UK Health Security Agency

UKHSA RCCE
Emergency Response Exercise 2025
Biological and physical dosimetry

Comparison of techniques for full and triage dose estimations in the event of a mass casualty nuclear incident

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1.1 Introduction

The UK Health Security Agency (UKHSA) is the UK's primary authority on public health protection in radiation emergencies. This function is delivered through its Radiation Protection Sciences Division, which integrates specialist expertise, operational capability, and research and development to provide evidence-based information and strengthen national resilience.

As a Category 1 responder under the Civil Contingencies Act (CCA) 2004, UKHSA maintains a suite of emergency plans to respond to and recover from health security incidents, including radiological or nuclear emergencies, hereafter termed radiation emergencies. Additionally, UKHSA is a statutory consultee under the Radiation (Emergency Preparedness and Public Information) Regulations (REPPIR) 2019, ensuring that emergency plans for regulated premises meet public health requirements.

Central to UKHSA's mission is the advancement and continuous improvement of both radiation protection science and the operational delivery of emergency response. A key mechanism for achieving this is through comprehensive emergency exercising. UKHSA actively participates in a wide range of exercises, both regulatory and non-regulatory, external and internal, on an annual basis. These exercises provide an opportunity to test existing plans, validate operational procedures, and identify potential lessons.

UKHSA's Radiation Effects Department (RED) has extensive expertise relating to the health effects of ionising and non-ionising radiations, including biological dosimetry. The RED's Chromosome Dosimetry Service has contributed to the establishment of internationally approved methods and techniques (ISO standards) to quantify radiation exposure and perform dose assessment following suspected radiation overexposure.

RED continually evaluates its capability and capacity to respond to large scale radiation emergencies, whilst building resilience to respond both nationally and internationally through international assistance networks. The Cytogenetics Group at UKHSA also provide a service for individual radiation exposure assessment through the Chromosome Dosimetry Service (UKHSA Chromosome Dosimetry Services - Introduction).

RED has previously demonstrated that it can routinely provide accurate and reliable biological and physical dosimetry through its radiation dosimetry services. Specifically, responding to suspected overexposure cases of individuals or as part of wider occupational monitoring efforts. The emergency response exercise presented within this report aims to assess the effectiveness and capacity of rapid dose response across the range of available dosimetry provided by UKHSA.

Additionally, UKHSA's Personal Dosimetry Service (PDS) Department has over 50 years' experience in providing high-quality personal radiation dose monitoring, underpinned by vast radiation protection expertise and research. PDS provides a high-quality dosimetry service capable of measuring and recording radiation doses received by customers and their employees. All PDS's services are Approved Dosimetry Services (ADS), meaning they have been approved by the British Health and Safety Executive (HSE) under the Ionising Radiations

Regulations (IRR) 2017. All dosemeters as part of the PDS) are assessed within UK laboratories (Personal Dosimetry Service - Introduction.

1.2 Background

Dosimetry seeks to assess doses received, not only absorbed, to estimate the effective dose delivered to matter. In the context of this report, dosimetry provides quantitative data on the absorbed dose of ionising radiation in individuals or materials, and it plays a critical role in radiation protection and emergency response. Dosimetry tools are essential for accurate risk assessment, clinical decision making, and regulatory compliance. There are two primary categories of dosimetry: physical dosimetry, which involves the direct measurement of ionising radiation using devices such as Thermoluminescent dosimeters (TLDs) and optically stimulated luminescence (OSL) systems; and biological dosimetry, which estimates absorbed dose based on measurable biological responses, such as chromosome aberrations, protein biomarkers, or radiation-induced gene expression changes.

Both physical and biological retrospective dosimetry are established and recognised techniques demonstrated to provide critical assistance for the triage of populations of individuals during incidents involving large numbers of casualties following radiation exposure events [1]. Triage categories most commonly consist of low (< 1 Gy), medium (1-2 Gy) and high (> 2 Gy) dose exposures and they have been used in a number of inter-laboratory comparisons (ILCs) and collaborative international response networks [2, 3], however triage dose categories can vary across different countries, assistance networks and federal bodies. Triage dose categorisation is vital to complement the assessment of radiation casualties based on clinical symptoms and identify individuals in need of immediate medical intervention and to reassure the ‘worried well’ (who would likely make up the majority of persons requesting testing. Several techniques have been firmly established over recent decades to support this initiative.

Physical dosimetry uses physical devices or materials to directly measure radiation exposure. Most commonly, these include dosimeters or detectors but can also incorporate commonly used or everyday materials to quantify radiation exposure and estimate dose. Most persons working with radiation, or exposed medically, will have their exposure measured using thermoluminescent or optically stimulated luminescent (OSL) dosimeters, ionisation chambers or other detection equipment. However, these devices may not be present in the event of an unplanned nuclear release or exposure to the general population. In this event, many materials and objects have been investigated and validated to measure radiation exposure and estimate dose that a person may be in possession of during the time of exposure, including mobile phones, fabrics and credit cards for example.

Electron paramagnetic resonance (EPR), also known as electron spin resonance, is a technique used to measure stable radiation-induced free radicals in materials such as tooth enamel, fingernails and bone. When exposed to IR, these tissues can retain radicals whose signals intensify following the trapping of delocalised electrons induced by exposure to IR [4]. While it offers high sensitivity and long-term stability, challenges such as signal interference and sample variability must be taken into consideration.

Biological dosimetry infers absorbed dose by detecting and measuring quantifiable biological effects resulting from IR exposure [5-7]. Techniques and methodologies established for

biological dosimetry most notably include the analysis of cytogenetic biomarkers such as chromosomal aberrations, protein biomarkers such as γH2AX foci and chromosome translocations in peripheral blood lymphocytes [8-10]. In more recent years, molecular biomarkers have emerged as useful tools for biological dosimetry, particularly gene expression profiling. Among these, the ferredoxin reductase (*FDXR*) gene has demonstrated high sensitivity and specificity as a radiation-responsive transcript, showing dose-dependent upregulation even at low doses [11]. All techniques deployed in this exercise are discussed in more detail in sections 4 and 5 below.

