local therapy in one session avoiding 3−6 weeks of post-operative therapy. This may be preferable to many women including those seeking breast-conserving surgery in the developing world and for women living in remote areas of the Western world.

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Late toxicity and long term results after partial breast irradiation with high-dose-rate brachytherapy: results from a phase II prospective study

I. Palumbo[1], A. Farneti[1], M. Margaritelli[1], C. Raymondi[2], A. Cavalli[1], E. Perrucci[1], C. Aristei[1]. *[1]Perugia Hospital, Surgical Radiological Odontostomatological Sciences, Perugia, Italy; [2]Perugia Hospital, Medical Physics, Perugia, Italy*

Background: radiation therapy aims at achieving disease control with a low risk of side effects. Here late toxicity and long term results are analyzed in patients who received partial breast irradiation (PBI) with high-dose-rate (HDR) brachytherapy after conservative surgery.

Materials and Methods: 4 Gy were administered twice daily in 8 fractions over 4 consecutive days to 96 patients (median age 65 years; range 49−84). Tumors included 79 infiltrating and 13 ductal in situ carcinoma. Median tumor size was 7 mm (range 2−18). Estrogen receptors were positive in 82 cases, progesterone in 61 and HER2 in 3; Ki-67 was overexpressed (>25%) in 14 and p53 (>20%) in 7. Implantation was intra-operative in 18 cases and post-operative in 78 (median time after surgery 8 weeks; range 4−12) with implant geometry being defined with pre-implant computed tomography (CT). In the last 82 patients treatment planning was CT-based. At a median of 24 (range 1−43) days after PBI 8 patients received adjuvant chemotherapy. In 1 case PBI was performed between the first and the second CMF cycles. Adjuvant hormone therapy was given to 77 patients.

Results: median V100 was 105 cm^3 (range 22.3–271), median V150 was 27 cm^3 (range 8.04–57.10), median V200 was 11.65 cm^3 (range 4.21–27.20), median DHI was 0.751 (range 0.612–0.810). At a median follow-up of 45 months (range 14−72) late side effects were breast pain in 1 case, teleangectasis in 13 (12 G1 and 1 G2), 2 sieromas, 8 liponecrosis (1 G1 e 7 G2), 9 subcutaneous fibrosis (8 G1 and 1 G2) and 1 G3 cutaneous fibrosis. Patients and the radiation oncologist judged cosmetic results as good or excellent in all cases except 1, judged as fair. Late toxicity occured in 4/8 patient who received chemotherapy: 1 (starting CMF 43 days after PBI) developed G2 teleangiectasia and G1 subcutaneous toxicity, 1 (starting CMF 6 days after PBI) developed G1 teleangiectasia, 1 (starting EC plus paclitaxel 24 days after PBI) presented G1 subcutaneous toxicity, 1 (starting FEC 31 days after PBI) presented G1 teleangiectasia, G2 subcutaneous toxicity, G3 cutaneous toxicity and liponecrosis. The 1st, 3rd and 4th patients were implanted during surgery. Two local relapses occurred. One (48 months after PBI) was in a different quadrant to the original tumor. The second (19 months post-PBI), in a patient with a previous superior internal quadrant, was very close to the mediosternal line. One patient with negative sentinel node developed axillary metastases 7 months after PBI. All relapsed patients are alive, the first 2 in NED, the 3rd with disease.

Conclusions: Our results demonstrate that PBI, administered with HDR brachytherapy, is associated with very low relapse and late toxicity rates. Late toxicity was higher in patients implanted during surgery, in whom the dose to the skin was >70% of the prescribed dose, which may account for the teleangectasis development. PBI-chemotherapy timing does not seem to affect toxicity.

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Can total lung volume increase predict the benefit in respiratory gated patients with left-sided breast cancer?

C. Sweldens[1], K. Erven[1], S. Petillion[1], C. Weltens[1]. *[1]University Hospital Leuven, Radiotherapy, Leuven, Belgium*

Background: To investigate the proportion of left-sided breast cancer patients that may have an advantage of respiratory gated radiotherapy. To investigate whether the increase in lung volume can predict which patients have the highest benefit.

Materials and Methods: Twenty-one left sided-breast cancer patients, treated with radiotherapy on the breast alone were sequentially enrolled in this study. 18 patients underwent a non-gated CT-scan on the virtual simulator (Siemens Sensation Open™), followed by a CT scan using prospective gating (PG). To perform the PG CT-scan, the RPM system (Varian™) was used to record the patients breathing pattern and patients were audio-coached to breath deeply. A gated window was chosen in deep inspiration and by an automatic interface between the RPM system and the CT scanner, CT acquisition was triggered in this window. For 3 patients, only a non-gated (NG) CT scan was performed because coached breathing was too difficult or they were belly-breathers, these patients were excluded from the study. The clinical target volume (breast) and normal tissues (heart and lung) were delineated on both the NG and PG CT-scans. For each patient, a treatment plan was designed on both CT-scans, using an isocentric photon technique. Dose volume histograms were used to evaluate the normal tissue doses.

