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An Exploratory Study of DNA and Chromosomal Damage in UK Nuclear Medicine Technologists

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Abstract: Objectives**.** Nuclear medicine technologists are chronically exposed to ionising radiation, yet the biological effects of chronic low-dose exposure remain poorly understood. This exploratory pilot study investigated DNA and chromosomal damage in technologists as biomarkers of occupational radiation exposure. Methods**.** DNA double-strand breaks were quantified by γH2AX immunofluorescence in cultured lymphocytes from blood samples of 20 technologists before and after radiotracer administration as well as from age- and sex-matched controls. The frequency of dicentric chromosomes, a well-established marker of radiation damage, was also scored. Participants completed questionnaires on occupational and lifestyle factors. Historical dose records were reviewed and dosimetry practices assessed by observation of dosimeter use. Results**.** Following routine radiopharmaceutical administration, technologists showed higher background γH2AX foci/cell than controls. Technologists also showed higher dicentric chromosome frequencies than controls while higher frequencies were observed among participants with a family history of cancer. There was a modest difference in the mean γH2AX foci/cell frequency between female and male participants. No significant associations were observed with smoking status and age. Weak correlations were noted with years of employment. Compliance with wearing personal dosimeters was high among technologists. Conclusions**.** γH2AX foci and dicentric chromosome frequencies were highly variable across groups and higher in nuclear medicine technologists. These findings provide preliminary evidence of differences in biomarkers of DNA and chromosomal damage in occupationally exposed technologists, suggesting that these biomarkers may have potential for detecting biological effects of low-dose occupational radiation exposure. Larger long-term studies are needed to determine whether these differences are related to occupational radiation exposure or to other factors that vary between individuals, and to assess the potential utility of these biomarkers for individualised routine biological monitoring as a supplement to dosimetry monitoring.

Keywords: γH2AX; dicentric chromosomes; nuclear medicine technologist; biomarkers; occupational exposure



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1. Introduction

Nuclear medicine uses radioactive tracers for diagnosis and therapy, with nuclear medicine technologists (NMTs) exposed to ionising radiation during tracer handling, administration and from patients after tracer administration [1]. Technologists working in positron emission tomography (PET) face relatively high radiation exposures as the field expands due to technological developments and new radiotracers [2–4]. While staff working in conventional nuclear medicine facilities typically receives annual effective doses of 0.1 mSv, occupational doses in PET are frequently close to 6 mSv [5]. In the UK, radiation safety follows the 'as low as reasonably practicable' (ALARP) principle by minimising exposure time, maximising distance, and using radiation effective shielding. However, protecting personnel can be challenging as approximately 90% of radiation exposure comes from unavoidable patient contact [6,7]. The use of unsealed sources also presents high exposure to the hands as technologists prepare, draw up, and inject radiopharmaceuticals [8].

Current estimates of health risks from low dose-rate radiation are largely derived from population-level studies of Japanese atomic bomb survivors [9,10]. Despite increased use of radiation in modern medical diagnostics, there are no up to date long-term epidemiological studies on cancer risks among medical radiation workers; the few longitudinal studies that previously reported cancer risks in medical radiation workers have mostly focused on general radiology workers [10–18]. An ongoing US longitudinal study of radiologic technologists employed between 1926 and 1982, based on surveys from 1983–1989, 1994–1998, and 2003–2005, found that those who performed nuclear medicine procedures had slightly higher risks for some health outcomes than those who did not, although the authors emphasised that longer follow-up is needed [18]. However, a later survey in 2012–2013 found an increased risk of cataracts was observed among technologists who had performed a nuclear medicine procedure but no increased risk of cancer incidence or cancer deaths [19,20]. Once again, the authors emphasized the small sample size, a need for longer follow-up and possible exclusion of older workers who had died or developed a cancer from this last analysis. The data relating to nuclear medicine technologists in this study unfortunately does not include nuclear medicine technologist registered after 1982. Considering the increasing demands for nuclear medicine studies, especially PET/CT since then, it would be useful to follow those certified later also to get a more up-to-date representation of nuclear medicine technologists today. The Million-Person Study is another large ongoing US cohort examining long-term health effects of low-dose ionising radiation in over one million workers and veterans, but published dose–response cancer risk analyses so far mainly involve industrial and nuclear workers, with no separate peer-reviewed results yet for medical imaging workers [21]. As such, research on nuclear medicine technologists remains limited due to scarce data, as this would require further long-term observation and large-scale epidemiological studies [19]. There are also challenges in determining combined internal and external exposures [9,10] for each individual in such a dose/risk study. For example, personal dosimetry may underestimate the actual exposure to technologists due to cumulative doses being unknown with monthly or quarterly readings occasionally being below detection thresholds and affected by improper dosimeter placement [22].

The lack of relevant epidemiological data and despite remaining within occupational dose limits, worries around cumulative low-dose radiation exposure and its impact on each individual's health remain amongst UK nuclear medicine technologists prompting this stakeholder-driven research initiative. Also, health estimates focus on dose risk at the population level, but this does not translate to individual outcomes as radiation susceptibility may vary due to multiple biological confounders and genetic diversity [23]. As such, it is important to investigate the biological effects of radionuclide occupational exposure in individual nuclear medicine technologists and biomarkers could provide more timely and effective insights into potential individual radiation sensitivities [24].

