CHRC

Centre for Health Effects of Radiological and Chemical Agents

Annual Report 2019 - 2020

The Nuclear Community Charity Fund

Making that difference

Brunel University London

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Background

The British Government undertook a series of atmospheric nuclear weapons tests at various sites in Australia and the South Pacific between 1952 and 1958. Associated with these tests was an experimental programme in which radioactivity was dispersed into the environment, this programme ended in 1963 although operations continued through to 1967. Additionally, UK personnel participated in a series of American tests based at Christmas Island in 1962. It is estimated that over 20,000 UK servicemen participated in at least one of these British and American tests.

An ongoing concern within the nuclear test community has been whether veterans of these programmes could have received sufficient radiation exposure to adversely affect their health. This concern extends to whether they might also have passed on genetic alterations to their children, thereby potentially affecting their family's health.

Who are we?

The Centre for Health Effects of Radiological and Chemical Agents (CHRC) was established in September 2017, funded by the Nuclear Community Charity Fund (NCCF) through funds received by the Armed Forces Covenant Aged Veterans Fund and Brunel University London.

Figure 1: A number of CHRC staff, students and Advisory Board members.

Our purpose is the generation, promotion and integration of new, multi-disciplinary research that is particular to the British nuclear test veteran community, their genomic health and the impact of uncertainty on health more broadly. Our work is also investigating other scenarios in which people may be exposed to radiation and chemicals such as in the workplace or as a medical treatment.

Our aim is to build to become a credible, independent, evidence-based source of information for interested test veteran, scientific, health professional and political communities.

CHRC Affiliates and Governance Bodies

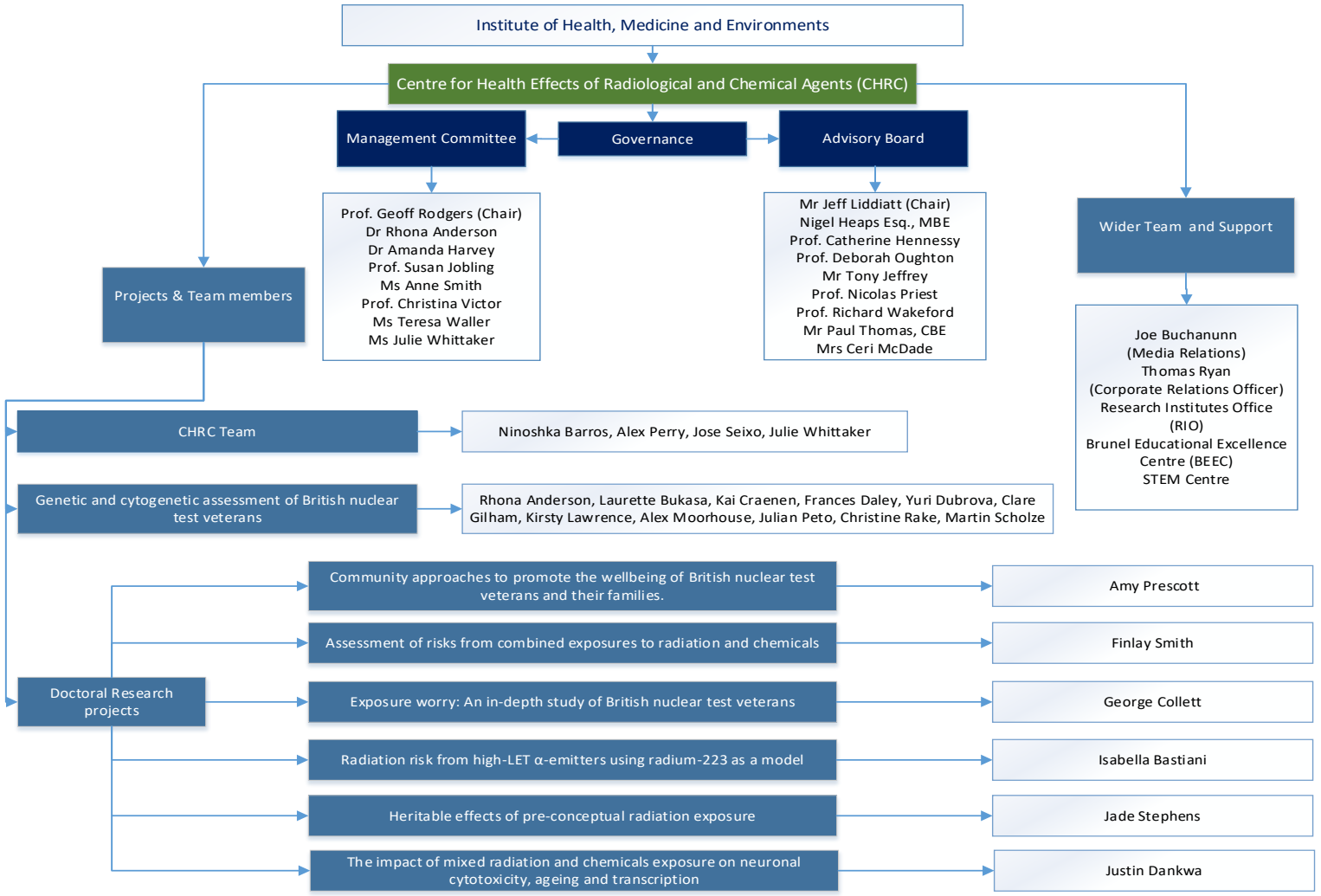


Figure 2: CHRC Affiliates and Governance Bodies

CHRC multi-disciplinary research

The CHRC sits within the Institute of Health, Medicine and Environments and, College of Health, Medicine and Life Sciences at Brunel University London. Our work exploring the human health impact of radiological and chemical agents is organised as disciplinary projects (Figure 2) within a network of interdisciplinary and inter-institutional collaboration. These can be grouped broadly as (1) Genetic markers of radiation exposure (2) Understanding health risks of exposures (3) Health and Wellbeing and, (4) Education and Engagement.

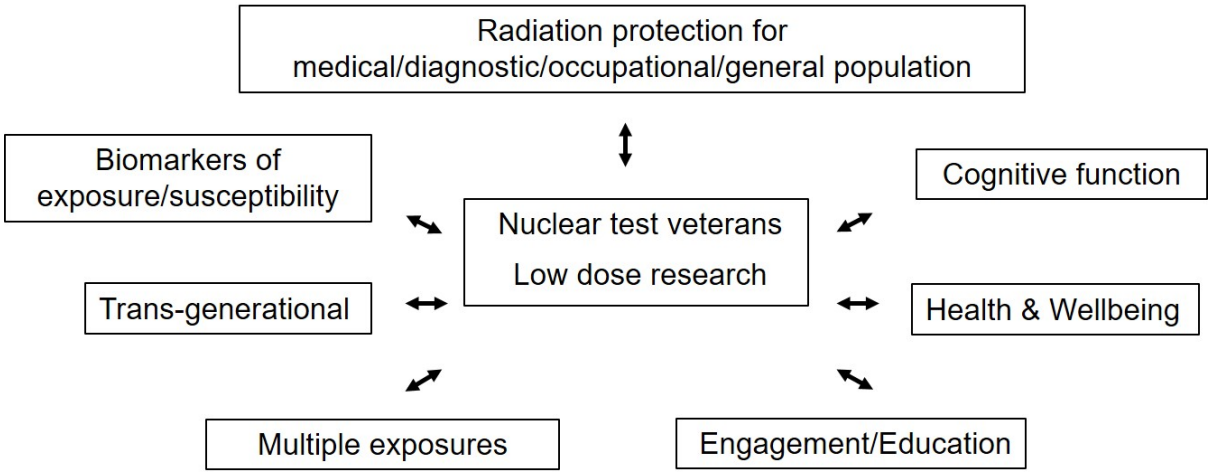


Figure 3: Current project areas exploring the human health impact of radiological and chemical agents.

The following section provides an overview of our current research activities.

1. Genetic markers of radiation exposure

The major component of the research programme currently underway at the CHRC is a genetic and cytogenetic assessment of nuclear test veterans (NTV) and their families. This work is funded by two project grants (Cytogenetic assessment of British nuclear test veterans and their families. Anderson RM (PI) and Peto J. £449,672, June 2016-Sept 2021 (Aged Veterans Fund) and Genetic and cytogenetic assessment of British nuclear test veterans and their families. Anderson RM (PI), Peto J and Dubrova Y. £826,027, Sept 2017-Aug 2021 (Aged Veterans Fund)).

