on the right side and vice versa, to diminish artifacts. This first phase was performed as a training program for radiologist and radiation oncologists to prepare the second phase of the study where the CT scan in treatment position was used without injection. For this second group of patients with one arm raised above head (treated side) and the other was kept by the side (contralateral side). Measurements were performed on both sides to evaluate the influence of the arm position. The depths of IMC and SC vessels were measured at 5 points: 1) the origin of the internal mammary artery, 2) the sterno-clavicular articulation, 3–5) the first, second and third rib interspaces (RI). Measurements of the depth and of the distance between the internal mammary vessels and the middle plan of the sternum were obtained using electronic calipers on a PACS workstation.

Results: Twenty diagnostic Ct scans and 26 CT scans in treatment position have been studied. The results of all measurements showed

differences in the depth between diagnostic CT scan and CT in treatment position. Definitive results compared by the method of Fischer will be presented at the Meeting. Table 1 shows the lateral limits of IMC-the distance between the IM vessels and the middle axis of the sternum (I, II, III rib interspaces): diagnostic CT and CT scan in treatment position (treated side).

Lateral limits [mm]	Diagnostic CT scan (n=20)	Treatment CT scan* (n=26)
I RI		
Median value [range]	30 mm [17–40]	31.5 mm [22–35]
Mean±SD	29.8±5.3	30.9±3.2
II RI		
Median value [range]	26 mm [21–39]	28.5 mm [25–37]
Mean±SD	28.2±4.7	29.8±3.5
III RI		
Median value [range]	27 mm [19–39]	29 mm [24–39]
Mean±SD	27.6±4.9	29.9±3.9

Conclusions: This study shows the importance of the patients' position between diagnostic and therapeutic CT scan, the large variability in the depth of SCN and IMLN. It is important to visualize these regions to permit an individual dosimetric optimization.

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Breast radiotherapy in women with pectus excavatum (funnel chest): is the lateral decubitus technique an answer? – a dosimetric study

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Purpose: Breast radiotherapy is a technical challenge in women with pectus excavatum. This study aimed to assess isocentric lateral decubitus (ILD) technique as a means to irradiate breasts for patients with pectus excavatum.

Methods and Material: Four women presenting with left-sided breast cancers and found to have pectus excavatum were offered breast-conserving treatments. Postoperative breast radiotherapy was indicated (50 Gy at ICRU point in 25 fractions over 5 weeks) with, in two patients, an additional boost to the tumour bed (16 Gy in 8 fractions over 1.5 weeks). Both ILD and standard decubitus (SD) techniques were simulated. We report the dosimetric comparison of these techniques and the acute skin toxicity (RTOG toxicity scale) of ILD radiotherapy.

Results: ILD permitted the same breast dose-homogeneity as SD while decreasing breast thickness by 41 to 62%. The width of lung and/or heart receiving > 20 Gy ranged between 2.1 and 4.3 cm with SD and between 0.5 and 1.1 cm with ILD. The estimated percentage of ipsilateral lung receiving > 20 Gy ranged from 21% to 34% with SD and from 0% to 5% with ILD. Acute skin toxicity was scored 1 for all patients at completion of ILD radiotherapy, with no interruption of treatment.

Conclusion: ILD is an effective breast radiotherapy technique for patients with pectus excavatum that preserves the underlying heart and lung from unnecessary irradiation.

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Evaluation of irradiated breast tissue volume and cosmetic outcome in conserving treatment using intraoperative Ir 192 HDR brachytherapy boost

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Introduction: Radiotherapy boost is a standard procedure during breast conserving treatment in patients with breast cancer, resulting in lower incidence of local recurrences. One of the methods may be the intraoperative Ir 192 HDR brachytherapy. Our study evaluates the irradiated breast tissue volume and cosmetic outcome in such a modality.

Material and Method: Between January 1998 and May 2003, 40 breast cancer patients received intraoperative Ir 192 HDR brachytherapy in the course of their breast conserving treatment (group A). Control group of 75 women received brachytherapy boost after finishing the full teleradiotherapy regimen (group B). The characteristics of both groups were similar. Patients in both groups received the boost in 1 fraction of 10 Gy, the dose specification was also identical (the dose was specified 5 mm from the source). The volume was measured for isodose of 10 Gy. All patients in