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Astronaut Biodosimetry at Health Canada

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YOUR HEALTH AND SAFETY... OUR PRIORITY.

Motivation for Astronaut Biodosimetry

Cytogenetic analysis of blood from astronauts provides a **sensitive**, ***in vivo*** **measurement** of the biological effects of exposure to space radiation

Biodosimetry is currently a medical requirement as specified in the ISS MED Vol. B Appendix A, Matrix 1 (CSA) & 2 (ESA):

Matrix 1 – CSA

C1.01 BIODOSIMETRY TESTING (OCCUPATIONAL MONITORING)

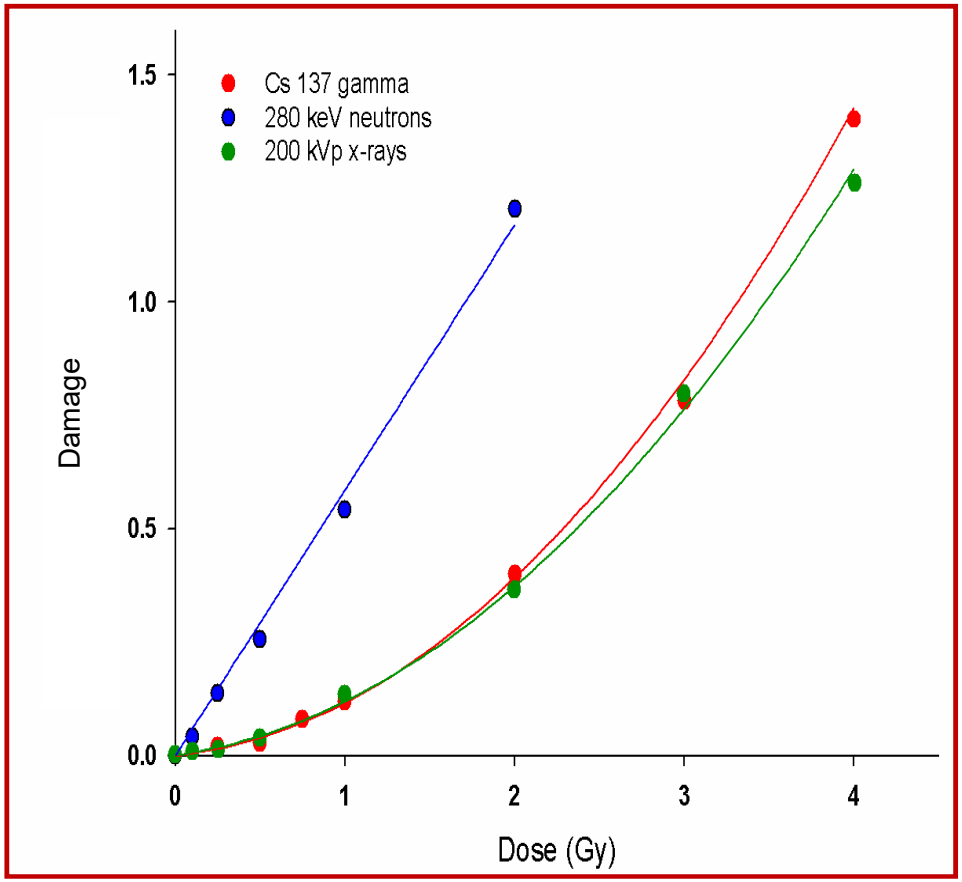
Requirement : Biodosimetry data will be collected preflight and post flight on all CSA crewmembers as part of the Occupational Health Monitoring Program. The data will be included in the individual crewmember's medical record.

Rationale : These data are not used for risk assessment, but should be available as a measure of individual radiosensitivity and for screening for potential post-mission health effects for individual crewmembers.

Health Canada heads the Canadian Biodosimetry Network; as such, the Ionizing Radiation Health Sciences Division of CCRPB is equipped to house the astronaut biodosimetry program.

Biodosimetry

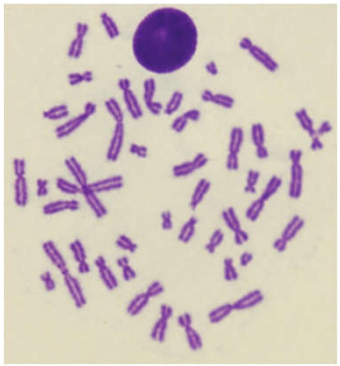
- Radiation-induced damage to DNA can be measured using cytogenetic endpoints
  - These endpoints can be related to levels of exposure
- Essential for triage in the case of a large-scale r/n event, these endpoints are also used for various research projects at Health Canada including:
  - Automation of cytogenetic assays
  - Identification of biomarkers of radiation sensitivity
  - **Cytogenetic analysis of blood samples from astronauts**



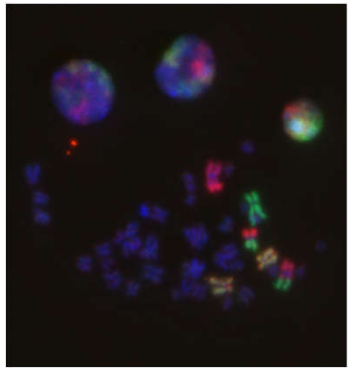
Biodosimetry Assays

- Dose assessments can be performed from blood samples using a number of different types of assays:

