2009 POSTER

An objective assessment of cosmetic outcome after intraoperative radiotherapy or external beam radiotherapy for early breast cancer in patients from a randomized controlled trial

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Background: Non-inferiority between the novel technique of TARGIT (Intra-operative radiotherapy with Intrabeam ®) and conventional whole-breast external beam radiotherapy (EBRT) in women with early breast cancer, in terms of the primary outcome measure of risk of local relapse within the treated breast, has been demonstrated in the international randomised contolled TARGeted Intraoperative radioTherapy (TARGIT) trial. The very low recurrence rates have increased the importance of cosmesis as an outcome after breast conserving treatment with both surgery and radiotherapy. This study was performed to determine if the single high dose of TARGIT leads to impaired cosmesis, compared with a fractionated dose of radiotherapy given as EBRT.
Material and Methods: BCCT.core software is a validated, objective assessment tool for the evaluation of cosmetic outcome from frontal digital photographs. Images were analysed at baseline (before TARGIT or EBRT) and yearly thereafter for up to five years. The analysis produces a composite score (Excellent, Good, Fair, Poor) based on symmetry, colour and scar.
Results: 342 patients from two centres participating in the TARGIT Trial were assessed. All were over 50 years old with a median age at baseline of 64 years (IQR 59 to 68). Scores were dichotomised into Excellent and Good (EG), and Fair and Poor (FP). There were statistically significant increases in the odds of having an outcome of EG for patients who received TARGIT group relative to those who received EBRT group at year 1 (OR=2.07, 95% CI 1.12 to 3.85, p = 0.021) and year 2 (OR=2.11, 95% CI 1.0 to 4.45, p = 0.05).
Conclusions: This objective assessment of aesthetic outcome in patients from a randomised setting demonstrates that those treated with targeted intraoperative radiotherapy have a superior cosmetic result compared with those patients who received conventional whole-breast external beam radiotherapy.
No conflict of interest.

2010 POSTER

Analysis of different clinical target volumes of whole breast after breast-conserving surgery based on three-dimensional CT and four-dimensional CT images

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Background and Purpose: The four-dimensional CT (4D-CT) has more information of tumour movement comparing with three-dimensional CT (3D-CT) during the whole respiratory. However, the workload of target delineation for the whole breast was heavier and the capacity of workload on the target delineation was increased greatly. In order to identify the necessary of the 4D-CT used for simulation in the IMRT of the whole breast after breast-conserving surgery, this study investigated the difference of the clinical target volumes of whole breast (CTVs) based on 3D-CT and the 4D-CT for patients after breast-conserving surgery.
Materials and Methods: Thirteen patients after breast-conserving surgery underwent 3D-CT simulation scans followed by 4D-CT simulation scans of the thorax during free breathing. Then data sets for 3D-CT and 4D-CT scans were transferred to Eclipse treatment planning software. The clinical target volumes (CTVs) of whole breast were manually delineated on the registered images of the 3D-CT, 4D-CT and maximum intensity projection (MIP) images by a radiologist under the same delineation criteria. And all the CTV delineated on the 10 phases of the 4D-CT images were fused into an internal target volume (ITV). The CTV_0, CTV_{20}, CTV_{50}, CTV_{MIP}, CTV_{3D} were defined on 0%, 20%, 50%, MIP and 3D-CT images. The volumes of the CTV, the matching index (MI) and the degree of inclusion (DI) were compared respectively.
Results: There was no difference in the CTV delineated by the same radiologist no matter based on 3D-CT or 4D-CT (P >0.05). The volume demonstrated no significant difference between CTV_{3D} and CTV_0, CTV_{20}, CTV_{50}, CTV_{MIP} (P >0.05). The difference of the MI and DI between CTV_{3D} and CTV_0, CTV_{20}, CTV_{50} was not statistically significant as well. The volume of ITV was larger than that of CTV_{3D} and CTV_{MIP}, the DI of ITV in CTV_{3D} and CTV_{MIP} Vs. DI of CTV_{3D} and CTV_{MIP} in ITV were significant as well (P <0.05).
Conclusions: The 3D-CT and MIP showed limited target movement information and it would not be a reliable clinical approach to replace 4D-CT by 3D-CT and MIP images when the clinical target volume of the whole breast was been delineated. It was more reasonable to construct ITV of whole breast based on 4D-CT after breast-conserving surgery.
No conflict of interest.

