



Invitation to Tender for a Dosimetry Work Package

Background

Since the Chernobyl accident in April 1986 the incidence of thyroid cancer has increased in the population who were children or adolescents at the time of the accident and resident in areas of Russia, Ukraine and Belarus affected by high levels of radioactive fallout .

The Chernobyl Tissue Bank (CTB), established in 1998, is an international collaboration currently funded by the European Commission, the NCI of USA and the Sasakawa Memorial Health Foundation of Japan. The objectives of the project are to:

- Collect and curate biological specimens with appropriate consent, from patients operated for thyroid cancer or cellular follicular adenoma who were born on or after the 26th April 1967 (i.e. aged 19 or under at the time of the Chernobyl accident).
- Provide quality assured materials (both in terms of pathology and molecular biology) for research to the wider research community
- Provide a database to the wider research community that links dosimetry data with information on age at clinical presentation and at the accident, residency and pathology of tumour
- Provide a web-accessible data warehouse for future bioinformatic studies on data from research projects funded by the EC and other

The CTB currently holds tissue from 3215 cases.

The tissue banks are maintained at The State Institute of Endocrinology and Metabolism in Kiev, Ukraine (IEM) and the Medical Radiological Research Centre in Obninsk, Russia (MRRC, RAMS) both of which are partners in the collaboration. Patients in the defined age range attending clinics in Kiev and Obninsk for treatment for thyroid cancer, are asked to consent to their tissue being used for international research studies. Each bank houses only material and information from its own population. Detailed pathology information along with relevant data about the patient (date of birth, date of operation, sex, oblast of residence at the time of the accident and operation) are recorded in a database in each centre. In addition, a back-up copy of each of the databases is maintained at the Coordinating Centre at Imperial College London.

Researchers wishing to use the resources of the CTB to address biological and epidemiological questions relating to the development of thyroid cancer following radiation exposure in childhood, apply for access via the Coordinating Centre. Applications are evaluated by external experts in the relevant areas of research.

In order to maximise the availability of what is a limited resource of material in the CTB, most researchers are supplied with DNA and RNA extracted from the tissues, rather than the frozen blocks.

The biological material provides the opportunity to study the malignant transformations in the thyroid after exposure to ionizing radiation. However, in order to make best use of such information, the doses to which the patients have been exposed need to be linked to the molecular biological data, which has not been done so far.

The CTB Dosimetry Work Plan

A number of studies have been carried out on the populations exposed following the Chernobyl accident and, as a consequence, there is a significant amount of dose reconstruction data maintained in Russia and in Ukraine. Following the accident, various measurements of radioactive contamination were made. Many people living in the most contaminated areas were monitored individually and the dose of ^{131}I to the thyroid was measured, or calculated. Some of the individuals who were monitored individually also completed a questionnaire to determine their residential history and the dietary habits of their family. Others had individual measurements taken but did not complete questionnaires, and a third group did not have measurements taken but an average dose has been estimated based on their residence and related to the deposition of radioactive ^{131}I . Most of the dose of radioactive iodine in the children resulted from ingestion of contaminated vegetables and milk.

Funding has been provided by the EC, as part of the overall support for the CTB, to enter dosimetry data into the CTB database in a way that will be useful for researchers. A number of research studies already use material from the CTB to investigate the molecular biology of thyroid cancer and its relationship to radiation exposure. The inclusion of dose in the CTB database will enable findings from these studies to be linked more closely to radiobiological parameters.

Over the next 2-3 years a research database will be built into which researchers who are using material from the CTB for approved projects, will add experimental data, much of it derived from studies using modern molecular biology platforms, such as Affymetrix, BAC and SNP arrays. The research data and corresponding clinical and dosimetry data from the CTB database will be brought together in a data warehouse from which researchers will either be able to use tools within the data warehouse to carry out on-line analyses, or to down-load the data and apply their own bioinformatics tools.

Work required for dose estimation

Current status

The dose estimations for the population in the Chernobyl-affected areas are based on various data sets:

- Direct measurements of radionuclides: Immediately after the Chernobyl accident, a campaign started to monitor ^{131}I in human thyroids. The thyroid exposure was estimated from the ^{131}I content in the thyroid at the day of monitoring, the time elapsed since deposition, the iodine kinetics in the thyroid and the whole body. In general, thyroid monitoring provides a reliable base for dose assessment. However, the measurements had to be performed in an emergency situation under field conditions, which caused uncertainties in the monitoring results.
- Although the monitoring campaign broadly covered the affected areas, ^{131}I measurements in human thyroids were not performed in all settlements. In these cases, the dose estimation is based on radioecological and dosimetric models. Input for those models are the ^{137}Cs (which acts as a tracer for ^{131}I), the main day of the passage of the plume, the contribution of wet and dry deposition to the total deposition, the day of start of grazing cattle, intake rates for milk and green vegetables.

In general, the accuracy of the dose estimation based on the model is less than for those that are based on thyroid monitoring. However, both approaches lead to similar results for the age-dependence of the thyroid exposure.

Work to be done for CTB patients

For each tissue sample in the CTB, the dose to the thyroid and whole body has to be estimated and entered in the data base along with an indication of the iodine status of the patient at the time of exposure and, if practicable, subsequently. Average dose estimates to the thyroid are available (within MRRC) for all Russian patients included in the CTB data base and individual doses for those who have been involved in case control epidemiological studies. Dosimetric estimates are, likewise, available for all Ukrainian patients in the CTB data base; the quality or precision of the data, however, varies between those available within IEM and those estimated for the purposes of case control studies and held by other Ukrainian organizations.

For the dose estimations, the currently available approaches should be applied. The preferable approach is the use of data on direct measurements of ^{131}I in the thyroid. If not available, other appropriate approaches should be applied that make use of regional data such as the time of the passage of the plume, the deposition mode, and the day of start of grazing cattle.

A Dosimetry Working Group has been set up to advise the CTB on the strategy to implement the dosimetry work plan, to assist in the oversight of the work and to prepare reports for the CTB Scientific Advisory Board. The WorkStream is being led by Dr G. Pröhl, Helmholtz Zentrum München, Institute of Radiation Protection, Germany.

Expressions of interest in this tender

Funding will be available from May 2009 and it is anticipated that the work will be completed within an 18 month period. Working with the CTB Dosimetry Working Group, the successful institutions will be required to collate all available dosimetric data held in Russia and the Ukraine, with the cases whose tissues are held in the CTB. A total of approx €50k is available for allocation to two centres, one in Ukraine and one in Russia, to carry out this work.

Expressions of interest outlining a proposed approach to carry out this tender should be submitted on a single side of A4 paper to a.galpine@imperial.ac.uk, Project Manager of the CTB by 31st March 2009.