

axillary lymph nodes although the same exists for patients with 4 or more positive nodes. But several recent publications (20 year result of British Columbia Study and DBCG 82 Protocol published by Overgaard et al) challenge this separation between '1 to 3' and '4 or more' positive axillary nodes as a relevant descriptor of indication of PMRT. This was the impetus that led us to review and analyze retrospectively from our institute data, the impact of post mastectomy radiotherapy (PMRT) in this controversial group.

Material and Method: Records of 785 patients with T1, T2 tumors who were registered in our department following mastectomy with axilla dissection with <4 positive axillary nodes between 2002 and 2009 were analyzed. 127/785 patients had 8 or less nodes dissected (as found in histopathology reports) and as such were excluded from the analysis. Of the remaining 658 patients, 528 received no PMRT, as per consensus. But 130 patients, as found in record, had received PMRT (possibly they appeared to be non-compliant regarding follow up). Locoregional recurrence, distant failure, disease free survival and overall survival of these 130 patients were studied and compared with 528 patients who were not offered PMRT.

As per erstwhile institutional policy, all patients had received FAC chemotherapy for 6 cycles. Receptor positive patients (164/528 of non-PMRT and 42/130 of PMRT subsets) were on Tamoxifen or an A.I.

Results: At a median interval of 30 months 132/528 patients not receiving PMRT suffered locoregional recurrence (chest wall recurrence alone in 36/528, supraclavicular recurrence in 81/528, chest wall + supraclavicular recurrence in 15/528, axillary and IMN recurrence in none). On the contrary only 4/130 patients receiving PMRT had locoregional failure ($p < 0.0001$). Distant metastasis was recorded in 37/528 of non PMRT subset and 8/130 of PMRT subset ($p = \text{NS}$). Survival data till September 2008 showed 4/130 deaths among PMRT subset against 26/528 of non PMRT ($p = \text{NS}$). 121/130 of PMRT are living without disease, contrary to 432/528 of non PMRT ($p = 0.001$).

Conclusions: This retrospective analysis revealed statistically significant reduction in locoregional recurrence as well as increased disease free survival with PMRT in T1 or T2 breast cancer patients with 1-3 positive axillary nodes. Deprivation of adjuvant radiotherapy for this subset of patients appears to be unjustified.

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Outcome of Breast Cancer Patients with Isolated Supraclavicular Fossa Lymph Node Recurrence Treated with Radiotherapy

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Background: The incidence of isolated supraclavicular fossa (SCF) nodal recurrence in breast cancer is between 4.5-7% [1, 2]. Published 2 & 5 year survival rates for patients with SCF node metastases are 52% & 34% [3]. It is unclear whether isolated SCF recurrence is a harbinger of distal disease or whether aggressive local treatment can result in cure. This is a retrospective study of the outcomes for breast cancer patients who received radiotherapy (RT) for isolated SCF recurrence.

Materials and Methods: Breast cancer patients who had received treatment with RT for SCF disease recurrence between 2005 & 2010 were identified from the Mount Vernon Cancer Centre (MVCC) coded 'Oracle' treatment database. RT treatment & fractionation were obtained from the database & clinical outcomes were assessed from the patient notes. Local lymph node control (LLNC), overall survival (OS) from SCF recurrence & distant disease free survival (DDFS) from radiotherapy were evaluated according to treatment received.

Results: 33 patients were identified with a median age of 57 (range 34-89). The ER/PR status was: 20 (61%) positive & 13 (39%) negative. The HER2 status was: 12 (35%) positive, 15 (45%) negative & 6 (20%) unknown. The RT regimens (Gy/#) used were: 40 Gy/15# in 3 weeks ($n = 13$), 20 Gy/5# in 1 week ($n = 5$), 50 Gy/25# in 5 weeks ($n = 9$), 30 Gy/10# in 2 weeks ($n = 2$), 18 Gy/4# in 1 week ($n = 1$), 8 Gy/1# in 1 day ($n = 1$), 45 Gy/15# in 3 weeks ($n = 1$) & 27 Gy/6# in 3 weeks ($n = 1$). 18 (55%) patients received chemotherapy & 21 (64%) received endocrine therapy prior to RT. Median LLNC was 45 (range 1-133) months with a median DDFS of 12 (range 3-60) months. Median OS was 25 (range 2-85) months from recurrence with 4 (12%) patients surviving >5 years from SCF recurrence. A significant difference was seen for DDFS & OS in favour of ER +ve status ($p < 0.05$ & $P < 0.001$) & in OS for longer RT regimens ($P < 0.05$).

