The Chernobyl Tissue Bank – an infrastructure for systems biology of thyroid cancer

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What is the CTB?

Established in October 1998

- Inclusion criteria
  - Diagnosis of thyroid carcinoma or cellular follicular adenoma
  - Born on or after 26/4/67 i.e. 19 or under at the time of the accident
  - Resident in the most highly contaminated areas of Ukraine (Cherkasse, Chernigov, Kiev, Rovno, Sumy, Zhitomyr) or Russia (Bryansk, Kaluga, Tula, Oryol)

Financial support from the EC, the NCI and the SMHF (japan), and has the support of the governments of Ukraine and Russia

Coordinated from the UK (Imperial College, London) – working with Institute of Endocrinology in Kiev, Ukraine and MRRC RAMS, Obninsk, Russia

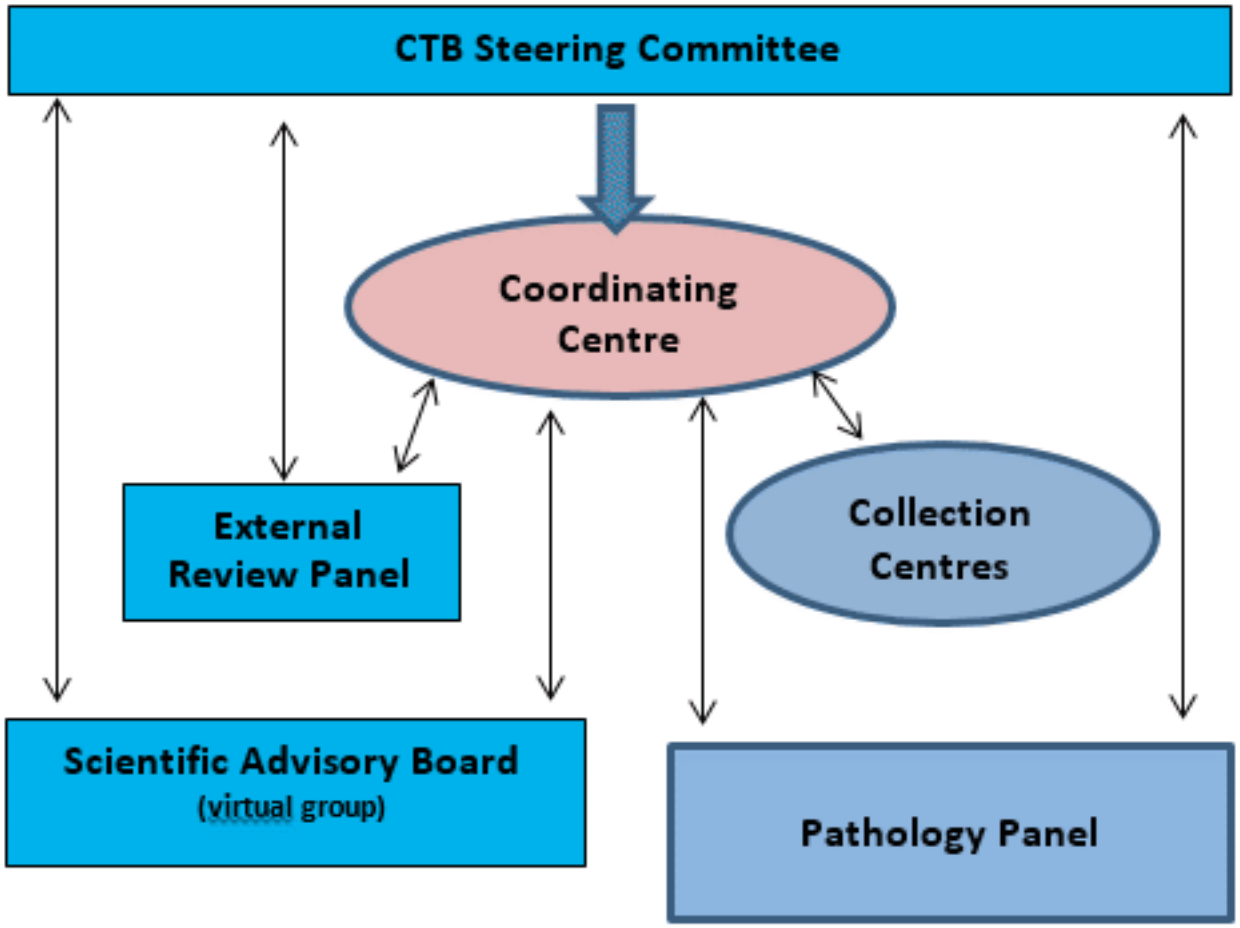
Ethics

- Annual review of project by IRBs in Ukraine and Russia, Imperial College Research Ethics Committee and by NCI IRB

