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Purpose or Objective

To analyze the tolerance in the French randomized phase 3 trial (BONBIS) that investigated the role of the boost to the tumor bed after breast-conserving surgery for ductal carcinoma in situ (DCIS).

Material and Methods

From November 2008 to July 2014, 2004 DCIS patients were treated by tumorectomy followed by whole-breast irradiation (WBI) to a dose of 50 Gy in 25 fractions for 5 weeks. Patients were randomized after surgery and before WBI between an additional boost to the primary tumor bed (16 Gy in 8 fractions of 2 Gy, n=1002) and no further treatment (n=1002). Stratification factors were centre, age (below or above 40), hormone therapy (yes or no), histological grade (low or intermediate or high), diagnosis mode (clinically or by mammography), surgical margins (1-2 mm vs 3 mm). Acute toxicities were prospectively recorded from baseline to 3 months after radiotherapy completion.

Results

A total of 1928 DCIS patients were evaluable for acute tolerance. Median age was 57 years. Re-excision was needed in 20% of patients in each treatment arm, mainly due to involved margins or postoperative complications. Median time for radiotherapy initiation was 54 days from surgery [min; max=5; 146]. Mean volumes of breast (CTV1) and of boost (CTV2) were 545 cc [min; max= 6; 2818] and 25 cc [min; max= 0; 754], respectively. A significant higher rate of radiotherapy disruption was observed in boost arm (3.9% vs 1.5%; p=0.015) due to acute toxicities occurrence with a mean time of disruption of 3 days. A significantly higher rate of grade ≥2 overall toxicities (including skin, edema, pain) was observed in the boost arm (54.6% vs 36.4%; p<0.001). Similarly, grade 3 erythema was significantly increased in the boost arm (5.4% vs 2.1%; p<0.001).

Conclusion

In the boost arm, a higher rate of grade ≥2 acute toxicities was observed compared to the control arm. However, grade 3 erythema was quite low even though its occurrence was significantly higher in the boost arm. A multivariate analysis of acute toxicities will be presented at the congress.

OC-0595 Does seroma predict patient-reported adverse effects following breast radiotherapy in IMPORT HIGH?

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Purpose or Objective

Seroma describes collection of serous fluid within a cavity and can occur following breast surgery. A seroma prevalence of 37-57% has been reported. Seroma is associated with adverse effects (AE) following breast radiotherapy. These AE have been predominantly assessed by clinicians and photographs, and not by patients. This study investigates if seroma is associated with patient-reported AE in IMPORT HIGH (CRUK/06/003).

Material and Methods

IMPORT HIGH (ISRCTN47437448) is a randomised, multi-centre phase III trial testing dose-escalated simultaneous integrated boost against sequential boost each delivered by intensity modulated radiotherapy (RT) in women with breast cancer. AE assessment included patient-reported outcome measures (PROMs) in a planned sub-set of patients. A case-control methodology was used to investigate the association of seroma with patient-reported AEs at 3 years. Cases were patients who reported moderate/marked breast appearance change and controls were those who reported none/mild changes. One control was selected at random for each case (unmatched). Seromas were identified on RT CT planning scans and graded as not visible/subtle or visible/highly visible. Logistic regression models were used to test associations between seroma and moderate/marked breast appearance change at 3 years, adjusting for patient and tumour/treatment factors. Tumour and treatment factors were reported by clinicians.

Results

2621 patients were recruited to IMPORT HIGH. 1078/1149 patients at centres participating in the PROMs sub-study consented to PROMs. 836 patients responded to whether they had breast appearance change at 3 years, of whom 231 (28%) patients reported moderate/marked changes (cases); 231 controls were identified. RT CT planning data were available for 202 cases and 205 controls. 156/231 (68%) cases and 148/231 (64%) controls received chemotherapy respectively. Seroma prevalence was 41/202 (20%) in cases and 32/205 (16%) in controls. No significant association was found between visible seroma and moderate/marked breast appearance change [odds ratio 1.38 (95% confidence interval 0.83-2.29), p=0.22] regardless of chemotherapy use. Larger seroma volume was significantly associated with worse breast appearance change on univariate analysis only [1.21 (1.02-1.44), p=0.03]. Treatment group was not significant on univariate analysis. On multivariable analysis, independent risk factors for worse breast appearance change were larger tumour size [1.43 (1.13-1.82), p=0.003], haematoma [5.96 (2.20-16.11), p<0.001], current smoking [2.25 (1.06-4.74), p=0.03] and body image concerns at baseline [1.04 (1.00-1.09), p=0.04].

Conclusion

Seroma prevalence in this study was lower than previously reported, perhaps reflecting the proportion of patients receiving chemotherapy in whom seroma resolves. Seroma was not associated with patient-reported breast appearance change but haematoma was a significant risk factor. Smoking cessation pre-radiotherapy should be encouraged to reduce AE.

OC-0596 Importance of dose to the atherosclerotic plaque in the LAD for cardiac toxicity in breast cancer

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Purpose or Objective

Recent studies have demonstrated a dose-effect relationship between radiation dose to the heart and the risk of an acute coronary event (ACE). However, knowledge on the exact underlying mechanisms behind this radiation-induced cardiac toxicity is lacking. Such information is crucial for the development of new strategies to optimize radiotherapy (RT) treatment planning.

