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Title: The REQUITE-AB study: Validating predictive models and biomarkers of radiotherapy toxicity to reduce side-effects and improve quality of life in breast cancer patients

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Body: Clinically significant side-effects from radiotherapy affect around a quarter of breast cancer patients and may impact considerably on outcomes from treatment. An increasing number of replicated genetic associations for radiotherapy toxicity are being reported[1],[2]. The international REQUITE consortium aims to validate genetic markers and clinical factors implicated in radiotoxicity. The purpose of the REQUITE-AB project is to develop an integrated set of predictors for acute radiotherapy side-effects in breast cancer patients to be used as a clinical decision-making tool.

As part of the REQUITE prospective cohort study, 2,000 patients eligible for adjuvant breast radiotherapy will be recruited in nine centres across Europe and North America between April 2014 and August 2016, with centralised data management, biobanking and two years' follow-up using a standardised data collection protocol. Patient characteristics and treatment details being captured also include dose-volume histograms and DICOM files. Genotyping will take place in fall 2016. Primary endpoints are acute skin toxicity (CTC-AE v4.0) and quality-of-life (QoL) on completion of radiotherapy and at 3 months from start of radiotherapy. Secondary endpoints are late side-effects including change in breast appearance.

1,766 breast cancer patients have been recruited to date with standardized documentation of toxicity and QoL. Among patients who completed radiotherapy so far, 21.6% of patients developed grade 2 skin toxicity (brisk erythema) and 1.3% grade 3 (moist desquamation). The ability of patient, treatment and genetic variables to predict clinical outcomes and QoL will be examined. The REQUITE study includes the largest radiogenomics cohort of breast cancer patients to date recruited under a single standardised protocol. Findings of the REQUITE-AB project are likely to inform the development of interventional biomarker trials and personalise breast cancer care in the future.

[1] Talbot et al, *Br J Cancer*, 2012; 107: 748-53.

[2] Seibold et al, *Int J Radiat Oncol Biol Phys*, 2015; 92: 1084-92.