1.3 Emergency preparedness

Large scale radiation emergencies such as nuclear power plant accidents, radiological dispersal device (RDD) detonations, and criticality accidents, can all potentially expose large populations to IR. However, in most scenarios, what becomes more critical than many people actually being exposed is the large number of ‘worried well’ or those who are worried that they might have been exposed to radiation and require reassurance. The scale of these events can vary widely, from hundreds to hundreds of thousands of individuals requiring triage assessment, more accurate dose estimation, or long-term health monitoring. Historical examples include the Windscale fire (UK, 1957), where radioactive iodine release posed a public health risk, the Three Mile Island accident (USA, 1979), which caused widespread concern despite minimal actual exposure, and the catastrophic reactor failures at Chernobyl (USSR, 1986) and Fukushima Daiichi (Japan, 2011) both of which triggered mass evacuations and international emergency responses. At present, the UK national threat level for terrorism and other national emergencies is ‘Substantial’. Thus, practical exercises such as this emergency response exercise are vital within UKHSA’s plan to prepare for and respond to a radiation emergency.

2: European and international response networks

Running the European Network of Biological and Retrospective Physical Dosimetry (RENEB – www.reneb.net) is a collaborative network established under the 7th EU Framework EURATOM Fission Programme that was fully established as a legal entity in 2016. Comprising 26 organisations across 16 European countries, RENEB is designed to provide coordinated mutual assistance in individual dose estimation during large-scale radiological and nuclear emergencies [1, 6, 12]. As part of this initiative, the Personal Dosimetry and Radiation Effects departments at the UK Health Security Agency (UKHSA) contribute expertise and capability in biological and physical dosimetry, supporting rapid and standardised dose assessment across Europe in emergency scenarios as part of a multi-institutional rapid response network.

Standardisation across a network is vital for the mutual collaboration efforts required in the event of a radiological emergency which could overwhelm a single institute, therefore regular inter-laboratory comparison (ILC) exercises are conducted to validate these methods [13] as well as establishing ISO standards for protocols and analysis techniques where possible and testing logistics or sample or data transfer. Current capacities per week for physical and biological dosimetry have been calculated (Table 1). ILC exercises typically assess parameters such as scoring consistency, calibration curve comparability, dose estimation accuracy, and inter-observer variability to overall validate various dosimetry techniques.

Technique for analysis	**UKHSA**	**RENEB**	**BioDoseNet**
Dicentric chromosome aberrations	300	2075	5188
Micronuclei	400	1485	
γH2AX	1000	1990	
Gene expression	1000	4036	
Mobile phones (OSL)	100	230	
TLDs	7000		

***Table 1**. Current capacity for physical and biological dosimetry techniques per week*

The BioDoseNet established by the World Health Organisation (WHO) in 2008 similarly is a network of international laboratories which supports international collaboration and validation and harmonisation of biodosimetry techniques [14]. Surveys completed every 5 years, the most recent being in 2021, confirm the trend capacities and capabilities of the network and underline the global status of cytogenetic biodosimetry [14]. Table 1 includes a dated BioDoseNet figure, however it is the only version currently available so might not entirely represent up to date capacities of this network.

The European Radiation Dosimetry Group (EURADOS), founded in 1982, is a non-profit association for promoting and harmonising research and development of dosimetry techniques and practices consisting of a network of 83 mainly European institutions and agencies [15, 16]. This network includes deep specialists and experts, both reference and research laboratories and dosimetry service providers. Under EURADOS, focused working groups have been established, regular intercomparisons organised for quality assurance of dosimetric procedures, and the promotion of education and training to enable ongoing contribution to strategic radiation research and development of techniques and standards. There are also a large number of other networks at a worldwide which include but are not limited to: the Asian Radiation Dosimetry Group (ARADOS), the Korean Biodosimetry Network (K-Biodos), the North American Biodosimetry Network (NABDN) and the Latin American Biological Dosimetry Network (LBDNet).

3: Biological dosimetry techniques

3.1 Chromosomal aberrations

The Dicentric Chromosome Assay (DCA) has long been considered the 'gold standard' biological dosimetry assay for the accurate dose estimation of potentially overexposed individuals. This well-established technique is used to identify and quantify the number of dicentric chromosomes found, typically in peripheral blood lymphocytes, after a suspected exposure to IR. Dicentric chromosomes are those with 2 or more centromeres and are formed, with a high level of specificity to IR, as a result of DNA damage and subsequent mis-repair. Damaged cells have multiple pathways they are able utilise to effectively repair double-strand breaks (DSB) in the DNA [17]. However, these pathways can sometimes lead to mis-repair, resulting in the rejoining of two or more similarly damaged chromosomes and the formation of aberrant chromosomes with multiple centromeres.

The prevalence of dicentric chromosomes has been shown to predictably increase with increasing exposure to IR, following a Poisson distribution. Dicentric yields have been shown to have a half-life of approximately 2-3 years [18, 19], meaning dose estimates can still be achieved in the years post-exposure. This assay has a time window of up to 1 year after exposure. The specificity of dicentric formation to ionising radiation-induced damage and low interindividual variability allows the DCA to provide accurate dose estimations down to extremely low exposure limits (>100 mGy), making it one of the most reliable tools in radiation biodosimetry. DCA follows an ISO standard for both the technical aspects (ISO 19238) and principles around its application during radiation protection (ISO 21243:2022).

3.2 γH2AX

γH2AX is a rapid and effective biological dosimetry technique especially useful for initial rapid dose assessment to determine whether potentially overexposed individuals need immediate healthcare. γH2AX is a phosphorylated form of the histone protein H2AX that forms rapidly at sites of DNA double-strand breaks (DSBs), which are a primary type of damage caused by IR. Studies have shown a strong correlation between the number of γH2AX foci and DSBs, demonstrating that γH2AX is a reliable and sensitive marker for detecting and quantifying radiation-induced DNA damage in individual cells [20]. The assay can be performed very rapidly, with around 4 – 5 hours to generate slides that can be scored for a rapid dose estimate following sample receipt [8, 21-23].