2011 POSTER

Breath hold and volumetric IMRT for accelerated partial breast irradiation (APBI)

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Purpose/Objective To investigate the effect of using volumetric modulated arc therapy (VMAT) and/or voluntary moderately deep inspiration breath-hold (vmDIBH) for patients treated with external beam APBI.
Materials and Methods: For three left-sided breast cancer patients, two CT-scans were acquired, in free breathing (FB) and in vmDIBH. On each scan, five tumour volumes were contoured: upper-inner, lower-inner, central, upper-outer, and lower-outer. For each tumour location 3D conformal radiotherapy (3D-CRT) and VMAT plans both in FB and vmDIBH were made. The prescribed dose was 38.5 Gy given in 10 fractions, two fractions per day. Dose parameters for the planning target volume (PTV), heart, lungs, ipsilateral (IL) non-involved and contralateral (CL) breast were assessed and compared.
Results: VMAT dose conformity was significantly better compared to that of 3D-CRT (conformity index =0.8±0.1 vs. 0.6±0.1). The PTV volume covered with 95% of the prescribed dose increased from 94.6% for 3D-CRT to 98.7% for VMAT. IL breast receiving ⩾50% of the prescribed dose was on average reduced by 30% with VMAT compared to 3D-CRT. For dose to heart and ipsilateral lung, the tumours were grouped: 1) inner and central location, and 2) outer location. For group 1, the mean heart dose decreased from 2.1±1.8 Gy for 3D-CRT(FB) to 1.0±0.9 Gy with VMAT(FB), and 0.6±0.5 Gy for VMAT(vmDIBH). The heart V5 Gy was reduced to 2.3% with VMAT(vmDIBH) compared to 14.9% and 3.8% with 3D-CRT(FB) and 3D-CRT(vmDIBH). For group 2, the mean heart dose was 0.2−0.5 Gy for all techniques. The heart V5 Gy was 3.2% in 3D-CRT(FB) plans, while no heart received 5 Gy in VMAT(vmDIBH). VMAT(vmDIBH and FB) resulted in significant reduction of the ipsilateral lung dose: V5 Gy = 8.8±7.6% vs. 24.2±1.7% for 3D-CRT(FB). VMAT showed a slight but acceptable increase in the maximum CL breast dose (from 0.8 to 4 Gy), with the mean dose always below 1 Gy.
Conclusions: APBI with VMAT offers improved PTV dose conformity and delivers lower doses to the ipsilateral breast and lung compared with 3D-CRT, at the cost of a slightly higher but acceptable dose to the contralateral breast. VMAT shows the largest reduction in heart dose for patients with tumours in the inner and central parts of the breast. Combining VMAT and vmDIBH only slightly reduces the heart dose further.
No conflict of interest.

2012 POSTER

Screening patients for deep inspiration breath hold to reduce cardiac doses for adjuvant left breast irradiation

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Background: When delivering radiotherapy to left-sided breast cancers, deep inspiration breath hold (DIBH) using active breath control (ABC) can significantly reduce radiation dose to heart and coronary arteries in selected patients. Currently, at our institution a cutoff of heart V50% >10cc is used to determine which patients require ABC. This dose-volume measurement requires generation of a radiation plan to select patients for ABC, delaying the second ABC CT simulation. The purpose of this study is to determine if simple 2-D measurements of the heart at the time of CT simulation can adequately screen patients for ABC. This would facilitate a streamlined process that minimizes delays for left-side breast radiation.
Materials and Methods: This study evaluated CT simulation scans from 50 randomly selected left-sided breast cancer patients treated with tangent RT alone from November 2009 to August 2012 (era when ABC was standard), where 50% of these patients were treated with ABC and 50% were not. On each CT dataset, a tangential line was drawn between the medial

