and postoperative seroma. In a recent study, no association between the irradiated target volume and the original tumor size was found in patients with DCIS and early stage breast cancer [den Hartogh et al., Breast cancer res treat, October 2011]. Therefore, two hypotheses were developed:

1. Tumor delineation on pre-operative imaging could lead to smaller target volumes, which are associated with superior cosmetic results and lower radiotherapy toxicity outcomes.
2. Supine breast MRI acquisition for RT delineation would result in superior soft-tissue contrast compared to the standard CT imaging in RT.

We have performed a feasibility study to test these hypotheses in order to perform a larger prospective cohort study.

Material and Methods: To test the first hypothesis, 9 patients with early stage breast cancer (pT1N0) who were treated with breast-conserving therapy (BCT), were retrospectively analyzed. Breast tumors were delineated on pre-operative prone contrast-enhanced MRIs. Clinical target volumes (CTVs) were created by adding a 1.5 cm surrounding margin. These MRI-CTVs were compared to the CT-CTVs acquired from post-operative delineations on RT planning CT scans. CT-CTVs were created by adding a 1.5 cm margin minus the minimal microscopic margin. Consequently, a 1.5 cm margin around the tumor was minimally treated.

To test our second hypothesis, we developed a protocol for MRI of the breast in RT position, since diagnostic MRI acquisition in prone position is not suited for supine RT delineation. Patients were positioned supine on a MRI compatible wedge board.

Results: The median tumor size was 12 mm (range 11−20 mm). The median excised specimen volume was 63 ml (range 26–174 ml). The median pre- and post-operative CTV values were 49.3 ml (range 28.6–96.8 ml) and 66.9 ml (range 20.0–218.6 ml), respectively. The median relative volume reduction was 31% (range −146−87%).

Furthermore, it was technically feasible to acquire high quality MRIs in supine RT position when using a 1.5T Philips Ingenia wide bore magnet. Within 25 minutes, the following 3D MRIs with fat suppression were acquired: T1 weighted FFE (DIXON), T2 weighted TSE (VISTA) and a dynamic series of contrast enhanced T1 (THRIVE) MRIs after Gadovist® administration. The Flexcoverage anterior receive coil was positioned on a PMMA support to prevent deformation of the outer contour of the patient.

Conclusions: In early breast cancer patients, treated with BCT, preoperative irradiation can result in a substantial reduction of irradiated target volumes in BCT. The developed MRI sequences are applied in a prospective cohort study which is currently running at our department. Pre- and post-operative target volume delineation and interobserver variability will be compared on both CT and MR imaging.

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Radiation-induced Pulmonary Injury After Radiotherapy for Early Breast Conserving Therapy

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Purpose: We observed a rare and unique occurrence of radiation-induced pulmonary injury after radiotherapy for early breast conserving therapy. We separated the pulmonary injury into inside and outside the tangential field. The goal of this study was to report and determine the incidence, analyze the characteristics of the pulmonary lesions on the images.

Materials and Methods: A retrospective analysis was conducted of 750 consecutive patients that underwent breast-conserving therapy (BCT) from January 1992 to December 2010. The patients were observed at least one year after radiotherapy for BCT. Radiotherapy was administered by 4 MV photons in all patients. The patients underwent chest X-rays and/or computed tomography (CT) periodically. We divided the appearance time of radiation pneumonitis into the super-early stage (during radiation therapy to 3 months after radiotherapy), the early stage (3 to 12 months after radiotherapy), and late stage (over 12 months after radiotherapy). If the pneumonitis was found on chest X-P, chest CT was conducted to identify the characteristics of the pulmonary lesion inside and/or outside the radiation field.

Results: The findings outside radiation field appeared to be idiopathic and were called radiation-induced bronchiolitis obliterans organizing pneumonia (BOOP) syndrome. The incidence of the radiation-induced BOOP syndrome was about 1.8%. We did not find a relationship between the characteristics of patients and the occurrence of radiation-induced BOOP syndrome. The pulmonary findings were classified into four patterns on chest CT. Progression of the pulmonary lesions observed on chest X-ray was classified into three patterns. Pneumonitis appeared within 6 months after radiotherapy was completed and disappeared within 6−12 months after its onset. The incidence of rate of the interstitial pneumonitis outside radiation field appeared in the super-early stage is 0.1%. On the other hand, the occurrence of the pulmonary findings inside field appeared in the early and late stage is approximately 85%. But these patients have no respiratory symptoms.