Genetic and cytogenetic assessment of British nuclear test veterans and their families.

This work is being carried out by Ninoshka Barros, Kai Craenen, Frances Daley, Kirsty Lawrence, Jose Seixo, Martin Scholze, Jade Stephens and Rhona Anderson in collaboration with Laurette Bukassa, Clare Gilham, Christine Rake and Julian Peto from the Department of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London and, Alex Moorhouse and Yuri Dubrova from the Department of Genetics and Genome Biology, University of Leicester, Leicester.

Background

The British Government undertook a series of nuclear tests at various sites in the South Pacific between 1952 and 1958. Associated with these atmospheric tests was an experimental programme, conducted largely at Maralinga in Australia, in which radioactivity was dispersed into the environment. This programme ended in 1963 although clean-up operations continued through to 1967. According to official records the dose received by the majority of personnel was negligible, although a number of 'special groups' were identified as potentially liable to higher exposure. These estimates were based primarily on film badge measurements of external dose. There are no recorded measurements of internal contamination through inhalation or ingestion of radionuclides. Over the intervening decades, the question of adverse health effects in both the veterans and descendants of this testing programme remains an unresolved issue.

Aim of research

This research seeks to address whether a genetic legacy could exist in families due to historical participation in various military operations during the British nuclear testing programme in the 1950s and 60s.

For this, we are undertaking a 'family trio' study that involves:

i. Recruitment of military veteran families
ii. Asking if there is any cytogenetic evidence of historical exposure of the test veterans
iii. Asking if there is any evidence of genetic anomalies in 1st generation children of test veterans.

i. Recruitment of military veteran families

All necessary permissions and full HRA approval were obtained after a 17-month process allowing participant recruitment to start in January 2018. Our target is to recruit 50 nuclear test veteran family trios (veteran, child, child's mother) who had participated in two or more Operations including the GRAPPLE series and Maralinga test sites and/or who had 'special group' status. We are matching (on age and service) with veterans who served in the tropics at the same time but who are verified as not present at any test sites. After family consent is obtained, whole blood is sampled and shipped to Brunel University London and University of Leicester where it processed for cytogenetic and whole genome sequence analyses.

Since January 2018, we have sent ~3600 study invitations to GP practices and in return have reached our recruitment target for the number of eligible nuclear test veteran couples responding. Work to convert all eligible couples into fully consented families and to receive their blood samples was near completion by spring 2020, when we were required to pause due to covid-19 restrictions. Outstanding samples will be sought from participating families after this time.

ii. Cytogenetic evidence of radiation exposure

Cytogenetic markers of historical and/or ongoing internal exposure in veterans

The potential health risks of exposure to ionising radiation can be estimated from individualised biological assessments of dose. Some prior knowledge as to the radiation quality and conditions of exposure are necessary if these estimates are to be robust however, as biological effect is influenced by linear energy transfer (LET) and dose-rate in addition to dose. In unknown or mixed dose exposure scenarios this may not always be the case. Current biological monitoring relies heavily on the quantification of chromosome aberrations that are detected using various means in the peripheral blood lymphocytes (PBL) and include reciprocal translocations and dicentrics. Indeed, the induction of simple reciprocal translocations and dicentrics by low-LET radiation such as γ-rays and their application as bio-dosimeters is very well characterized. Complex chromosome aberrations are defined as any exchange that involves three or more breaks in two or more chromosomes and are established as being strongly dependent on dose in the low-LET range but largely independent of dose after exposure to high-LET radiation. This has been shown for α-particles, neutrons and heavy ions.

24-colour chromosome karyotyping (multiplex-fluorescence in situ hybridisation (M-FISH)) is a cytogenetic technique that enables the detection and quantification of simple reciprocal translocation and dicentrics and, complex chromosome aberrations.

Work is ongoing to analyse the occurrence of these different types of chromosome aberration in anonymised samples of veterans PBLs. Upon completion and de-coding to ascertain test and control status of the samples the observed frequencies within nuclear test veteran and control veteran groups will be statistically evaluated to look for any differences between the two veteran groups.

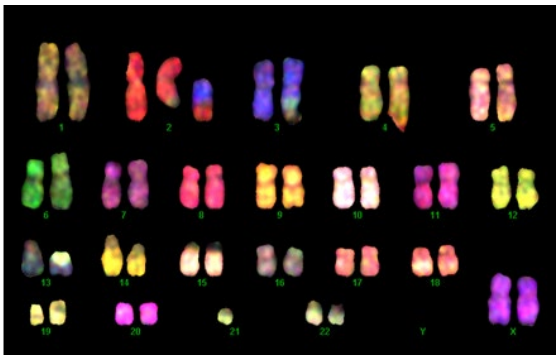


Figure 4: Representative M-FISH karyotype showing chromosomal abnormalities as colour changes.

Cytogenetic markers of radiation-induced delayed effects in veterans

Radiation is known to destabilise the genome; whereby cellular descendants of irradiated cells express newly arising (non-clonal/sub-clonal) genetic alterations. The mechanisms and relevance to health risk of this radiation-induced genomic instability phenomenon continue to be debated; however, its detection can be determined through the accumulation of newly arising or *de novo* chromosome and chromatid aberrations.

To test for evidence of radiation-induced genomic instability in veterans, chromatid-type aberrations and unstable structural and numerical chromosome type aberrations are being scored by staining with a dye called DAPI. This analysis is being followed by up as necessary by Giemsa staining to determine the frequency and type of abnormality. Upon completion and decoding the observed frequencies within test veteran and control veteran groups will be statistically evaluated to

look for any differences between the two veterans.

iii. Evidence of genetic anomalies in 1st generation children

The lack of reliable approaches for monitoring germline mutation represents the main obstacle to evaluating the genetic risk of human exposure to mutagens. For this reason, germline mutation induction in mice has continued to be the main source of experimental data used to evaluate the genetic risk of human exposure to mutagens including radiation. In recent years, researchers have demonstrated the validity of whole genome sequencing (WGS) approaches for the characterisation of newly arising mutations in the mammalian germline. We are employing such WGS approaches with the aim of determining the frequency (number) and spectra (type) of newly arising (*de novo*) DNA mutations in the offspring of nuclear test veterans, and comparing these to those identified in control veteran family trios.

Using Illumina WGS, we have sequenced to at least 30x genome coverage the genomes of 30 nuclear test veteran family trios and 30 control family trios (veteran, child, child's mother). This represents the completion of the whole genome sequence generation for the target number of 60 family trios for this part of the project. The sequence data is in the final stages of being validated. After this time, the data will be decoded and interrogated to investigate if there are any significant differences in the frequency and spectra of *de novo* germline mutations in the 1st generation children of test veterans compared with those of the control family group. This analysis is also exploring the potential for health consequences that may be attributable to paternal radiation exposure during participation in nuclear bomb tests.

Some studies have demonstrated that offspring of human and animal models exposed to high radiation doses of radiation show an increase in genomic instability. It has been hypothesized that germ cells of an exposed individual can develop a genetic memory, which leads to genomic instability in subsequence generations, termed as transgenerational genomic instability.

To test for cytogenetic evidence of trans-generational genomic instability in the descendants, chromatid-type and unstable chromosome type aberrations are being scored by Giemsa solid stain analysis. Upon completion and decoding the observed frequencies within test and control groups will

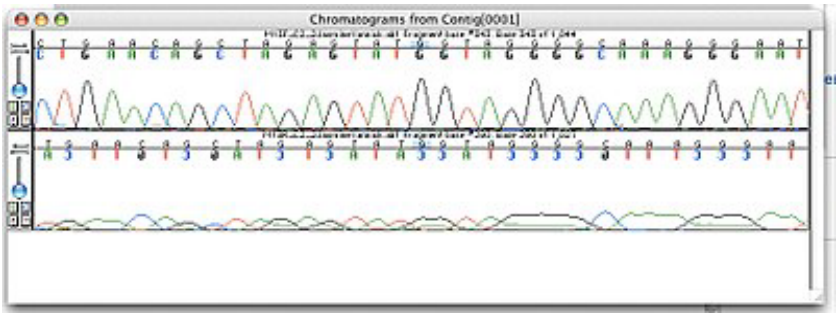


Figure 5: Representative image showing output from whole genome sequencing analysis for the detection of *de novo* mutations such as single nucleotide variants (SNVs), indels and structural variants.

be statistically evaluated to look for any differences between the two descendant groups.