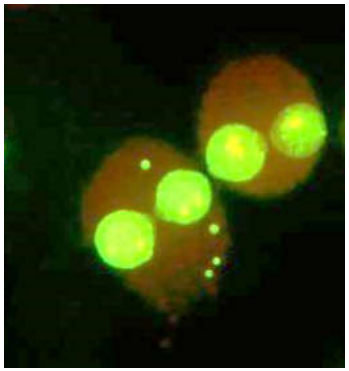
DCA



FISH



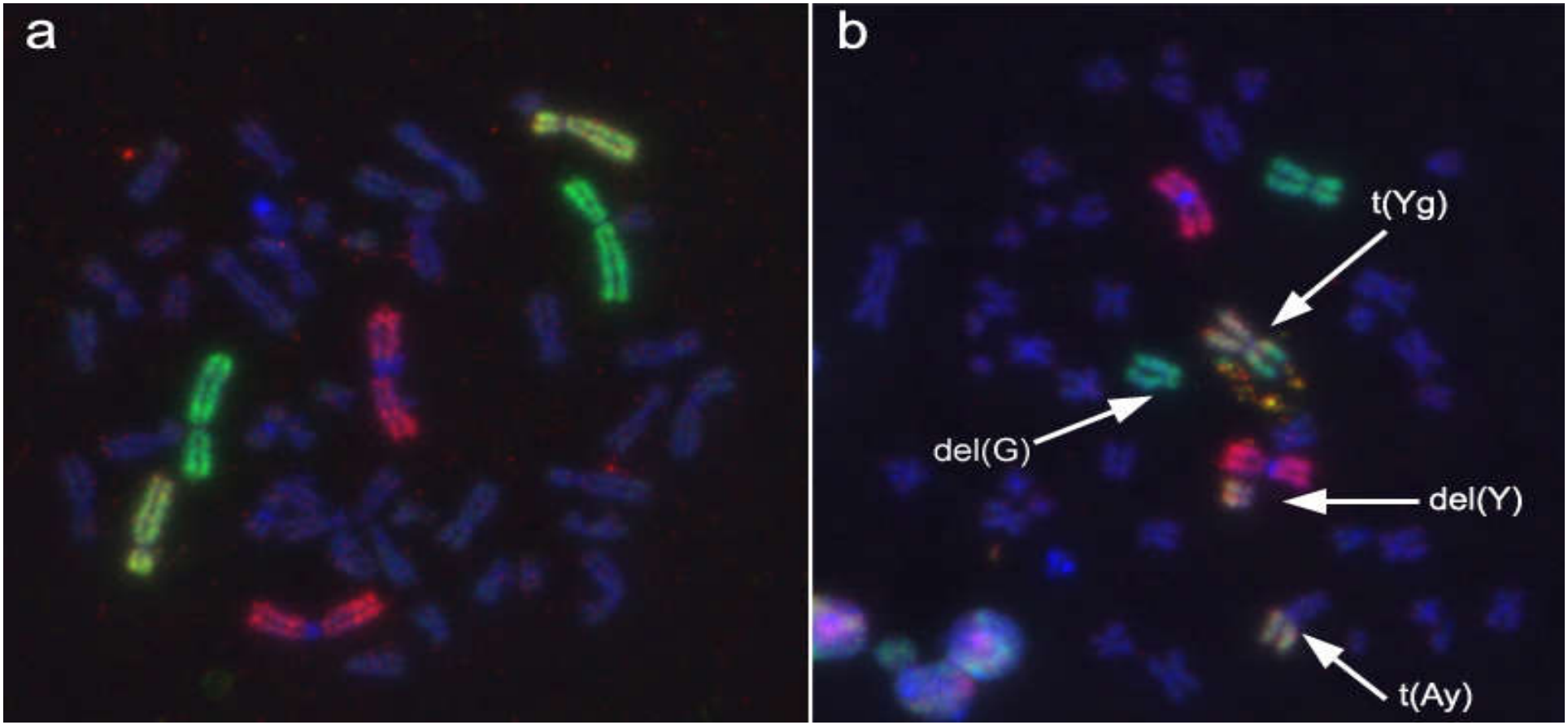
CBMN



- DCA: Dicentric Chromosome Assay
- Translocation Assay (FISH): Fluorescent *in situ* Hybridization
- CBMN: Cytokinesis Block Micronucleus Assay
- Additionally: Lymphocyte isolations can be done on any remaining blood and cryogenically frozen in case it's needed in the future