Results: For all patients (N = 18), a significant reduction in mean heart dose [3.1 Gy (NG) to 2 Gy (PG), $p < 0.0005$] and heart V30 [3.9% (NG) to 3.2% (PG), $p < 0.0006$] was achieved with respiratory gating. The total lung volume increased by 66% [2800 cm^3 (NG) to 4652 cm^3 (PG)]. Mean lung dose was comparable in both CT scans [3.1 Gy (NG) and 3 Gy (PG)] and V20 was the same (3%). Mean reduction in heart dose in all patients was 35%. 9 patients (50%) had an advantage in mean heart dose of >35% and were considered for treatment with respiratory gating. Patients that were selected for gated treatment based on an advantage for the heart, had a significant higher increase in total lung volume (87%) [2388 cm^3 (NG) to 4464 cm^3 (PG)] compared to patients not treated with gating (53%) [3130 cm^3 (NG) to 4802 cm^3 (PG)].

Conclusions: In this study, respiratory gating leads to a significant heart (>35%) sparing effect in 50% of left-sided breast cancer patients, irradiated on the breast alone. The patients with the highest increases in total long volume correlate with the patients which benefit most from the gated treatment.

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Is exclusive radiotherapy an option for early breast cancers with complete clinical response after neoadjuvant chemotherapy?

C. Daveau[1], A. Savignoni[1], S. Abrous-Anane[1], J.Y. Pierga[1], F. Reyal[1], Y. Kirova[1], R. Dendale[1], F. Campana[1], A. Fourquet[1], M.A. Bollet[1]. *[1]Institut Curie, Paris, Paris Cedex 05, France*

Background: Neoadjuvant chemotherapy (NCT) emerged in the 1990s as a treatment option that challenged primary surgery for non-metastatic operable breast adenocarcinomas, especially when they were deemed too large to be treated by breast-conserving surgery. The study was designed to determine whether exclusive radiotherapy (ERT) could be an option after complete clinical response (cCR) to NCT for early breast cancers (EBC).

Material and Methods: Between 1985 and 1999, 1477 patients received NCT for EBC considered to be too large for primary conservative surgery. Of 165 patients with cCR, 65 were treated by breast surgery (with radiotherapy) and 100 by ERT.

Results: Median follow-up was 12 years. The two groups were comparable in terms of baseline characteristics, except for larger initial tumor sizes in the ERT group. There were no significant differences in overall, disease-free and metastasis-free survivals. Five-year and 10-year overall survivals were 91% and 77% in the no surgery group and 82% and 79% in the surgery group, respectively ($p = 0.9$). However, a non-significant trend towards higher locoregional recurrence rates (LRR) was observed in the no surgery group (31% vs. 17% at 10 years; $p = 0.06$). In patients with complete responses on mammography and/or ultrasound, LRR were not significantly different ($p = 0.45$, 10-year LRR: 21% in surgery vs. 26% in ERT). No significant differences were observed in terms of the rate of cutaneous, cardiac or pulmonary toxicities.

Conclusion: Surgery is a key component of locoregional treatment for breast cancers that achieved cCR to NCT.

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Single dose intra-operative radiotherapy for breast cancer patients where external beam radiation was not feasible − results after 3 years of follow-up

M. Keshtgar[1], J.S. Tobias[2], J.S. Vaidya[1], C. Stacey[3], T. Corica[4], D. Joseph[4], A. Keller[5], F. Wenz[5], N.R. Williams[1], M. Baum[1]. *[1]University College London, Department of Surgery, London, United Kingdom; [2]University College London Hospital, Department of Medicine, London, United Kingdom; [3]University College London Hospital, Department of Radiotherapy, London, United Kingdom; [4]Sir Charles Gairdner Hospital, Department of Radiotherapy, Perth, Australia; [5]Universitätsklinik für Strahlentherapie und Radioonkologie, Department of Radiotherapy, Mannheim, Germany*

Background: Intra-operative radiotherapy (IORT) with Intrabeam® (Carl Zeiss, Germany) has been used since 2000 in the international randomised TARGIT Trial to determine if there is equivalence between IORT and conventional external beam radiotherapy (EBRT) in women with early breast cancer. The primary endpoint is local recurrence. Some patients were unsuitable for inclusion in our trial for a number of reasons and were given IORT as a single treatment off-trial.

