Predicting acute radiotherapy side-effects in breast cancer

Using precision medicine to improve patient care

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Cancer survivorship
- Over 80% of women now survive breast cancer long-term (10 years).
- Patients may live many years with side-effects (toxicity) of their treatment.

Radiotherapy side-effects
- After breast-conserving surgery (lumpectomy), radiotherapy (RT) is used to treat the breast in the majority of patients.
- The severity of RT side-effects varies between patients, but 20-25% of patients will experience significant breast skin breakdown (acute toxicity).
- This may interfere with onco-plastic procedures increasingly used by surgeons, affecting cosmetic outcome and quality of life.

Predicting radio-toxicity
- Different factors have been investigated but at present the severity of side-effects cannot be predicted with certainty.

Radiogenomics is an area of precision medicine studying the association of genetic variation, usually single nucleotide polymorphisms (SNP), with response to RT.
- A SNP is a variation in a single nucleotide of DNA at a specific position in the genome, present in a proportion of the population.

Developing a predictive statistical model
1. I developed the predictive statistical model in existing radiogenomics RGC cohorts.
2. I recruited 350 breast cancer patients undergoing RT in Leicester as part of the REQUITE prospective cohort study, taking blood samples for genotyping (see Table).
3. I validated the predictive statistical model in the REQUITE breast cohort and examined the effect of adding genetic markers (SNPs) on model performance.

Predictive test for acute toxicity
- Final model to predict ≥ 1 acute desquamation:
  - Age
  - Age # BED*
  - BP_CVD # age
  - BED*
- BED = biologically effective dose, # interaction term

Calibration plot showing actual vs. predicted probability in the REQUITE cohort.

Qualitative study
I also conducted 21 semi-structured interviews with Leicester REQUITE breast cancer patients to explore attitudes towards future radiogenomics testing for breast radio-toxicity.

Conclusions
- A predictive radiogenomics test for acute breast toxicity has the potential to personalise breast cancer care. In the future, this could be tailored towards different endpoints, e.g. pain, fibrosis (scarring).
- Patients have the confidence in a predictive radiogenomics test, but would prefer the result to be provided to healthcare professionals. Except in cases of significant chronic side-effects, advance knowledge of their toxicity risk is unlikely to influence personal treatment decision-making.