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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INTRODUCTION

Recently the first replicated genetic associations for adverse reactions to radiotherapy were reported. Predictive clinical models for radiotherapy side effects are also being developed. It is now timely to start a project that aims to validate known clinical and genetic predictors of adverse reactions and develop the statistical models for clinical use. REQUITE is a European Union funded FP7 project aiming to validate clinical models and biomarkers of radiotherapy toxicity and design future trials using the models.

OBJECTIVES

1. Perform a multi-centre, cohort study collecting: blood samples, epidemiology and treatment data, and longitudinal side-effect and quality-of-life data (before and after treatment, years 1 & 2) in 5,300 patients with prostate, breast or lung cancer.
2. Produce a centralised biobank of DNA and a centralised database including radiotherapy plans
3. Validate published biomarkers of radiosensitivity – genetic and apoptosis assays
4. Validate clinical predictive models 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.

WORK FLOW
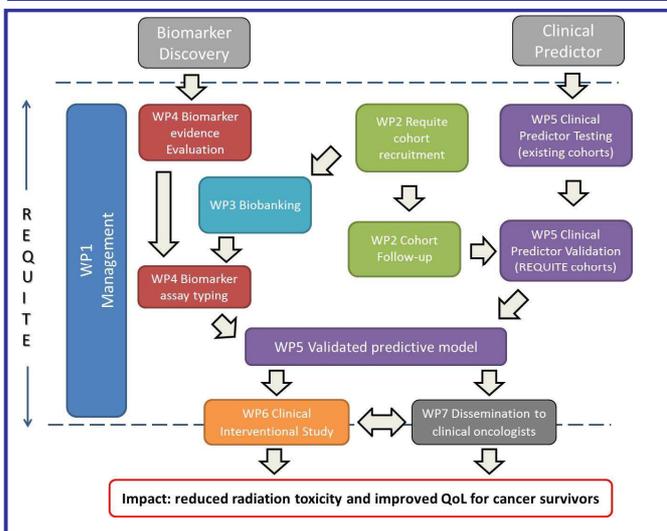
CURRENT STATUS

- Standardised data collection forms and validated patient reported toxicity questionnaires were developed, with responses stored in an online centralised database alongside treatment planning and physics data.
- Questionnaires were translated into multiple languages then back translated to check for consistency, and finally tested in small cohorts of patients for acceptability. These are available for use by other research groups at our website: www.requite.eu.
- By May 2016 >3,600 patients recruited (68% of target); with DNA extracted from >2,000 blood samples ready for genotyping to start in September 2016. Apoptosis assay carried out on >1,090 patients (109% of revised target)
- Undertaken clinical prediction modelling of normal tissue toxicity in radiation therapy.

BIOMARKERS

- ~5,300 samples will be genotyped for SNPs and CNVs associated with radiotherapy toxicity.
- ~1,800 samples will be assayed for radiation-induced lymphocyte apoptosis using FACS analysis.

TIMESCALE

Project start	Oct 2013
Recruitment starts	Apr 2014
Recruitment ends	Mar 2017
Follow-up ends	Mar 2018
Project complete	Sep 2018

PATIENT ADVISORY GROUP

- Four international patient representatives actively engaged with cancer research and patient communities.
- Participate in bi-monthly dissemination meetings and attend annual meetings to provide ongoing feedback and ensure patient views are fully considered throughout the research process.
- Provide valuable input and practical advice on design and accessibility of the website (www.requite.eu).
- Collaborated on the development of the study documentation set including protocol, consent form, patient information sheet and toxicity questionnaires.
- Review (alongside the steering committee) associated sub-studies that aim to answer additional research questions beyond the original scope of the project.

PARTNERS
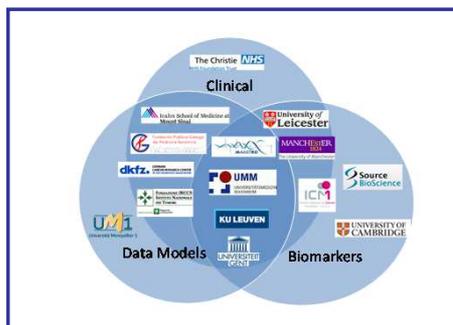
KICK OFF MEETING

SUMMARY

- REQUITE has developed standardised data collection forms including questionnaires for collecting patient reported CTCAE toxicity in multiple languages. These forms are freely available via the website to improve the standardisation of data collection in other studies.
- The REQUITE project will develop and validate statistical models incorporating biomarker data to predict radiotherapy side effects. Future interventional trials will use these models to help optimise radiotherapy.
- The project welcomes collaborations that add value to the project, particularly additional datasets for validating clinical models.

REQUTE
Validating Predictive Models and Biomarkers of Radiotherapy Toxicity to Reduce Side-Effects and Improve Quality-of-Life in Cancer Survivors