- Generic (enduring) informed consent obtained from patient (if over 18) or their parent or guardian (if under 18)

- Right to withdraw from the study at any point, and patients made aware that samples may be sent abroad for study

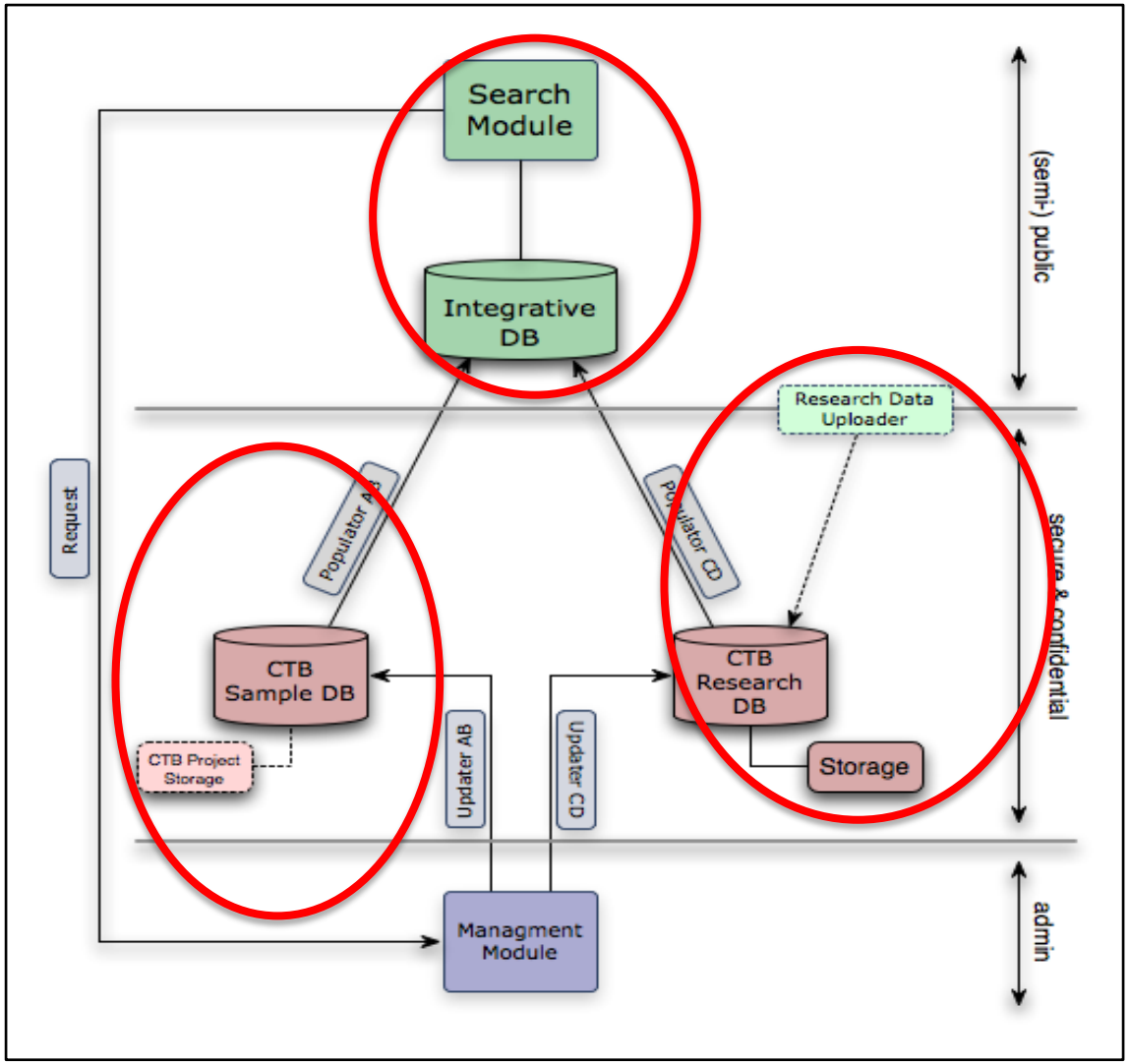
Governance


CTB Steering Committee
Coordinating Centre
External Review Panel
Collection Centres
Scientific Advisory Board
(virtual group)
Pathology Panel