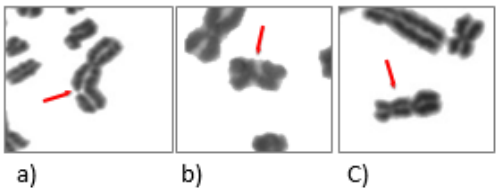


Figure 6. Examples of chromatid type gaps and breaks (a and b) and a dicentric chromosome (c).

Progress on all elements (recruitment, cytogenetic and WGS analysis) of the above work has been impacted by covid-19 restrictions. We now anticipate different elements of the work to be drafted and submitted for peer-review publication through 2021.

2. Understanding health risks of exposures

Genomic instability and cancer risk

The genomic instability phenotype is recognised as an enabling characteristic of neoplasia facilitating the acquisition of the hallmarks of cancer. There is as yet no validated biomarker of cancer induced by ionising radiation, but the frequency of chromosome aberrations in PBLs has been reported to correlate with cancer risk in human populations. We are exploring this in veterans and children's samples to evaluate any occurrence of radiation-induced and/or transgenerational genomic instability observed with respect to age-expected norms and estimated risks for cancer. This work is being carried out using data generated in sections 1ii and 1iii.

Pre-conceptional radiation exposure and transgenerational health

The adverse consequences of radiation exposure *in utero* are known but the heritable effects of parental radiation exposure pre-conception remain to be fully understood. The consensus within the radiation research community is that no epidemiological study has yet conclusively demonstrated a detrimental health effect in the offspring of radiation-exposed people, yet this is tempered by some evidence from cellular and animal studies that support the presence of detrimental outcomes as a result of parental exposure to radiation.

We are undertaking a number of projects examining this.

A study of pre-conceptional radiation exposure and transgenerational health.

This work is being carried out by Jade Stephens as part of her Doctoral studies, supervised by Dr Rhona Anderson and Dr Joanna Bridger.

The heritable effects of parental radiation exposure before conception in humans remain poorly understood and controversial. This project seeks to examine this complex question using a number of different approaches.

1. Evaluate the strength of published evidence on health outcome.
2. Identify any constitutional aberrations in offspring of nuclear test veterans.
3. Employ cytogenetic biomarkers for the assessment of health risk among offspring of nuclear test veterans.

To evaluate the strength of the published evidence, we are undertaking a full systematic review of the published literature. Specifically,

we are asking whether there is sufficient human evidence to support a trans/intergenerational effect on morbidity, mortality, mutation and/or other heritable genetic change following parental pre-conceptional radiation exposure.

reference lists also screened, resulting in 101 human papers for full analysis. Our protocol is registered with the international prospective register of systematic reviews (PROSPERO registration:123237).

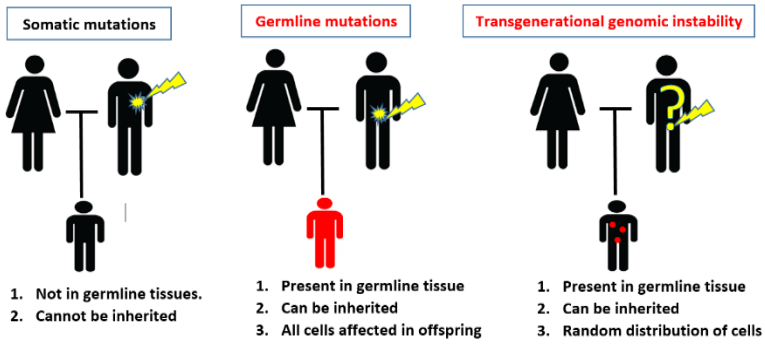


Figure 7: Schematic of somatic and germline mutations

The study population are human offspring, and/or members of subsequent generations, of a parent(s) who were exposed to ionising radiation prior to conception. Human studies published over the past 30 years were sourced in accordance with guidelines from the Office of Health Assessment and Translation/National Toxicology Program. We constructed a Boolean search which generated 2441 publications for review. Each of these have been screened for eligibility, and

Relevant data has been extracted from each eligible publication and an assessment for *risk of bias* carried out. Data from each paper has been grouped according to health outcome; sex ratio (4 papers), stillbirth (7 papers), congenital abnormalities (32 papers), DNA anomalies/mutations (19 papers), solid (23 papers) and non-solid (23 papers) cancers, in order to assess the body of evidence for each health outcome grouping. For this, an initial confidence rating is assigned based upon key

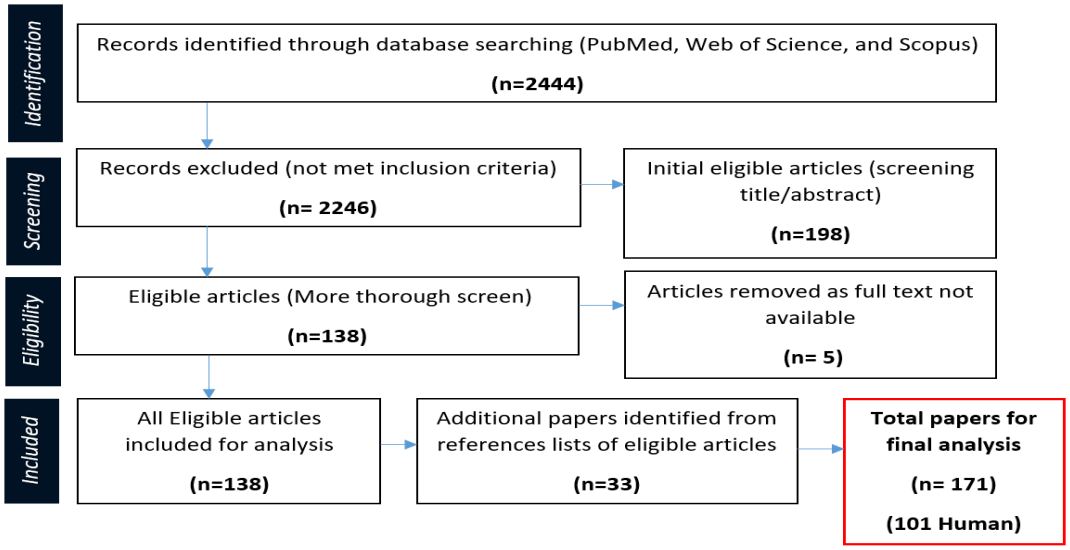


Figure 8: Flow chart of articles selected

risk of bias domains (selection, detection and confounding) before factors including inconsistency, imprecision (e.g. large confidence intervals), magnitude of effect, existence of a dose response and, residual confounding is considered. From this, a final confidence rating in the strength of published evidence for or against an effect for each health outcome grouping is derived. We are currently analysing the data within each health outcome group and evaluating our findings. A random effects meta-analysis will also be carried out on small homogenous sub-sets of data for a quantitative analysis. Additional contributors to this work include kai Craenen, Alex Moorhouse and Fotios Drenos.

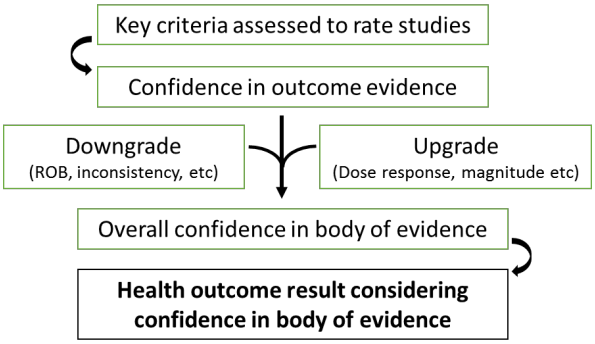


Figure 9: Health outcome analysis

To identify any constitutional aberrations in offspring of nuclear test veterans, blood samples of nuclear test veteran's descendants has been collected, and cytogenetic analysis is being performed. This involves culturing peripheral blood lymphocytes, harvesting chromosome preparations and G-band staining the resulting metaphase cells. Constitutional abnormalities will be identified if present, using the unique pattern of G-light and G-dark bands (Figure 10). This analysis is ongoing.