Here, we conducted an exploratory pilot study to investigate observable biological effects in peripheral blood lymphocytes from individual UK nuclear medicine technologists exposed to chronic, low-dose occupational radiation in a real-world occupational setting. We assessed γH2AX as an indicator of early DNA damage alongside dicentric chromosomes as a marker of more persistent, radiation-specific mis-repaired chromosomal damage.

2. Materials and Methods

2.1. Ethics

The study had local ethical approval and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants (Figure S1).

2.2. Selection and Exclusion Criteria

A total of 20 technologists and 20 controls were approached for participation. All consented but four controls were excluded; three due to needle phobia and one due to having undergone a CT abdomen scan in the preceding week. The final study population comprised 20 technologists and 16 controls. The NMTs were recruited from both general nuclear medicine and PET imaging in UK National Health Trusts alongside age and sex matched healthcare worker controls from the same Trusts to reduce healthy worker bias (Table 1). Participants were >18 years old and able to provide written informed consent. Exclusion criteria included cancer diagnosis, being on chemotherapy or radiotherapy, and recent CT, nuclear medicine, PET, or fluoroscopy imaging within 12 months.

Table 1. Characteristics of nuclear medicine technologists (n = 20; 55% male, median age 20–39 years) and of control participants (n = 16; 50% male, median age 20–39 years). Smoking history and parental cancer history are indicated (N = no, Y = yes) as is place of work (P = PET department, RP = Radiopharmacy, NM = general nuclear medicine).

Participants	Sex	Age	Smoking	Cancer History	Department	Years in Employment
T1	F	20–39	N	N	P	4
T2	F	20–39	N	N	P	5
T3	F	20–39	EX	N	P	11
T4	M	20–39	N	N	P	6
T5	F	40–59	N	N	P	28
T6	F	20–39	N	PARENT	P	5
T7	M	20–39	N	N	P	3
T8	F	20–39	N	N	P	3
T9	M	20–39	EX	N	RP	8
T10	M	40–59	N	N	P	25
T11	F	20–39	N	N	RP	8
T12	M	20–39	N	N	RP	11
T13	F	20–39	N	N	P	3
T14	F	20–39	N	PARENT	NM	8
T15	M	20–39	N	PARENT	NM	14
T16	M	20–39	Y	N	RP	9
T17	M	40–59	EX	PARENT	NM	20
T18	M	60+	N	PARENT	NM	40
T19	M	20–39	N	PARENT	NM	9
T20	M	20–39	N	N	NM	11
C1	F	20–39	N	N	N/A	N/A
C2	M	20–39	N	N	N/A	N/A
C3	M	20–39	N	N	N/A	N/A
C4	F	20–39	EX	N	N/A	N/A
C5	F	40–59	N	N	N/A	N/A
C6	F	20–39	N	N	N/A	N/A
C7	M	40–59	EX	N	N/A	N/A
C8	F	20–39	N	N	N/A	N/A
C9	F	20–39	N	N	N/A	N/A
C10	F	20–39	N	PARENT	N/A	N/A
C11	M	20–39	N	N	N/A	N/A
C12	M	20–39	N	N	N/A	N/A
C13	M	60+	N	N	N/A	N/A
C14	F	20–39	N	PARENT	N/A	N/A
C15	M	20–39	N	N	N/A	N/A
C16	M	20–39	EX	PARENT	N/A	N/A

2.3. Questionnaire

Participants completed a questionnaire (Figures S2 and S3) and self-reported the number of years working in the field of nuclear medicine, the type of facility worked in, procedures performed (e.g., radiopharmaceutical preparation, generator elution), the frequencies of diagnostic and therapeutic procedures performed, and radiation safety measures employed (e.g., shield use, distance from patient). Personal data included height, weight, physical activity, family history of cancer, smoking status, and personal diagnostic and therapeutic radiation procedures.

2.4. DNA Damage: γH2AX

The γH2AX assay was used to assess short-term DNA damage. All blood sampling was performed between approximately 08:00 and 09:00. For NMTs, venous blood samples were collected at two time points during the same morning: a baseline sample collected prior to radiopharmaceutical administration, and a second sample collected within 30 min following drawing up and administering a radiopharmaceutical to a patient. The radiopharmaceuticals administered were 350 MBq [^{18}F]FDG for PET, 170–220 MBq [^{99m}Tc]Tc-Myoview for general nuclear medicine, 19.6–22.0 GBq [^{18}F]FDG for PET radiopharmacy and 11 GBq [^{99m}Tc]Tc-Myoview for nuclear medicine radiopharmacy.

Controls were chosen from participants who do not work with radiation. Samples from controls participants were collected in the morning before they started their working day. Controls were therefore sampled at a comparable time of day, although a second time-matched control sample was not collected.

All blood samples were immediately placed on ice following collection and maintained under these conditions until sample preparation. Lymphocytes were isolated by density gradient centrifugation, washed and γH2AX assessed microscopically. Samples for which staining was unsuccessful or unsuitable for reliable quantification were excluded from the γH2AX analysis. For further details, see supplementary methods.

