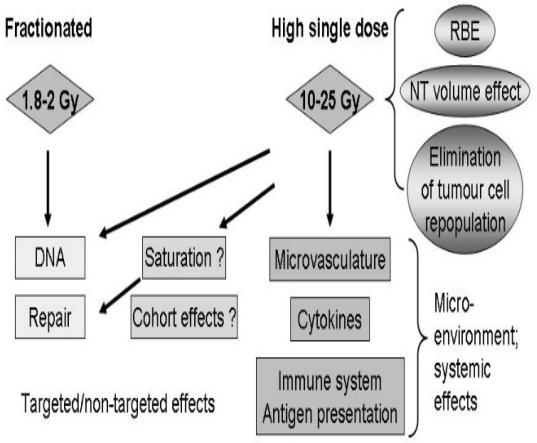


In conclusion, the conventional model of cell inactivation based on *in vitro* survival curves which can be described by the L-Q formalism is being complemented by complex mechanisms involving the cellular radiation response, interaction with other target cells, and the influence of the microenvironment and systemic factors.

**SP-0381**
**Full dose IORT with electrons during breast conserving surgery**
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Abstract not received

**SP-0382**
**Update on TARGIT trial**
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**Background**: In 2010, we reported data on local control and early toxicity for theTARGIT-A trial of intraoperative radiotherapy after lumpectomy for early breastcancer (n = 2232, Vaidya et al, Lancet). Randomisation continued until a totalnumber of 3451 patients were included in June 2012. We present the updatedresults on local control and the first analysis of survival of the wholecohort.
**Methods**: TARGIT-A was a randomised trial in patients >=45 years with invasive ductal carcinoma undergoing breast conserving surgery comparing standard fractionated whole breast EBRT (3-6 weeks) with single dose TARGIT (20 Gy)either given at the time of the primary operation (prepathology stratum) or ina delayed second procedure (post pathology stratum). The experimental arm mandated additional EBRT excluding a boost, if adverse features were detected on final pathology making this a "risk-adapted policy". 3451, 2020 and 1222 patients have a median follow-up of 2.5, 4 and 5 years, respectively. The primary outcome was ipsilateral within breast recurrence (IBR) with an absolute non-inferiority margin of 2.5% at 5 years and secondary outcome was survival.
**Results**: 1721 patients were randomly allocated to receive TARGIT and 1730 to EBRT. Primary events have increased from 13 to 34 since2010. For the primary outcome of ipsilateral breast recurrence, the absolute difference at 5-years was 2.0% (3.3% vs. 1.3%), which was higher with TARGIT; in prepathology the absolute difference in 5-year IBR was 1%; in post pathology it was 3.7%. For the secondary outcome, there was a non-significant trend for improved overall survival with TARGIT (HR = 0.70) due to fewer non-breast cancer deaths (17 vs. 35, HR 0.47).
**Conclusion**: Patients in the TARGIT-A trial have excellent 5 year outcomes (local control > 96%, overall survival >= 94%) in both arms of the trial.

**SP-0383**
**Update on HIOB Trial: hypofractionated WBI plus intraoperative boost (IOERT) in early stage breast cancer**
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**Background:** To assess the role of an intraoperative electron boost (IOERT) in combination with hypofractionated whole breast irradiation (WBI) in terms of in-breast tumor control and cosmeticoutcome.
**Methods:** Starting in Jan 2011, a prospective multi-center single arm trial is conducted by the ISIORT. Patients receive an IOERT boost of 10 Gy ( Dmax 11.1 Gy) followed by a WBI of 40.5 Gy in 15 fractions (2.7 Gy single dose). 5-year in-breast-recurrence rates will be analyzed in 3 different age groups (35-40y, 41-50y, >50y) and tested against the respective best published results from randomized prospective trials by the use of a sequential probability ratio test (SPRT). Acute reactions are assessed by CTC-scoring, late reactions according to LENT-SOMA criteria. Cosmesis is evaluated by a 5-point-Scoring System (van Limbergen, double evaluation) starting prior to WBI on the basis of repeated photodocumentation in standardized positions.
**Results:** As of Jan2013, within six active institutions 327 patients have been recruited, 204 of them already in follow-up. Patient and tumor characteristics are summarized in Table 1.