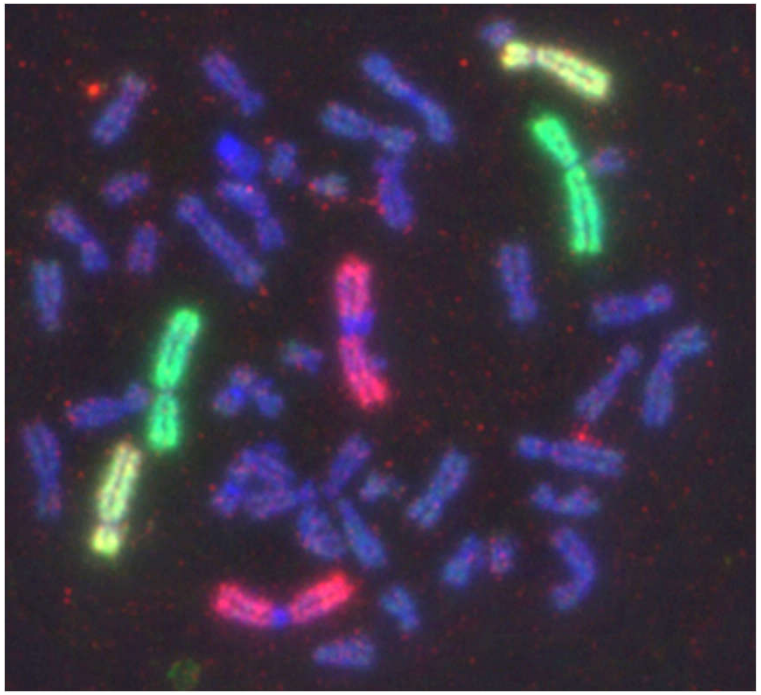
Fluorescence in situ hybridization (FISH)

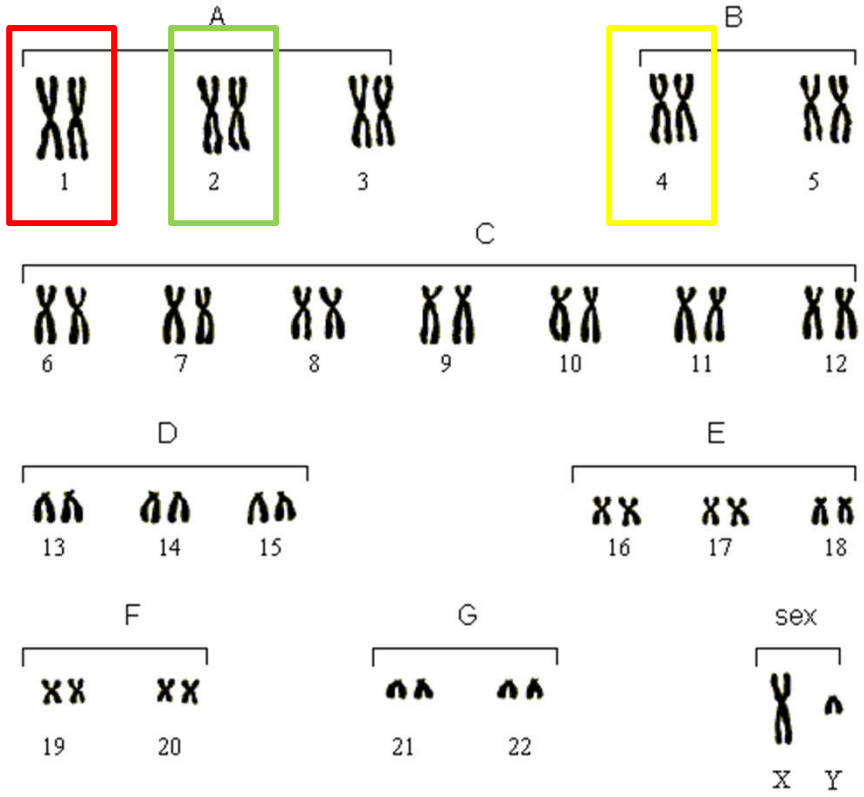
Whole chromosome fluorescence *in situ* hybridization (**FISH**) allows for the detection and identification of chromosome translocations in metaphase spreads.



Fluorescence in situ hybridization (FISH)

