



Oxford University Hospitals
NHS Foundation Trust

CT doses in Ethics: methods and pitfalls

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Summary

- Ethics process
- Common ethics CT examinations
- CT dose calculation methods
- Discussion points





Ethics process

- Studies with research exposures involving ionising radiation require MPE and CRE (Clinical Radiation Expert) statements for Part B section 3 of the IRAS submission form.
- Requires nature and number of exposures (both additional and standard of care) and estimate of dose and risk.
- Seems straightforward enough...??





IRAS form (excluding nuclear medicine)

B. Other ionising radiation

B1. Details of other ionising radiation

Give details by completing the table below:

Procedure	No of procedures	Estimated procedure dose (use national Diagnostic Reference Levels where available)

C. Dose and risk assessment

C1. What is the total participant dose from all the exposures in A1 and/or B1, and what component of this is the additional dose over and above standard practice? What are the risks associated with these two doses (total and additional)?

The dose and risk assessment should be set out below. This should be prepared by a Medical Physics Expert (MPE) who is a registered clinical scientist registered with the Health Professions Council and has expertise relevant to the planned exposures. Where the study involves different types of exposure (for example, both radioactive materials and other ionising radiation, or more than one imaging method), advice may need to be sought from other MPEs with relevant expertise. The lead MPE should produce a combined assessment for the ethics committee, giving the names of any other MPEs who have contributed to the assessment. Further guidance is available by clicking on the information button.



HRA process

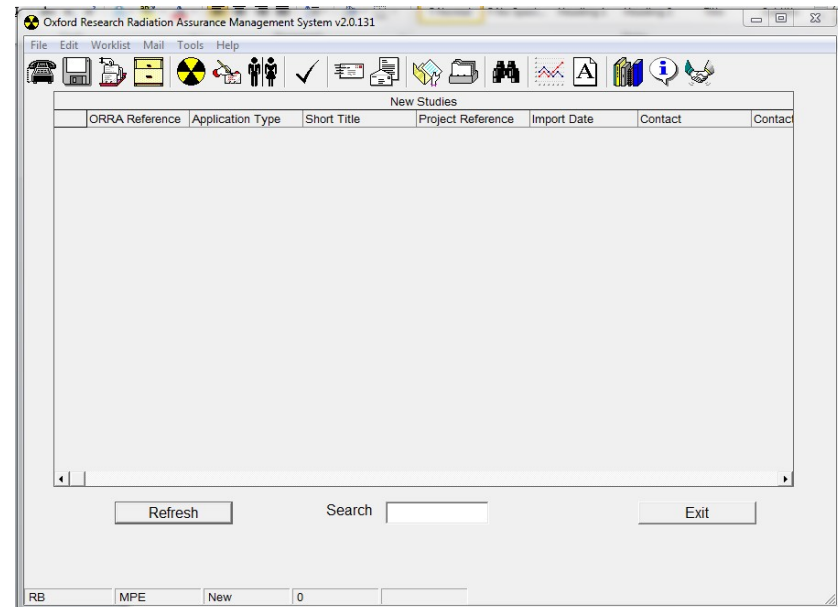
- HRA (Health Research Authority) have published guidance for MPEs and CREs on:
 - PIS (Patient Information Sheets) statements – typically do not put a numerical estimate on risk.
 - MPE and CRE statements depending on type (standard of care vs. additional) and extent of exposure as well as prognosis of study group.
 - Recommended references for dose estimates (CT – *Shrimpton et al 2015 BJR paper*).



Oxford process



- Use in-house software ORRA (Oxford Research Radiation Assurance) to track trials.
- Work closely with research radiographers to assess trial exposures.
- HRA guidance is used for IRAS and PIS statements and dose estimates.





Oxford process: risk assessment

The screenshot shows the 'Radiation Risk Assessment' software interface. It is divided into several sections:

- Research Exposures:** Contains two tables for 'Details of proposed research exposures involving radioactive materials (Question A1)' and 'Scientific or therapeutic research exposures (Question B1)'. The B1 table has columns for Description, Code, Routine, and Additional. One entry is 'CT Chest' with code 'CCHES', Routine '0', and Additional '1'.
- Form Fields:** Includes ORRA ID (1644 - Automatic), ID, Type of investigation/therapy, Exposure, Projection, Effective Dose (mSv), Routine Exposures, Additional Exposures, and Cohort.
- Risk Assessment:** Includes input fields for Additional Dose (mSv), TRPD (mSv), Background Radiation, Additional Risk Estimate, TRPD Risk Estimate, Days/Months/Years, and Cohort. It also has radio buttons for Risk Expression (1 in... or %) and Prognosis (<5yrs or >5yrs).
- Text Areas:** 'The cohort description appropriate for this study:', 'Risk Statement to be included in the Risk Assessment (C1)', and 'Risk statement for the Participant Information Sheet (PIS)'. There is also a 'Notes about this assessment' area.
- MPE (Medical Practitioner Examination) Details:** Lists MPE (NM), MPE (DR), and MPE (RT) with checkboxes for various names like Dr Matthew Walker, Mr Steve M..., Mr James Harries, Mrs Helen Amatiello, Mr Maxwell Robinson, and Mrs Charlotte Hector.