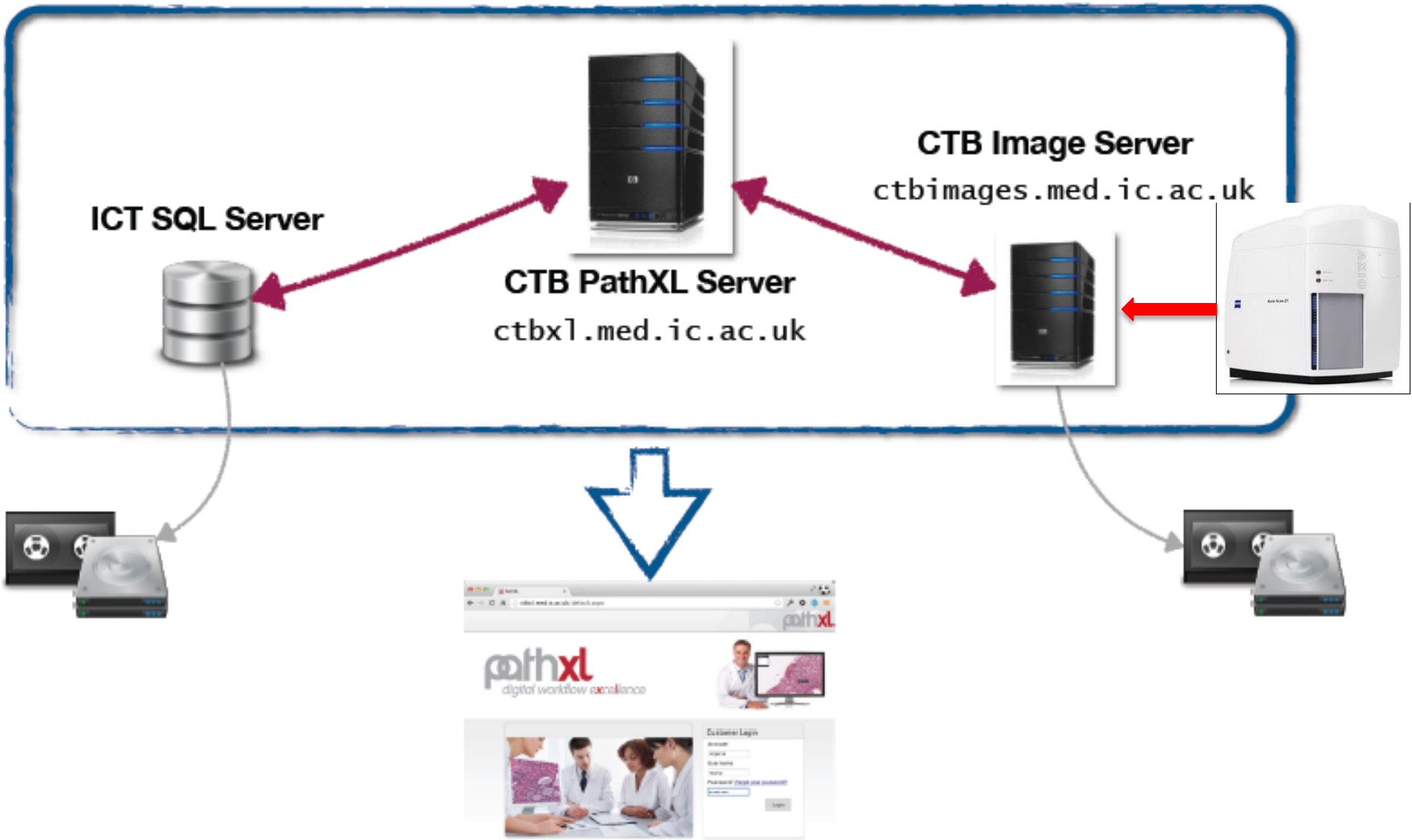
What does the CTB collect?