Conclusions: We have to understand the occurrence of the radiation induced or related pneumonitis, and its associated prognosis are not significant, the patients' clinical condition must be carefully followed.

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Does the Effect of Clip Displacement On Target Volume Potentially Hamper the Concept of Partial Breast Irradiation in Prone Position?

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Background: To analyse and compare the displacement of surgical clips in prone (*Pr*) and supine (*Su*) positions and assess the consequences on target volumes in case of partial breast irradiation (PBI).

Material and Methods: 30 post-lumpectomy breast cancer patients underwent CT imaging in *Su* and *Pr*. Displacements of the surgical clips were measured by the distances from the chest-wall (CW) and from a common fix bony reference point (3D vector analysis). On each dataset, the tumour bed (TB = clips ± seroma), clinical target volume (CTV = TB+1.5 cm) and planning target volumes (PTV = CTV+1 cm) for PBI were determined and the volume pairs were compared. Volumes were studied by multiple regression analysis with respect to a set of covariates: age, body weight, left/right side, cup size, localization within the breast, number of clips, presence of seroma and 'deep' clips (defined as located <1 cm from CW).

Results: Clip displacements varied considerably with respect to their position to the CW. The largest displacement was observed for clips situated close to the skin ($p < 0.0001$). The mean volumes of seroma (8.61 ± 8.61 (*Pr*) vs. $7.67 \pm 7.51\,cm^3$ (*Su*), $p = 0.037$), CTV (88.5 ± 37.0 vs. $75.0 \pm 32.3\,cm^3$, $p = 0.0001$) and PTV (233 ± 76.4 vs. $211 \pm 70.1\,cm^3$, $p = 0.0008$) were significantly higher in *Pr* than in *Su*. The PTV volume difference (*Pr-Su*) was significantly higher in patients with presence of seroma (48.1 ± 33.2 vs. $10.8 \pm 24.8\,cm^3$, $p = 0.002$), TB locations in the superior-internal-quadrant (SIQ) and at the border of superior quadrants (bSQ) (46.4 ± 31.2 vs. $5.72 \pm 20.6\,cm^3$ $p = 0.0002$) and in case of 'deep' clips (31.2 ± 32.8 vs. $0.47 \pm 17.2\,cm^3$, $p = 0.013$). When combining these factors in a multivariate analysis, two variables remained significant: seroma ($p = 0.0037$) and localization in SIQ-bSQ ($p = 0.0006$).

Conclusions: *Pr* position in selected patients potentially leads to a significant increase in target volumes in the frame of PBI. Factors independently predicting this volume increase are the presence of seroma and location of TB in the SIQ-bSQ.

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Improved Cosmetic Outcome After TARGIT Compared with External Beam Radiotherapy for Early Breast Cancer

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Background: Early results from the randomised controlled TARGIT Trial have demonstrated non-inferiority between the novel technique of TARGIT [intra-operative radiotherapy with Intrabeam® (Carl Zeiss, Germany)] and conventional external beam radiotherapy (EBRT) in women with early breast cancer, in terms of local relapse within the treated breast and clinically significant toxicity. We report here data from a sub-protocol assessing cosmesis in 114 women over 50 years of age participating in the TARGIT Trial from one centre (Perth, Australia).

Material and Methods: Frontal digital photographs from were assessed, blind to treatment, using specialist software (BCCT.core 2.0, INESC Porto, Portugal) which produces a composite score based on symmetry, colour and scar. Statistical analysis was by generalised estimating equations (GEE) on all of the data, and logistic regression analysis at year 1.