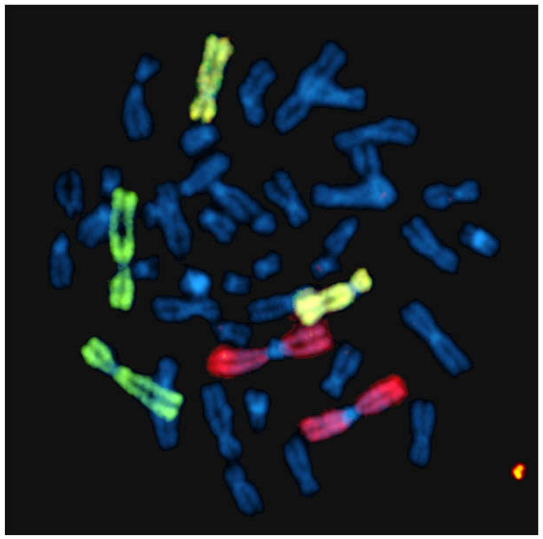
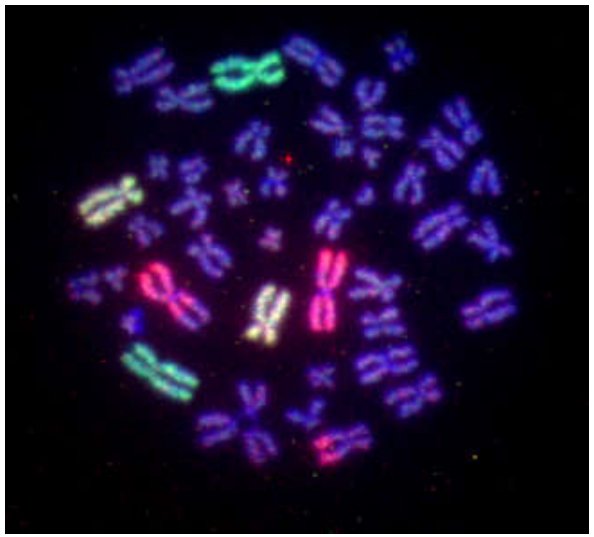
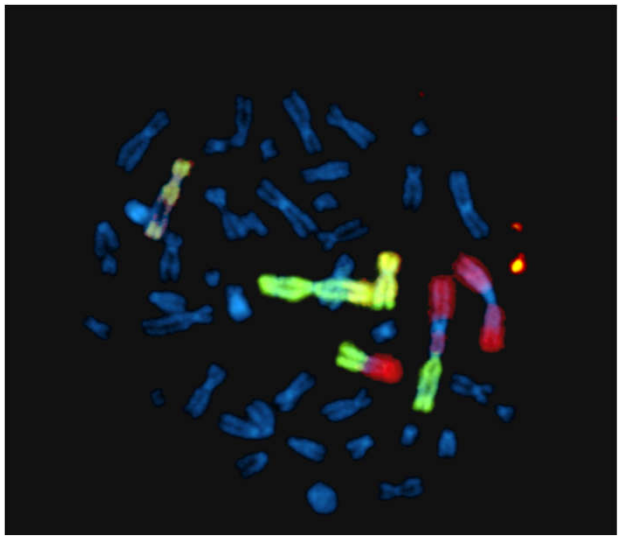
Metaphase spreads are scored for: stable and unstable translocations, colour junctions, deletions, insertions, inversions, dicentrics, rings, and acentric fragments





Fluorescence in situ hybridization (FISH)

- Simple translocations are stable and provide a measure of the cumulative lifetime dose

Chromosome Damage: Simple Damage

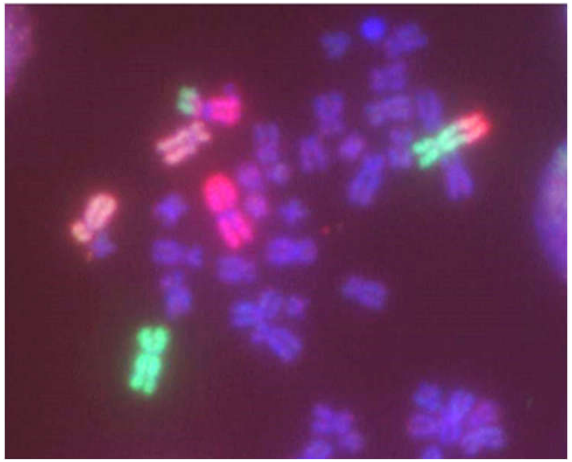
Simple (AST, TIT, PIT)

Apparently Stable Translocation

Direct swap between 2 chromosomes

t(Ar) + t(Ra) + R

t(Rg) + t(Gr) + R + G



Pseudo-Incomplete Translocation

1 translocation and 1 deletion

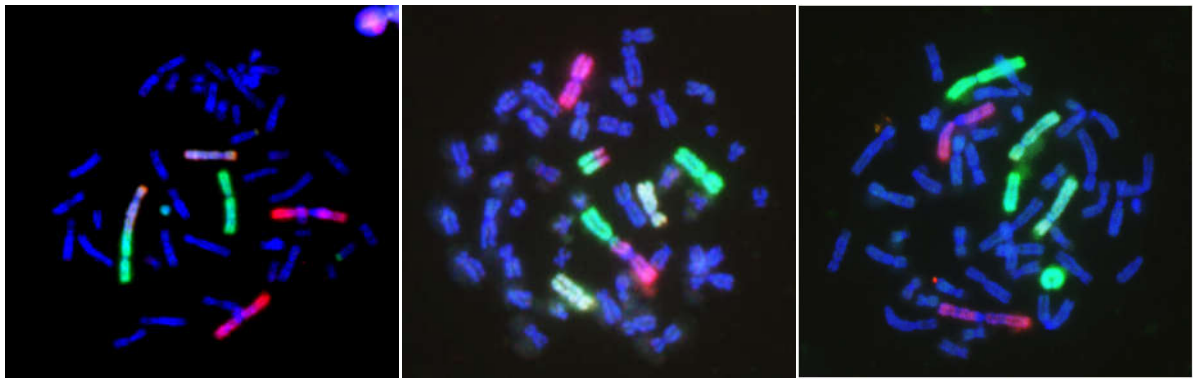
t(Ar) + del(R) + R

Totally Incomplete Translocation

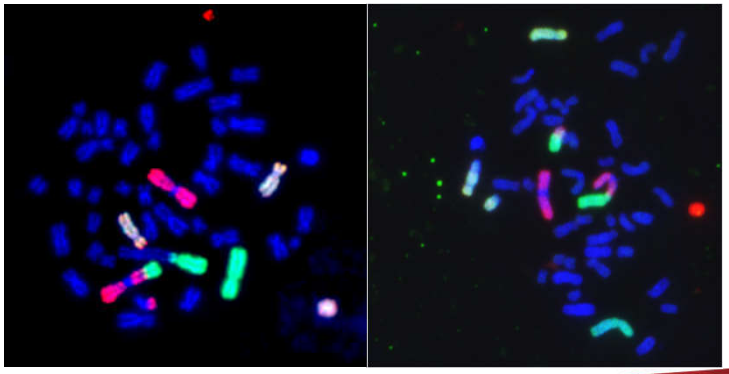
t(Ra) + R (missing **r**)