Conclusions: Outcomes at MVCC are akin to those published as only 12% of patients survived for >5 years following RT. Our data also demonstrates that ER status influences DDFS and OS is better with longer hyperfractionated regimens & +ve ER status. This however, may have been biased by confounding factors, such as co-morbidity, and furthermore the sample size was small. A prospective analysis is suggested to establish a stronger evidence base for best practice in this patient group, including evaluation of outcomes for those patients not treated with RT.

References

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Preclinical Assessment of Multidirectional Firing Laser Ablation in Porcine Liver and Human Breast Tissue

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Background: Minimally-invasive thermal ablation is a promising new tool for local destruction of small carcinomas of the breast. Currently, cryosurgery, radiofrequency ablation, laser-induced thermal therapy, microwave ablation, and high-intensity focused ultrasound ablation are clinically available local ablation modalities. Laser-induced thermal therapy requires a laser fiber to guide the light energy directly into the tissue to be treated. Most laser fibers are designed for forward firing i.e. the light is emitted at the distal end along the optical axis of the fiber. But laser ablation using a forward firing fiber cannot transmit the energy evenly to the lesion, so the exact size of the thermal lesion cannot be predicted.

We developed multidirectional firing laser fiber using the femtosecond laser and an arc discharging process. The aim of this study was to compare the ablation properties of forward firing laser fiber and multidirectional firing laser fiber in relation to the application time and power.

Materials and Methods: Laser ablations with each fiber were performed in porcine liver and human breast tissue ex vivo. Laser energy was applied at powers of 5, 7.5 W and 10 W, with exposure times between 5 and 15 minutes. Directly after ablation, the tissues were cut open along the applicator axis. The lesions were macroscopically inspected. We regarded clearly demarcated portions of the visibly damaged area as necroses and measured each axial and transversal diameter.

Results: Gross pathologic examination showed a bullet-shaped thermal lesion applied with forward firing fiber and more circular-shaped thermal lesion with multidirectional firing fiber. We got the same results in porcine liver and human breast tissues. When a forward firing fiber was used, the greatest ablation diameters ranged from 15 mm at the lowest dose (5 W, 5 minutes) to 30 mm at the highest dose (10 W, 15 minutes). Multidirectional firing fiber created ablation zones as large as 40 mm in greatest diameter with the lasers operating at 10 W for 15 mins.

Conclusions: The results of this study demonstrated a dose response relationship for laser-induced thermal therapy. The application of higher energy volumes leads to the induction of larger lesions up to complete coagulation of the available organs. And we found the thermal lesions with multidirectional firing fiber were more spherical shape and easily predictable the size.

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The Role of VEGF Gene Polymorphisms in the Development of Distant Metastases in Postmenopausal Breast Cancer Patients

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Background: Vascular endothelial growth factor (VEGF) is a key regulator of tumor-induced angiogenesis and is required for tumor growth and distant tumor spread. Aim of the present study was to evaluate the role of VEGF polymorphisms and haplotypes for metastatic progression of breast cancer in postmenopausal women.

Methods: We carried out a prospective study including 584 postmenopausal breast cancer patients from the Austrian TIGER ("tumor of breast tissue: incidence, genetics, and environmental risk factors") study. Development of metastases was examined in regular follow-up investigations. Seven VEGF polymorphisms were selected and determined by a 5'-nuclease assay (TaqMan). Haplotypes and linkage disequilibrium were determined using the Haploview program.

Results: Within a median follow-up time of 77 months (range 0-121 months), 122 (21%) patients developed distant metastases.