**Table 1. Patient characteristics**

| Patient age (y) | n | Histology | n |
|---|---|---|---|
| 35-40 | 13 | IDC | 197 |
| 41-50 | 79 | ILC | 26 |
| > 50 | 235 | mixed | 27 |
| | | mucinous | 4 |
| | | tubular | 10 |
| **T-Stage** | | medullary | 1 |
| 0 | 1 | metaplastic | 1 |
| 1 | 219 | | |
| 2 | 44 | **EIC-status** | |
| 3 | 1 | negative | 247 |
| Tx | 1 | positive | 19 |
| | | **Multifocality** | |
| **N- Stage** | | no | 226 |
| 0 | 232 | yes | 40 |
| 1 | 30 | | |
| 2 | 2 | **HER2-status** | |
| X | 2 | neg | 233 |
| | | pos | 33 |
| **Resection status** | | **HR- status** | |
| R0 | 265 | neg | 27 |
| R1 | 1 | pos | 239 |

For IOERT, the median energy chosen was 6 MeV(range 4-12) with median tube diameters of 6 cm (3-8) and mean prescription depths of 20 mm (13.8 SD), resulting in mean D90 volumes of 37 ml.
Perioperatively, no major complications were observed. Four weeks after the end of WBI, 60 patients (29.8%) showed no reactions (CTC 0), 130 patients (66.2%) presented with faint (CTC 1) and eight (4%) with moderate to brisk erythema (CTC 2),respectively. Four to five months after the end of treatment, late reactions according to LENT-SOMA criteria were assessed in 159 patients, all of them scored as grade 0. At one year post WBI, 74 patients still presented as grade 0, one patient as grade 1.
Cosmesis was assessed postoperatively in 217 patients, 159 were evaluated 4-5 months and 75 one year after the end of WBI, respectively. Baseline appearance prior toWBI was scored as excellent (E0) in 31.8/17.5% (patients/doctors), good (E1) in 52/50.4%, moderate (E2) in 14.3/27.6%, bad (E3) in 1.4/4.5% and complication (E4) in 0.5/0%. At 4 months post RT, there was a trend towards better rating: E0: 34.6/21.3%; E1: 51.6/46.9%; E2: 12.6/27.3%,E 3: 1.2/4.5%. Results at 12 months follow-up were similar.
At a median follow-up period of 12 months (3-16), no recurrence was noted.
**Conclusion:** Tolerance of a combined IOERT / hypofractionated WBI regimen is excellent, acute reactions moderate and late reactions insignificant in short-term assessment. With regard to postoperative appearance, early cosmetic results are not impaired. Both tumor control and cosmetic outcome have to be evaluated on long-term follow-up.