2.5. Chromosomal Damage: Dicentric Chromosomes

The dicentric chromosome assay was carried out on the first baseline blood samples from technologists and the control group and followed standard protocols [25,26]; for more details, see supplementary methods.

2.6. Assessing Dosemeter Practices

With participant consent, occupational radiation exposure was assessed using individual passive dosimetry records from local radiation protection services. Dose records were unavailable for two technologists. Whole-body dose records covering the 12-month period preceding blood sampling were used for each participant. Where records were incomplete, the available data were extrapolated to estimate the corresponding 12-month cumulative dose. Historical dosimetry records were then used to relate biomarkers to recorded radiation doses. To assess the reliability of these records, compliance with dosimeter use was evaluated through observational monitoring of passive dosimeter use at two UK sites: a general nuclear medicine department (8 observation days, 5–8 technologists per day; Panasonic UD-802AT-D) and a PET department (8 observation days, 9–15 technologists per day; Luxel Landauer). Compliance was assessed by observing whether each technologist was wearing their dosimeter during routine work. Technologists were not informed that the observations were being conducted, to minimise the potential for behaviour to be altered by awareness of being observed. For each observation day, the number of technologists wearing their dosimeter and the number not wearing their dosimeter were recorded.

2.7. Statistical Analysis

Data are presented as mean ± standard deviation. Statistical analysis was carried out using GraphPad Prism v10.6.1 and significance annotated as, * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; and **** $p < 0.0001$. Multiple unpaired *t*-tests were carried out for the γH2AX and dicentrics assays. For γH2AX foci, pre- and post-injection measurements from the same nuclear medicine technologists were compared using a paired *t*-test.

The Welch's *t*-test was used to compare group means due to unequal variances for cancer history for the γH2AX and dicentric assays. Simple linear regression with Pearson correlation analysis was used for comparison of body dose to dicentrics and finger doses to γH2AX foci. A multivariable linear regression sensitivity analysis was performed to assess the association between historical annual whole-body dose and dicentric chromosome frequency, adjusting for sex, smoking history and family history of cancer. Current and former smokers were combined into an ever-smoker category and compared with never-smokers. The analysis focused on dicentric chromosome frequency because γH2AX foci reflect a transient DNA damage response following irradiation, whereas dicentric chromosomes can persist in circulating lymphocytes and may provide a more stable indicator of accumulated chromosomal damage.

3. Results

3.1. DNA Damage: γH2AX

Four technologist samples and one control sample were excluded due to unsuccessful γ-H2AX staining, resulting in 16 technologists and 15 controls included in the analysis. An unpaired t-test showed that baseline γH2AX

frequency in technologists was 0.35 ± 0.31 foci/cell, which was not significantly different from that in controls at 0.35 ± 0.19 foci/cell. A paired t-test showed a statistically significant increase in γH2AX frequency following tracer administration from 0.35 ± 0.31 to 0.64 ± 0.46 foci/cell in the same technologists ($p = 0.0024$; Figures 1 and 2).

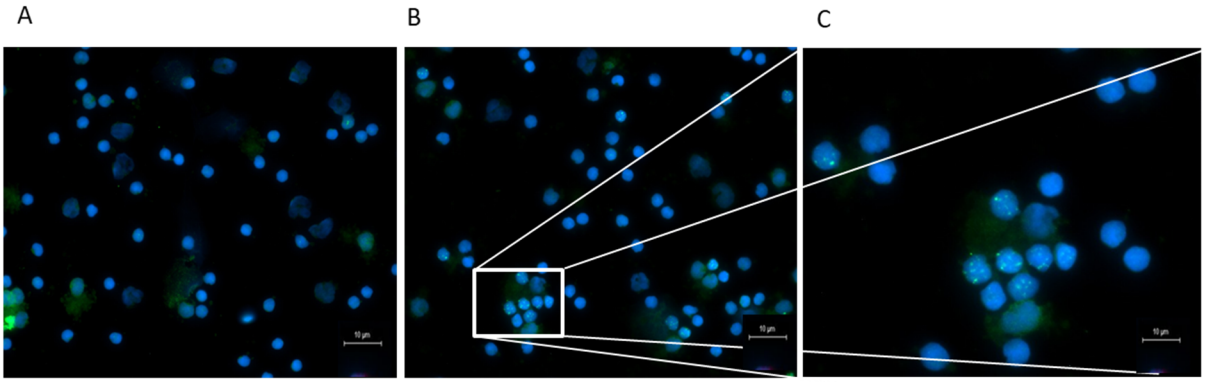


Figure 1. γH2AX immunofluorescence image of a technologist's blood lymphocytes. (**A**) is before administering a radiopharmaceutical to a patient and (**B**) is after radiopharmaceutical injection. (**C**) is a magnified version of the box in (**B**) for better visualisation of the γH2AX foci in nuclei. The scale bar is 10 microns.

