

## 2674

**Real-Life Impact of Hypofractionated IMRT in Early Breast Cancer on Cardiovascular Risk**

A.A. Diaz-Gavela,<sup>1,2</sup> E. del Cerro,<sup>1,2</sup> F. Counago,<sup>3</sup> S. Sanchez,<sup>4</sup> C. Andreu,<sup>1</sup> I.J. Thuissard,<sup>1</sup> L. Guerrero,<sup>4</sup> M. Pena,<sup>1,2</sup> V. Duque-Santana,<sup>1,2</sup> Y. Molina,<sup>5</sup> and D. Sanz-Rosa<sup>1</sup>; <sup>1</sup>Medicine Department, School of Biomedical Sciences, Universidad Europea, Madrid, Spain, <sup>2</sup>Quironsalud Madrid University Hospital. Radiation Therapy Department, Madrid, Spain, <sup>3</sup>San Francisco de Asís and La Milagrosa Hospitals. National Chair of Research. GenesisCare Spain, Madrid, Spain, <sup>4</sup>La Luz Hospital. Radiation Therapy Department, Madrid, Spain, <sup>5</sup>Hospital Quironsalud Madrid. Radiophysics Department, Madrid, Spain

**Purpose/Objective(s):** Various meta-analyses and studies based on historical registries have shown an excess of mortality and significant cardiovascular (CV) morbidity in breast cancer (BC) patients who receive adjuvant radiotherapy (RT) on the left side. However, these patients were treated with obsolete RT techniques, with conventional fractionation and without a precise knowledge of the heart dose-volume histograms (DVH) or CV-risk factors. We now know that the use of ultra-conformal techniques (IMRT) has led to a significant decrease in the heart dose, as reflected in the DVHs. In parallel, hypofractionated protocols -which result in lower EQD2 in organs at risk- have become the standard of care. The aim of our study was to assess whether the combination of both could reduce CV events compared to historical series and to identify clinical or dosimetric factors that could have a negative impact.

**Materials/Methods:** All BC patients at our institution who received hypofractionated (40.05Gy/15sessions) adjuvant forward-planned IMRT after conserving surgery were included. Patients in indication for elective lymph node RT and those who had received previous mediastinal RT were excluded.

**Results:** 882 patients with invasive BC or DCIS were analyzed (450 right breast; 432 left). After a median follow-up of 8ys (maximum 14), 35 CV events were identified (5 myocardial infarction/angina, 20 arrhythmias, 2 severe valvular disease and 7 "other non-ischemic"). No statistically significant differences were observed according to breast laterality ( $P=0.15$ ). With regard to heart DVHs, none of those analyzed had a deleterious effect, although there was a slight and progressive trend towards statistical significance (Table). Patient-dependent CV risk factors that were found to have a significant impact on the incidence of late CV events were dyslipidemia, hypertension, family history of heart disease and overweight/obesity ( $P=0.03$ ,  $<0.001$ ,  $<0.001$  and  $0.02$  respectively).

**Conclusion:** Although the deleterious impact of thoracic RT on CV late events is well known, in our cohort it has been shown to be less determinant than patient-dependent baseline risk factors for any CV event. Further long-term follow-up will be necessary to determine whether these results are sustained over time and, if event curves continue to diverge, to assess the extent to which they do so. On the other hand, a precise understanding of the impact of CV risk factors may help to design targeted primary prevention strategies from which BC patients may benefit.

Abstract 2674 – Table 1

Long term cardiac toxicity			
Heart DVH (median [ICR])	Yes (n = 35)	No (n = 847)	P value
V16 <sup>1</sup>	0 [0.28]	0 [1.12]	0.88
V8 <sup>1</sup>	0 [0.64]	0 [1.72]	0.086
V1 <sup>1</sup>	4.32 [12.49]	7.48 [13.65]	0.070
V0.5 <sup>1</sup>	11.93 [17.54]	17.30 [18.22]	0.069
Dmax*	4.08 [33.4]	7.12 [35.32]	0.054
D2*	2.12 [5.20]	2.52 [20]	0.128
Dmed*	0.60 [1.32]	0.68 [1.64]	0.391

<sup>1</sup> % of the heart who receives 16, 8, 1 and 0.5Gy respectively; \* Expressed in Gy; DVH: dose-volume histograms; ICR: Interquartile range. Dmax: Maximum heart dose; Dmed: Mean heart dose.