Chromosome Damage: Other Damage

- Other types of damage are also visible
  - Dicentrics and rings – can be produced by any type of ionizing radiation

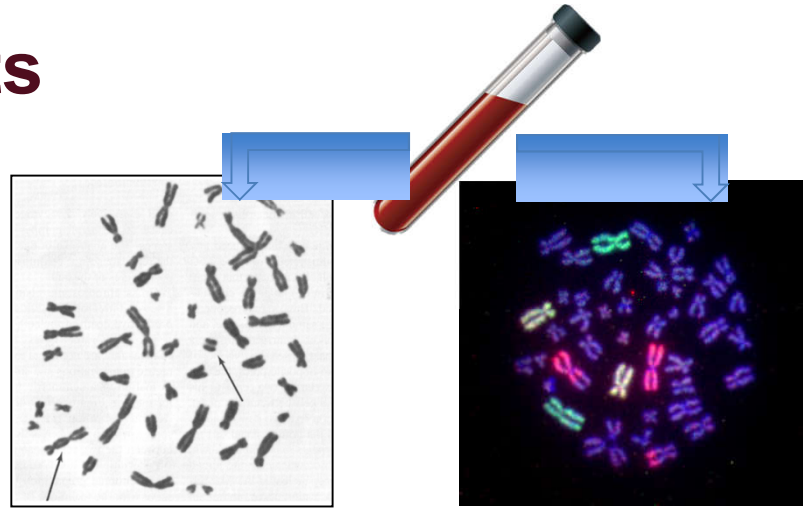


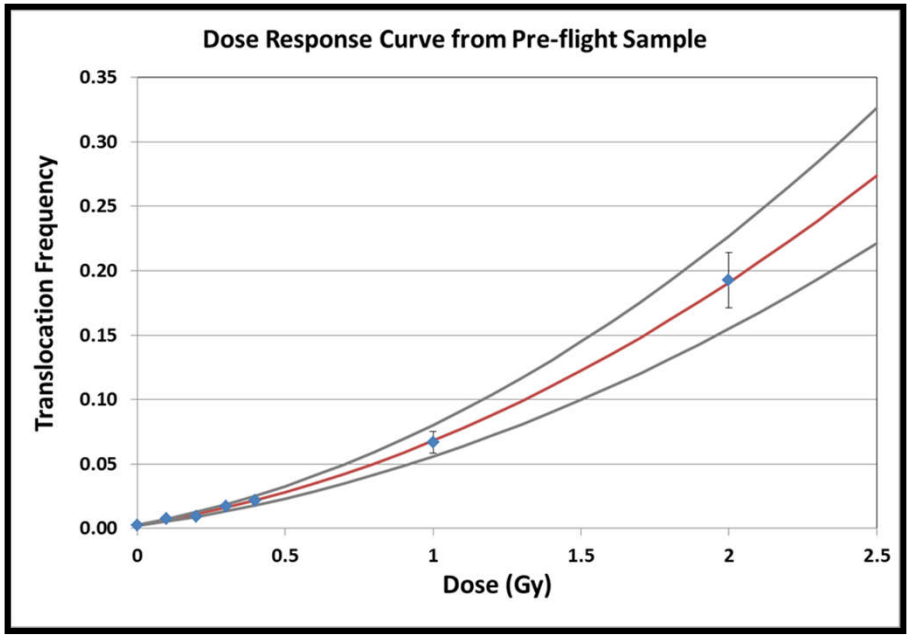
- Complex damage (damage involving 3 or more breaks in 2 or more chromosomes)
  - Less likely after low LET radiation
  - HZE are capable of producing extremely complex patterns



Biodosimetry on Astronauts

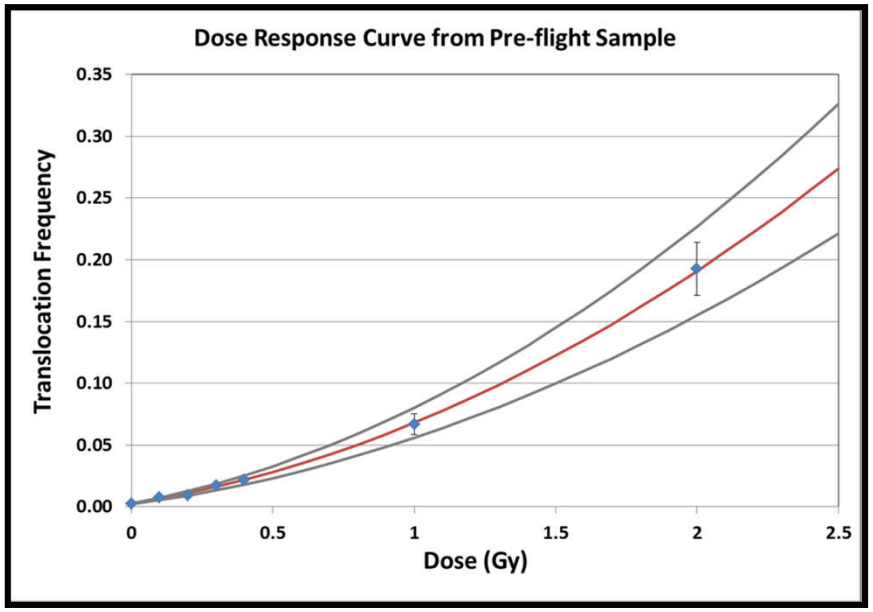
- For each astronaut, we receive a venous blood sample prior to their flight, and 2 more samples post-flight
  - PRE-FLIGHT:
    - 34 mL: L-35/90 days
  - POST-FLIGHT:
    - 17 mL: R+7/14 days
    - 17 mL: R+6/18 months
- Using the pre-flight sample, we generate a FISH dose response curve, now with doses ranging from 0-2 Gy
  - Each astronaut is their own baseline