Materials and Methods: Patients with invasive breast cancer underwent wide local excision followed by IORT (n = 74). Low energy x-rays are

emitted from a point source, delivering a dose of radiation (~20 Gy at the surface and ~5 Gy at 1 cm) directly to the tumour bed. The women could then proceed to have chemotherapy and/or adjuvant hormonal therapy as required. In addition, patients who were deemed unfit for surgery (n = 3) received interstitial radiotherapy alone under local anaesthetic. Women were followed-up for local recurrence.

Results: Over the past 7 years in centres in 3 countries (UK, Germany and Australia), 77 patients have been treated in this way, with median age of 66 (56−77 IQR) years and a median follow-up of 37 (25−54 IQR) months. To date there have been two local recurrences, which gives an estimated annual local recurrence rate of 0.78% (95% CI 0.09% to 2.77%).

Conclusion: This cohort adds to the evidence that targeted radiotherapy using IORT offers a safe and effective method of delivering radiotherapy to breast cancer patients in whom EBRT is not feasible or is not an option.

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Pragmatism in the TARGIT trial encouraged wider participation of centres yet yielded an unexpected homogeneous patient profile

J.S. Vaidya[1], on behalf of Targit Trialists's group. [1]*University College London, Division of Surgery and Interventional Science, London, United Kingdom*

In 1999, we designed a randomised controlled trial to test whether TARGeted Intraoperative radioTherapy (TARGIT) was equivalent to post-operative external beam radiotherapy (EBRT).

To cater for a wide level of equipoise, our design was pragmatic with minimal restrictions for age ($\geqslant$45) and tumour size (preferably smaller than 3.5 cm), and no restrictions for grade and nodal status. At the outset, each centre specified these options in a treatment policy document.

This analysis of the treatment policies includes 1674 patients from 24 centres ransomised until April 2009. The minimum age at entry was specified to be 40, 45/48, and 50 by 2, 8 and 14 centres that randomised 243 (14.5%), 514 (30%) and 917 (55%) patients. However, 1566 (93.5%) of patients randomised were $\geqslant$50; 45−49y = 83 (5%) and 40−44y = 21 (1.25%). 10 (525 patients) centres did not restrict tumour size while 8 (800 patients), 1 (187 patients), 5 (152 patients) centres restricted the size to $\leqslant$2 cm, $\leqslant$2.5 cm, $\leqslant$3 cm. However, 84% patients had tumour size $\leqslant$2 cm and <4% were >3.5 cm. Grade 3 was excluded by only 4 centres (278 (16.6%) patients), but only 13% of all randomised patients had grade 3 cancers.

TARGIT could also be delivered either as a first or second procedure, and 37% more patients were randomised because of this. Furthermore, if patients randomised and given intraoperative radioatherapy were found to be high risk of elsewhere-recurrence (e.g. lobular cancers or EIC or other prespecified features) EBRT could be added within the protocol which essentially tested the two strategies and not techniques. Only 10% patients randomised to IORT received additional EBRT.

Allowing clinicians to be liberal in their intended inclusion criteria increased appeal and encouraged wider participation, yet led to a relatively homogeneous patient sample, demonstrating an unexpected conservatism in this pragmatic trial.

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Accelerated partial breast irradiation (APBI) after breast conserving surgery − early tolerance, dosimetric and volumetric parameters of interstitial multicatheter implant

B. Lange[1], B. Bialas[2], M. Szlag[2], S. Kellas-Sleczka[2], J. Rogozinska-Szczepka[1], B. Lkaszczyk-Widel[1], T.W. Rutkowski[1]. [1]*Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology Gliwice Branch Poland, Department of Radiation Oncology, Gliwice, Poland;* [2]*Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology Gliwice Branch Poland, Department of Brachytherapy, Gliwice, Poland*

Purpose: The aim of the study was to analyze early tolerance and dosimetric and volumetric quality of interstitial multicatheter implant in Accelerated Partial Breast Irradiation (APBI) in select early stage breast cancers following BCT.

Materials/Methods: From May 2006 to October 2009 in Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch 60 patients with preinvasive ductal breast cancer (DCIS − 7 women) or invasive ductal breast cancer (53 women) were selected to prospective Phase II trial. The mean age was 62 years (range 45−80 yrs). All women underwent mammography, usg and MRI for breast to exclude multicentrcity and multifocality. In all cases postoperative specimen histopathology was classified as pT1N0 with a pathologically negative margin (margins from 2 to 15 mm). One patient received adjuvant systemic chemotherapy (AC 4 cycle), the others received adjuvant hormonotherapy. APBI treatment was delivered with High Dose Rate Brachytherapy. Treatment planning was based on CT. Catheters were inserted in local anaesthesia. Median number of catheters 14 (range 10−18). All women received total dose 32 Gy (fractionation dose 4 Gy twice a day, in first and last day only one fraction) in 5 days.

