in the COMD was found, from 5.5 mm to 2.9 mm, in favour of the use of a pre-op CE-CT.

Conclusions: With agreement of tumour location in 19 of 20 patients, the tumour visibility on pre-op CE-CT was good.

Using a pre-op CE-CT, an increased CI and a decreased COMD was found, resulting in an improved accuracy of the boost volume delineation.

460   Poster discussion

A Seven-gene Signature Predicting Benefit of Postmastectomy Radiotherapy in High Risk Breast Cancer

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Background: Recommendations for postmastectomy radiotherapy (PMRT) are well established in patients estimated to have a high risk of loco-regional recurrence (LR) (e.g. tumor size >5 cm or $\geqslant$ 4 positive lymph nodes). Large randomized trials, including the DBCG82 trial (Danish Breast Cancer Cooperative Group), have also shown a substantial overall survival benefit after PMRT in patients with low risk of LR (e.g. 1−3 positive nodes), and shown that the largest translation of LR reduction into breast cancer mortality reduction occurs within the most favorable prognosis group. Our hypothesis is that a more refined partitioning of patients likely to benefit from PMRT can be established through identification of genes whose transcription interacts with PMRT to modify the hazard of LR.

Material and Methods: The DBCG82bc cohort constitutes high risk patients (tumor size >5 cm and/or positive lymph nodes and/or invasion in skin or pectoral fascia) diagnosed between1983−89, treated with mastectomy and partial axillary lymph nodes dissection and randomized to +/− PMRT. From 267 DBCG82bc patients, fresh frozen samples histologically verified to contain invasive tumor were available. Whole genome arrays (Applied Biosystem Human Genome Survey Microarray v2.0®, Applied Biosystem, Foster City, USA) were successful in 195 samples. Genes, whose expression levels interacted with PMRT on the association with LR, were identified through a two step Cox Proportional Hazard model with lasso penalty.

Results: Seven genes were identified whose expression interact with the effect of PMRT, and a specialized index was generated based on the expression levels of these genes. Among patients not receiving PMRT, a low index was associated with a significantly higher risk of LR compared to patients with a high index. PMRT significantly reduced the risk of LR in patients with a low index; equalizing the risk to patients with a high index, who showed no LR reduction by PMRT. Among the seven genes, only two were associated with risk of distant metastasis (DM) in patients with 1−3 positive nodes, and yet another gene in the group of patients with $\geqslant$4 positive nodes.

Conclusion: A seven gene-signature attaining prognostic and predictive impact was identified. The gene-signature may provide a method to identify patients expected to benefit from PMRT in terms of LR. The gene-signature is only weakly associated with risk of DM after PMRT in patients who may already have disseminated disease at time of diagnosis.

461   Poster

Clinical Outcomes of Proton Beam Therapy for Accelerated Partial Breast Irradiation

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Background: Previously we reported dosimetric advantage of proton beam therapy for accelerated partial breast irradiation (PB-APBI). Clinical use of PB-APBI for patients with early-stage breast cancer was prospectively evaluated.

Materials and Methods: Thirty-one patients with breast cancer were treated with PB-APBI in a Phase II clinical trial. A total dose of 30 Cobalt Gray Equivalent (CGE) was delivered to the lumpectomy bed in 5 fractions, daily 6 CGE over 5 working days consecutively.

Results: At the median follow-up of 40 months (range, 23−48 months), one ipsilateral axillary lymph node recurrence has been detected. PB-APBI produced acute skin toxicity with moderate erythema in 9 (29%) at 2 months and 4 (13%) patients at 6 months, and among these, 2 patients persistently exhibited moderate hyper-pigmentation at 3 years. Cosmetic outcome judged by physician was good or excellent in 84% of patients before PB-APBI, which gradually changed during follow-up to be 75% and

70% of patients at 2 and 3 years, respectively. The mean the percentage breast retraction assessment index (pBRA) in all patients before PB-APBI (10.5%) and at 3 years (15.5%) significantly differed ($p = 0.02$). Although single field PB-APBI group ($n = 15$) showed significantly worse pBRA at 3 years than at baseline ($p = 0.005$), pBRAs of two field PB-APBI group ($n = 16$) did not change by time ($p = 0.3$).

Conclusions: In addition to dosimetric advantage, PB-APBI with five consecutive fractions achieved in excellent local control in this clinical study of patients with early stage breast cancer. However, relatively high incidence of skin toxicity and worse cosmetic outcome by time are the main factors limiting use of this treatment modality. Modifications of technique such as 3-dimensional proton technique as well as schedule of fractionation and overall treatment time should be explored to avoid skin toxicity and to improve better cosmetic outcome.

462   Poster

Pre Radiotherapy Calcium Scores of Coronary Arteries in Women with Breast Cancer: a Comparative Study

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Background: Breast cancer radiotherapy has been associated with an increased risk of cardiac toxicity. However, no data are available on the probability of developing coronary artery disease (CAD), specifically in the group of breast cancer patients when compared to that of healthy women. Therefore, baseline Coronary Artery Calcium (CAC) scores were determined in a cohort of breast cancer patients (R-cohort) and compared to the CAC scores of a healthy, asymptomatic cohort, the M-cohort. This M-cohort was designed from 2000–2002, to study the prevalence, risk factors and progression of subclinical cardiovascular disease in a population-based sample of 6814 men and women aged 45−84 years [1].

Material and Methods: Eighty consecutive patients with ductal carcinoma in situ or infiltrative breast cancer referred for radiotherapy after breast conserving surgery were included in our study. Their cardiovascular risk-profile was registered and a 64multi-slice CT-scan was performed.

The CAC scores of an unselected (Caucasian only) R-cohort, as well as of those of a selected (co morbidity and race adjusted) R-cohort, were determined. The scores of both R-cohorts were compared to those of the female (Caucasian only) M-cohort.

Results: For the unselected R-cohort ($n = 62$) we found significant ($p < 0.01$) higher scores for women in the age category '55−64' when compared to those of the M-cohort. This becomes apparent in the percentiles of the CAC scores, see table.

Table: Calcium values

Cohort	45−54		55−64		65−74	
	R	M	R	M	R	M
Caucasian, n	11	379	33	356	18	379
25th	0	0	0	0	12	0
50th	0	0	1	0	46	13
75th	0	0	100	16	131	119
90th	7	8	474	102	323	391
95th	8	31	666	209	415	674

In the selected R-cohort ($n = 55$) the CAC scores of the women in the age category '55−64' were significantly ($p = 0.02$) higher when compared to the M-cohort. No significant differences were noted in the other age categories.

Conclusions: The unselected as well as the selected R-cohort revealed, that CAC scores in the age category '55−64' were significantly higher than the CAC scores in the asymptomatic (female) M-population. These data suggest that breast cancer patients bear a higher risk of developing coronary heart disease before the start of radiotherapy. Therefore, measures to (further) decrease cardiac dose in breast cancer radiotherapy are even more important.

References

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