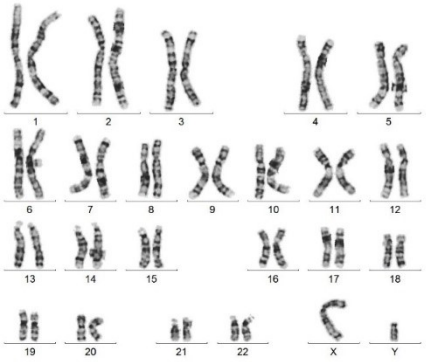


Figure 10: Representative G-band karyogram for the assessment of constitutional chromosomal abnormalities.

We are also building upon work briefly described in order to assess the potential of using cytogenetic markers to make assessments of health risk among offspring of nuclear test veterans. These include the occurrence of any genomic instability by detection of unstable chromosomal aberrations and, also the potential for measuring telomere length.

A systematic review of animal evidence for the transgenerational effects of parental pre-conceptual exposure to ionising radiation.

This work is being carried out by Kirsty Lawrence, Jade Stephens, Kai Craenen, Alex Moorhouse, Ewald Schroder and Rhona Anderson.

In addition to the review of human published studies, we are also undertaking a full systematic review of the published literature of animal studies. Animal models are often used to explore this inter/transgenerational question as they can be pre-conceptionally exposed to radiation with (or without) controlled exposure to other DNA-damaging

events. We are reviewing these published works to determine the strength of current evidence. Specifically, we are asking whether there is sufficient evidence to support an inter/transgenerational radiation effect on morbidity, mutation and other heritable genetic change following parental pre-conceptional exposure to ionising radiation.

Animal studies published over the past 30 years were sourced using a Boolean search construct which targeted publications for review. Each of these papers and their reference lists were screened for eligibility, resulting in ~80 papers for full analysis. This study is registered with PROSPERO, a prospective register for systematic reviews (No.123238) and has been undertaken in accordance with Office of Health Assessment and Translation/National Toxicology Program (OHAT/NTP) and UNSCEAR recommendations.

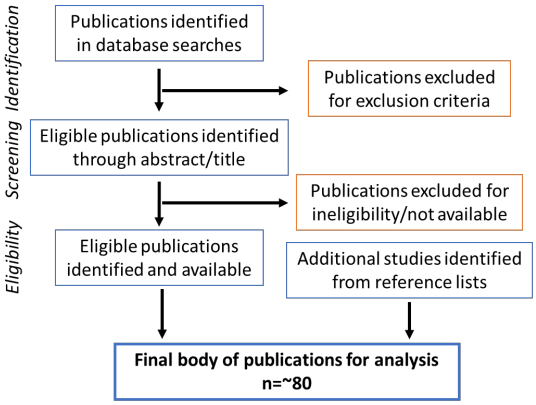


Figure 11: Flow chart of articles selected

Data extraction and risk of bias (ROB) analysis were performed on all qualifying papers. The ROB rated key elements pertaining to selection, confounding, performance, detection, statistical and publication bias issues for each paper. Key ROB questions were used to rate the confidence of each body of evidence or grouping, such as appropriate control comparison group, or unbiased/full detail of radiation exposure.

Three groupings of animal outcomes were identified; DNA mutation and damage (satellite mutation/DNA breaks/methylation), disease incidence (cancer/cataracts), and congenital outcomes (litter size/physical defects). Our systematic review also identifies inter/transgenerational radiation effects that may be associated with radiation quality, dose, parental sex or timing of parental exposure to conception.

From this evaluation of each body of evidence, each health outcome is assessed to consider if there is an effect and the confidence in the effect. We are currently analysing the data within each health outcome group and evaluating our findings.

Assessment of risks from combined exposures to radiation and chemicals.

This work is being carried out by Finlay Smith as part of his Doctoral studies, supervised by Prof Andreas Kortenkamp and Dr Rhona Anderson.

Mixture toxicology deals with the concept that chemicals with similar chemical structures or similar biological effects can have a combined mixture effect that has greater toxicity than its components' individual toxicities. This suggests that mixtures of chemicals can present a risk even if each individual component is below its recommended 'safe' limit. Mixture toxicity depends on:

- Exact mixture composition
- Whether toxicity is dose additive or independent
- Whether or not there are any synergies or antipathies in the interaction

Mixture effects are predicted using either Concentration (Dose) Addition (CA) for similar chemistry and routes of action, or via

Independent Action (IA) principles for stochastic or dissimilar routes of action.

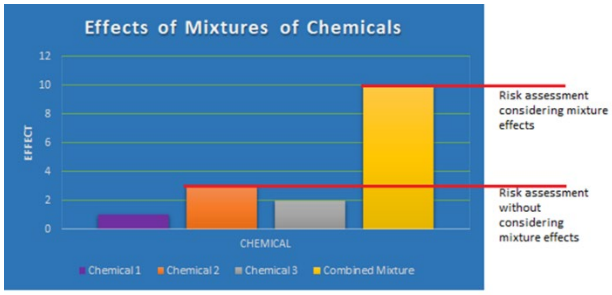


Figure 12: Representative illustration of mixture toxicology effects.

We are conducting proof of concept experiments with cultured cells to reveal whether combined genotoxic effects between radiation and chemical exposures can occur in principle. This approach will enable us to establish basic cell biological principles which will provide a solid foundation for examining whether combined risks exist under more realistic exposure scenarios.

Radiation risk from high LET alpha-emitters using radium-223 as a model.

This work is being carried out by Isabella Bastiani as part of her Doctoral studies, supervised by Dr Rhona Anderson and Dr Liz Ainsbury.

This is a collaborative project with Dr Liz Ainsbury, Public Health England and, Prof Joe O'Sullivan, Prof Kevin Prise, Dr Philip Turner and Dr Stephen McMahon from Northern Ireland Cancer Centre and Queens University, Belfast.

Prostate cancer is the most common cancer affecting men in the UK with over 400,000 new cases each year. Bone metastases are associated with stage IV prostate cancer, are linked with poor prognosis and often result in spinal cord fractures and/or compression leading to nerve damage and paralysis.

Radium-223 (^{223}Ra) is a radiopharmaceutical that delivers high-linear energy transfer α-particles to regions of bone metastatic disease. α-particles have a range of <100 µm and are effective in targeting bone metastases and delaying the onset of skeletal related events, however it remains unclear if this targeted radiotherapy may also result in unwanted exposure of normal neighbouring bone marrow cells.

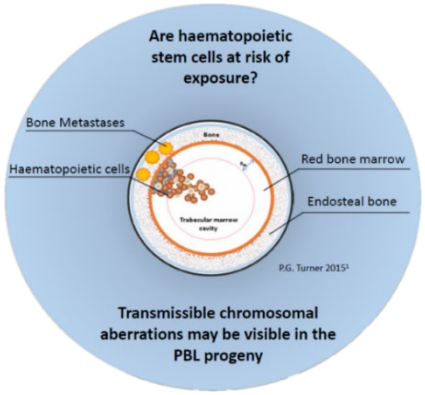


Figure 13: Image modified from Turner and O'Sullivan. British Institute of Radiology, vol. 88, no. 1050, 2015.

To assess this, whole blood is being sampled from metastatic castration-resistant prostate cancer patients who are receiving ^{223}Ra as part of the ADRRAD clinical trial in Belfast. The treatment schedule follows 6-monthly injections of ^{223}Ra (55 kBq/kg) in conjunction with 6 weeks of 2Gy/fraction external beam radiotherapy (EBRT) (Figure 14).

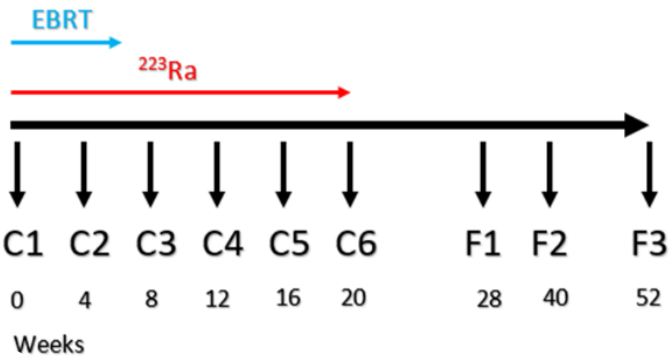


Figure 14. ADRRAD Clinical trial schedule. EBRT Daily 2 Gy fractions for 7.5 weeks, ^{223}Ra: 55 kBq/kg every 4 weeks. Sampling: Control (C1), during treatment (C2-C6) and follow ups (F1-F3).