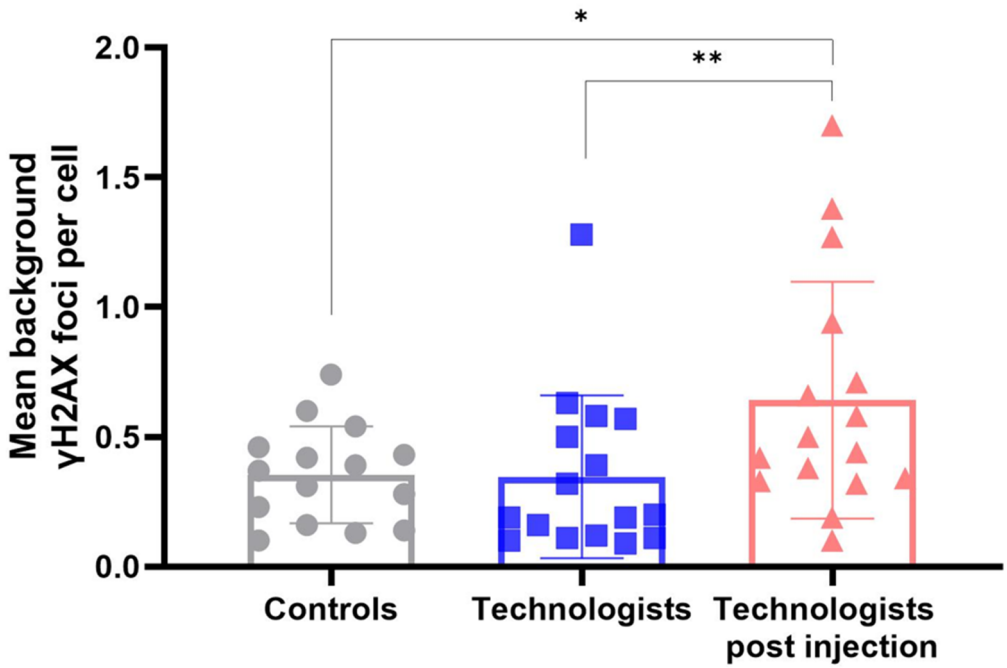


Figure 2. γH2AX foci in blood lymphocytes from control participants and technologists (before and after radionuclide handling and administration to patients). Background mean frequency of γH2AX foci/cell measured after blood sample collection in controls and technologists, before and after performing a radioactive injection. Samples with unsuccessful γH2AX staining were excluded from the analysis. An unpaired t-test was used to compare controls with technologists at baseline, and a paired t-test was used to compare technologists before and after administering a radioactive injection. Asterisks indicate statistical significance * $p < 0.05$; ** $p < 0.01$.

3.2. Chromosomal Damage: Dicentric Chromosomes

Dicentric chromosomes are chromosomes with two centromeres, which arise after ionising radiation exposure (Figure 3A). The dicentric chromosome assay was successfully performed on all blood samples from the technologists, with no samples excluded from the analysis. A higher proportion of these were found endogenously in the blood samples of technologists (0.11% ± 0.07%) versus in controls (0.07% ± 0.05%; $p = 0.03$; Figure 3B). Among technologists, those working in general nuclear medicine had a significantly higher frequency of dicentric chromosomes at 0.17% ± 0.04% compared to 0.08% ± 0.06% for those in PET imaging ($p = 0.002$), but there was no significant difference when compared to those in radiopharmacy at 0.09% ± 0.06% $p = 0.06$ (Figure 3C).

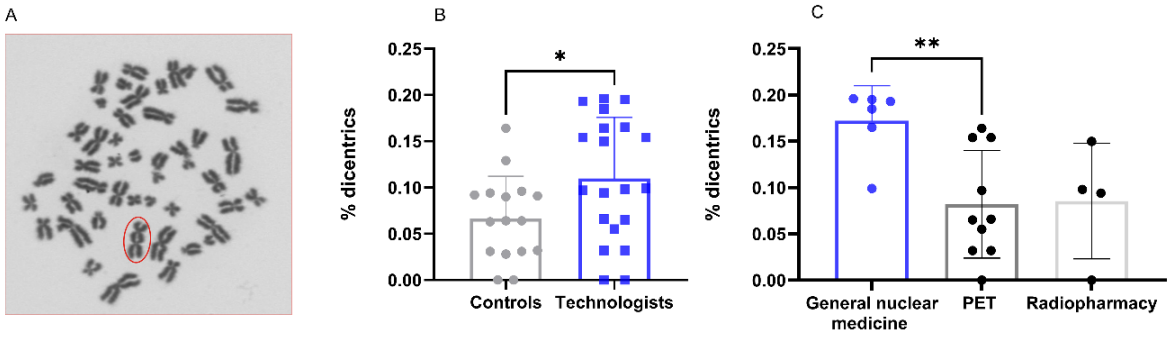


Figure 3. Dicentric chromosomes in blood samples of participants. (**A**) Blood sample from a technologist displaying a metaphase with a dicentric chromosome highlighted by a red circle. (**B**) The percentage of dicentric chromosomes in blood lymphocytes of control participants and technologists. (**C**) Percentage of dicentric chromosomes in technologists working in general nuclear medicine, PET, and radiopharmacy. Asterisks indicate statistical significance * $p < 0.05$; ** $p < 0.01$.