Whilst the assay is less sensitive than other cytogenetic biodosimetry techniques, the rapid processing time would ideally be used to distinguish critically exposed individuals from those unexposed or 'worried-well' to enable more efficient prioritisation of sample analysis by more sensitive but time consuming techniques (such as DCA) [8].To evaluate the performance of the γH2AX assay, various ILCs have taken place such as the RENEB 2021 ILC which aimed to simulate a real-life IR emergency which have validated the usefulness and application of γH2AX in categorising people into correct triage categories [21].

3.3 Gene expression

During recent decades, much international research effort has focused on developing new biomarkers of radiation exposure, chasing rapid and high-throughput techniques to assist in the triage of large-scale individual dose estimation following a mass casualty nuclear incident. Gene expression analysis based on peripheral blood sampling, is a valuable tool for determining radiation dose, especially in emergency situations. The technique is based on qPCR analysis to scan the genome for genes that show responsiveness to radiation exposure.

One of the most responsive genes revealed during this search was ferredoxin reductase (*FDXR*) expression, which demonstrates strong dose-dependent upregulation post-exposure in humans [24]. When cells are exposed to DNA-damaging agents like radiation, they rapidly activate specific genes as part of their initial response. This gene induction is controlled by complex regulatory mechanisms involving multiple signalling pathways [11]. Measuring these changes in gene expression provides a sensitive and early indicator of IR exposure, allowing for timely assessment of dose and potential biological effects. This makes gene expression profiling, using *FDXR*, particularly useful for quickly evaluating individuals in radiation emergencies where rapid and accurate dose estimation is critical for effective medical intervention. Subsequent studies have supported the use of *FDXR* as a suitable biomarker for gene expression analysis, with favourable triage categorisation of dose estimates reported and a time window of at least 72 hours post-exposure [2, 25].

3.4 Tachyon

Tachyon is an innovative point-of-care molecular diagnostics device that integrates nanopore sequencing with real-time gene expression analysis. This novel portable molecular diagnostic device is being developed by HQ Science Limited and supported by UKHSA. During this exercise, it was deployed to assess radiation exposure in real time using nanopore sequencing and advanced bioinformatics, offering a rapid and scalable solution in emergency contexts [26].

3.5 Fluorescent *in situ* Hybridisation (FISH)

Fluorescence in situ Hybridisation (FISH) is a high-resolution molecular cytogenetic technique widely employed in biological dosimetry for the detection of stable chromosomal aberrations, particularly reciprocal translocations. FISH is utilised in various research areas including cytogenetics, gene mapping, tumour biology and prenatal diagnosis due to its high specificity and ability to detect subtle chromosomal rearrangements with visual clarity [27]. Fluorescently labelled DNA probes are used to bind to either entire chromosomes or specific regions within chromosomes, enabling the hybridised regions to be clearly identified and differentiated. Specifically, for biodosimetry, FISH with whole chromosome painting (WCP) probes, typically for chromosomes 1, 2 & 4, enables the scoring of stable translocations that persist in peripheral blood lymphocytes post-exposure [28, 29].

While FISH remains a less time-efficient technique than the ‘gold standard’ DCA, its capacity to detect stable aberrations makes it a crucial technique for long-term biological monitoring,

radiation epidemiology, and historical dose reconstruction, particularly useful in scenarios involving protracted or chronic-low dose exposures [3]. Inter-laboratory validation of FISH is required in emergency preparedness contexts, as previous RENEB ILC exercises showed a trend in laboratories over-estimating the observed doses [13].

4: Physical dosimetry techniques

4.1 Thermoluminescent dosemeters (TLDs)

TLD badges are widely used for precise measurement of IR exposure in both occupational monitoring and emergency response scenarios. These devices contain thermoluminescent materials, such as lithium fluoride, which trap electrons in response to radiation. Upon heating to 250ºC in a lab, the trapped electrons are released and emit energy in the form of light proportionate to the radiation dose. The amount of the emitted light is collected and measured to determine the radiation dose received. TLDs can measure a broad dose range, with the lower limit of detection being 0.02 mSv for monthly handouts.

The Personal Dosimetry Service at UKHSA provides routine monitoring of radiation exposure from photon (X-ray and gamma) and beta radiation using TLDs [30]. For accurate dosimetry, especially in blinded studies involving a range of radiation doses, the analyst must be informed which samples exceed 1 Sv so that the appropriate filters can be applied during readout.

4.2 Mobile phones

Alternative materials for performing physical dosimetry where dosemeters or detectors are not possible have been explored in recent years, with methods using mobile phones and associated components being investigated and developed as a promising new tool. Studies have shown that ceramic substrates in resistors or glass displays (components of mobile phones) trap electrons when exposed to IR which can be measured retrospectively using OSL or TL to estimate absorbed dose [31]. OSL and TL dosimetry methods were implemented in a 2017 RENEB ILC exercise [32] to determine their validity and show the potential availability of mobile phones as personal dose proxies. UKHSA has a capability to perform dosimetry based on OSL of resistors (specifically 0201 and 0402 types) following exposure to photon radiation in the dose range of 0 – 10 Gy up to 7 days post-exposure [33].

Thus far, this technique presents a promising supplementary method for dose estimation in the instance of a real-life accident/emergency or mass-casualty incident due to the high accessibility of mobile phones. This is especially useful where biological dosimetry capacity may be overwhelmed. However, studies have shown that further validation and confinement are required as post-irradiation exposure to sunlight increases the complexity of the EPR signal analysis and the interindividual variability between different types of smart phones requires more comprehensive study [31, 32].