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**Prospective Evaluation of Acute Toxicity from Tumor Bed Boost Following Whole Breast Radiotherapy**

M.P. Dykstra,<sup>1</sup> K. Griffith,<sup>2</sup> A. Moncion,<sup>1</sup> M. Grubb,<sup>1</sup> R. Marsh,<sup>1</sup> M. Mietzel,<sup>1</sup> F.A. Vicini,<sup>3</sup> and L.J. Pierce<sup>1</sup>; <sup>1</sup>Department of Radiation Oncology, University of Michigan, Ann Arbor, MI, <sup>2</sup>Department of Biostatistics, University of Michigan, Ann Arbor, MI, <sup>3</sup>MHP Radiation Oncology Institute/GenesisCare, Farmington Hills, MI

**Purpose/Objective(s):** Tumor bed boost improves local control following whole breast radiotherapy (WBRT) for women with invasive cancer or ductal carcinoma in situ (DCIS) with high-risk features. However, tumor bed boost is also associated with more toxicity. We sought to evaluate acute toxicity associated with boost based on conventional (CF) vs moderate hypofractionation (MH) among women receiving WBRT using real world data.

**Materials/Methods:** This analysis includes women who underwent definitive WBRT without regional nodal irradiation for invasive carcinoma or DCIS, prospectively enrolled from 2012 to November 2023 at 27 radiation oncology centers in a state-wide quality consortium. Standardized patient, physician, and physicist forms were used to collect baseline and follow-up information. Acute toxicity evaluation included patient- and physician-reported outcomes at treatment end. A severe toxicity composite variable included patient- or physician-reported breast pain or moist desquamation. Multivariable models were used to find associations between boost and toxicity outcomes, accounting for relevant clinical characteristics and treatment planning techniques including use of a photon vs electron boost, stratified by fractionation scheme.

**Results:** Full clinical and treatment data were available for 15,711 women. MH was more common than CF (74.9% vs 25.1%). Boost use was less common with MH compared to CF, 71.1% vs 94.0% ( $P<0.001$ ). Of those receiving boost, photon (PB) and electron boost (EB) were used in 69.0% and 31.0% of women receiving MH and 58.7% and 41.3% of those receiving CF, respectively. Both PB and EB were associated with increased composite severe toxicity following MH, 26.3% and 19.5% vs 12.2% for no boost, respectively (OR 2.11 and 1.79,  $P < 0.001$ ), but not following CF (44.0% and 34.1% vs 47.4% for no boost, OR 0.92 and 0.78,  $P=0.16$ ). PB and EB worsened patient-reported moderate to severe breast pain following MH, 24.5% and 19.4% vs 13.6% (OR 1.62 and 1.36,  $P < 0.001$ ), but not CF (32.2% and 25.5% vs 35.9%, OR 0.90 and 0.72,  $P=0.03$ ). Physician-reported breast pain showed a similar trend, with 8.0% and 6.4% vs 3.2% (OR 1.91 and 1.95,  $P < 0.001$ ) following MH, and 15.0% and 10.7% vs 13.1% (OR 1.29 and 1.02,  $P=0.11$ ) after CF. Neither PB nor EB worsened severe fatigue in MH (24.0% and 21.5% vs 19.9%, OR 1.17 and 1.14,  $P=0.12$ ) or in CF (32.2% and 28.2% vs 34.7%, OR 0.79 and 0.79,  $P=0.47$ ). Physician-reported dermatitis was worse with PB and EB for both fractionation schemes: 28.9% and 24.3% vs 13.0% (OR 2.39 and 2.14,  $P < 0.001$ ) after MH and 48.9% and 44.4% vs 40.0% (OR 1.54 and 1.56,  $P < 0.001$ ) with CF.

**Conclusion:** Following MH, boost is associated with increased acute toxicity. CF led to more pronounced acute toxicity than MH, but boost is associated with less added toxicity. These data may help shared decision making when discussing the relative benefits of adding a boost following MH or CF.

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