In a Kaplan-Meier analysis, carriers of the -634G>C polymorphism were at decreased risk of developing distant metastasis ($p = 0.027$) and

in a Cox regression analysis, the hazard ratio for distant metastases was 0.69 (95% CI 0.52 to 0.92, $p = 0.012$). Furthermore, the CCCC haplotype formed by 5 polymorphisms upstream of the coding sequence including the -634G>C polymorphism demonstrated a significant association with distant metastases (HR 0.655, 95% CI 0.487 to 0.882; $p = 0.004$). In a multivariate analysis including tumor stage, tumor grade, initial lymph node involvement, hormone receptor status and HER2neu status as potential confounders, the CCCC haplotype remained a significant predictor of distant metastases (HR 0.614, 95% CI 0.416 to 0.906; $p = 0.014$).

Conclusion: We conclude that VEGF gene polymorphisms and haplotypes may influence the risk of developing distant metastases in postmenopausal breast cancer patients.

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Frequency and Anatomical Characteristics of Involved Regional Lymph Nodes in Recurrent and Advanced Breast Cancer and Its Impact On Target Definition for Radiotherapy

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Background: The role of radiotherapy (RT) has been well evaluated in the multidisciplinary management of breast cancer (BC). Local-regional RT is typically delivered with traditional field borders. An analysis of the frequency of lymphatic nodal involvements with corresponding anatomical extent in recurrent and advanced BC would help to evaluate the adequacy of target definition with regard to contour guidelines.

Materials and Methods: Recurrent or advanced BC patients with CT images to cover the whole regional nodes at the time of recurrence or staging prior to systemic therapy were eligible. Additional MRI or PET-CT images were collected if presented. The regional lymph nodes were categorized into 8 anatomical substructures: medial and lateral-supraclavicular (Sc-M, Sc-L); axilla (ALN)-I, II, III; infraclavicular (Ic); Rotter's nodes (RN) and internal mammary nodes (IMN). Frequency of involvement and the anatomical characteristics were analyzed.

Result: A total of 182 regional recurrent pts and 26 advanced BC pts from July 2003 to Jan. 2010 entered study, with 352 anatomical substructures of involved nodes. The frequency of involvement includes: Sc-M: 71(20.2%), Sc-L:38(10.8%), ALN-I: 43(12.2%), ALN-II: 38(10.8%), ALN-III and Ic: 58(16.5%), RN: 44(12.5%), IMN: 60(17.0%). Apart from IMN, in pts received axillary dissection, 85.8%(200/233) had recurrent nodes cranial to the axillary vein (AV), while in advanced pts without axillary dissection, ALN-III remained the most frequently involved regions: 39.0% and 18.6%. 58/60 of the involved IMN occurred within the first 3 intercostal spaces. The average depth from the center of the involved nodes in ScM and Sc-L was: 35.37±10.25 mm and 47.29±18.52 mm respectively, with 62.0% and 76.3% of these measured above 3 cm. The average distance from the center of involved IMN to the midline was 29.4±6.7 mm, which was also 5.5±4.8 mm to internal mammary vessels (IMV) laterally and 5.3±4.5 mm deeply.

Conclusion: Identification of involved regional nodes in recurrent and advanced BC pts would help to better understand the natural history of lymphatic spread. The data observed in our series confirms that current target definition of is consistent with the potential risk of regional nodes. Sc and axillary nodes cranial to the AV should be considered the primary risk target in post-operative radiotherapy after axillary dissection. Individual treatment planning would be feasible with increasing knowledge of nodal involvement.

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Perioperative Interstitial Brachytherapy as a Boost in Breast Cancer Conserving Therapy

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Background: The aim of breast-conserving treatment (BCT) in breast cancer, consisting of wide local excision (WLE) and whole breast radiation (WBR), is to obtain locoregional control of disease. Since a considerable percentage of local recurrences after BCT occurs close to the original tumor bed, WBR is supplemented with a boost on the original tumor bed. Application of perioperative brachytherapy allows more precise deposition of boost radiation energy to the lumpectomy cavity in a shorter period of time, as compared to conventional radiation schemes. This study evaluated treatment and clinical outcomes of patients with early staged breast cancer who received perioperatively placed catheters for Iridium-192 based brachytherapy.