4.3 Alanine pellets

Commonly used as reference dosimeters due to their precision, small size, and stability, alanine pellets have been a useful tool for measuring absorbed doses of IR. The pellets are made from L-α-alanine powder and 10-20% of a binder (as it is not convenient to just use a powder). Their sensitivity to all types of IR and long half-life makes these pellets ideal for use

as dosimeters. Their small form-factor also allows for further design optimisation i.e. the use of multiple pellets in a single device, with filters separating radiation types to provide more insight into the characteristics of an IR exposure event [34]. These solid-state dosimeters respond to IR by forming free radicals, which can be quantified using EPR dosimetry as the intensity of the EPR signal correlates directly with the absorbed radiation dose.

5: The exercise methodologies

5.1 Sample irradiation

To simulate a real-life emergency scenario, five of each sample type were irradiated using an X-ray irradiator at doses of 0.3 Gy, 0.8 Gy, 1.2 Gy, 1.5 Gy, and 2.4 Gy. This included five 2 mL lithium heparin blood samples (for H2AX, DCA manual, and DCScore), five 1.5 mL EDTA blood samples (for gene expression), five 6 mL EDTA blood samples (for Tachyon device), five mobile phones, five alanine pellets, and twenty-five (5x5) TLD badges. Each item was assigned a label from A to E, corresponding to a specific dose, in a blinded manner so that the analyst was unaware of which dose each sample received and the labelling of samples were in unique orders for each assay, to avoid results from one assay influencing the dose estimates of another.

X-irradiations were conducted using a self-contained 250 kVp X-ray unit (CD160/1, AGO X-ray Ltd, Martock UK) with aluminium and copper filtration (~1 mm) containing a Varian NDI-320 source. Acute doses of X-rays were delivered at 0.5 Gy min^{-1}. Dosimetry was performed with a calibrated reference ionisation chamber for the exact exposure setup used. Exposures were always monitored using a calibrated UNIDOS E electrometer and 'in-beam' monitor ionisation chamber (all from PTW, Germany) located at source. Correction factors are used to calculate exact dose.

5.2 Chromosomal aberrations

Following x-irradiation the whole blood was held for 2 h at 37 °C then mixed with Minimal Essential Medium, supplemented with 10% heat inactivated foetal bovine serum, 1% PHA, 100 units/mL penicillin plus 100 µg/mL streptomycin and 2 mM L-glutamine. 5-bromodeoyuridine was also added to the medium to give a final concentration of 10 µg/mL. All the cells were then cultured in an incubator at 37 ± 0.1°C with a humidified atmosphere of 5 ± 0.2% CO2 in air. Colcemid at 0.2 µg/mL was added 3 h before termination of the cultures. At the end of the 48 hour culture period, metaphases were harvested by a standard hypotonic treatment in 0.075 M potassium chloride for 7 min at 37°C followed by three changes of 3:1 methanol:acetic acid fixative. Fixed cells were dropped onto clean microscope slides and air dried. The slides were cleaned by RNAase treatment and stained by the fluorescence plus Giemsa technique to ensure that first division metaphases were scored. Slides were then mounted under a coverslip and dried overnight. These culture, fixation and staining procedures follow standard protocols commonly employed in radiation cytogenetics laboratories and recommended in a widely accepted manual published by the International Atomic Energy Agency [35]. All the microscope slides were coded for analysis and 50 or 150 metaphases per dose point were scored manually or captured for semi-automated scoring respectively.

The most accurate and sensitive method of analysing peripheral lymphocytes for radiation-induced dicentric chromosomes is through manual scoring of metaphase cells. We use a scanning microscope (Metafer 4 by Metasystems) to identify metaphase spreads of chromosomes (MSearch), which then captures high-resolution images of metaphase spreads for analysis (AutoCapt). For large numbers of cases, a total of 50 metaphase spread cells are

analysed per sample for initial triage dose categorising. Manual scoring of 50 cells takes around one hour per sample.

Dose estimates, based on the number of dicentrics per cell were calculated using BioDose Tools [36] and UKHSA standard 250 kVp X-ray calibration curve, with the following coefficients: C = 0.0005 ± 0.0005, α = 0.046 ± 0.005, β = 0.065 ± 0.00 [37] for manual scoring. A calibration curve for semi-automated scoring was constructed for 250 kVp X-ray using the standard method described above. The calibration scoring data, presented in Appendix A, were used to generate the following calibration coefficients using BioDose Tools C = 0.0007 ± 0.0009, α = 0.040 ± 0.010, β = 0.028 ± 0.005.

5.3 γH2AX

5.3.1 Culture and Lymphocyte isolation

Whole blood samples were incubated at 37°C for 24hr post-exposure. Following incubation, samples were diluted 1:1 with PBS (5 mL/5mL) in centrifuge tubes and carefully layered onto an equal volume of Histopaque. Tubes were centrifuged at 3000 rpm for 10 min at room temperature with the brake off (Mistral 3000E). The buffy coat was collected using a wide-bore pipette, washed twice in 10 mL PBS (1800 rpm) and resuspended after the supernatant was removed.

5.3.2 Fixing and Staining

Cells (20 µL per well) were placed onto Tekdon 14-well coated slides and allowed to adhere for 15 min. Cells were fixed in 2% formaldehyde/PBS (1:8 dilution from 16% stock) for 5 min, permeabilised with 0.25% Triton-X-100/PBS for 5 min and blocked with 1% BSA/PBS for 10 min. Primary antibodies (anti-γH2AX, 1:500; anti-53BP1, 1:400; diluted in BSA) were applied for 45 min at room temperature. After three washes in BSA, secondary antibodies (Goat anti-Mouse Alexa Fluor 488 (GaM 488), 1:500; Goat anti-Rabbit Alexa Fluor 555 (GaR 555), 1:500; DAPI, 1:500, diluted with BSA) were applied for 30 min. Slides were washed three times with PBS, air-dried in the dark, and mounted with Vectashield mounting medium and thickness 0 coverslips before being stored at 4°C prior to analysis.

