Purpose or Objective

Treatment of early stage breast cancer (BC) can be considered as a preference-sensitive care, where decision-making between treatment options can vary according to patient preferences. Typical factors that influence therapy choice in favour of mastectomy include: concerns about cancer recurrence or perceived consequences related to breast conserving surgery (BCT), including potential adverse effects of radiation therapy. Aim of the present study was to compare the oncologic outcome of mastectomy versus breast conserving therapy in patients treated in a modern clinical setting outside of clinical trials.

Material and Methods

Data were provided by the population-based Munich Cancer Registry. Between 1998 and 2014, all female patients diagnosed with early invasive BC (pT1pN0, pT2pN0, pT1pN1 and pT2pN1) and treated at two Breast Care Centres were included in this observational study. For comparison of the standard BCT and mastectomy approaches, we excluded patients with more than 3 positive lymph nodes (pN2) as postmastectomy RT (PMRT) would have been routinely recommended in these high-risk patients.

Results

The final study cohort consisted of 7565 women with a median follow-up of 95.2 months. After adjusting for age, tumour characteristics and therapies, Cox regression analysis for local recurrence-free survival identified BCS with RT as an independent predictor for improved local control (hazard ratio [HR], 1.476; 95% confidence interval [CI], 1.164-1.872, p<0.001) as compared to mastectomy without RT. Ten-year risk of local recurrences was 8.7% following BCS, compared to 14.8% in patients receiving mastectomy (p<0.001). Similarly, lymph node recurrences (10y LNR 2.4% vs 6.7%, p<0.001) and distant metastasis (10y DM 6.8% vs 15.2%, p<0.001) were more frequent in patients undergoing mastectomy only. This translated into an improved survival outcome among patients treated with BCS plus radiotherapy (10-year OS estimates 86.7% vs 77.6%, p<0.001), which was also significant on multivariate analysis (p<0.011).

Conclusion

In conclusion, the present study showed that patients treated with BCS followed by radiotherapy in clinical practice had an improved outcome regarding local control, distant control and overall survival as compared to mastectomy alone in a large cohort reflecting "real-life" clinical practice in this setting.

PV-0045 Is proton therapy a “pro” for breast cancer? A comparison of proton vs. non-proton RT using the NCDB

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Purpose or Objective

There is limited data demonstrating the clinical benefit of proton radiotherapy (PRT) in breast cancer. Here we investigate the impact of PRT on overall survival (OS) and evaluate predictors associated with PRT use for patients with breast cancer in the National Cancer Database (NCDB).

Material and Methods

Women with non-metastatic breast cancer treated with adjuvant radiotherapy from 2004-2014 were identified using the NCDB. Patients were stratified based on receipt of PRT or non-PRT (i.e. photons +/- electrons). A logistic regression model was used to determine predictors for PRT utilization. For OS, Multivariable analysis (MVA) was performed using Cox proportional hazard model. Subset analyses were performed for groups at risk for receiving higher heart dose.

Results

A total of 724,492 women were identified: 871 received PRT and 723,621 received non-PRT. 58.3% of the PRT patients were group stage 0-1. Median follow-up time was 62.2 months. On multivariate logistic analysis, the following factors were found to be significant for receipt of PRT (all p<0.05): academic facility (odds ratio [OR]=2.50); South (OR=2.01) and West (OR=1.43) locations; and mastectomy (OR=1.47); pT2-T4 disease predicted for decrease PRT use (OR=0.79).

PRT was not associated with OS on MVA for all patients: Hazard Ratio: 0.85, p=0.168. PRT remained not significant on MVA after stratifying for subsets likely associated with higher heart radiation doses, including left-sided (p=0.140), inner-quadrant (p=0.173), mastectomy (p=0.095), node positivity (p=0.680), N2-N3 disease (p=0.880), and lymph node irradiation (LNI) (p=0.767).

Conclusion

In this large national multicenter database, we found receipt of PRT to be associated with left-sided, ER+ tumors, mastectomy, South and West location, and academic facilities, but not higher group stages or LNI. PRT was not associated with OS, including in subsets likely at risk for higher heart doses.

In light of the high cost of proton RT, these data question the utilization of PRT, especially in early-stage patients with expected low heart doses, unless enrolled on a clinical trial.

PV-0046 Patient selection for proton therapy of early breast cancer - the DBCG phase II study strategy


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Purpose or Objective
Recently, overall survival gain from radiation therapy (RT) of the internal mammary nodes (IMN) was documented. IMN RT inevitably leads to more radiation dose to heart and lungs, thus often target coverage is compromised to meet constraints for doses to organs at risk (OAR). Here, doses to heart and lung are estimated when target coverage is not compromised in consecutive high-risk breast cancer (BC) patients. The aim is to establish dose cut-off points for selection of patients for proton therapy (PT) in the Danish Breast Cancer Group (DBCG) single-arm phase II trial.

Material and Methods
179 BC patients treated with adjuvant loco-regional RT including the IMN from 18 European departments were included in the study. Each department included 5 patients with left-sided and 5 patients with right-sided BC. The prescription dose ranged from 39.9 Gy to 51.52 Gy in 15 to 28 fractions. Planning techniques included both conformal and several inversely optimized techniques (see Table 1). If the clinically delivered treatment plan did not comply with defined target coverage requirements, the plan was modified retrospectively for this study until sufficient target coverage was reached by allowing OAR constraints to be exceeded. Sufficient target coverage was in this study defined as: V90% ≥ 95% of CTV_IMN, V90% ≥ 95% of CTVn and V95% ≥ 95% of CTVp_breast/chest wall.