and lateral tattoo and the following heart measurements were recorded by a blinded observer at 2, 3, 4, and 5 cm below the tattoos: (1) maximal heart distance (MHD) perpendicular to this line and (2) heart length (HL) along this line. The first 20 cases were measured by 2 observers to test interobserver variation. Correlation between each measurement and heart V50 (from the delivered RT plan) was calculated using linear regression. T-test was used to evaluate the association between heart measurements and ABC use. Predictive models were created using two strategies; (1) using a step wise approach utilizing the most significant factor and (2) using principle component analysis.
Results: 49 patients were analyzable as the heart dose from one patient was not available. Analysis of the first 20 patients shows the heart measurements between the two observers were similar with a correlation coefficient of 0.93 for the MHD and 0.94 for HL. For the 49 patients, the HL at 2 cm had the highest association with V50 (R^2 = 0.45; p < 0.0001). The other values that were significantly associated with V50 were HL at 3 cm (R^2=0.37; p= <0.0001), MHD at 2 cm (R^2=0.25; p = 0.0003), MHD at 3 cm (R^2=0.23; p = 0.0006) and HL at 4 cm (R^2=0.17, p = 0.0035). The predictive model using the most significant variable (HL at 2 cm) gave an adjusted R^2=0.4385 (P<0.0001). Adding other variables into the predictive model did not improve the adjusted R^2.
Conclusions: The results of this study suggests that a simple 2-D heart measurement, heart length across a line connecting the 2 tattoos at 2 cm, shows moderate correlation with the irradiated heart volume in the delivered RT plan. Although the correlation was modest, this may serve as an easy screening tool to select patients who may benefit from ABC. Appreciating the limitations of our retrospective study, validation of this predictive model is ongoing.
No conflict of interest.

2013 POSTER

Irradiation of the internal mammary nodes in breast cancer patients with morphologically verified metastasis at this zone

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Objective: Detection of regional lymph nodes involvement is an extremely important step in the diagnosis and treatment of breast cancer. As with axillary lymph node metastases, parasternal lymph nodes metastases are an important prognostic factor.
Goal: To detect metastasis in the internal mammary lymph nodes (IMN) and to find out the best way of radiation therapy at this zone.
Material and Methods: Retrospective study of 1125 patients with breast cancer who underwent thoracoscopic internal mammary lymphadenectomy in 1998–2008 was performed. Metastases were found in 204 of 1125 cases (18.3%), representing 33.9% of all cases of regional metastases (n = 601). Only patients with metastasis had radiation therapy at IMN zone. Standard regimen (2 Gy x 25, total 50 Gy) underwent 87 patients (42.6%) − Group A, hyperfractionated regimen (3 Gy x 13, total 39 Gy) − 80 patients (39.2%) − Group B, no radiation − 37 patients (18.1%) − Group C.
Results: No difference in overall survival was registered in all three groups. Median disease free survival was significantly worth in Group C (5.5 years) in comparison with Group A (7.8 years) and Group B (not achieved).
Conclusion: We believe that the thoracoscopic internal mammary lymphadenectomy should be a part of the diagnostic process in patients with breast cancer. Irradiation of IMN leads to better disease-free but not to overall survival at 8.1 years median follow up. Hyperfractionated regimen could be safely used for breast and IMN irradiation.
No conflict of interest.