Aberration Scoring

- Scored spreads for:
  - AST, PIT, TIT, colour junctions, deletions, insertions, inversions, dicentrics, rings, and acentric fragments



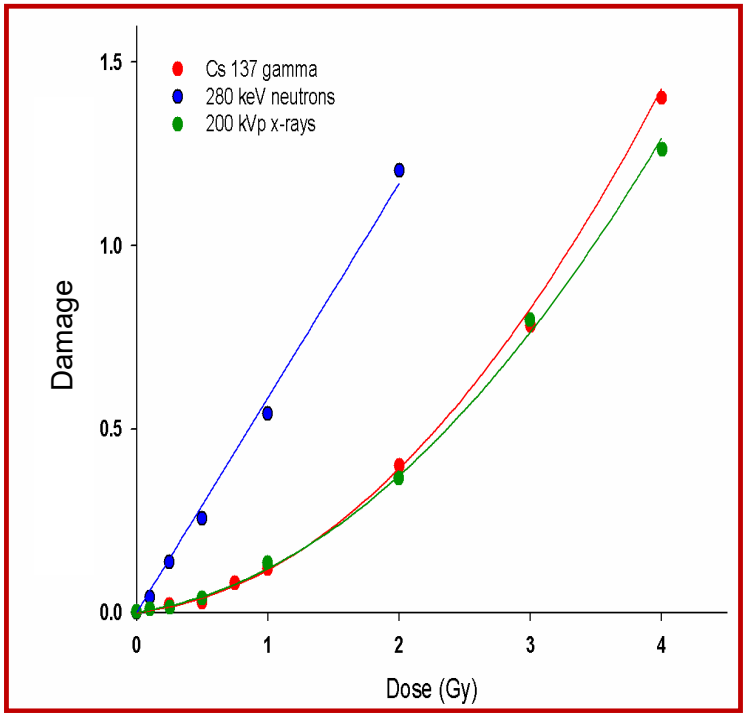
Dose (Gy)	# of cells to score
0 (pre-flight background)	10,000
0.10	4,000
0.20	3,000
0.30	3,000
0.40	3,000
1.0	1,000
2.0	500
Post-flight 1	10,000
Post-flight 2	10,000