Mature lymphocytes (PBL) originate from haematopoietic stem cells in the bone marrow and follow a hierarchical path of differentiation. Radiation-induced chromosome aberrations in surviving cells of the bone marrow and in PBL exposed in circulatory pool should be detectable in the resulting PBLs sampled. Multiplex-fluorescence *in situ* hybridization is being used to determine the type and frequency of chromosomal rearrangements induced in normal cells as a consequence of the treatment. The chromosomal aberrations are classified as simple, complex or as break only with complex chromosomal aberrations characterized by 3 or more breaks on 2 or more chromosomes.

Our findings show an increase in frequency and complexity in chromosome aberrations which coincides with the progression of treatment and which reflects the differing qualities of radiation exposure (low-LET X-rays and high-LET α-particles). We are using this information to make estimates of radiation dose to normal cells of the haemopoietic system to evaluate patient-specific responses. As part of this, we have developed a new method for estimating the dose contribution from each radiation type that could have broader usefulness for assessing mixed radiation exposure scenarios. To question whether PBL may have been exposed in circulation and/or whether their progenitor cells were exposed in the bone marrow, the stability and transmissibility of abnormal cells are being assessed. This work is nearing completion and is being prepared for drafting and submission of manuscripts for publication.

The impact of mixed radiation and chemicals exposure on neuronal cytotoxicity, ageing and transcription.

This work is being carried out by Justin Dankwa as part of his Doctoral studies, supervised by Dr Cristina Sisu and Dr Rhona Anderson.

In recent years, evidence has been emerging showing ionising radiation as a possible risk-factor for cognitive impairment. Cognitive impairment includes deficits in learning, memory, and information processing ability. At lower doses of radiation, the evidence is more equivocal thus research interest is steadily growing. Some studies show that prenatal exposures may affect brain development and cognitive functioning however there is much more uncertainty about its effects when exposed as on adolescents and adults. This emphasises the necessity of increasing our present understanding on the biological

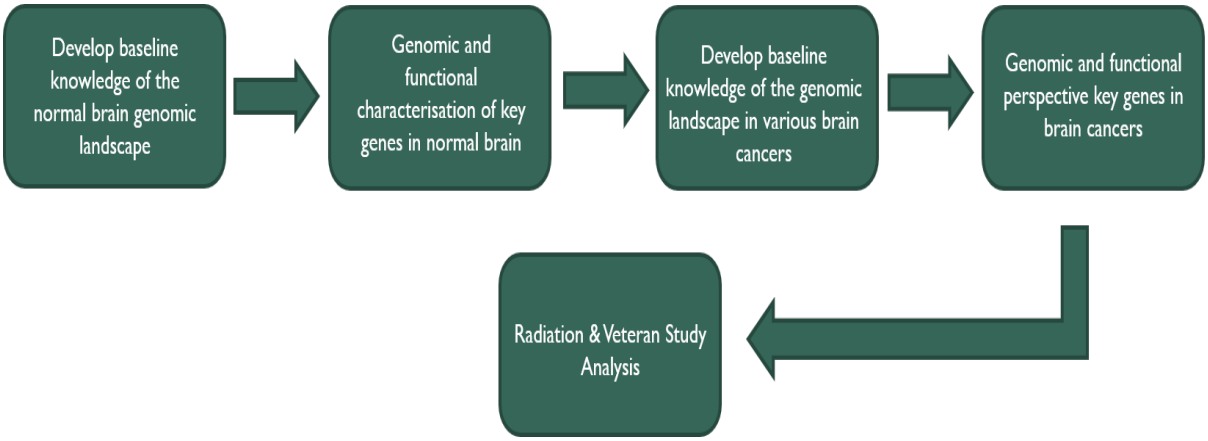


Figure 15: Methodology for Neuronal Effects

processes and pathways surrounding the adverse effects of radiation on neural cells.

Our current work is data-driven project, analysing publicly-available large-scale next generation sequencing brain datasets. Primarily, the work is focused on developing a working pipeline that will be used to evolve baseline knowledge of normal brain genomic landscape and subsequently the brain's genomic landscape in other cognitive impairments. Once completed, genes that are mutated or have a differential expression pattern in radiation exposed subjects compared to healthy individuals will be identified. This will inform on particular biological pathways of interest to explore further.

The aim of this study is to explore the adverse effects of radiation and chemical exposures on normal human brain functioning particularly after low-moderate doses. This study will elucidate on biological responses, new mutations, genetic biomarkers and the adverse pathways that can lead to cognitive impairments.

3. Health and Wellbeing

Exposure worry, ageing, and cognitive functioning*: An in-depth study of British nuclear test veterans*.

This work is being carried out by George Collett as part of his Doctoral studies, supervised by Dr Wendy Martin, Dr Rhona Anderson, Dr Will Young and Professor Mary Gilhooly.

Over 20,000 servicemen took part in the British nuclear testing programme in Australia and the Pacific islands from 1952 to 1963. Many claim that their health and the health of their descendants was negatively affected by their exposure to ionizing radiation. One aspect of health which has recently gained attention in relation to low-dose ionizing radiation exposure is cognitive functioning. Although studies have not conclusively shown an effect of low-dose exposure on cognitive functioning, the persistent psychological stress of potential exposure, may itself impact cognitive functioning in old age. As such, the original aim of this project was to explore the psychological impact of perceived radiation exposure (termed 'exposure worry') and the possible association with cognitive functioning in old age.

To examine the relationship between exposure worry and cognitive functioning, an appropriate measure was required. While relatively recent measures assessing similar constructs to exposure worry (e.g. 'radiation-anxiety') have been developed in the context of the Fukushima power plant disaster, previously available scales were not appropriate to measure exposure worry in British nuclear test veterans, primarily because some of the items are not relevant. Therefore, a significant part of this project was to develop an exposure worry scale and report the extent to which British nuclear veterans agree that they are worried about certain aspects of exposure worry. One focus group (n = 6 British test veterans) followed by four individual telephone interviews were conducted to assess the suitability and relevance of the proposed exposure worry items. Frequencies of responses were then assessed in 120 respondents, and the scale was modified by extending to 8-points to reduce skew and the addition of a seventh item to capture excessive exposure worry. Principle components analysis was conducted to confirm the assumption that each item pertained to unique components.

The proposed exposure worry scale was then used in a study to examine the relationship between exposure worry and cognitive functioning. A total of 91 participants completed the exposure worry scale and a sociodemographic questionnaire gathering data on age, proxy indicators of socioeconomic status (variables known to be correlated with cognitive functioning), their general anxiety, and information about their role in the nuclear testing programme and their health. A version of the Montreal Cognitive Assessment with the visuospatial items omitted (MoCA-BLIND) was administered over the telephone to measure cognitive functioning. After missing data was accounted for, a final sample of 76 British nuclear test veterans provided cognitive data.

It became apparent through anecdotal discussions with veterans who participated in the telephone cognitive assessments and from the four previous individual telephone interviews, that exposure worry may not be as persistent throughout life as it was presumed. Furthermore, the psychological impact may not relate specifically to worry but, rather, there was a broader psychological impact not captured by the proposed exposure worry scale. Therefore, a decision was made to conduct a qualitative study aimed to provide insights into the mechanisms and dynamics of exposure worry, and to explore the broader psychological impact of involvement in the testing programme. More specifically, this study explored what specifically are the perceptions, experiences and concerns for British nuclear test veterans and the underlying reasons for these views.

As such, twenty semi-structured interviews were conducted face-to-face and over the telephone with British nuclear test veterans who had participated in previous stages of the project. The interviews were recorded, transcribed and analysed using thematic analysis to produce a set of themes which best capture the data in relation to the research questions. The themes generally relate to worry about health effects in descendants, the role of time in any worry (for example the location in time that the tests took place and subsequent life events), and broader issues such a guilt and frustration. Since qualitative findings can be complicated (as they are in this study), the findings were translated into a conceptual model to describe the potential psychological impact of perceived ionizing radiation exposure in the context of the British nuclear testing programme.

