

VORTEX-BIOBANK

Prospective Sample Collection for the VORTEX Randomised Radiotherapy Trial in Patients with Extremity Soft Tissue Sarcoma

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INTRODUCTION

- Soft tissue sarcoma accounts for ~1% of adult cancers with ~1200 cases in the UK per annum
- Primary treatment is surgery with an adequate margin followed by adjuvant radiotherapy (XRT)



- Current standard treatment results in:
 - >80% local control
 - ~50% overall survival
- Most patients die of metastatic disease
- Tumour oxygenation status is an adverse prognostic factor for survival and predicts for the likelihood of distant metastases in sarcoma patients (Brizel *et al.* *Cancer Res.* 1996;56:941-943, Nordmark *et al.* *BJC* 2001;84:1070-1075)

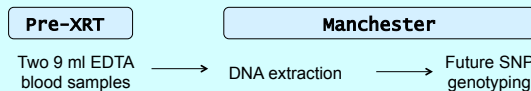
TRANSLATIONAL HYPOTHESES

- The development of a pre-treatment tumour molecular profile will help define patients with a high risk of failure following surgery and post-operative XRT
- The profile could be used to identify patients who might benefit from adjuvant systemic therapy with a hypoxia modifying agent
- There is an association between common genetic variation, reported by single nucleotide polymorphisms (SNPs) in relevant candidate genes, and individual patient variability in normal tissue radiation toxicity

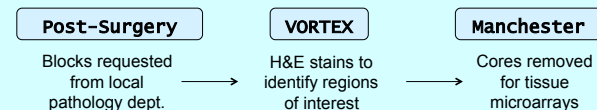
PATIENTS & LOGISTICS

- VORTEX-BIOBANK is multi-centre study funded by Cancer Research UK (TRICC).
- Co-ordinated from The University of Manchester, Christie Hospital
- Planned recruitment: 400 patients (from the VORTEX trial)
- To date: 121 people have registered to VORTEX; 98 have gifted tissue and/or blood samples to the VORTEX-BIOBANK
- Centres currently recruiting:
 - Queen Elizabeth Hospital
 - The Christie
 - UCL Hospital
 - Weston Park Hospital
 - Cheltenham General
 - Glan Clwyd
 - Royal Marsden Hospital
 - Manchester Royal Infirmary
 - Royal Orthopaedic Hospital
 - Robert Jones & Agnes Hunt
 - Royal National Orthopaedic Hospital
 - Western Infirmary
 - Nottingham City Hospital
 - Bristol Haematology & Oncology
 - St. James's University Hospital
 - University Hospital Leicester
- Kits are provided that contain all the necessary materials for preserving and transporting tissue and blood samples

1. BLOOD SAMPLE COLLECTION



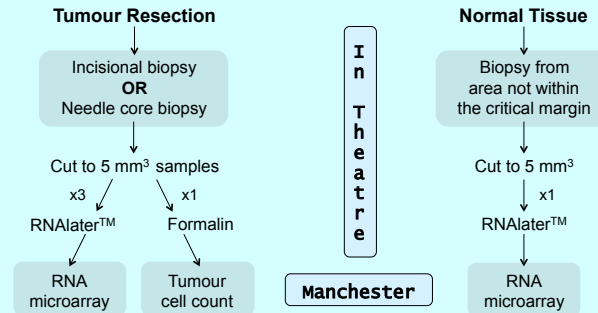
2. PARAFFIN TISSUE BLOCK COLLECTION



COLLABORATORS

Dr. Anna Cassoni; Mr. Rob Pollock; Dr. James Wylie; Dr. Charles Candish; Dr. Simon Gollins; Dr. Michael Sokal; Dr. Paula Wilson; Dr. Fiona Cowie; Dr. Frank Saran; Mr. John Skinner; Mr. Lee Jeys; Mr. Simon Carter; Dr. Claire Joynson; Zoe Wood; Liz Mollo; Andrea Hughes; Chris Ford; James Swinscoe; Gillian Brown; Catrina Forde; Anita Immanuel; Caroline Pemberton; Liz Andrzejewski; Galina Petrikova; Annette Bolger; Cathryn Leng; Anna Grier;

3. FRESH TISSUE SAMPLE COLLECTION

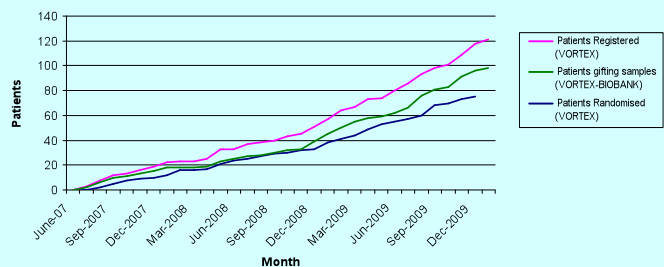


Biopsy samples should be taken in theatre following resection. Delaying sampling until pathology can cause tissue degradation.

SAMPLES RECEIVED TO DATE

- Fresh tumour & normal tissue: 91 samples
- Paraffin-embedded tissue: 23 blocks
- EDTA blood: 73 samples
- At least one sample is collected from >80% of patients registered to VORTEX

VORTEX Recruitment



TISSUE EXTRACTION RESULTS

- RNA has been extracted from over 75 tumour samples. The following indicate average values:
 - RNA concentration: 441 ng/µl
 - Total yield: 18.62 µg
 - RIN (RNA Integrity Number): 7.50
 - 260/230 ratio: 1.60
 - 260/280 ratio: 1.97
- Where high quality samples should have:
 - RIN > 6
 - 260/230 > 1.5
 - 260/280 > 2
- 260/230 ratio is an indicator of contaminants; 260/280 ratio indicates purity of the nucleic acid
- Phenol/chloroform or Trizol+ extractions were used

FUTURE

- Patients with a hypoxia associated tumour molecular profile could be selected for standard treatment plus a hypoxia modifying agent
- A link between the common genetic variation and normal tissue sensitivity could be used to predict response to radiotherapy and allow individualisation of radiation dose