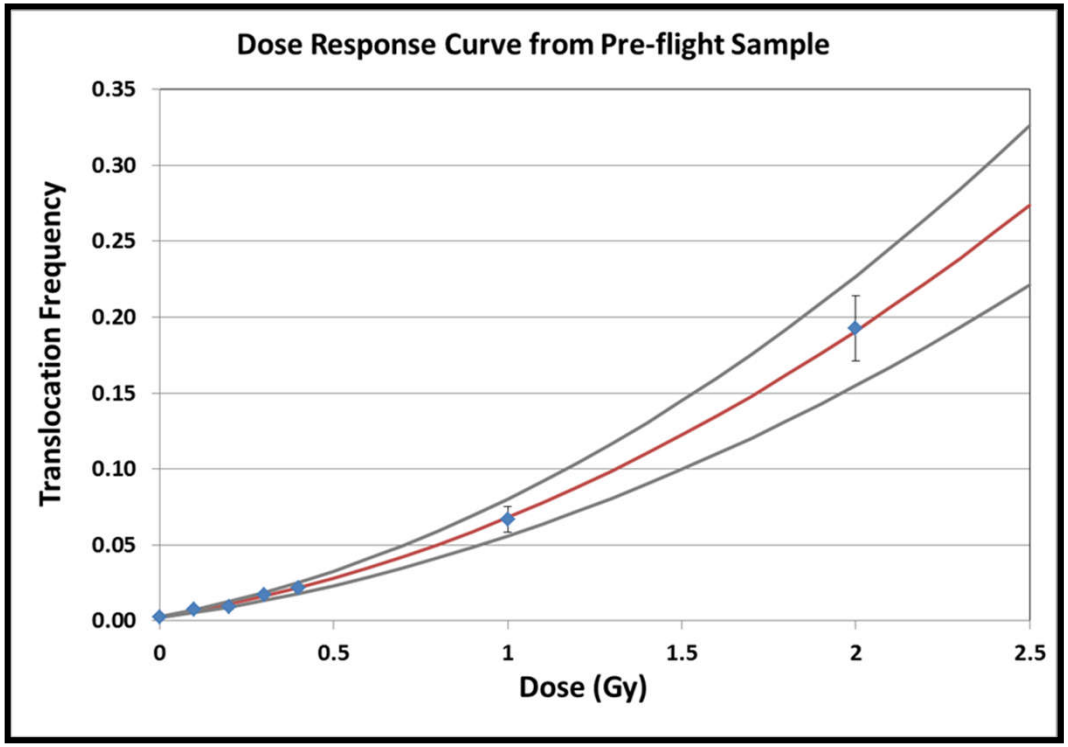

~0.7-3 mGy/day
USA
NASA


~0.05 mGy/h

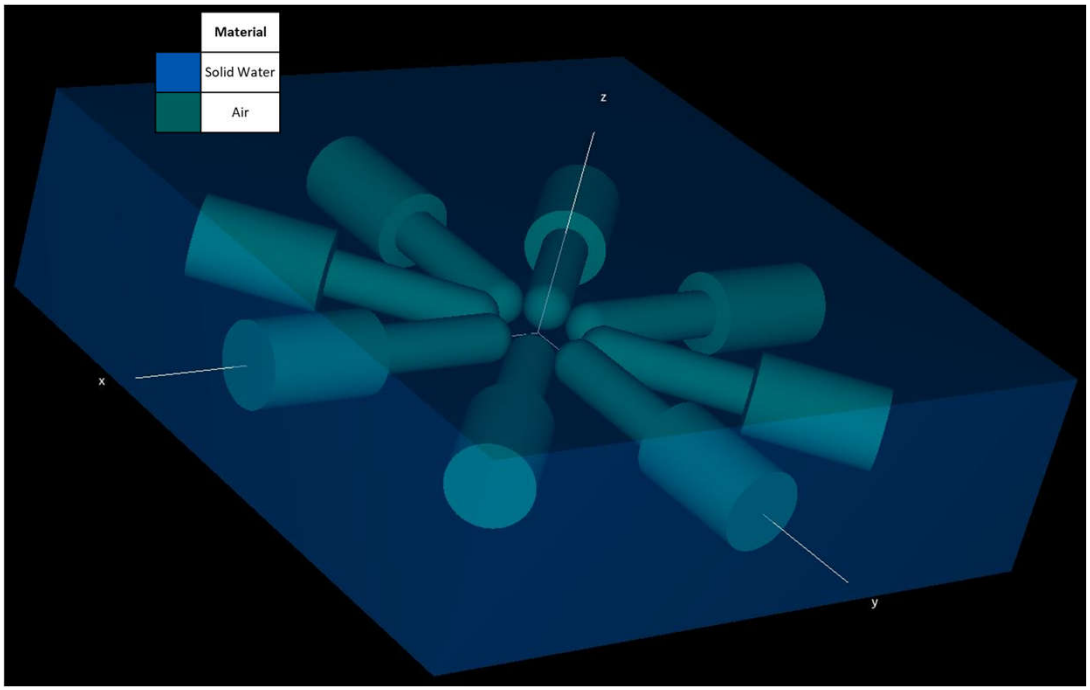

~0.8 mGy/day

Calibration Curves





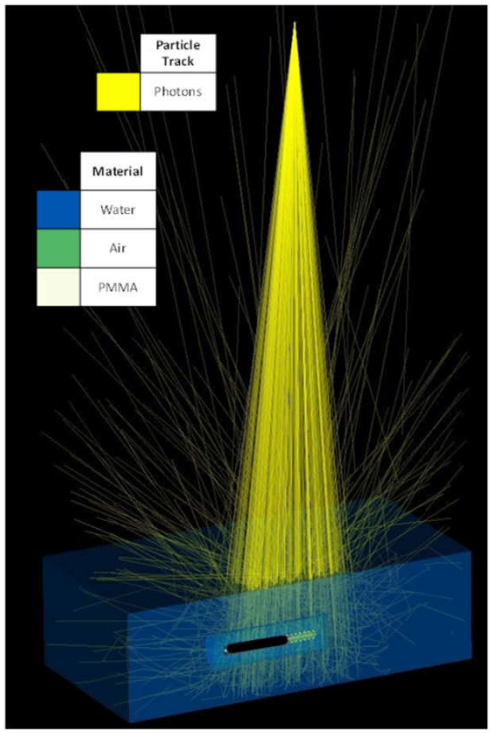
Current Work: Monte Carlo modelling

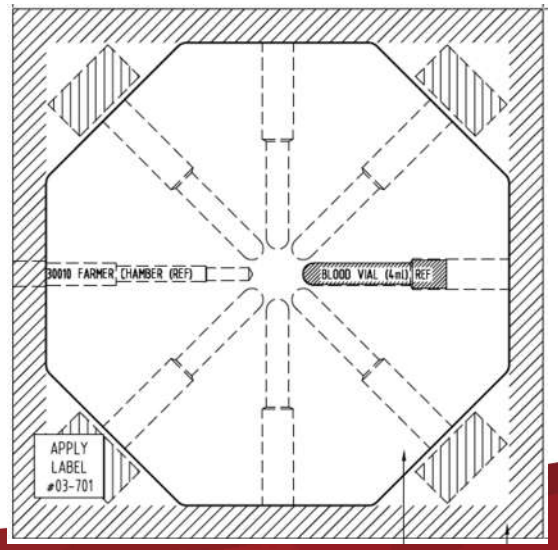


(top) 4 mL vial Slab Phantom model in EGSnrc

(right) Particle tracks after using SpekCalc spectrum as source for simulation (cross section):