Material and Methods: 107 breasts in 105 patients with cT1-2 non-luminal breast cancer were treated between 1996 and 2009 with BCT, including WLE combined with perioperative brachytherapy using Iridium-192 (15 Gy applied with low dose rate or 9 Gy with high dose rate) followed by whole breast irradiation (50 Gy in 5 weeks). Outcome analysis included treatment toxicity (according to Common Terminology Criteria for Adverse Events), local recurrence rate, disease-free survival, and overall survival.

Results: Median follow-up was 6.7 years (range 0.50-14.8). Mean age was 50.2 years (±10.5). Mean tumor diameter was 15 mm (±8 mm). Three patients (2.8%) developed a true in field recurrence. Five- and ten-year local recurrence free survival was 98% and 87%, respectively. Five- and ten-year disease-specific survival was 94% and 84%, respectively. Five- and ten-year overall survival was 92% and 78%, respectively.

Acute complications consisted of wound infections of the lumpectomy site ($n = 3$, grade 1), haematoma ($n = 3$, G1), venous bleeding due to removal of catheters, necessitating surgery ($n = 1$, G3), radiation induced mastitis ($n = 2$, G1). Late complications were fibrosis ($n = 19$, G1), temporary pain ($n = 6$, G2), circumscribed teleangiectasia ($n = 6$, G1).

Conclusions: Local recurrence rate and local toxicity after perioperative interstitial brachytherapy and whole breast irradiation for breast cancer appear to be similar to that seen after external beam radiotherapy schemes in BCT. The main disadvantage is the fact that the final histological reports concerning radicality are not available during the brachytherapy treatment. The advantages are the ability to visualize the excision site at the time of implantation and reduction of outpatient treatment.

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Palliative Radiotherapy in Patients with Metastatic Breast Cancer - Rates of Utilization, Distance Travelled and Incurred Costs

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Background: Palliative radiotherapy (PRT) is a well recognised treatment for the successful relief of symptoms associated with metastatic breast cancer (MBC). Improvements in up to 80% of MBC patients with complete resolution of pain in a third are recognised. Over half of female patients with MBC receive at least one course of palliative radiotherapy. Distance from radiotherapy centre is associated with reduced rates of PRT despite likely patient benefit. Our aim was to unveil the proportion of patients with MBC attending oncology clinics who received PRT, distance travelled and overall cost.

Materials and Methods: By reviewing the notes of 76 patients with MBC attending outpatient clinics between August 2010 and February 2011 at Wansbeck District General Northumbria, we recorded all courses of PRT received from the diagnosis of MBC for each patient. Number of attendances for delivery of treatment at the Newcastle Centre for Cancer Care (NCCC), fractionation schedule, technique used and distance travelled were recorded. IMRT costing was excluded. An estimated cost of each NCCC course of treatment was made.

Results: MBC patients comprised a median of 36% of outpatient clinic appointments, attending a median of 4 appointments each. 40 (52.6%) of these patients received at least one course of PRT since the diagnosis of MBC, totalling 463 PRT fractions with a median of 10 fractions per patient. 92.3% of patients' PRT was delivered with standardised single or parallel opposed field techniques. 3-D conformal IMRT techniques were required for 2 patients. One patient with bone metastases received stereotactic radiotherapy in a different radiotherapy centre. PRT was administered to bone in 31 (80%) of cases, 10 (27.5%) to soft tissue and 7 (17.5%) to brain. 8 (20.5%) of the patients were re-treated, 6 (15.4%) had one and 2 (5.1%) had two re-treatments. 90% of re-treatments were to bone. The total cost including transport was £37,632. The mean cost was £990 (median £800) per patient with an average price of £100 per fraction. Average distance travelled to the NCCC was 20.9 miles (range 3-63 miles).

Conclusion: Patients with MBC comprise a large proportion of outpatient consultations. Our utilization of PRT is comparable to a limited number of published reports. We show that PRT is an inexpensive and frequently used modality when treating symptomatic metastases in a majority of cases. Despite the average distance travelled to the NCCC this was not a barrier to PRT.

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Feasibility Study On Pre-operative MRI-guided Irradiation in Breast-conserving Therapy

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Background: Today's radiotherapy (RT) after breast-conserving surgery is prone to uncertainties due to high interobserver delineation variation