Exposure split

Dose estimate

Risk estimates

Prefills with suggested HRA statements based on dose/prognosis/split. Can be manually edited.

MPE details





Common CT exposures in ethics: NCAP/CAP

- NCAP/CAP studies for cancer staging in chemo drug trials. Required at fixed timepoints throughout the trial.
- Often patients have poor prognosis.
- Main difficulty is estimating number of scans and standard of care/additional split.
- Trials are often “open ended” and assessments continue as long as patient is tolerating treatment.
- **Can mean a patient receives many more scans than original IRAS assessment. Particularly if median survival time used for trial length estimate.**



<https://www.bbc.co.uk/news/health-49853878>

More than half of patients can now survive a deadly skin cancer that was considered untreatable just a decade ago, say UK doctors.

Ten years ago only one-in-20 patients would live for five years after being diagnosed with late-stage melanoma. Most would die in months.

But drugs to harness the body's immune system mean 52% now live for at least five years, a clinical trial shows.

Doctors said it was an extraordinary and rapid transformation in care.

What did the trial show?

The trial investigated two immunotherapy drugs which are designed to enhance the immune system and let it attack cancer.

There were 945 patients in the trial, a third were given nivolumab, a third were given ipilimumab and a third were given both.

Doctors then looked at the five-year survival rate - the proportion of patients still alive after five years.

The results showed:

- 26% were still alive on ipilimumab alone
- 44% were still alive on nivolumab alone
- and 52% were still alive when given both.

2 extracts from recent BBC article (28/09/2019)



Common CT exposures in ethics: HRCT

- HRCT used for pulmonary assessments.
- Patients are not healthy volunteers but typically have good prognosis.
- Often 2 phase scans specified at inspiration and expiration – **not clear if x2 NDRL is a good representation of this.**
- Patients not necessarily directly benefitting from scans, requires careful justification.
- **Can also be recommended as assessment for pneumonitis in cancer trials. ?Research exposure in this scenario.**



Example: Local HRCT

- Protocol includes inspiration and expiration so two phases but not equivalent scans in terms of dose. Combination of helical (inspiration) and axial (expiration).

The screenshot displays a medical software interface. At the top left, there is a small image of a chest scan with a green line and a box labeled 'x2'. To its right, the text reads 'CT CT Chest High Resolution CCHHR' and '5.10 C2 HRCT > 45Yrs'. Further right, there are four buttons: 'ICRP 103' (4 mSv), 'SSDE' (4.4 mGy), 'DLP Head' (- mGy-cm), and 'DLP Body' (196.2 mGy-cm). Below this is a navigation bar with tabs: 'Dosimetry', 'Acquisitions', 'Analysis', 'Contrast Report', 'Patient Protocols', 'RDSR', 'Protocol', and 'Logbook'. The 'Acquisitions' tab is selected, showing a table titled 'Examination Acquisitions'.

#	Series #	Description	Protocol	kVp	Mean mAs	CTDIvol	DLP	Irradiated Length	Slice Thickness	Target
2	6	Hi Res Exp	5.10 C2 HRCT > 45 Yrs	100	240	1.3	33.9	269.13	1.25	
1	2	Chest Insp	5.10 C2 HRCT > 45 Yrs	120	51.5	4.5	162.3	363.83	0.63	



Common CT exposures in ethics: Head CT

- Head CT may be performed at screening to check for metastatic spread or as a routine study assessment.
- **Can be easily missed in IRAS assessment as not necessarily performed on all patients and MRI often given as an option.**