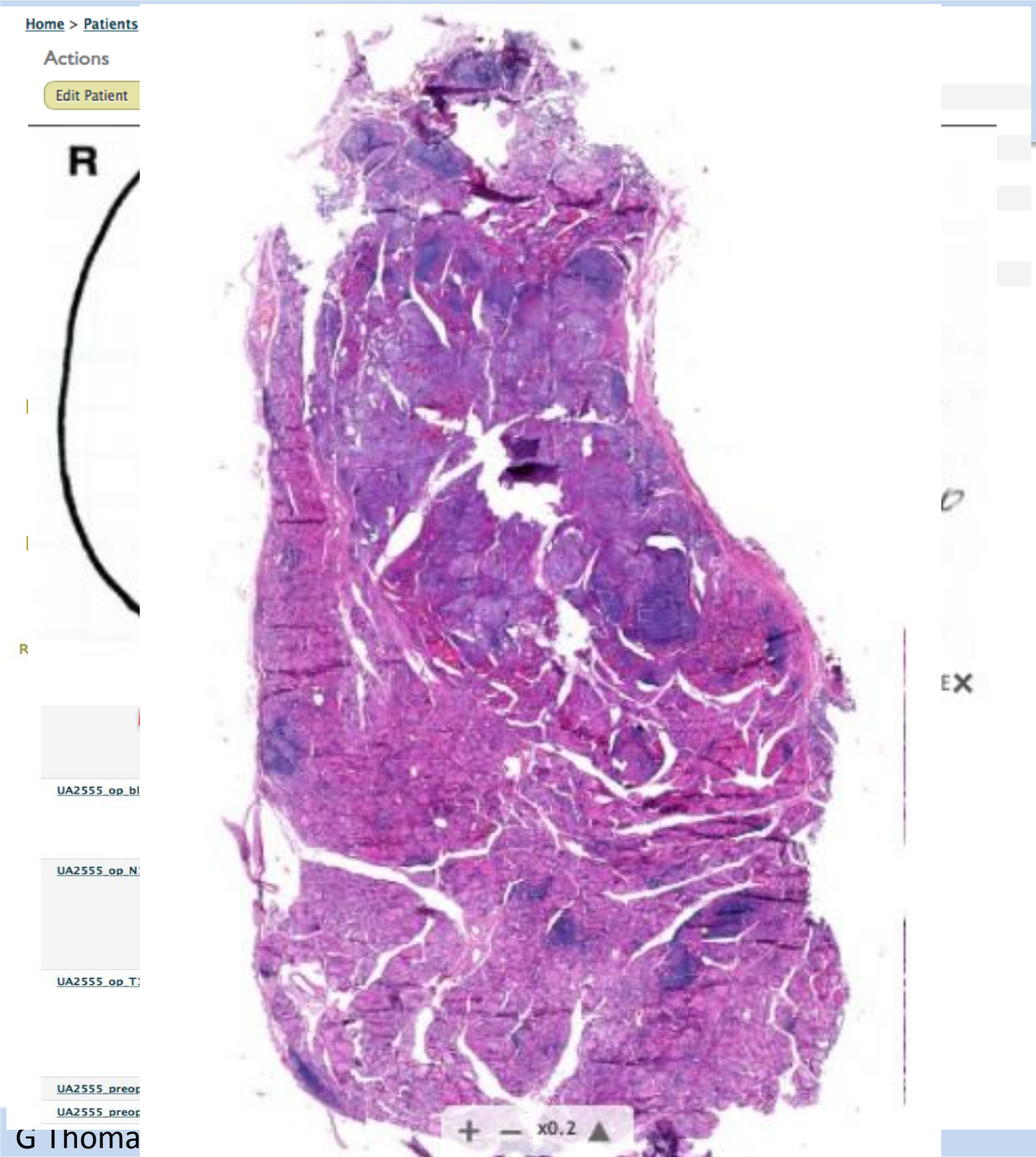
- Blood samples – DNA and serum markers
- Tissue – both frozen tissue and normal histological material
- Different types of sample from the same patient
- Detailed pathological annotation
- *Future - treatment and outcome*

IT infrastructure



Digital Pathology





Chernobyl Tissue Bank

Human Cancer Studies Group

Catalogues info on patient, dosimetry, operation, pathology, specimens taken, storage location, processing and issue of samples to researchers

Provides data to CTB portal

Dosimetry and the CTB

Each donor to the CTB has a calculation for radiation dose to the thyroid (plus an estimation of the error)