3.3. Relating Biomarkers to Health Questionnaire

Mean background γH2AX foci/cell frequency did not differ between individuals without or with a family history of cancer (Figure 4A); participants without a family history of cancer had a mean foci/cell of 0.37% ± 0.26% versus 0.26% ± 0.22% ($p = 0.32$) for those with a family history of cancer. There was a significant difference in the mean percentage of dicentrics between participants without (0.07% ± 0.05%) and with a family history of cancer (0.14% ± 0.06%; $p < 0.01$; Figure 4B), but this would need more participants in future studies to be conclusive.

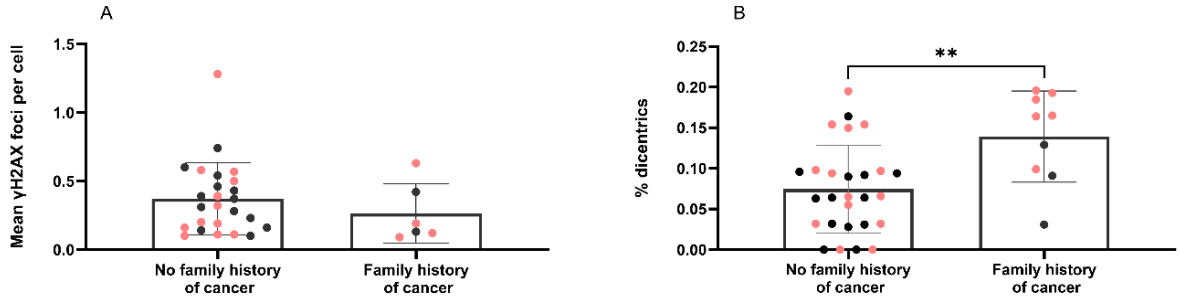


Figure 4. γH2AX and dicentric chromosomes in blood lymphocytes from control participants and technologists plotted against family history of cancer. (**A**) γH2AX foci/cell and (**B**) percentage of dicentric chromosomes in individuals without or with a family history of cancer. Coloured dots indicate technologists. Samples from technologists were taken before handling of radiopharmaceuticals. Samples with unsuccessful γH2AX staining were excluded from the analysis. In contrast, dicentric chromosome analysis was successfully performed for all 20 technologists and 16 controls. Asterisks indicate statistical significance ** $p < 0.01$.

There was also a modest difference in the mean background γH2AX foci/cell frequency between female and male participants (0.47 ± 0.31 vs. 0.25 ± 0.15; $p = 0.03$; Figure 5A), but the mean percentage of dicentrics did not differ between female and male participants (Figure 5B). There was also no significant difference in γH2AX foci frequency and dicentric frequencies when comparing against smoking or age (Figures S4 and S5). However, these comparisons were limited by the small numbers of participants in some categories, particularly ever-smokers and those aged 40 years and older. Age was recorded in categories rather than as an exact continuous measure, preventing analysis of age as a continuous variable.

There was no statistically significant association between dicentrics and years of employment in technologists; $r(18) = 0.11$, $p = 0.65$, n = 20 (Figure S6).

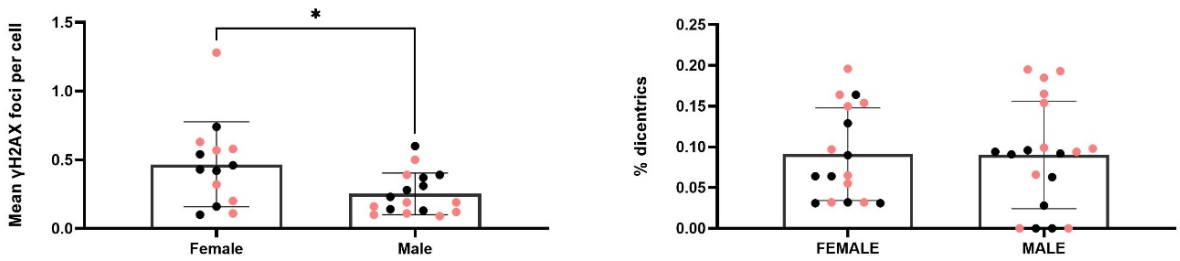


Figure 5. γH2AX and dicentric chromosomes in blood lymphocytes from control participants and technologists plotted against sex**.** (**A**) γH2AX foci/cell and (**B**) percentage of dicentric chromosomes in female and male participants. Coloured dots indicate technologists. Samples from technologists were taken before handling of radiopharmaceuticals. Samples with unsuccessful γH2AX staining were excluded from the analysis. In contrast, dicentric chromosome analysis was successfully performed for all 20 technologists and 16 controls. Asterisks indicate statistical significance * $p < 0.05$.

3.4. Relating DNA Damage to Live Doses

To evaluate whether occupational radiation exposure was associated with an increase or decrease in biomarkers of DNA damage compared to controls, we examined the relationship between live measured finger and whole-body doses on the day of sample collection and γH2AX foci and dicentric frequencies (Supplementary Table S1). Extremity dose i.e., acquired finger doses on the day of sample collection measured using a live dosimeter during the radiopharmaceutical injection, showed a moderate positive correlation with mean γH2AX foci per cell; however, this did not reach statistical significance, $r(9) = 0.40$ $p = 0.23$ (Figure S7A). Body doses showed a weak negative correlation with mean γH2AX foci per cell with no statistical significance; $r(14) = -0.19$ $p = 0.48$ (Figure S7B).