Results: 55 and 59 patients were randomised to receive EBRT or TARGIT, respectively. The median age at randomisation was 62 years (IQR 56 to 68). Photographs were taken at baseline (before surgery) and one, two, three and four years after initial breast conserving surgery; none had subsequent breast surgery. The scores were dichotomised into Excellent and Good (EG), and Fair and Poor (FP). There was a non-significant 45% increase in the odds of having an outcome of EG for patients in the TARGIT group relative to the EBRT group (OR = 1.45, 95% CI 0.78–2.69, $p = 0.245$)

after adjusting for tumour size. The results were similar when adjusted for tumour grade and age of the patient. For year 1 only there was a statistically significant 2.35 fold increase in the odds of having an outcome of EG for patients in the TARGIT group relative to the EBRT group (OR = 2.35, 95% CI 1.02–5.45, p = 0.047) after adjusting for age of the patient, tumour size and grade.

Conclusions: These results demonstrate a significantly better cosmetic outcome with TARGIT compared to EBRT in the first year after surgery.

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Effect of Radiation Therapy on Local Control in Patients with Positive Surgical Margins After Breast-conserving Surgery

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Purpose: The surgical margin status after breast-conserving surgery (BCS) has been associated with the risk of local recurrence. The purpose of study is to retrospectively evaluate the effect of a higher radiation dose on local control in patients with positive margins.

Patients and Methods: A total of 1,083 patients who underwent BCS followed by whole breast irradiation of 50 Gy between 1991 and 2009 were including in this study. 138 patients (13%) with positive margins were assigned to receive or not an extra boost dose of 10 Gy. **A positive margin was defined as tumor seen at 5 mm or less from the resection edge**.

Results: At a median follow-up of 8.5 years, the rate of local recurrence was 2.1% (23/1083). Positive margin status was found to be a significant risk factor for local recurrence. For patients with positive margins, the boost dose of 10 Gy reduced the local recurrence from 23% to 2%. There was no significant difference in local recurrence rate between patients with positive margin who treated with 50 Gy and boost and those with negative margin without boost. In addition, patients with positive margin who treated with 50 Gy and boost showed no significant difference in local relapse rate compared with patients who underwent additional local resection before whole breast irradiation.

Conclusion: Our results suggest that boost irradiation to the tumor bed in patients with positive margins after breast-conserving surgery reduces local recurrence.

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Patient Preferences for Adjuvant Radiotherapy in Early Breast Cancer − an Australian Sub-study of the International TARGIT Trial

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Background: The multicentre randomized TARGIT trial compares single dose intra-operative radiotherapy (IORT) with 6−7 weeks of conventional external-beam radiotherapy (EBRT) in women with early breast cancer (EBC) at low risk of local recurrence (LR). The primary endpoint is LR rates; the *a priori* hypothesis is that IORT will give a non-inferior risk of LR compared with EBRT. Early results suggest non-inferiority however mature results are not yet available. It is unclear what LR risk patients and clinicians consider 'non-inferior'. In order to guide women and their doctors making choices about radiotherapy for EBC, a Patient Preference study was performed to determine what increased risk of LR, without detriment to survival, women who have completed radiotherapy for EBC would accept, in return for the increased convenience and possibly decreased toxicity of IORT.

Methods: This is a cross-sectional study of patient preferences and their determinants in 209 women who had radiotherapy on the TARGIT trial in Western Australia. Preferences were obtained from 108 participants who received IORT and 101 who received EBRT. Preferences were determined by a self-rated questionnaire using validated trade-off methodology. Disease, treatment, and demographic details were collected, and quality of life during radiotherapy was self-rated by patients.

Results: While 36% of patients were prepared to accept a 4%-6% increase in risk of LR for the increased convenience of IORT, 22% would not accept IORT at all. Multivariate Poisson regression identified treatment received as the only significant determinant of patient preferences (p < 0.0001). This is despite significant differences found in two-sample Kolmogorov-Smirnov tests of quality of life scores during treatment all favouring IORT. Comparison of the treatment groups found that 60% of IORT patients would accept IORT at an increased risk of 4%-6% in contrast to 12% of patients in the EBRT group. Only 2% of IORT patients indicated they would not have IORT at all, in contrast to 43% of EBRT patients.