We hypothesized that radiation dose to atherosclerotic plaques leads to subsequent inflammatory reactions and increased risk of ACEs. Thus, dose to the plaques may be a stronger predictor of an ACE after RT than the dose to the left anterior descending coronary artery (LAD). Therefore, the aim of this study was to investigate the association between radiation dose to the LAD and the LAD-plaques and the risk of an ACE in breast cancer (BC) patients treated with 3D conformal radiation therapy.

Material and Methods

The study cohort consisted of 952 BC patients treated with postoperative RT after breast conserving surgery. The LAD was delineated using an auto-segmentation tool. After calculation of the coronary artery calcium score, LAD-plaques with Hounsfield units ≥ 130 were manually delineated. The primary endpoint was the cumulative incidence of an ACE (defined according to Darby *et al.*) 9 years after treatment. For each individual patient, the mean heart dose (MHD), mean dose to the LAD and the mean dose to the LAD-plaques were collected from planning CT scans.

First, the relation between the dose to the LAD and the LAD-plaques and ACEs was analyzed with an univariable Cox-regression analysis. Then, an association analysis using a Cox-regression model was performed, only including patients who had a LAD-plaque. Furthermore, we used a multivariable Cox-regression analysis to calculate the excess risk of an ACE per patient including age, cardiac risk factors (0 or ≥ 1) and mean dose to the heart and LAD-plaques.

Results

The median follow-up time was 7.5 years (range: 0.1-10.1 years). In total, 31 patients developed an ACE during follow-up. 167 patients (17.5%) had a LAD-plaque. Univariable Cox-regression analysis showed that the impact of the dose to the LAD-plaque was much stronger than the impact of the MHD and the mean dose to the LAD (Figure 1). A significant but modest association between radiation dose to the LAD and ACEs was found (regression coefficient 0.053 (95% CI 1.014-1.096), $P=0.008$). However, a much stronger and significant association was found between the mean dose to the LAD-plaques and ACEs (regression coefficient 0.323 (95% CI 1.129-1.689), $P=0.002$). In figure 2, the NTCP-curves are shown for a 50-year old patient in the presence of a cardiac risk factor for ACE.

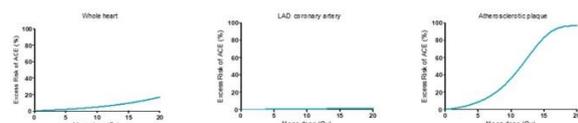


Fig. 1: Univariable Cox-regression analysis for the cumulative incidence of ACEs within the first 9 years after RT

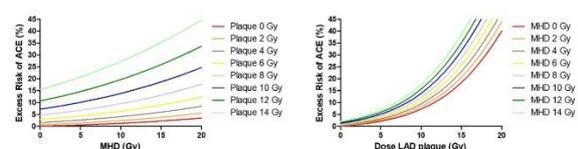


Fig. 2: NTCP-models for the cumulative incidence of ACEs within the first 9 years after RT in a 50-year old patient in the presence of a cardiac risk factor for ACE.

Conclusion

The results of this study suggest that mean dose to the atherosclerotic plaque in the LAD is more important for the development of an ACE in BC patients than the MHD, possibly due to radiation-induced inflammatory reactions in pre-existent plaques. This will be further investigated.

Proffered Papers: CL 12: Proffered papers : Health Economics and Health services research

OC-0597 Implementing a quality indicator project on a national basis: a feasibility study

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Purpose or Objective

Quality indicators (QI) are measurement tools that can be used as guides to evaluate and improve overall quality of patient care. Monitoring QIs amongst departments allows for clinical practice benchmarking leading to exchange of best practice and the delivery of best-quality care. Mandated by the Belgian Federal Government, radiotherapy (RT) specific structural, process and outcome indicators were defined in a collaboration of the College for Physicians in Radiation Oncology (RO) in Belgium and the Belgian Quality Managers (QM) in radiotherapy Association (QMRT.be). Subsequently, a voluntary national QI data collection started, with the aim of generating benchmarking reports and supporting departmental and national quality improvement projects.

Material and Methods

The QI were defined through a simplified Delphi approach by a panel of RO, QM and medical physics experts following the national requirement to collect quantitative data annually (e.g. number of treatments) but also based on established guidelines or good practice. As such, 18 structural (e.g. number of equipment and treatment activities), 30 process (e.g. timely delivery) and 6 outcome QIs (recorded acute toxicity related to treatment for breast, head-and-neck and prostate cancer patients) have been defined. To evaluate the feasibility of data collection in all Belgian RT departments, a test phase was launched in 2015, collecting the full set of structural QIs, but limiting the number of patient-specific QIs (n=5 per pathology/department). Upon validation of this dummy run, as of 2016, a broader capture of process and outcome QIs was started (n=25 patients/pathology/department).

Results

A high department participation rate to this national QI project was obtained, with 100% of departments participating in 2015 and 2016 and 92% in 2017. This success rate is highly attributed to the presence of QM in each RT department. Over the 3 year-period, 33.993 data points were collected contributing to the establishment of the 54 QIs. The analysis of the collected QIs gave insight into national activity levels, resource availability, clinical practice and acute toxicity levels. This resulted in a yearly global report but also in the generation of individualized benchmarking documents in which each department is able to identify its performance as compared to other departments which are anonymously identified (see fig 1).