3.5. Relating Chromosomal Damage to Historic Whole-Body Doses

All technologists working in a nuclear medicine department wore their passive body dosimeter at the time of observation; this was significantly higher than for technologists working in PET, where 91.43% ± 5.40% compliance was found ($p = 0.0005$) (Figure S8A). Compliance with wearing passive dosimeters was high, and as such, the accuracy of historical dose records was deemed acceptable. Annual whole-body dose for the year prior to blood sampling was then used and, in the case of incomplete dose records, average monthly dose readings from the months prior to sample collection were extrapolated to 12 months. Dose records were unavailable for two technologists. Incomplete and missing dose records often result from technologists having changed jobs or dosimetry providers. Only a weak negative correlation with the dicentric frequency with no statistical significance was observed $r(16) = -0.26$, $p = 0.29$, n = 18 (Figure S8B). A sensitivity analysis using linear regression was performed to assess whether this association remained after adjustment for sex, smoking history, and family history of cancer (Supplementary Table S2). The association was non-significant in both the unadjusted model, with a regression coefficient (β) of −0.024 and a 95% confidence interval (CI) from −0.070 to 0.022 ($p = 0.292$), and the adjusted model, β = 0.001, 95% CI −0.059 to 0.060 ($p = 0.976$).

4. Discussion

Physical dosimetry is routinely used in nuclear medicine technologists to monitor occupational radiation exposure levels and to ensure that exposures remain within recommended limits. However, dosimetry measures radiation exposure rather than the biological effects of that exposure. Although radiation risk estimates provide useful information at the population level, they do not necessarily reflect differences in individual susceptibility or biological response. With the registration of classified workers and higher workloads, there is now an increasing recognition amongst UK-based technologists of the need to understand their own personal risk. Equally, determining and understanding individual biological effects of exposure may contribute to more accurate and personalised occupational risk assessments [27]. In a previous review, we comprehensively evaluated the use of biological markers of radiation exposure in healthcare workers, highlighting evidence from micronucleus, comet, sister chromatid exchange, γH2AX and dicentric chromosome assays [24]. Building on this evidence, the present study provides a pilot exploratory assessment of short-term biological responses and the investigation of potentially persistent chromosomal effects associated with occupational exposure history. Two biomarkers with different biological characteristics were examined. The γH2AX measurements obtained immediately before and after radiotracer administration were used to assess an acute cellular response to occupationally relevant radiation

exposure occurring around the time of blood sampling. In contrast, dicentric chromosome frequency was used to investigate whether a measurable chromosomal signal was present in peripheral blood lymphocytes of technologists in relation to their occupational exposure history. The findings demonstrate a measurable increase in γH2AX foci following radiotracer administration and a higher frequency of dicentric chromosomes among technologists compared with controls. Together, these findings suggest that biological responses may be detectable even at the relatively low occupational doses encountered in this workforce. However, the two assays reflect different biological processes and timescales and should not be interpreted as direct measures of cumulative occupational radiation exposure.

4.1. Short-Term Biological Effects: Acute γH2AX Response

Background γH2AX foci levels were comparable between technologists and controls while technologists demonstrated increased foci formation following radiotracer administration. The increase in γH2AX foci is of particular interest given the low doses recorded in this study. The γH2AX DNA damage assay is a sensitive and well-validated biomarker across multiple clinical settings, detecting radiation-induced DNA damage [28,29]. The assay demonstrates high sensitivity, capable of detecting DNA damage induced by radiation doses as low as 1 mGy [30]. The doses recorded in the present study were considerably lower, in the range of 1–8 μSv. However, personal dosimeter readings cannot be directly equated with the absorbed dose received by circulating lymphocytes, nor can they be directly compared with the experimental dose thresholds used to establish the sensitivity of the γH2AX assay. Consequently, the observed increase in γH2AX should not be interpreted as demonstrating that the assay directly detected an absorbed blood dose of 1–8 μSv. Rather, the findings indicate that a measurable biological response occurred following radiopharmaceutical administration despite the low external doses recorded by personal dosimetry.

Of particular interest is the distribution in γH2AX foci counts, which point to a large variation across both groups in response to radiation exposure. Such variability is consistent with the recognised sensitivity of γH2AX measurements to biological and technical factors [29,31]. γH2AX measurements can also show considerable day-to-day variation, meaning that a single measurement may not fully capture an individual's usual biological response or longer-term variability [32]. This may partly explain the wide range of responses observed and suggests that a single physical dose estimate may not fully explain individual biological responses. This is particularly relevant in nuclear medicine, where exposure can vary over time and across different tissues.