5.4 Gene expression

5.4.1 Blood sample processing and RNA extraction

Blood samples were incubated at 37°C with 5% CO_2 for 24hr post-exposure. Following incubation, 1 mL of whole blood was mixed with 2 mL of TRI Reagent (Sigma-Aldrich, UK) and stored at -80°. RNA was extracted using the Direct-zol™ RNA MiniPrep kit (ZymoResearch) with a modified phase separation. Samples were thawed at room temperature for 15 minutes, then 400 µL chloroform and 40 µL acetic acid were added, vortexed, incubated for 3 minutes, and centrifuged at 12000xg for 15 minutes at 4°C. The aqueous layer was collected, mixed with an equal volume of 100% ethanol, and applied to Zymo-Spin™ IIC columns. Columns were washed, treated with DNase (75 µL buffer + 5 µL DNase, 15 minutes RT), washed again,

and RNA eluted in 30 µL RNase/DNase-free water. RNA quantity and integrity were assessed using a Nanodrop ND2000 and Tapestation 2200 (RIN values), respectively.

5.4.2 Reverse transcription and qPCR

cDNA was synthesised from 500 ng RNA using the iScipt™ Advanced cDNA Synthesis Kit (Bio-Rad) with thermocycling at 46°C for 20 minutes and 95°C for 1 minute. Quantitative PCR was performed on a Rotor-Gene Q (Qiagen) using PerfeCTa MultiPlex qPCR SuperMix (Quanta Bioscience) in 10 µL reactions, run in triplicate with 1 µL cDNA and 300 nM primers and probes. Multiplexed reactions included FAM- and Texas Red-labelled probes for target genes *FDXR* and housekeeping gene *HPRT*. Cycling conditions were 95°C for 2 minutes, then 45 cycles of 95°C for 10 s and 60°C for 60 s. Ct values were normalised to *HPRT* and converted to transcript quantities using standard curves generated from serial dilutions of PCR-amplified DNA fragments (6-log range, efficiencies 93-103%, $R^2 > 0.998$). Blind samples were analysed alongside a calibration curve prepared from pooled RNA (500 ng) representing doses 0-4 Gy.

5.5 Point-of-care transcriptome-based biodosimeter device Tachyon

5.5.1 Blood samples processing and RNA extraction

Peripheral blood mononuclear cells (PBMCs) were isolated from whole blood using the EasySep™ RBC Depletion Reagent (STEMCELL Technologies, Vancouver, Canada) according to the manufacturer's protocol, then aliquoted in LGM-3 medium to yield 5 independent samples. After irradiation, flasks were incubated for 24 h at 37 °C in a humidified 5% CO_2 atmosphere. Cells were then harvested, lysed in 2 mL RLT buffer (Qiagen, Manchester, UK), and stored at −80 °C. Total RNA was extracted using Qiagen RNeasy Midi Kit (Qiagen, Manchester, UK). RNA integrity was assessed using Tapestation (Agilent) with all samples exhibiting RNA Integrity Number (RIN) values > 7.0.

5.5.2 Library preparation and sequencing

For each sample, cDNA libraries were generated using the Oxford Nanopore PCS-SQK114 chemistry following the manufacturer's standard protocol. Sequencing was performed on R10.4 PromethION flow cells. One flow cell was used per sample.

The real-time data analysis is proprietary and currently UKHSA and HQ Science Limited are in the process of submitting the patent covering the methodology of the Tachyon technology.

5.5.3 Data processing and transcriptomic analysis

5.6 Mobile phones

5.6.1 Aluminium Oxide Resistors in Mobile Phones

Commercially available mobile phones were used in this experiment and were irradiated in working condition. Aluminium oxide ceramic substrate, present in the resistors, functions as an optically stimulated luminescent (OSL) dosemeter material [33]. After irradiation, the devices were dismantled, and the resistors were extracted and analysed. OSL measurements are carried out with an automated luminescence reader (Risø model TL/OSL DA-20) [38]. Approximately ten extracted resistors are collected into a sample cup that is subsequently illuminated with blue light (wavelength: 470nm). This stimulation causes stored energy in the resistors to be released as light, which is detected by the luminescence reader. There are two different protocols for dosimetry using phones, one conducted at room temperature and one that preheats samples to 120 ^{0}C before readout and maintains a temperature of 100°C during readout [39]. Preheating the samples makes the signal more stable and reduces uncertainty in measurements; however, it is more time consuming, which would affect efficiency in an emergency situation [40]. For the purposes of this exercise, the preheat protocol was used.

The luminescent signal emitted by the sample resistors is dependent on the dose received; however, there is also a dependence on the size, shape and number in a sample-cup which can vary with each device that is used. Therefore, a calibration dose of a known quantity must be given to the resistors after the initial measurement is made, and the read-out process repeated; comparison of the respective luminescence signals allows the unknown dose to be reconstructed [31]. In the current measurements, a calibration dose of 2 Gy was applied.
Over time the OSL signal will fade from the Al_2O_3 substrate, thus, even when a calibration measurement is taken, the dose can still be underestimated. The relationship between time and signal fading has been studied in previous work [33]; therefore, with knowledge of the fading time, the correct dose can be estimated.

5.7 Thermoluminescent dosemeters (TLDs)

The dosemeters used in this exercise consisted of a badge insert containing an aluminium card with two pellets of lithium fluoride doped to enhance radiation sensitivity. For this emergency response exercise, 5 dosemeters per dose group were irradiated as above, in controlled conditions rather than being worn. Following irradiation, the dosemeters were heated to approximately 250°C by automated laboratory processors. This thermal stimulation released stored energy in the form of light, proportional to the cumulative radiation dose. Calibration factors were applied to convert light output to dose, with the minimum reportable dose being 0.05 mSv.