- 6% direct thyroid measurements
- 7% personal history questionnaires
- 74% residency only
- 12% no dose (born after 1/1/87)

Archive so far

4500 cases reviewed by the Pathology Panel

- 3017 from Ukraine, 1483 from Russia
- 3442/4500 cases have frozen tissue available
- 3094 come from exposed oblasts, 1406 from unexposed oblasts
- 758 born after 1/1/87 (475 from exposed oblasts and 283 from unexposed oblasts)
- 3232/4500 (72%) are cancer, of these 2926 are PTC (90.5% of all cancers, 65% of all cases)
- Further 357 cases are currently under review

Access to samples

- Application on line

https://cisbic.bioinformatics.ic.ac.uk/ctb/html_ctb_public - also link from website (www.chernobyltissuebank.com)

- All applications reviewed by an independent external review panel
- Material transfer agreements signed between the Eastern European Institutes and the Coordinating Centre and the Coordinating Centre and the PI

Access to samples

- Samples issued via the Coordinating Centre to ease import/export problems and so that each shipment can be verified
- Researchers asked to provide their results back on a case by case basis
- Web-accessible database for researchers return results

- CTB MDTA binds researchers to return of data
- Sample list provided with MDTA serves as template for researchers to upload data

Approved Project Code 003/2011

Patient UID	dob	dop	sex	columns	diagnosis	tumour UID	no sections	normal UID	no sections
UA0033	09/01/1982	12/01/1999	Female	Zhytomyr	PTC	UA0033_op_blockA_cut1s02-6	5	UA0033_op_blockB_cut1s02-6	5
UA0037	14/05/1985	20/01/1999	Female	Chernigov	PTC	UA0037_op_blockA_cut1s02-6	5	UA0037_op_blockD_cut1s02-6	5
UA0067	16/08/1983	23/04/1999	Female	Zhytomyr	PTC	UA0067_op_blockA_cut1s02-4	3	UA0067_op_blockB_cut1s02-4	3
UA0076	15/05/1982	14/05/1999	Female	Cherkassy	PTC	UA0076_op_blockA_cut1s02-4	3	UA0076_op_blockB_cut1s02-4	3
UA0133	22/06/1984	14/01/2000	Female	Chernigov	PTC	UA0133_op_blockA_cut1s02-4	3	UA0133_op_blockB_cut1s02-4	3

Research data uploader

- CTB portal provides uploading facility for researchers – data as raw as possible
- Log on using approved project code – template for upload based on MDTA
- Data on individual samples can be combined and used by others
- Metadata collected on protocols used to derive data
- Links to public repositories and to published papers

Material supplied

Samples supplied to 33 projects. Several ongoing projects looking at "omic" approaches on mRNA, miRNA and sequencing of RNA and DNA (incl WGS)

Issued so far:

- 853 frozen blocks*
- 1137 FFPE blocks*
- 2828 aliquots of RNA from tissue
- 2377 aliquots of DNA from tissue
- 375 vials of whole blood*
- 428 aliquots of DNA from blood
- 9107 paraffin sections