The absence of correlation between γH2AX foci counts and extremity dose measurements is consistent with partial-body exposure to the hands, whereas γH2AX was assessed in circulating peripheral blood lymphocytes. Whole-body dose provides an estimate of external exposure and may also not accurately represent the dose received by circulating lymphocytes, which may explain the lack of correlation between γH2AX foci counts and whole-body dose. The observation of γH2AX induction following radiotracer administration should, however, be interpreted cautiously. A limitation of the γH2AX study design is that only a single control sample was collected, and therefore a time-matched control comparison was not performed. All baseline samples were collected under standardised conditions between 08:00 and 09:00, before participants began their working day. The post-administration samples were collected within 30 min of radiopharmaceutical administration. Although the significant increase observed within technologists supports an acute response associated temporally with radiotracer administration, other short-term factors occurring during this interval cannot be completely excluded. A time-matched control group with repeated sampling would therefore provide stronger evidence for attributing the observed increase specifically to radiation exposure.

4.2. Long-Term Biological Effects: Dicentric Chromosome Findings

Here, we also investigated the presence of dicentric chromosomes in lymphocytes of nuclear medicine technologists; these are highly radiation-specific, with only a limited number of genotoxic and chemical agents capable of inducing dicentric chromosomes [33]. Unlike γH2AX foci, which represent an early response to DNA damage, dicentric chromosomes are a downstream chromosomal consequence of radiation exposure. Dicentrics appear rapidly after exposure but gradually diminish over time due to their instability, with an estimated biological half-life of three years [25,33]. The dicentric chromosome assay can detect damage resulting from doses as low as 0.1 Gy when analysing up to 1000 metaphase cells [28,33].

Because dicentric chromosomes are relatively persistent compared with γH2AX foci, they provide an opportunity to explore biological effects that may remain detectable beyond the immediate exposure period [25,33].

This study showed a 1.5-fold increase in the number of dicentrics in technologists compared to controls, highlighting the fact that despite the low occupational doses received by technologists, there remains a measurable

biological effect. The increase was particularly evident among technologists working in general nuclear medicine, suggesting that the pattern and nature of occupational tasks may be relevant to biological response. However, this finding should not be interpreted as evidence of a clinically meaningful increase in radiation-related disease risk. Rather, it represents a measurable biological difference that warrants further investigation in larger populations and through longitudinal study designs. The background frequency of dicentric chromosomes in the control population was within the range generally reported for the general population, which is set at 0–2 per 1000 cells [34,35]. It is therefore important to match the control group to the population investigated as much as possible, as done here with the control group being age- and sex-matched hospital workers with no exposure to radiation occupationally or otherwise. Nevertheless, differences in background exposures and other individual characteristics cannot be completely excluded and may contribute to variation in dicentric frequency.

4.3. Relationship between Dicentric Chromosomes and Historical Dosimetry

An important distinction when interpreting the dicentric findings is between detecting a measurable chromosomal change and measuring cumulative long-term biological effects. Historical dose records that we used focused on the whole-body dose recorded during the 12 months prior to blood sampling. This period was chosen because it provided the most complete and recent record of occupational exposure available for comparison with the biological measurements. The use of the previous 12 months of personal dosimetry data to compare with dicentric chromosome frequency was based on the fact that dicentric chromosomes are unstable and decrease over time after radiation exposure [36]. Therefore, more recent radiation exposure is more likely to contribute to the dicentric frequency measured at the time of blood sampling. The 12-month period was chosen as a practical timeframe that allowed occupational dose to be compared with the biological measurement.

When comparing the number of dicentrics in technologists with whole-body doses acquired over the last 12 months, there was no clear correlation, likely due to the circulating profile of lymphocytes, the biological half-life of dicentrics, and likely inaccuracies in dose measurement, which is often incomplete, thereby necessitating dose extrapolations. Dose measurements can also underestimate actual exposure due to factors such as improper device usage or doses falling below detection thresholds [22,37]. These factors may reduce the strength of any relationship between recorded dose and biological effect.

The absence of an association between the previous year's dose and dicentric frequency should not be interpreted as evidence that cumulative occupational exposure has no biological effect. The 12-month whole-body dose does not capture total occupational exposure over an individual's career, nor does it account for duration of employment or exposures incurred earlier in the individual's working history. Instead, the dicentric analysis should be considered as an initial assessment of longer-lasting chromosomal effects rather than a full measure of cumulative occupational radiation exposure. Future studies incorporating cumulative career dose, employment duration, and repeated biological measurements would provide a stronger assessment of occupational long-term effects.

The limitation of historical dosimetry highlights the importance of improving exposure monitoring. Variability in dosimeter wearing, i.e., on the waist versus chest, could have influenced historical recorded doses, although this was partially addressed by using live dosimeters on the day of sample collection to record doses. Historical measurements remain dependent on compliance and appropriate device use. Improved compliance with dosimeter wearing and the development of centralised, accessible occupational dose registries could therefore strengthen future epidemiological and biomarker studies.

4.4. Individual Factors Associated with Biological Response

The study also explored whether individual characteristics were associated with variation in DNA or chromosomal damage. Higher dicentric frequencies were observed in individuals reporting a family history of cancer, suggesting a potential genetic predisposition to chromosomal aberrations, though the small sample size limits definitive conclusions. No difference was found for γH2AX foci counts in those with or without a family history of cancer. The absence of a corresponding difference in γH2AX foci may reflect differences in the biological processes measured by the two assays. γH2AX primarily reflects an early DNA damage response, whereas dicentric chromosomes represent a downstream chromosomal consequence that may persist for longer. However, no genetic analyses were undertaken in the present study, and family history is not a direct measure of inherited radiosensitivity. The finding should therefore be considered hypothesis-generating rather than evidence of a genetic predisposition to radiation-induced chromosomal damage. Larger studies using genetic analyses and DNA damage response and repair measures are needed to determine whether inherited differences in radiosensitivity explain this variation.