**SP-0384**
**IORT Boost: randomised prospective trial**
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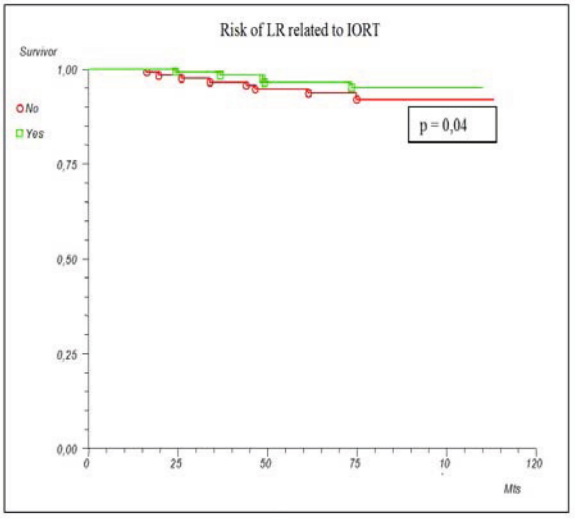
**Purpose:** Many published reports have demonstrated that early stage breast cancer patients need a radiotherapy boost on tumor bed after breast conserving surgery (BCS) and whole breast irradiation. Linac-based IORT boost with electrons was implemented to prevent the contamination with subclinical tumor cells in the vicinity of tumor site, followed by external beam radiotherapy. A IORT boost may allow to reduce the incidence of local recurrence, obtaining good esthetical results compared to external beam boost, due to skin sparing. In addition to whole breast irradiation (WBI), it has yielded excellent long-term results. The aim of this study is to present the long term follow up results on local control, esthetic evaluation and toxicity of a randomized prospective study on early stage breast cancer patients treated with IORT boost of 10 Gy versus the same external beam dose.
**Material and Methods:** A randomized prospective study on IORT versus external beam boost in early breast cancer patients was carried on in our Institution. Primary endpoints of the study were the evaluation of local recurrence(LR), toxicity and cosmetic result.
From April 1999 to April 2004, 244 patients were enrolled: 126 in IORT arm (131 treatments for 5 bilateral) and 118 in no IORT arm. The average age was 49.2 and 50 7 respectively.
Toxicity valuation was assessed using EORTC/RTOG scale. The cosmetic result was detected on five parameters: hyper-pigmentation, telangiectasias, hypertrophic scar, profile asymmetry and difference in consistency.
**Results:** The median follow-up was 130,6 months (range 96-156 months). Ten patients were lost at the follow up. Sixty women (24,6%) were younger than 45 years, 33 in IORT and 27 in no IORT arm. Two and five true local recurrences were observed in IORT and no IORT arm respectively. Both of the IORT arm recurrences were observed at more than 100 months follow up: one of them (in field) was a 62 years old woman, with apT1bN0M0 G2 infiltrating ductal carcinoma (IDC), after 100 months and the other (marginal) was a 56 years old pT1cN0M0 G3 IDC, after 112 months follow up. A third patient presented an ipsilateral out of field recurrence: she was a 72 years old with a pT1cN0M0 G3 IDC, after 120 months follow up. The mean time to recurrence in no IORT group was earlier (55,2 months). One patient was a 46 years old, pre-menopausal, with a pT2N2M0 G3 IDC, after 50 months; one was a 51, pre-menopausal, pT1cN0M0 G3 medullary carcinoma, after 40 months; one patient was 69 pT1cN0M0 G2 IDC after 45 months; one was 67, pT1cN0M0 G3 IDC, after 56 months; the last was a 71 years old woman, pT1cN0M0 G2 infiltrating lobular carcinoma, after 90 months.
No local failures were observed in the group of IORT pre-menopausal women.
As acute toxicity 12 patients developed post-surgical seromas and 7 wound healing problems occurred (7,8%). No late complications associated with IORT were observed, but three cases of liponecrosis in the treatment area. In 5 patients, a secondary mastectomy was performed for tumour multi centricity or excessive intraductal component. Cosmetic result was very good (objective valuation 92,8% good or excellent, subjective valuation 90,2%) and comparable to patients treated with external boost (87,4% good or excellent). The DFS was 89,1% and 86,4% in IORT and no IORT arm, 22 patients developed distant metastasis and 19 died (fourteen of them for disease).
**Conclusion:** Our data suggest that IORT as anticipated boost after breast-conserving surgery can be performed without significant morbidity and it's a reliable alternative to conventional postoperative external beam boost, particularly in younger women, for whom published studies indicate higher risk of local recurrence. The incidence of recurrence with the IORT boost, for any age, including young women, is quite low. Further research is required to clarify several issues such as identification of the most appropriate subgroups of patients for IORT as boost or complete replacement of postoperative radiotherapy.




## DEBATE: DOES THIS HOUSE BELIEVE THAT WE CAN AVOID SURGERY IN RESPONDER RECTAL CANCER PATIENTS?

**SP-0385**
**For the motion: We can avoid surgery in responder rectal cancer patients**
G. Lammering[1], J. Buijsen[1], R.G.P.M. van Stiphout[1], G. Beets[2], R. Beets-Tan[3], V. Valentini[4], P. Lambin[1]
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Chemoradiation (CRT) has been shown to lead to downsizing in an important part of rectal cancers. In 15-20% of cases even a pathological complete response (pCR) occurs. In order to tailor treatment at an earlier stage, predictive models are being developed. Accurate prediction could enable more individualised surgical approaches, including less extensive resection or even a wait-and-see policy. Furthermore, also CRT could be tailored based on tumor response prediction.
In our research groups several response prediction models for rectal cancer have been developed, mainly based on longitudinal PET-imaging, on MR imaging and on multifactorial nomograms including clinical parameters. Furthermore, an innovative method consists of adding CT- based features for pre-treatment response prediction in rectal cancer, the so-called "radiomics" approach. More recently, also biomarkers have been added to the prediction models, since they can add important biological information to the prediction model and can be collected very easily in clinical practice. We conclude that imaging based models and the nomogram developed based on clinical, biological and sequential imaging data can accurately predict tumor response, and can be used as a decision support tool for individualized treatment approaches including surgery avoidance after prospective validation. Inclusion of patients developing a clinical complete remission after chemoradiation in a wait and see protocol helps us further to identify the group of patients in whom surgery can be safely omitted.

**SP-0386**
**Against the motion**
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Abstract not received