Conclusion: Willingness of patients to accept IORT was discordant between the two treatment groups. The EBRT group were risk-averse, whilst patients who had IORT valued the convenience of IORT highly. Participants of this study have justified the treatment they were randomly allocated to, which questions the validity of post-treatment patient preference studies. Further research targeting patients who have not yet received radiotherapy will now follow, in order to better inform future patients and their clinicians. Given the early results of the TARGIT trial however, it is unlikely that the clinical difference in LR between IORT and EBRT will exceed what patients will accept.

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Simultaneous Integrated Boost in Breast Conserving Radiotherapy − Is Replanning Necessary Following Tumor Bed Change?

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Background: Tumor bed (TB) change is well-known phenomenon during the whole breast irradiation (WBI) in early stage breast cancer patients. The aims of this study were to evaluate change in seroma volume on repeat Computed Tomography (CT) scans and to explore whether replanning is necessary in breast conserving radiotherapy (RT) using the intensity modulated radiotherapy with simultaneous integrated boost (IMRT-SIB).

Methods and Materials: Thirty patients underwent WBI with 84 CT scans (24 patients with three CTs and 6 patients without the third CT) during the five weeks of RT were reviewed. TB and other target volumes on all CTs were delineated and compared. IMRT-SIB treatment plans with 50.68 Gy to the whole breast and 64.4 Gy to the boost in 28 fractions were constructed in the first CT. Replanning and hybrid plan (without replanning) on the second CT were reproduced. Dosimetric difference between the replannings and hybrid plans were compared.

Results: The mean TB volumes for the 1st CT, 2nd CT and 3rd CT were 42.1 cm^3, 20.1 cm^3 and 17.0 cm^3, respectively. The mean TB reduction was 40.5% from the 1st CT to 2nd CT and 4.3% from the 2nd CT to 3rd CT. The difference of TB volumes between the 1st CT to 2nd CT was statistically significant (p < 0.001), but not significant between 2nd CT to 3rd CT (p = 1.000). For all patients, target coverage remained adequate with either hybrid plans or replannings. However, replanning can significantly decrease the whole breast mean dose (35.2 Gy vs.35.6 Gy, p = 0.026) and breast volume outside the boost receiving 95% of the boost prescribed dose (39.5 cm^3 vs. 68.2 cm^3, p < 0.001).

Conclusions: TB change existed significantly during the WBI. Although boost volume could irradiate adequately without replanning after the shrinkage of seroma with IMRT-SIB, replanning could avoid the undesired high dose irradiation to the breast volume.

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Late Radiation Toxicity After Intraoperative Radiotherapy (IORT) for Breast Cancer: Results From the Randomized Phase III Trial TARGIT A

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Background: The first results from the randomized phase III trial TARGIT A (Vaidya et al., Lancet 2010) showed non-inferiority of intraoperative radiotherapy (IORT) compared to whole breast radiotherapy (WBRT) after breast-conserving surgery (BCS) regarding local recurrence. Here, we analyse long term toxicity.

Materials and Methods: Between February 2002 and December 2008, 109 patients were treated within the TARGIT A trial in a single center (Arm A (IORT, 20 Gy), n = 34 IORT, n = 20 IORT + WBRT (46−50 Gy); Arm B (WBRT 56 Gy) n = 55). Patients (n = 196) receiving an IORT boost followed by WBRT were used as a control. Follow-up was performed every six months during the first two years and yearly thereafter. Toxicity was assessed according to the LENT SOMA scales. Additionally mammography, ultrasound and photo documentation were done routinely. Cumulative incidences were calculated with Kaplan-Meier-estimates.

Results: In general long term toxicities were in range with the expected toxicities after radiation treatment of the breast. Fibrosis had a cumulative rate of 5.9% for Arm A IORT, 37.5% for Arm A IORT + WBRT and 18.4% for Arm B (38.2% for non-randomized control group) at 3 years. Chronic skin toxicities were very low after IORT alone (0% Arm A IORT vs. 17.5% Arm A IORT + WBRT vs. 17.7% Arm B). The calculated Hazard ratio