2014 POSTER

Case selection for targeted intraoperative radiotherapy (TARGIT)

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Background: The TARGIT-A randomised trial compared a risk-adapted approach using targeted intraoperative radiotherapy (TARGIT) with whole breast external beam radiotherapy (EBRT) after lumpectomy for early breast cancer. At the San Antonio update, it was suggested that the preferred option is to give TARGIT concurrently with lumpectomy (prepathology). In this analysis we describe patient and tumour factors that may help select patients for TARGIT based on the results of an *a priori* statistical analysis plan.
Methods: In this large international trial, 3451 patients (age>=45, unifocal invasive ductal carcinoma, size $\leqslant$3.5 cm) from 33 centres in 10 countries were randomly allocated to either TARGIT or EBRT. Primary outcome was ipsilateral breast recurrence and secondary included mortality. Before unblinding for this analysis, we hypothesised that progesterone receptor (PgR) status, as an expression of a functionally active oestrogen receptor (ER), is a surrogate for radiation responsiveness and could predict a difference between the outcome for local control in the two randomised groups and pre-specified a detailed analysis by PgR status. We also assessed whether a Cox proportional hazard model including age, margin status, tumour grade, ER, PgR, HER2, vascular invasion and node positivity was consistent with our results.
Results: For PgR positive cases, there was no significant difference in the primary outcome of Ipsilateral breast recurrence between TARGIT and EBRT (2.3%(1.3−4.3) vs. 1.5%(0.75−3.0) p = 0.51, while in PgR negative cases there were significantly more local recurrences after partial breast irradiation using TARGIT: 7.0%(3.5–13.6) vs. 0.5%(0.1−3.7) p = 0.017. By contrast, age, margin status, tumour grade, tumour size, vascular invasion, node positivity, ER and Her2 status were not found to be significant predictors. Even age younger than 50 or grade 3 cancers had similar outcome with TARGIT or EBRT. Exploratory analyses in conjunction with the timing of TARGIT, revealed that when TARGIT was given concurrently in PgR positive cases (n = 1625) the results were (TARGIT vs. EBRT): ipsilateral breast recurrence 4 vs. 5, 5-year risk 1.4%(0.46−3.9) vs. 1.2%(0.48−2.9) HR 0.82(0.22–3.06), and overall mortality 18 vs. 31, 5-year risk 3.3%(1.83–6.04) vs. 6.4%(4.3−9.6) HR 0.60(0.34–1.08).
Conclusions: It appears that progesterone receptor status is useful in selecting cases for using the TARGIT concurrently with lumpectomy for breast cancer. Progesterone receptor negative patients may fall in the cautious or unsuitable category and progesterone receptor positive cases are in the suitable category for partial breast irradiation with TARGIT.
Conflict of interest: *Other substantive relationships: Carl Zeiss (travel to meetings and honoraria).*

2015 POSTER

Late toxicities and outcomes after one year of adjuvant radiotherapy associated with concurrent bevacizumab in patients with non-metastatic breast cancer

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Background: Few data are available regarding the safety of the concurrent combination of bevacizumab (BV) with adjuvant locoregional radiotherapy (RT) for breast cancer, especially in terms of late toxicity. The aims of this study were to determine late toxicities and outcomes among patients with non-metastatic BC treated with this combination.
Materials and Methods: In our multicenter prospective and descriptive study, we analyzed toxicities of adjuvant RT in patients with non-metastatic BC receiving concurrent BV. Early and late toxicities were assessed by the Common Terminology Criteria for Adverse Events (v3.0). Evaluation was done 12 months after the end of RT. All patients provided written informed consent before enrollment.
Results: Among patients enrolled in our study from October 2007 to August 2010, evaluation at 12 months was available for 63 patients. Mean age was 51 years. Among tumors, 17% were luminal BC, 24% HER2+ and 70% triple negative. A total of 56 patients had an invasive ductal carcinoma. Nineteen patients were stage I (30%), 21 patients stage II (33%) and 22 patients stage IIIB (35%) without patients stage IV (no data for one patient). A total of 23 patients (37%) received neoadjuvant chemotherapy plus BV followed by surgery then RT whereas 40 patients (63%) had surgery followed by adjuvant chemotherapy plus BV then RT. A total of 28 patients (44%) achieved post mastectomy RT and 35 patients (56%) had a whole breast RT with a boost in the surgical bed. Lymph node RT was performed in 42 patients (67%) with internal mammary chain RT in 25 patients (40%). Concurrent trastuzumab with RT and BV was performed in 15 patients (23%). Mean time of BV treatment was 10.2 months (2−13)