The quantitative data from the cognitive functioning study is now being revisited and currently being analysed to extend the conceptual model of exposure worry produced

by the qualitative work. The qualitative findings confirmed the possibility that exposure worry is too complex to be reduced to a quantitative measure and, therefore, renders any analysis examining its relationship with cognitive functioning to be limited. Therefore, rather than examining the correlates of cognitive functioning, I am currently analysing the correlates of exposure worry to further extend the conceptual model. An analysis will also be conducted to address the original aim of the project, by examining the relationship between exposure worry and cognitive functioning, but methodological issues for this will be discussed in depth.

This project has extended our understanding about the possible psychological impact of perceived ionizing radiation exposure in a unique cohort. Not only are they unique in the fact that they are nuclear test veterans, but they are also older men. This project provides insight into the possible psychological impact of perceived ionizing radiation exposure over a life course, for which little research exists.

Figure 16: Components of exposure worry

British Nuclear Test Veterans: The complexities of identity, health and wellbeing, and the ageing process.

This work is being carried out by Amy Prescott as part of her Doctoral studies, supervised by Professor Louise Mansfield and Dr. Alistair John.

Between 1952-1958, the UK conducted 21 atmospheric nuclear tests in Australia and South Pacific, involving ~22,000 individuals. The servicemen's experiences are profound, yet the health effects of radiation dominate the discourse. Research on ageing veterans is limited, but research on BNTVs as a specific ageing population group is sparse. Also, no published studies are examining the impact of nuclear testing experience on wellbeing and identity within the BNTV community. This community consists of nuclear test veterans, their families, and their friends. Therefore, the nuances of ageing for this unique community and the interventions required to improve wellbeing have not been fully investigated.

It is known that among older people, the percentage of those living with poor wellbeing and quality of life has risen. Furthermore, older adults have a higher risk of becoming disengaged from society and community and experiencing loneliness and social isolation. Physical activity and the arts can provide a wealth of physical, mental, and social benefits, including improving self-confidence, morale, social cohesion, depression, and alleviating feelings of loneliness and social isolation. Thus, it has been suggested that physical and leisure activities may address the health and wellbeing issues of older people. The aim of the present study, is to identify and understand the possible mechanisms by which cultural, physical, and/or leisure activities may help and contribute to improving the health and wellbeing of the ageing BNTV community. The objectives are: (i) to understand the complexities of BNTV identity within the community, (ii) to critically explore health and wellbeing issues within the BNTV community, and (iii) to identify and analyse the types of leisure activities that can enhance wellbeing

and the reasons for engagement within this unique ageing population.

Adopting a narrative methodology, this qualitative study recruited 29 participants from the BNTV community for two rounds of life history interviews (30 telephone; 13 face-to-face). This approach centres on listening to individuals' stories and to identify actions that may be taken by both individuals and the community to address issues that affect their health and wellbeing. The life history interview allows for the participants to do this, through expressing their political, socio-cultural, and personal views and feelings on particular topics. Round one data was analysed using thematic analysis (TA). Round two further explored perceptions of nuclear testing, identity, the ageing process, and current life activities. Narrative analysis (NA) and TA were used for analysis and creation of life stories; consisting of the 'bigger' story regarding specific life events (e.g. witnessing a nuclear explosion) and, the 'smaller' story (typically mundane everyday interactions) that are often overlooked.

The findings of this doctoral research are represented using creative non-fiction (CNF). CNF is story creation grounded within the data but using fictitious conventions (metaphors, narration in the 1st/3rd person, imagery, and character creation), but is based on systematically collected data and occurrences during the data collection process. It captures the experiences, feelings, thoughts, and real words of the participants but as a consolidation of the 29 members of the BNTV community. The three CNF stories within a so-called Book of British Nuclear Test Veteran Experiences (Betrayal and BNTV Identity; The Ageing Veteran; and, Staying Connected) are an amalgamation of 19 life history

'monologues' constructed from the interview verbatim. Importantly, the 'big', 'small', 'shared' and 'exceptional' stories that this narrative study has identified are: identity and feeling like an outsider, forces life, perceived health effects of radiation, conspiracy and betrayal, ageing, loneliness, disability and accessibility, and engagement in physical and leisure activities for wellbeing.

This biographical narrative study is part of an emerging body of nuclear test veteran research. With this in mind, it is recommended that future research should look to develop interventions to help alleviate the health and wellbeing issues connected to ageing, social isolation, and loneliness.

4. Education and Engagement

CHRC created an external website (www.chrc4veterans.uk) to share information on our research projects and to act as source of education which is accessible to all stakeholders.

Over the past year, we have developed the sites 'knowledge hub' content in a number of ways. We have expanded our basic information education series covering topics which are relevant to CHRCs research (Figure 17).

Our intention is for these to act as a foundation for achieving a deeper scientific understanding of the key methods and processes involved in CHRCs research. All are available in either interactive or booklet formats online with hard copies available to order.

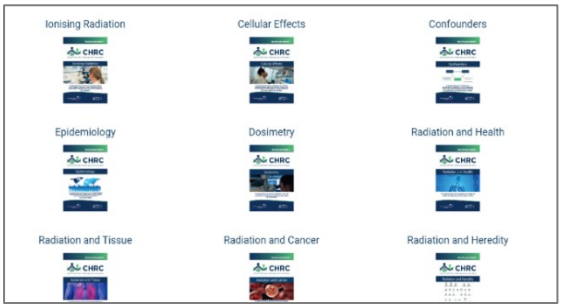


Figure 17: Basic information education series.

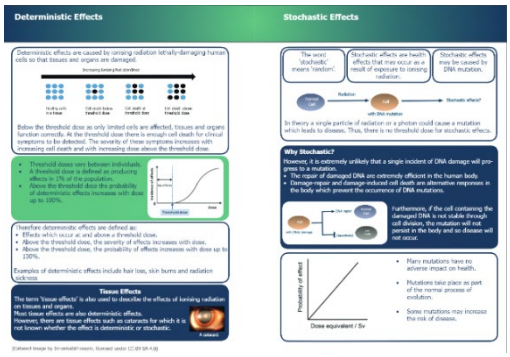


Figure 18: Example content within Basic information booklet.

We have also started a catalogue of Lay Summaries which aims to present published scientific research in an easy-to-read, accessible format for the non-scientist. The research question, the approach taken to address this and, the key findings are summarised to enable the reader to follow the scientific evidence and to draw their own understanding. This catalogue will continue to grow with topics aligned with CHRC associated research.

The knowledge hub content is supported by reference lists and other resource links.

CHRC information is also shared directly to members of the nuclear community through publication of non-peer reviewed articles and comment in 'Exposure' magazine. This is published near quarterly by the Nuclear Community Charity Fund and is sent free of charge to ~700 households.

Education through STEM

Brunel University's STEM (Science, Technology, Engineering and Maths) Centre aims to get children of all ages excited about science and technology. It features an array of exhibitions and work areas to help inspire young minds and ordinarily hosts 1000s of children per year through its programme of STEM events.

CHRC worked in partnership with Digital Design students and staff from Brunel's College of Engineering, Design and Physical Sciences and also, staff from the Brunel STEM Centre and Head of Digital Education to create and deliver an educational, digital resource called the 'Radiation Biomarkers Module', using Adobe® Captivate® e-learning software. The module features animations showing interactions between radiation and DNA and, how this results in the formation of chromosome aberrations. It also takes users through the process of how to make estimations of radiation dose by counting the number and type of chromosome aberrations in human cells, illustrating how chromosome aberrations are useful biomarkers of radiation exposure. To make it engaging for schoolchildren aged 14-16 it is stylised as a 'digital game' and contains quizzes to assess the children's learning.

STEM Ambassadors were being trained to support their effective delivery of this module in spring 2020. The target was thirty STEM programme events over the academic year, each involving thirty children in each STEM Wednesday Programme and sixty children at each STEM Saturday Masterclass Programme. Unfortunately, these on-campus events were cancelled due to covid-19 restrictions. STEM Brunel are currently reviewing their delivery for academic year 20/21 with a view for the 'Radiation Biomarkers Module' to be incorporated into 'online Brunel STEM'.