**Preliminary work from*
Dinindu Gunasekara (MSc student, Medical Physics)

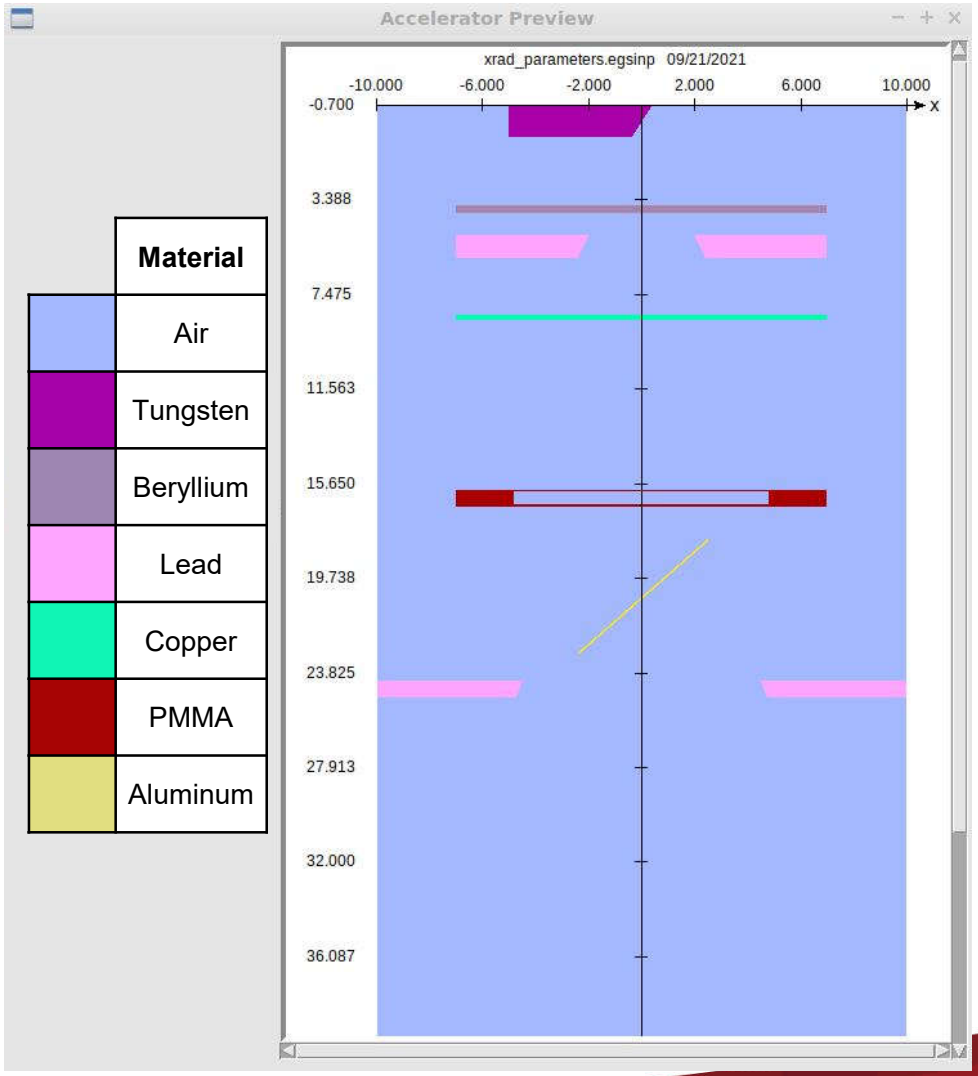




Future Work: Monte Carlo modelling

- XRAD-320 used to irradiate samples (below)
- Modelled in EGSnrc application BEAMnrc (left)
  - Can be used in previous model for more realistic radiation delivery

**Preliminary work from Dinindu Gunasekara (MSc student, Medical Physics)*



Future work

- Evaluation of other cytogenetics endpoints in astronaut samples analysed by FISH

- Pooling of the CSA and NASA data will provide better data in order
  - to compare doses from astronauts,
  - do a more in depth analysis other types of damage to determine if there are better indications of exposure and radiation quality,
  - look at variation in radiation sensitivity from the individual dose response curves.


Credit: NASA

- Evaluate stored samples for molecular endpoints

Conclusions

- Biodosimetry has been completed for 10 astronauts to date, and the results tend to lie in the range expected from physical dosimetry
  - Takes into account individual radiosensitivity
  - Biological response to radiation damage, particularly in a microgravity environment and stress

- As plans are being made for longer duration space travel, it would be ideal to maintaining robust, well harmonized biodosimetry methods between the space agencies.

- There are many gaps in the knowledge of biological effects of space radiation that could be addressed by a continuing collaboration between HC and CSA


Credit: NASA

Acknowledgements

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