Dosemeter performance has been evaluated in line with the European Commission's *Radiation Protection 160 recommendations* for monitoring individuals occupationally exposed to external radiation [41]. In Health and Safety Executive (HSE) performance tests, TLDs typically demonstrated an overall relative standard deviation of 5% and an overall bias of 5%. Both values fall well within the recommended limits of 10% and 20% respectively.

5.8 Alanine Pellets

Alanine pellets used in this experiment were 60mg Harwell tape tab pellets. Irradiations were carried out The Bruker EMX EPR spectrometer was used to measure the EPR spectrum of each pellet. Each tape tab was trimmed, while keeping the pellet laminated, and placed in a PTFE sample holder. Each pellet was then then placed in the spectrometer, tuned for approximately 2-5 minutes, and measured for 2:40 minutes. Each pellet therefore took a maximum of 10 minutes in total to measure. The measurement parameters of the spectrometer and example spectra are shown in appendix.

To determine the microwave power used for each measurement, a 2D power sweep was measured on the 10 Gy sample, and 0.5 mW was found to provide maximum signal without saturating the sample. This power was used for all further measurements to avoid non-linearities in the dose calibration and estimates.

The calibration curve was constructed with 20 pellet measurements of doses 0.1, 0.5, 1, 2, 3.5, 5 and 10 Gy. The peak-to-peak amplitude of each spectrum was used to estimate dose, as there was background noise from the sample holder that prevent fitting the spectra, or a double integral spin count.

3 pellets were irradiated and measured per dose – an average dose was estimated, and the resultant error was propagated using the fitted covariance matrix of the calibration curve and standard deviation of the three estimated values.

6: Results

Dose categories are Low (<1 Gy), Medium (1-2 Gy) and High (>2 Gy)

6.1 DCA Manual Scoring

2 mL LiHep Blood	Exposed Dose (Gy)	Lower confidence limit	Dose Estimate (Gy)	Upper confidence limit
A	2.4	2.8	3.4	4.0
B	1.2	0.9	1.3	1.9
C	0.3	0.3	0.7	1.2
D	1.5	1.5	2.0	2.6
E	0.8	0.4	0.8	1.4

Table 2. *Dose estimation for five blind doses using Lithium Heparin Blood for DCA Manual scoring*

Table 2 compares the received dose against the blind dose estimate calculated after 50 metaphase cells were analysed. Only sample D was incorrectly triaged, being categorised in as 'high dose' instead of 'medium dose'.

6.2 DCA DCScore (Semi-automated)

During emergency response, the number of samples for chromosome aberration (dicentric) analysis will increase significantly. To match this demand, DCA capacity can be greatly increased using the DCScore module of Metafer 4 by Metasystems [10]. Using this semi-automated system (experienced staff confirm false positives), we analyse 150 captured metaphase cells per sample, which takes around 30 mins per sample, with only two minutes of staff effort needed. Table 3 shows that, aided with the larger number of metaphase cells analysed, the semi-automated DCA analysis accurately triaged all 5 blind samples while further improving the accuracy of the dose estimate over manual scoring of 50 cells. The reason for scoring more cells with DCScore is because the software only detects about 50% of dicentrics, so by scoring more cells the aim is to have similar accuracy to manual score.

2 mL LiHep Blood	Exposed Dose (Gy)	Lower confidence limit (Gy)	Dose Estimate (Gy)	Upper confidence limit (Gy)
A	2.4	1.7	2.3	3.4
B	1.2	0.7	1.3	2.1
C	0.3	0.0	0.3	0.9
D	1.5	1.2	1.8	2.8
E	0.8	0.4	0.9	1.7

Table 3. Dose estimation for five blind doses using Lithium Heparin Blood for DCA DCScore (automated) scoring.

6.3 γH2AX (24 hours post-exposure)

The γH2AX foci assay is a useful tool to provide a rapid dose estimate based on blood sampling during a mass casualty nuclear incident. In triage mode, a total of 50 lymphocytes isolated from peripheral blood samples are analysed for the presence of γH2AX foci (representing double strand breaks) that increase with radiation dose following exposure and can be quantified and dose estimated using appropriate calibration curves.

2 mL LiHep Blood	Exposed Dose (Gy)	Lower confidence limit	Dose Estimate (Gy)	Upper confidence limit
A	1.2	1.2	1.6	2.0
B	2.4	1.7	2.2	2.6
C	1.5	1.6	2.1	2.5
D	0.8	1.0	1.2	1.3
E	0.3	0.2	0.4	0.6

Table 3. *Dose estimation for five blind doses using Lithium Heparin Blood for γH2AX*

Using the rapid γH2AX assay, as demonstrated here, shows strong correlation of estimated triage dose estimate and categorisation with the actual exposed doses. Sample C was categorised higher than the actual dose, although could have been correctly triaged based on the lower dose estimate. Nevertheless, the assay would be used to identify high dose categories for further cytogenetic testing with the DCA assay and so serving its purpose to streamline throughput in a real-life exposure scenario.

6.4 Gene Expression (24 hours post-exposure)

Utilising gene expression to separate individuals into medically triaged categories has proven to be an accurate and valuable tool in the instance of a large-scale IR emergency, especially in doses under 1 Gy as seen in the 2023 RENEB Intercomparison exercise [2]. To determine each dose estimate, the endogenous level of each of the calibration curves was used to construct the dose estimation curve using a polynomial fit using Excel software for analyses.

1.5 mL EDTA Blood	Exposed Dose (Gy)	Dose Estimate (Gy)
A	1.2	1.3
B	2.4	1.5
C	0.8	0.8
D	0.3	0.1
E	1.5	1.1

***Table** 4. Dose estimation for five blind doses using EDTA blood for FDXR expression*

6.5 Tachyon device

The Tachyon system offers an in-the-field addition to emergency response efforts. After loading with a sample of isolated PBMCs from a suspected exposed individual, the self-contained system utilises Nanopore technology to analyse the samples. IR doses are estimated using a polygenic approach, with multilinear regression analysis. The system

provides the end-user early exposure detection, identifying exposed versus unexposed samples in 10 minutes. By 60 minutes, it classifies samples into clinically relevant dose categories (<2 Gy, ≥2 Gy, or 0 Gy), enabling the triage of individuals who fall into the highest triage category to seek medical intervention at the earliest opportunity. The thresholds for the clinical triage "<2 Gy, ≥2 Gy" is based on the METREPOL guidelines.