Results: The mean follow-up period from the beginning of treatment was 18 months (range from 7 to 40 months). Median V100 − 91.12 cm^3, median V200 − 9.76 cm^3. D10 and D2 for lung was 18% and 29% referent dose, respectively. Maximal dose on the skin surface was 44.7% (range 19% to 67%).

Early complications: 21 patients (35%) had bruises after catheters implantation and 2 women (3.3%) experienced implant infection (dermatitis) treated with antibiotics. In 6 cases antibiotics were used as a prophylaxis (10%).

Conclusions: Multicatheter HDR APBI, in selected subgroup of patients, has good early tolerance and good dosimetric and volumetric quality of implant. Longer follow-up and randomized trials are necessary.

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Effect of breathing on contralateral breast doses in patients with breast carcinoma receiving radiotherapy

E. Tezcanli[1], E. Goksel[2], M. Garipagaoglu[1], O. Senkesen[2], H. Kucucuk[2], M. Sengoz[1], I. Aslay[3]. [1]*Acibadem University, Radiation Oncology, Istanbul, Turkey;* [2]*Acibadem Kozyatagi Hospital, Radiation Oncology, Istanbul, Turkey;* [3]*Istanbul University Oncology Institute, Radiation Oncology, Istanbul, Turkey*

Background and Purpose: Radiotherapy (RT) for breast cancer results in scattered radiation doses to the contralateral breast which is found to be associated with an increased risk of secondary malignancy. This prospective study investigates the dosimetric and volumetric changes in contralateral breast as a consequence of breathing cycle.

Methods and Patients: Ten patients with left breast carcinoma underwent breast conservative surgery or mastectomy receiving RT (breast or chest wall and regional lymph nodes) are included. All patients were positioned supine on breast board and a body cast was fabricated for shoulder and trunk immobilization. For this study, planning CT (computerized tomography) images were obtained during deep inspiration (I) and end of expiration (E), besides free breathing (FB) in order to simulate the changes during respiratory cycle. CT images were taken in the treatment position on a flat table top for 3 different series: during FB, I and E, with 3 mm intervals. I and E images were registered to FB using rigid bony anatomy references. Targets and contralateral breast volumes were contoured by the same Radiation Oncologist on 3 different image series. Three dimensional conformal or intensity modulated RT planning was done to obtain dose-volume information using 3 different CT series. Treatment plans and dose calculations were constructed using CT images taken during free breathing. Then, plan was exported to I and E image series. No changes in the initial FB scan treatment plan such as gantry angles, number of monitor units delivered per beam were permitted. The significance of dose and volume changes was investigated with "repeated measures ANOVA" test.

Results: Maximum contralateral breast dose to a 2 cc volume was higher for I, then FB and E for all patients. Median values for maximum contralateral breast dose to a 2 cc volume for FB, I and E were 284 cGy (127–1458 cGy), 353.5 cGy (231–5709 cGy) and 294 cGy (137–4264 cGy) respectively ($p = 0.2$). Median values for volume (cc) receiving more than 100 cGy for FB, I and E were 74 cc (14–445 cc), 108 cc (53–650 cc) and 72 cc (17–650 cc), respectively ($p = 0.1$). However, contralateral breast dose and volume variations during breathing were not found to be statistically significant.

Conclusion: Results of this study suggest that there are variations in contralateral breast volume and dose; however these differences are not statistically significant. This can be further investigated especially in left breast cancer patients where contralateral breast dose might be sacrificed in order to limit the dose to heart and its components.

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Prospective trial for Japanese breast cancer patients treated with accelerated hypofractionated whole breast irradiation for breast conserving treatment

Y. Kagami[1], A. Imai[1], M. Morota[1], H. Mayahara[1], Y. Ito[1], M. Sumi[1], J. Itami[1], S. Akashi[2], T. Hojo[2], T. Kinoshita[2]. [1]*National Cancer Center Hospital, Radiation Oncology Division, Tokyo, Japan;* [2]*National Cancer Center Hospital, Breast Surgery Division, Tokyo, Japan*

Background: Randomized controlled trials have demonstrated that breast irradiation after lumpectomy substantially reduces recurrence of cancer in the breast and thereby increases the likelihood of breast conservation. Though there were several trials with hypofractionated whole breast irradiation, few patients enrolled in the trials. In Japan, the most commonly