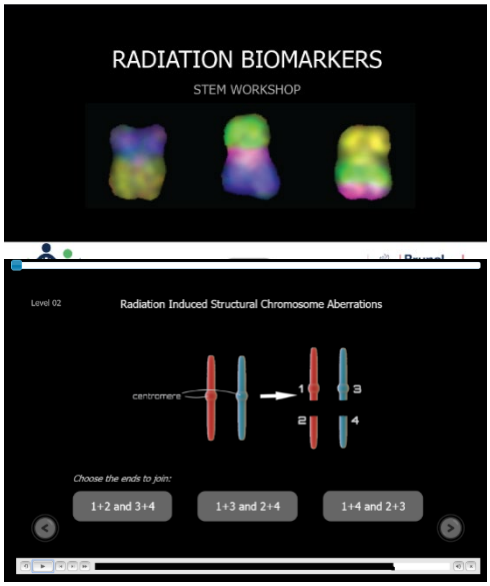


Figure 19: The *Radiation Biomarkers* module for 14-16 year schoolchildren.

A second STEM project is currently under development. CHRC, the NCCF and STEM Brunel are working together to pilot the 'Military Veterans for nuclear testing programs' project. This project is aimed at school students aged 14-16 who will collaborate to produce an information pack that would be informative for the members of the nuclear test veteran communities and the general public. Each group of students will focus on one of a number of identified themes drawn from veterans' experiences.

Impact and reach

The data received from Google Analytics from September 2019 to October 2020 show 1,248 total visits to www.chrc4veterans.uk with over 10,000 pages viewed; 48% returning visitors and 52% new visitors. The top 10 countries by users are UK (majority), US, China France, India, Bangladesh, and Iran.

Public Engagement Events

CHRC was invited to participate in a Health Protection Research Unit (HPRU) / EU-funded stakeholder meeting on low dose radiation in Newcastle on 30th March 2020. The actual event was cancelled due to covid-19. In its place, information on CHRCs work was shared to forum groups through VOICE (a stakeholder engagement platform). Taya Franco a recent 2019 graduate from Newcastle Universities' Fine Art program, was commissioned by the HPRU to design artwork as part of this stakeholder event. She used the information provided on VOICE together with discussions with CHRC to inspire her work. The finished piece is a blend covering radiation protection research and how to make information accessible.

Figure 20: HPRU commissioned art

All other external events identified for participation through the first 6 months of 2020 were cancelled due to covid-19 restrictions. Materials prepared and engagement activities planned are being future-proofed for 'live' and 'online' events.

Publications

Collett, G., Kai, C., William, Y., Mary, G. and Anderson, R. (2020) 'The psychological consequences of (perceived) ionizing radiation exposure: a review on its role in radiation-induced cognitive dysfunction.'. *International Journal of Radiation Biology*. pp. 1 - 56. ISSN: 0955-3002

Anderson, R., Williams, K., Jeggo, P., Hammond, E., West, C. and Badie, C. (2020) 'Meeting Report of the 16th International Congress of Radiation Research and the 12th International Symposium on Chromosomal Aberrations.'. *Journal of Radiological Protection*, 40 (1). pp. 361 - 365. ISSN: 0952-4746

Williams, KJ., Hammond, EM., West, C., Anderson, RM., Badie, C. and Jeggo, PA. (2019) 'Meeting Report on ICRR2019, the 16th International Congress on Radiation Research'. *International Journal of Radiation Biology*, 96 (2). pp. 167 - 171. ISSN: 0955-3002

Sabin, R., Pucci, G. and Anderson, RM. (2019) 'DNA damage processing is perturbed in both proliferative and non-proliferative cells of increased chronological cellular age.'. *Radiation Research*, 19 (2). pp. 200 - 207. ISSN: 0033-7587

Anderson, RM. (2019) 'Cytogenetic biomarkers of radiation exposure'. *Clinical Oncology*, 31 (5). pp. 311 - 318. ISSN: 1433-2981

Exposure Magazine *published by Nuclear Community Charity Fund*

Summer 2020:

Article: Ionising Radiation and Tissue Effects Part 2.

April 2020:

Article: Ionising Radiation and Tissue Effects Part 1.

August 2019:

Article: Radiation Exposed Populations.

April 2019:

Article: Assessment of Risks from Combined Exposures to Radiation and Chemicals by Finlay Smith.

December 2018:

Article: Investigating the DNA of British Nuclear Test Veterans and their Families by Alex Perry.

Article: Sport, Culture and Wellbeing by Amy Prescott.

August 2018:

Article: Exposure Worry, Ageing and Cognitive Functioning by George Collett.

Article for Genome Biology series: Techniques to study *de novo* mutations by Alex Moorhouse.

April 2018:

Article: Why can't I volunteer for the genetic study? By Ewald Schroder.

Scientific Conferences attended

Radiation Research Society Annual Meeting, San Diego, 2nd-6th November 2020 https://www.radres.org/mpage/RRS2019Home

- Chromosome indicators of LET in the assessment of mixed or internal exposures. Oral presentation by Rhona Anderson.
- Radiation risk from High LET α-emitters using Radium-223 as a model. Poster Presentation by Isabella Bastiani

British Sociological Association Sport Study Group Student Conference, Oxford Brookes University, 5 September 2019. *Sport, culture & wellbeing: community approaches to promote wellbeing among British nuclear test veterans and their families.* Oral presentation by Amy Prescott.

16th International Congress for Radiation Research (ICRR), Manchester Central, 25-29 August 2019 http://icrr2019manchester.com/ CHRC was very well represented:

- *A genetic and cytogenetic study of British nuclear test veterans and their children.* Rhona Anderson oral presentation in 'non-targeted and transgenerational effects' session.
- *Exposure Worry, Ageing and Cognitive Functioning: An in-depth study of British Nuclear Test Veterans.* Poster presentation by George Collett. Co-chair of 'psycho-societal' session.
- *An M-FISH study to assess the presence of radiation-induced chromosomal damage in British nuclear test veterans.* Poster presentation by Kai Craenen. Co-chair of 'non-targeted and transgenerational effects' session.
- *A Radiation Biomarkers Module: A Digital Resource for Education and Public Engagement.* Poster presentation by Alex Perry.
- *A solid stain approach to assess genomic stability in British nuclear test veterans and their children.* Poster presentation by Jose Seixo.
- *Assessment of Risk from Combined Exposures to Radiation and Chemicals.* Poster presentation by Finlay Smith.
- *A Systematic Review of Evidence for the Transgenerational Effects of Parental Pre-conceptual Exposure to Ionising Radiation*. Poster presentation by Jade Stephens.
- *Radiation risks from high-LET α-particle emitters using Radium-223 as a model*. Poster presentation by Isabella Bastiani.

12th International Symposium for Chromosome Aberrations, Manchester, 27th August 2019. Presentations included:

- *Complex chromosome aberrations as biomarkers of internal exposures*. Oral presentation by Rhona Anderson.
- *Dose estimation of radium-223 treated patients*. Oral presentation by Isabella Bastiani.

3rd European Radiological Protection Research Week 1 – 5th October 2018, Rovini - Rovigno, Croatia https://erpw2018.com/. *A genetic and cytogenetic study of British nuclear test veterans and their children*. Oral presentation by Alex Moorhouse.

US Annual Meeting for Radiation Research and the 24th Meeting of the Conference on Radiation & Health. Chicago, Illinois,23 – 25th September, 2018. *A genetic and cytogenetic study of British nuclear test veterans and their children.* Poster presentation by Rhona Anderson.

Global Co-ordination of Low-Dose Research: Scoping Meeting, Milan 17 – 18th September, 2018, Milan University, Milano Italy https://www.oecd-nea.org/rp/workshops/science-values2018/. Attended by Paul Leonard (on behalf of Rhona Anderson).

Association for Radiation Research 2018: Health and Environmental Implications of Multidisciplinary Radiation Research. - Riddel Hall, Queen's University Belfast, 25 - 27th June, 2018. https://www.le.ac.uk/cm/arr/home.html.

- *A genetic and cytogenetic study of British nuclear test veterans and their children.* Oral presentation by Rhona Anderson.
- *Radiation risk from High LET α-emitters using Radium-223 as a model.* Oral presentation by Isabella Bastiani.