6 mL EDTA Blood	Exposed Dose (Gy)	10 min Exposure Detection	60 min Dose Estimate (Gy)	60 min Threshold Result (Gy)
A	0.8	Exposed	1	<2
B	1.5	Exposed	0.6 - 1	<2
C	2.4	Exposed	1.8 - 2	<2
D	0.3	Exposed	0.25	<2
E	1.2	Exposed	1	<2

***Table** 5. Dose estimation for five blind doses using isolated PBMCs for Tachyon device*

As table 6 shows, the Tachyon system was able to successfully identify that all five samples had been exposed after the first 10 minutes of analysis. After the full 60 minutes, the Tachyon system's METREPOLE-based triage threshold of 2 Gy has accurately placed 4 out of the 5 samples, although it is important to note that sample C is the only sample that would need to be triaged as a high dose exposure. It is also worth mentioning that Tachyon's calibration model is only based on the blood samples from three human donors and the resulting dose-response curve, which includes 0, 0.1, 0.25, 0.5, 1, 2, 3, 4, and 5 Gy. Therefore, it is recommended and encouraged the further training dataset generation to improve the accuracy of Tachyon's biodosimetry model.

6.6 Mobile Phones

Resisters isolated from mobile phones were processed using a RisØ OSL/TL reader (model DA-20), with a read out generated from a set procedure of heat and light stimulation and collection of the OSL signal. Of the 4 mobile phones, 3 were able to be correctly triaged, with only sample E was triaged into the 'medium dose' category rather than 'low dose'. Sample B was not readable.

Mobile Phone	Dose (Gy)	Dose Estimate (Gy)
A	2.4	3.0 ± 0.5
B	1.2	N/A
C	0.3	0.25 ± 0.05
D	1.5	1.1 ± 0.2
E	0.8	1.0 ± 0.2

Table 6. *Dose estimation for five blind doses for Mobile phone analysis*

6.7 Thermoluminescent Dosimeters (TLDs)

For each dose, the reported estimate represents the mean of five TLD readings, with the standard deviation reflecting measurement variability.

	Exposed Dose (Gy)	Dose estimate I (Gy)	Dose estimate II (Gy)	Dose estimate III (Gy)	Dose estimate IV (Gy)	Dose estimate V (Gy)	Mean Dose Estimate ± SD (Gy)
A	0.3	0.320	0.314	0.314	0.306	0.311	0.313 ± 0.004
B	0.8	0.722	0.732	0.734	0.740	0.754	0.736 ± 0.010
C	2.4	2.251	2.276	2.374	2.227	2.166	2.259 ± 0.068
D	1.5	1.261	1.428	1.375	1.347	1.383	1.358 ± 0.055
E	1.2	1.113	1.083	1.057	1.102	1.093	1.090 ± 0.019

Table 7. *Dose estimation for five blind doses for TLD analysis*

6.8 Alanine Pellets

Dose Label	Actual Dose (Gy)	Dose Estimate (Gy)
A	0.8	0.79 ± 0.032
B	1.5	1.51 ± 0.045
C	1.2	1.15 ± 0.054
D	0.3	0.32 ± 0.050
E	2.4	2.16 ± 0.049

Table 9. displays the estimated dose for each set of irradiated pellets.

6.9 Average Absolute Error (AAE)

AAE was calculated to compare on average how far the reported dose was from the actual dose using Excel for each biological/physical dosimetry assay (Table 10). It must be noted that when only 50 cells are scored, the statistical power becomes limited. This is especially true for higher doses as dicentric yield increases steeply with dose, but the limited sample size (for triage mode) does not capture this relationship accurately. With few cells, the variance around the expected dicentric frequency is large, and even small random fluctuations in observed aberrations can produce disproportionately high dose estimates when applied to the calibration curve. Furthermore, higher doses may introduce more complex damage visually, which can increase the likelihood of observer-dependent error and make the identification of aberrant chromosomes more challenging. Comparatively, automated systems, as seen here, show more accurate results likely due to the increased sample size scored. As seen on table 10, although DCA manual has a high AAE, it was still able to successfully categorise 4/5 simulated ‘persons’ into the specified broad triage dose categories.

	Method							
Dose (Gy)	**DCA Manual****	**DCA Automated**	**γH2AX**	**Gene Expression**	**Tachyon Device**	**Mobile Phones**	**TLDs**	**Alanine Pellets**
0.3	0.366	0.020	0.099	0.200	0.25	0.050	0.013	0.32
0.8	0.007	0.074	0.387	0.000	1	0.200	0.064	0.79
1.2	0.145	0.061	0.418	0.100	**1**	**-**	0.110	1.15
1.5	0.524	0.340	0.550	0.400	0.6-1	0.400	0.142	1.51
2.4	0.984	0.054	0.248	0.900	1.8-2	0.600	0.141	2.16
AAE	0.405	0.110	0.340	0.320	0.33	0.312	0.094	0.066
Doses correctly categorised	**4/5**	**5/5**	**3/5**	**4/5**	**2/5**	**2/4**	**5/5**	**5/5**

Table 10. *Absolute Errors (Estimate – Reference) and Average Absolute Errors showing average spread of predicted data for each assay compared to actual dose given. Blank spaces indicate that no dose estimate was provided. Lower number indicates that the predicted DE was closer to the actual DE. AAE = (1/n) * Σ|y_i - $\hat{y}_i$|. AAE = Average Absolute Error, n = the number of data points, y_i = the actual value, $\hat{y}_i'$ = the predicted value.*

**** This is for triage of 50 cells only to categorise individuals – Routinely 1000 cells are analysed to warrant accurate DE**

To evaluate the performance of the different methods, estimated doses obtained for each technique at reference doses 0.3, 0.8, 1.2, 1.5 and 2.4 Gy were plotted showing on each figure the point estimate with associated confidence intervals (Figure 1). These visually compare the accuracy and variability of each method and highlight which fall within a suitable success range.