There was also no correlation between DNA and chromosomal damage levels and smoking status or age. On the other hand, female participants did show higher γH2AX frequencies than males. Current literature does not provide consistent evidence for sex-related differences in baseline γH2AX. As the number of γH2AX foci can be affected by many confounding factors at once [29,31] and no long-term biological effects in terms of dicentric numbers were identifiable, the observed difference in γH2AX foci numbers may not reflect a true sex-specific effect but rather the influence of unmeasured or uncontrolled variables.

A sensitivity analysis was also performed to examine whether the association between historical annual whole-body dose and dicentric chromosome frequency changed after adjustment for sex, smoking history, and family history of cancer. The association remained non-significant following adjustment. However, given the small sample size, these findings should be interpreted cautiously.

4.5. Occupational Exposure in Nuclear Medicine

The present findings also need to be considered in the broader context of occupational radiation exposure in healthcare. Biomarker studies in medical imaging personnel have previously demonstrated biological effects using micronucleus, comet, sister chromatid exchange, and other approaches [1,22,24,38–41]. Nuclear medicine technologists are of particular interest because their exposure profile differs from that of many other healthcare workers. Rather than being exposed predominantly to fixed imaging equipment, nuclear medicine technologists routinely work with unsealed radionuclides and radiopharmaceuticals and may experience repeated low-level exposures associated with preparation, administration, and handling of radioactive materials and with close contact with patients following administration. These activities cause uneven radiation exposure. The hands may receive much more radiation than the whole body because they are often close to radioactive materials. However, the exposure of circulating blood lymphocytes may differ from that indicated by either extremity or whole-body dose dosimetry. Lead aprons provide limited protection against the higher-energy gamma radiation used in nuclear medicine and may produce additional scattered radiation. Therefore, they are not routinely relied upon for radiation protection in nuclear medicine, where distance, time, and appropriate shielding are more effective [42,43]. These characteristics distinguish nuclear medicine from many other healthcare radiation environments and provide an important context for interpreting the biological measurements observed in this study.

4.6. Overall Interpretation, Study Limitations and Future Directions

Taken together, the findings suggest that biological measures can detect variation in response among UK NMTs that is not fully captured by conventional physical dosimetry. The acute increase in γH2AX following radiotracer administration indicates a short-term DNA damage response, while the higher dicentric chromosome frequency indicates differences in chromosomal damage between technologists and matched controls. These biomarkers are complementary, as γH2AX reflects early DNA damage whereas dicentric chromosomes provide evidence of more persistent chromosomal damage. However, the small sample size, single-day γH2AX measurements, lack of a time-matched repeated control measurement, and reliance on 12-month whole-body dosimetry limit the strength and generalisability of the findings. The substantial variation between individuals may reflect differences in exposure, biological susceptibility, lifestyle or other factors, and therefore should not be interpreted as evidence of individual clinical risk. Larger longitudinal studies are required to validate these findings, clarify the factors contributing to biological variation, and determine the potential role of these biomarkers in individualised occupational radiation risk assessment.

5. Conclusions

In this pilot study, nuclear medicine technologists showed differences in markers of short-term DNA and chromosomal damage in lymphocytes compared with controls. These findings may indicate biological effects associated with occupational exposure to ionising radiation. The large interindividual variability in the chromosomal damage assays highlights the need for further investigation into factors contributing to biological variation and the potential value of individualised monitoring. Further studies with larger sample sizes may help in understanding the biological significance of these findings and whether they have any implications for the long-term health of nuclear medicine technologists chronically exposed to low-dose ionising radiation. Overall, this study emphasises the need for further research around dosimetry precision, the development of centralised dose registries to ensure complete and accessible exposure records, comprehensive health monitoring, and studies examining the relationship between physical dosimetry and biomarkers of biological effect. These findings support continued optimisation of occupational exposure practices in line with ALARP principles and underline the importance of maintaining effective radiation protection in nuclear medicine settings.

Supplementary Materials

The additional data and information can be downloaded at: https://media.sciltp.com/articles/others/2611241611492410/WAH-26060233-SI.pdf.

Author Contributions

I.M.-A.: conceptualization, investigation, data curation, formal analysis, writing—original draft preparation; J.M.: conceptualization, methodology, training, writing—review and editing; H.M.: formal analysis, writing—review and editing; S.B.: conceptualization, methodology, training, writing—review and editing; B.M.: supervision; E.A.: supervision, conceptualization, methodology, writing—review and editing; S.Y.A.T.: supervision, conceptualization, methodology, writing—review and editing. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

The study was reviewed and approved by the London–City & East Research Ethics Committee (16/LO/1111) on 13 June 2016, with an amendment on 6 January 2023, and conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Data Availability Statement

The data of this study are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

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