Governance

CHRC Management Committee

Professor Geoff Rodgers: Vice-Provost Research

Dr Rhona Anderson: Director, CHRC

Dr Amanda Harvey: Division Lead (Biosciences), Department of Life Sciences

Professor Susan Jobling: Director, Institute of Environment, Health and Societies

Ms Anne Smith: Institute Manager (Institute of Environment Health and Societies)

Professor Christina Victor: Vice Dean Research (College of Health and Life Sciences)

Ms Teresa Waller: Director, Research Support and Development Office

Ms Julie Whittaker: Centre Manager, CHRC

CHRC Advisory Board

Mr Jeff Liddiatt (Char): President (Hon) NCCF

Mr Nigel Heaps Esq., MBE: Director, BH Associates

Professor Catherine Hennessy: Professor of Ageing at University of Stirling

Professor Deborah Oughton: Professor in Environmental Chemistry and Head of the research school in Ecotoxicology at the Norwegian University of Life Sciences

Mr Tony Jeffrey: Chairman of the Nuclear Community Charity Fund

Mrs Ceri McDade: Chairperson of the British Nuclear Test Veterans Association

Professor Nicholas Priest: Visiting Professor at Middlesex University and Adjunct Professor at the Medical University of South Carolina, USA

Professor Richard Wakeford: Professor in Epidemiology, Manchester University and Dalton Nuclear Institute

Mr Paul R Thomas CBE: Chief Operating Officer (COO), Brunel University London (retired July 2020)

Staff at CHRC

Dr Rhona Anderson Director

Dr Rhona Anderson is a Reader in Radiation Biology in the Department of Life Sciences and, a member of the Institute of Institute of Health, Medicine and Environments at Brunel University London. Rhona started her career as a clinical cytogeneticist before developing her research interests in radiation biology at the Medical Research Council Radiation and Genome Stability Unit, Harwell (1996-2005). She gained her PhD from Brunel University in 2004 before taking up a lectureship in 2005. She has held offices in the UK Association for Radiation Research, including acting as Chair (2012-14), was appointed Honorary Membership of Royal College of Radiology in 2017 and is currently serving as Councillor (at large) for the International Association for Radiation Research.

Professional staff

Julie Whittaker Centre Manager

Julie joined the CHRC in September 2017 at the start of the project, but has been working for Brunel University London since September 1999, when she joined the Department of Information Systems and Computing (DISC) as an administrator for undergraduate final year projects. Whilst in DISC Julie studied part time with the Open University and was awarded BSc Hons in Computer Science in 2010. During her time at Brunel Julie has taken on several secondments which has allowed her to gain knowledge in a wide range of research areas and activities.

Dr Alex Perry Communications and Engagement Officer (Nov 2018-June 2020)

Dr Alex Perry joined the CHRC in November 2018 as a Communications and Engagement Officer. Alex holds a BSc and a Doctorate in chemistry from Southampton University. He worked as a post-doctoral researcher in the USA for 4 years and as a scientist in the pharmaceutical industry for 15 years. In 2017 Alex moved into the field of science communication and public engagement and obtained a Master's degree in this subject from Edinburgh University.

Research staff

Ninoshka Barros - Research Technician

Ninoshka joined the CHRC as a Research Technician in March 2020. Ninoshka was awarded a BSc (Hons) degree in Biomedical Sciences from Brunel University London. She continued her studies at Brunel University and gained a MSc degree in Disease Mechanisms and Therapeutics, specializing in Cancer Biology. Ninoshka has investigated the uptake of coated and uncoated nanoparticles in cells and in the tumor microenvironment, as a form of specific targeted cancer therapy.

Dr Kai Craenen - Postdoctoral Research Fellow (Nov 2018 - Sept 2019)

Dr Kai Craenen joined the CHRC as a postdoctoral fellow in November 2018. After gaining a BSc and an MSc in biochemistry and biotechnology from the University of Antwerp, Kai went on to complete a Doctorate in Biochemistry at the Catholic University of Leuven in Belgium and the Belgian Nuclear Research Centre SCK-CEN. He is the author of several scientific papers and has won a number of awards. Kai brings a highly multidisciplinary background to the CHRC, having worked in the fields of radiation biology, teratology, neuroscience, nutraceuticals and behavioural science.

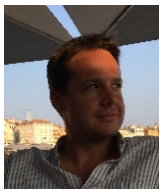
Frances Daley - Research Assistant (August 2017 – February 2020)

Frances joined the Veterans Cytogenetic Project at Brunel University in August 2017 having moved from the Institute of Cancer Research Molecular Pathology department. Frances is a senior biomedical scientist and holds an MSc in Medical Molecular biology from the University of Westminster. She has accumulated vast experience working in a pharmaceutical, diagnostic and research environments.

Dr Kirsty J. Lawrence – Postdoctoral Research Fellow

Kirsty joined the CHRC as a postdoctoral research fellow in November 2019. Kirsty was awarded a BSc degree in Biological Sciences (Genetics) from the University of Leicester. She then went on to gain both a master's degree and a PhD at the University of Birmingham in DNA damage repair and genome instability. She has experience in molecular and cellular biology and has completed a postdoctoral fellowship at Imperial College London. Kirsty has also worked as a science copy editor, editing articles and managing the review process for an oncology journal, and advising on human and animal ethics within publishing.

Alex Moorhouse - Postdoctoral Research Fellow



Dr Alex Moorhouse is a Postdoctoral Research Fellow based at the University of Leicester. Alex has gained degrees from the University of Exeter in bioinformatics and from UCL in human evolution. He has worked with a range of model organisms including Zebra fish, infectious yeast species of the genus *Candida*, the budding yeast *Saccharomyces cerevisiae* and mouse models of the malaria parasite *Plasmodium berghei*. Alex gained his PhD at the University of Aberdeen studying yeast genomics, population genetics and ancient DNA at the MRC Centre for Medical Mycology and Fungal Immunology with placement at the Australian Centre for Ancient DNA.

Jose Seixo - Research Technician (November 2018 – January 2020)

Jose joined the CHRC in November 2018 as a Research Technician. He has an MSc in Molecular and Cellular biology from the University of Porto and a BSc in Genetics and Biotechnology from the University of Trás-os-Montes and Alto Douro. Prior to joining the CHRC Jose worked at the Centre for Medical Genetics in Portugal in the field of human cytogenetics.

Doctoral students

Projects being carried out by our Doctoral Researchers are shown; delivering new research and building research capacity for the future.

Isabella Bastiani supervised by Dr Rhona Anderson and Dr Liz Ainsbury.

Radiation risk from high LET alpha-emitters using radium-223 as a model.

Start Date: 1st Aug 2017 Funded by: Public Health England

George Collett supervised by Dr Wendy Martin, Dr Rhona Anderson and Professor Mary Gilhooly.

Exposure worry, ageing, and cognitive functioning: An in-depth study of British nuclear test veterans.

Start date: 8th Jan 2018 Funded by**:** CHRC

Justin Dankwa supervised by Dr Rhona Anderson and Dr Cristina Sisu.

The impact of mixed radiation and chemicals exposure on neuronal cytotoxicity, ageing and transcription.

Start date: 6th April 2020 Funded by**:** CHRC

Amy Prescott supervised by Professor Louise Mansfield, Dr Alistair John and Dr Rebecca Hings.

Sport, culture & wellbeing: community approaches to promote wellbeing among British nuclear test veterans and their families.

Start Date: 2nd October 2017 Funded by: CHRC

Finlay Smith supervised by Prof Andreas Kortenkamp and Dr Rhona Anderson.

Assessment of risks from combined exposures to radiation and chemicals.

Start Date: 8th Jan 2018 Funded by: CHRC

Jade Stephens supervised by Dr Rhona Anderson and Professor Joanna Bridger.

Pre-conceptional radiation exposure and transgenerational effects.

Start Date: 8th January 2018 Funded by: CHRC

CHRC

Centre for Health Effects of Radiological and Chemical Agents

Contact Details

For further information about the centre and the research projects please contact:

CHRC@brunel.ac.uk

Visit our website:
www.chrc4veterans.uk

+44(0)1895 266018

The Nuclear Community Charity Fund

Making that difference

Brunel University London