

THE REQUITE PROJECT: Validating predictive models and biomarkers of radiotherapy toxicity to reduce side-effects and improve quality-of-life in cancer survivors

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Recently the first replicated genetic associations and GWAS for adverse reactions to radiotherapy have been reported. These will help to build predictive statistical models for optimising radiotherapy delivery or interventions to alleviate the side effects. It is now important to validate known predictors of adverse reactions and develop the statistical models to become clinically useful. The REQUITE project is a European Union funded FP7 project that aims to do this.

REQUITE's objectives:

1. Perform a multi-centre, cohort study collecting: blood samples, epidemiology and treatment data, longitudinal side-effect and QOL data (before and after treatment, years 1 & 2).
2. Produce a centralised biobank of DNA from 5,300 patients with centralised data management.
3. Validate published biomarkers of radiosensitivity.
4. Validate clinical predictors of radiotherapy toxicity in breast, prostate and lung cancer and incorporate biomarker data.
5. Design interventional trials to reduce long-term side-effects.
6. Provide a resource for dissemination and exploitation to the radiotherapy community.

REQUITE is funded for 60 months from October 2013 and organised into seven work packages. WP1 is responsible for overall management and scientific oversight run by Manchester. The central activity of the project is a multi-centre, observational study organised through WP2, led by DKFZ. Enrolment began in April 2014 and will proceed for 2 years in nine clinical centres, with 2 years follow-up. Current recruitment has exceeded 1400 patients. The primary endpoints are change in breast appearance; rectal bleeding (prostate); pneumonitis (lung). The integrated database has been designed at Leicester. Blood samples are being collected before radiotherapy. Tracking, biobanking and DNA preparation is handled in WP3 at CIGMR in Manchester. Validation of biomarkers (genetic markers and apoptosis assays) as predictive factors is being carried out in WP4 led by Leicester. Preliminary work has reduced inter-laboratory variation in the FACS-based apoptosis assay between Leicester, Mannheim and Montpellier. The assay is now being carried out on all samples collected through the three centres. The data will establish whether the assay can be used as a standard test to predict radiotherapy toxicity. In WP5 Gent is leading in validating published models in existing cohorts, leading to replicated models that can be validated using the REQUITE cohorts. In WP6 Leuven will use the predictive models to design clinical interventional trials and produce protocols that seek to lower radiotherapy side-effects in those individuals at high risk of developing them without affecting tumour control. Dissemination and Outreach is being co-ordinated through WP7 led by MAASTRO.