* Only released in exceptional circumstances

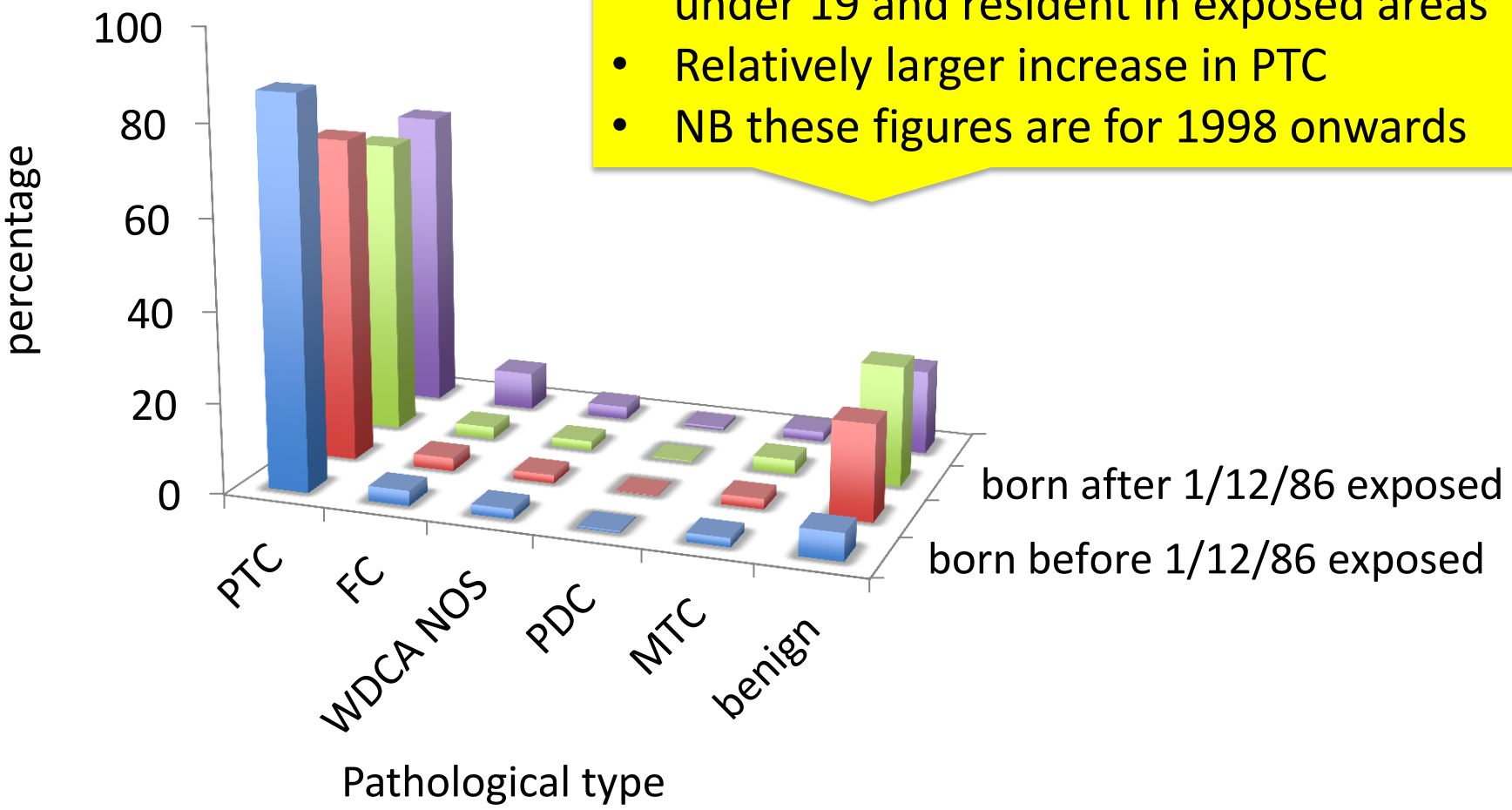
>40 publications so far see www.chernobyltissuebank/papers

Use of resource

- To date 25% of all accrued cases have been used in research
- 51% of those cases with the highest thyroid doses (>500 mGy) have been used in research compared with 16% with the lowest doses (<100 mGy)
- Majority of projects focus on PTC, but projects on MTC and FT also supported

Pathology of post Chenobyl TC

- Larger number of cancers in those aged under 19 and resident in exposed areas
- Relatively larger increase in PTC
- NB these figures are for 1998 onwards



Clinical outcome

Cohort	Paediatric thyroid cancer arising after exposure to Chernobyl fallout	Paediatric thyroid cancer arising after exposure to external beam irradiation	Paediatric thyroid cancer developing without previous radiation exposure	Adult thyroid cancer developing without previous radiation exposure
N1	60–70%	60–70%	40–90%	30–40%
M1	10–15%	10–15%	5–25%	2–5%
Recurrence	30–50%	30–50%	30–50%	20–30%
Death	1%	1%	1%	5%

R.M. Tuttle et al. / Clinical Oncology 23 (2011) 268–275

- Post Chernobyl thyroid cancer similar to young onset thyroid cancer arising from other causes
- Although recurrence rate range is higher, mortality is lower than for adult onset
- Recent evidence suggests molecular phenotype of young onset disease leads to retention of the iodine symporter

Summary

- The CTB facilitates integrated research across international boundaries to a rare resource
- Different formats of biological material available from the same patient to facilitate systems oncology
- Will continue to lead to new insights into the molecular biology of childhood thyroid cancer
- The CTB is a paradigm for modern tissue banking in the omics era – and has been used as a model to set up more wide-ranging collections

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www.chernobyltissuebank.com