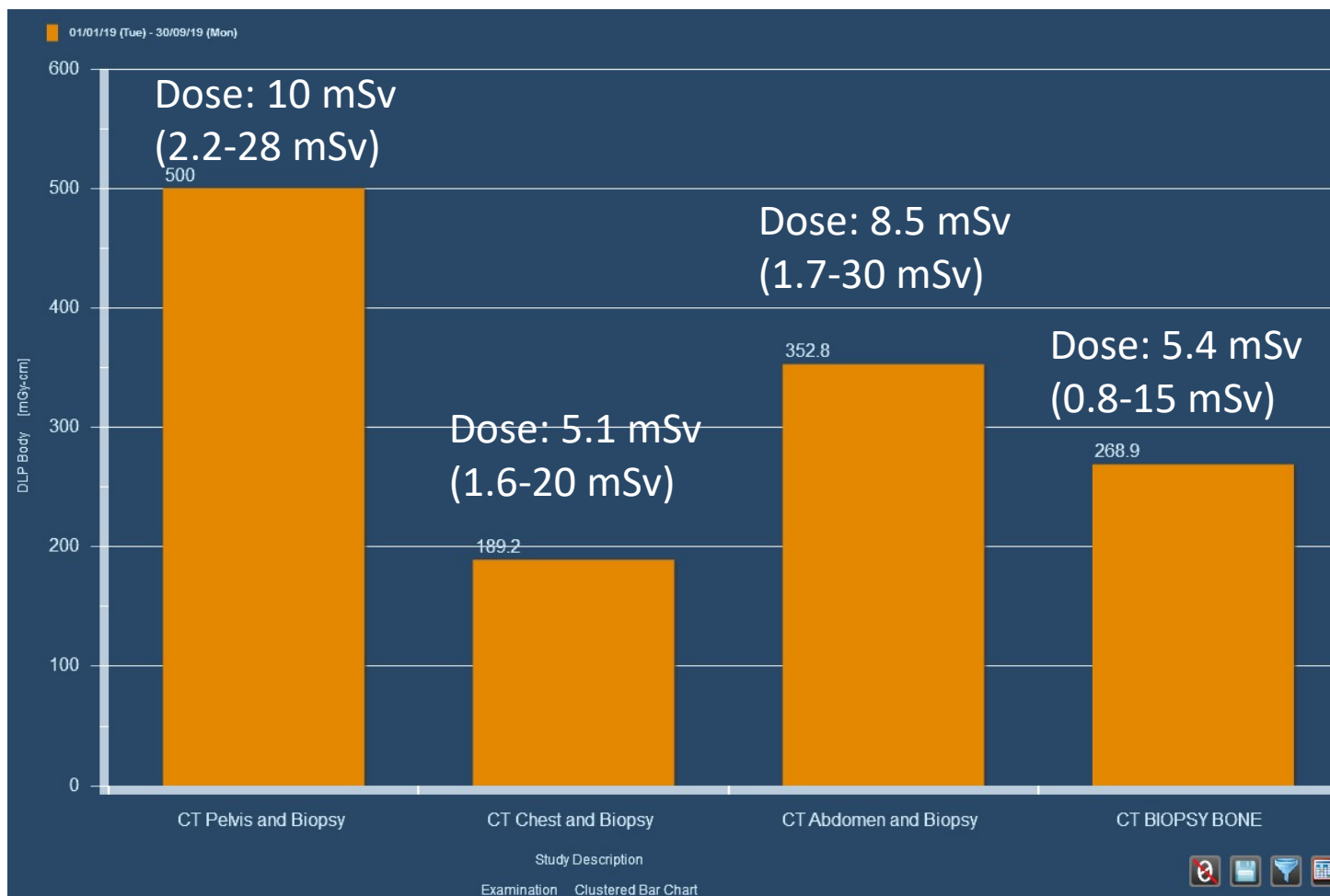


Common CT exposures in ethics: CT guided biopsies/injections

- Often given as an option for biopsies if ultrasound not considered suitable (dependent on location of lesion).
- Many studies also have additional paths involving a biopsy, which a patient can sign up to separately.
- Assessing dose can be difficult as dependent on location/complexity.
- **Can also involve additional imaging not specifically specified in protocol – lung biopsies are often followed up by chest x-rays as standard (pneumothorax risk).**



CT guided biopsies doses





Common CT exposures in ethics: Other

- Often protocols specify that imaging should include “other locations” if clinically relevant.
- Could be extremities, neck, head...
- Could be every scan or treatment might terminate if disease has spread.
- **Difficult to assess a dose as no clarity on scan location or numbers – different approaches: increase dose estimate by e.g 10% to account for variations or include specific dose estimates for additional scan regions.**



Low dose WB (whole body) CT

- Often proposed as an alternative to skeletal surveys for bone lesion assessments.
- Not performed at our site.
- No NDRLs but some good papers, which can be used as references.
- **Can be difficult to assess a protocol without local data or indication of how it would be performed.**



Calculation methods

- Typically start with examination DLP and use software or conversion factor to obtain effective dose.
- IRAS asks for NDRLs to be used where possible but often mean doses (*Shrimpton et al BJR 2015*) or best achievable doses (*Iball et al NM Comm. 2017*) used.
- Some big differences in doses with older references.
- Shrimpton provide generic conversion factors but need to be clear on phantom used. ImPACT can allow more detailed estimates and may be useful if an imaging protocol is available.