Results
Forty percent of the treatment plans needed modification to fulfill the required dose for target coverage. Median mean heart dose (MHD) was 3.0 Gy (range, 1.1-8.2 Gy) for left-sided BC and 1.4 Gy (range, 0.4-11.5 Gy) for rightsided BC. For left-sided BC patients the median MHD was 2.8 Gy (range, 1.1-7.4 Gy) when breath hold (BH) was used (71%) and 5.2 Gy (range, 2.2-8.2 Gy) when no BH was used (29%). Median mean (ipsilateral) lung dose was 13.4 Gy (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy). Median V17Gy/V20Gy (hypofractionated/normofractionated plans) for lung was 31% (range, 5.1-24.9 Gy).
Conclusion
Using thresholds of MHD ≥ 4 Gy and lung V17Gy/V20Gy ≥ 37% in departments using 3DCRT and BH, we estimate that 22% of all the patients requiring loco-regional IMN RT will be eligible for the DBCG phase II PT study.

PV-0047 IMRT versus VMAT for elderly patients with breast cancer: comparison of acute and late toxicities
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Purpose or Objective
To evaluate the differences between conventional fractionated intensity modulated radiotherapy (cIMRT) and hypofractionated (HypoRT) volumetric modulated arc therapy (VMAT) in elderly women affected by early stage Breast Cancer (BC) in terms of RT-related acute and late side effect.

Material and Methods
Between October 2011 and July 2015, 80 consecutive elderly BC patients were treated with cIMRT for 5 weeks (40 patients) or HypoRT-VMAT for 3 weeks (40 patients). Inclusion criteria were: age ≥ 70 years, early stage BC (pT1-2 pN0-1), no prior neoadjuvant chemotherapy and non-metastatic disease. For patients receiving cIMRT or HypoRT-VMAT, a total dose of 50 Gy (25 fractions) or 40.5 Gy (15 fractions) were prescribed to the whole ipsilateral breast, respectively. All patients received a simultaneously integrated boost (SIB) up to a total dose of 60 Gy for cIMRT and 48 Gy for HypoRT-VMAT. Acute and late side effects were evaluated using the RTOG/EORTC radiation morbidity scoring system.

Results
Median follow-up was 45 months. Compliance to treatment was 100% for each RT schedule, without any interruptions. The median age was 75 years (range 70-83). The median PTV breast was 929 cc (range 330-2527). In each group, 90% and 92% of patients received hormone-therapy, respectively. During RT delivery, only low grade acute skin toxicity was observed, with an advantage for the HypoRT-VMAT group; grade 1 in 25 cases (62.5%) of the cIMRT group and 21 cases (52.5%) of the HypoRT-VMAT group (p=0.2); while grade 2 toxicity was reported in 10 cIMRT patients (25%) and 1 HypoRT-VMAT patient (2.5%) (p=0.001). No skin G3 or other side effects were observed at all. Regarding late adverse events, skin toxicity was overall mild without any grade 2 or higher toxicity, but resulted in significantly better outcome for patients treated with HypoRT-VMAT. Grade 1 side effects were reported in 13 cases (32.5%) of the cIMRT group as compared to 2 cases (5%) of the VMAT group (p=0.001). G1 fibrosis was registered in 4 cIMRT (10%) cases and 2 HypoRT-VMAT patients (5%) (p=0.4). No other late toxicities (e.g. pulmonary or arm edema) were observed. In patients treated with cIMRT, only the breast volume >700 cc was statistically associated with acute G2 skin adverse events (p=0.04). In patients receiving Hypo-RT, factors like age or breast volume did not have any influence on the onset of acute or late skin toxicity. No differences in fatigue were observed for the two groups of treatment groups: 11 cIMRT patients vs 16 HypoRT-VMAT (p=0.1).

Conclusion
The present study showed that whole breast cIMRT and HypoRT-VMAT are feasible and well tolerated in early stage BC elderly patients and that HypoRT-VMAT is affected by lower risk of acute and late RT-related side effects.

PV-0048 The Radiosensitivity Index (RSI) predicts for outcomes in triple negative breast cancer
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Purpose or Objective
While genomic biomarkers have been utilized to predict outcomes in ER+ breast cancer, further investigation is needed to develop similar predictors for triple negative breast cancer (TNBC). RSI is a previously validated multi-gene expression index that is thought to be radiotherapy (RT)-specific. Here, we evaluate whether RSI is an RT-specific predictive biomarker in TNBC.

Material and Methods
Prospectively gathered breast tumor samples were identified from an IRB-approved tissue biorepository representing one academic and two community hospitals. Gene expression of tumor samples was assessed with Affymetrix microarray chips and the RSI 10-gene signature was calculated for each sample using the previously published rank-based algorithm. As in prior studies, radiophenotype was determined by dichotomizing at RSI=0.3745, where RSI<0.3745 is radiosensitive (RS) and RSI>0.3745 is radioresistant (RR). Clinical information was obtained by chart review. Endpoints were loco-regional recurrence-free survival (LRFS), distant metastasis-free survival (DMFS), overall survival (OS), and progression-free survival (PFS). Outcomes were estimated with Kaplan Meier (KM) methods and compared with log-rank tests. Associations between characteristics and outcomes were explored with univariable (UVA) and multivariable (MVA) Cox regression.

Results
97 TNBC tumors with available genomic profiling were identified for analysis. The median age was 55 years (range 25-82). 97.9% of tumors were pT1-T2, and 37.1% had positive lymph nodes. 80% of tumors were high grade. 40.2% were treated with mastectomy alone, 14.4% with...