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The REQUITE project: integrating biomarkers and clinical predictors of radiotherapy side effects

Biography

Dr Christopher Talbot is a Senior Lecturer in Medical Genetics at the University of Leicester. He has been involved in researching radiotherapy toxicity since 2008, working closely with Prof Paul Symonds. In that time the group has been involved in Radiogenomics and researching other predictive factors. Dr Talbot initiated the EU-funded REQUITE project, which is co-ordinated by Prof Catharine West. He is Honorary Secretary of the Association for Radiation Research.

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Abstract text

The European Union funded REQUITE consortium aims to validate predictors of radiotherapy-related adverse reactions to develop clinically useful tools. Potential predictors include clinical and dose parameters, genetic markers, gene expression and the radiation-induced lymphocyte apoptosis (RILA).

REQUITE is a multi-centre, observational study (www.requite.eu). Enrolment was open for two and a half years through 10 hub centres (nine in Europe and one in the United States) each collecting through multiple hospitals. Follow-up is being collected for two years ending in September 2018. The primary endpoints are change in breast appearance at 24 months (breast), rectal bleeding at 24 months (prostate) and breathlessness at 12 months (lung). 4442 patients have been enrolled in REQUITE: 2071 breast, 562 lung and 1809 prostate cancer patients. In addition a further 383 lung cancer patients from another study have been integrated. All the patient data is held in a central database, including clinical, treatment, CTCAE scored toxicity, patient-reported outcomes, DVH & DICOM and biomarkers. All blood samples are held in the CIGMR Biobank at the University of Manchester.

All patients who complete the study are being SNP genotyped using Infinium OncoArrays, which tests for ~250,000 genome-wide SNPs and a similar number of cancer-specific SNPs, including some chosen from

Radiogenomics studies. RILA was carried out in three of the European centres using a standardised protocol; it assesses the percentage radiation-induced apoptosis in lymphocytes, detected by flow cytometry, 48 hours after ex-vivo irradiation of whole blood. 1322 samples have been analysed using the apoptosis assay. The levels of apoptosis 48 hours after ex-vivo irradiation increase over baseline in a range from 2.4% to 62.4%, confirming large inter-patient variability. Factors that affect RILA have been identified, including cancer type and smoking status. Preliminary analysis has been carried out of acute toxicity data. A pilot RNA sequencing experiment has been carried out using 50 lung cancer cases to identify differentially expressed transcripts as potential predictors.

18 sub-studies have been approved for use of the REQUITE data and/or samples to address a number of important questions e.g. the role of mitochondrial DNA, circadian rhythm effects, effect of integral dose on fatigue, modelling of the α/β ratio for prostate toxicity, exploring patient attitudes to predictive testing.

This large scale prospective observational study will be the largest to date to assess the use of predictive biomarkers for assessing radiotherapy related toxicity.