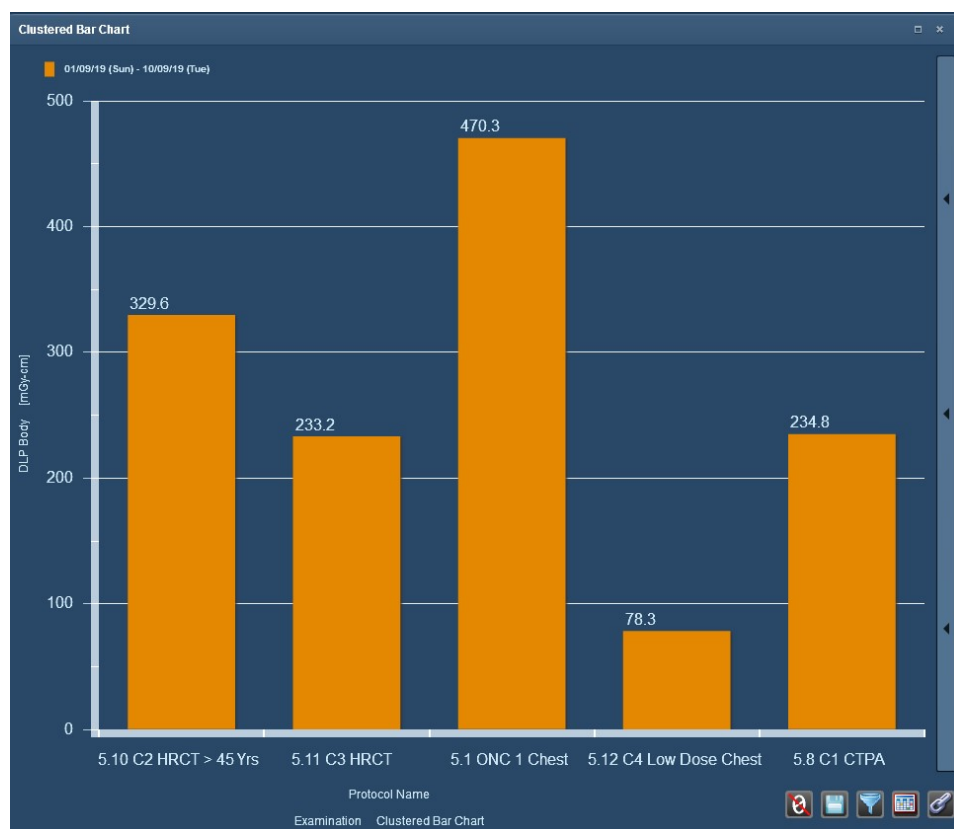
Calculation methods: comparison

						using NDRL as target DLP		
	NDRL	dose (Shrimpton BJR Table 6 conversion factor)	Mean DLP	dose (Shrimpton BJR Table 6 conversion factor)	HPA-CRCE-012	ImPACT (Siemens Sensation 64)	ImPACT (GE Lightspeed VCT)	ImPACT (Phillips brilliance 64)
CAP (cancer staging)	1000	21	900	19	10	18	18	17
CT Head (acute stroke)	970	1.9	890	1.8	1.4	2.2	2.5	2.2
Chest (lung cancer)	610	16.5	500	14	6.6	13	12	12
Abdomen (liver metastases)	910	22	670	16	5.6	17	16	16
units	mGycm	mSv	mGycm	mSv	mSv	mSv	mSv	mSv

- Use of NDRLs and BJR conversion factors appear to provide most conservative estimates.



Calculation methods



- Require clarity on scan indication, graph shows different local chest protocols.
- If particular number of phases is required and/or particular scan parameters – can be different to local practice.
- Better to ask questions now than after the patient has had the scan!



Discussion points

- What is considered acceptable dose variation? 50%? 100%? Dose assessment needs to be generous to cover different equipment/sites but does not remove need for local optimisation.
- Also studies in cohorts with good prognosis – maybe tighter dose assessments are a good thing?
- Tightrope in IRAS assessment as do not want patient scans/treatment delayed as waiting for amendments in order to increase number of scans
- Is one extra scan an issue? 2...3....10?