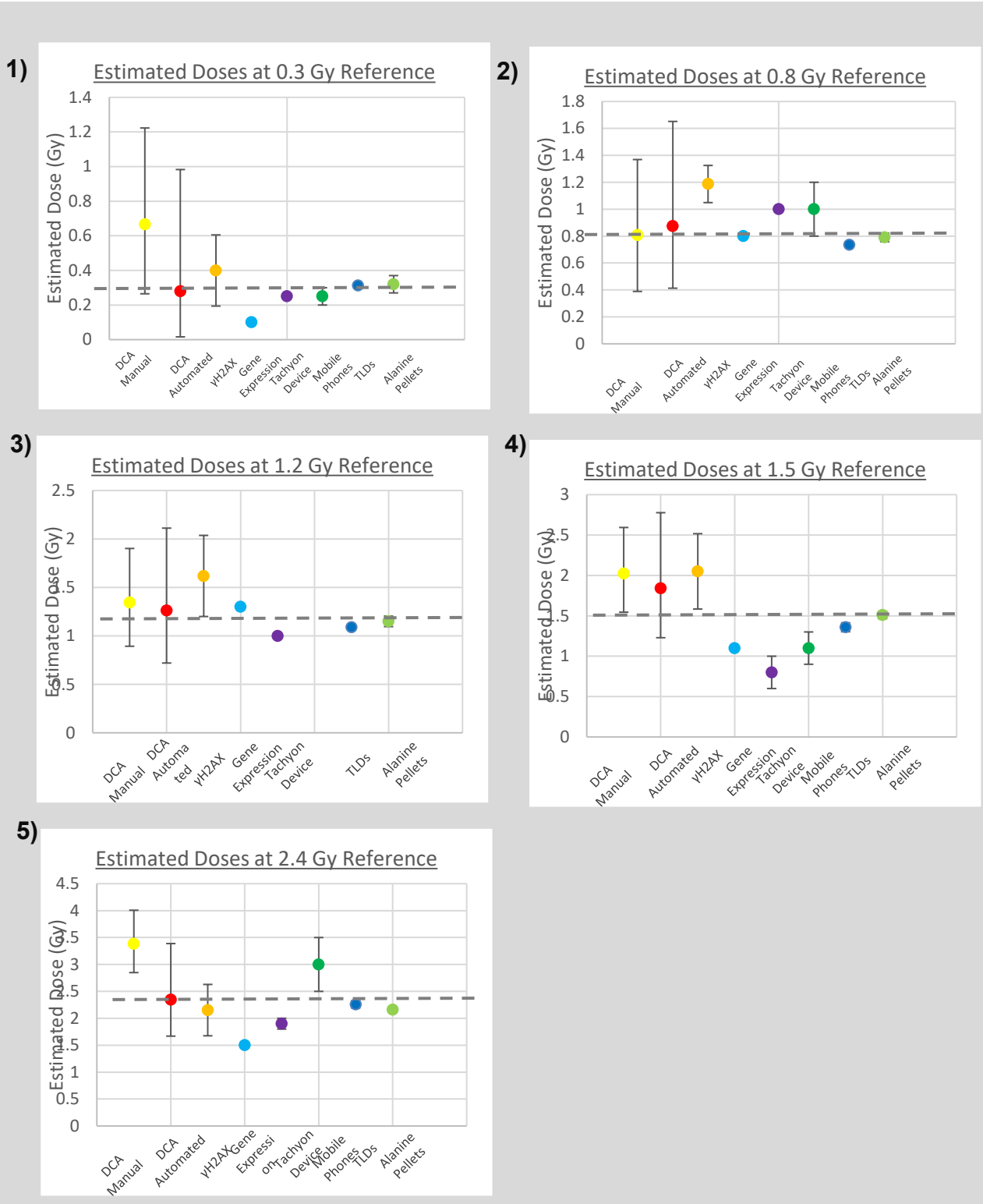

Figure 1. Comparison of estimated radiation doses across multiple biodosimetry methods at reference doses of 0.3, 0.8, 1.2, 1.5 and 2.4 Gy. Left panels show dose estimated for each method relative to the corresponding reference dose (Grey dashed line), with vertical error bars representing the reported confidence intervals. Each point represents an individual dose estimate obtained by specific method (DCA manual, DCA automated, γH2AX, gene expression, Tachyon device, mobile phones, TLDs and alanine pellets).

7: Discussion

Large-scale radiological emergencies present a major challenge for emergency preparedness, highlighting the importance of regular practical and table-top exercises and intercomparisons across all emergency response plans. High throughput analysis of samples will be essential for determining the extent of radiation dose exposure and characteristics as efficiently as possible, and to streamline triage and sample prioritisation. RENEB and EURADOS continue to play a vital role in this area by regularly organising exercises that demonstrate the capability of various laboratories in maintaining routinely competent biological and physical dosimetry techniques across European countries, including UKHSA. Evaluating global preparedness is vital in driving the development of emerging technologies and techniques as well as strengthening the community of laboratories responsible for dosimetry. Historically, biodosimetry is well embedded in UKHSA and wider emergency response plans across the UK, whereas newer techniques, including gene expression and physical retrospective dosimetry, need further validating and standard operating procedures (SOPs) to be developed, embedded in response plans and further exercising to establish robustness.

The γH2AX assay was first identified and refined at UKHSA over a decade ago, showing promise as a new biodosimetry tool to identify radiation dose exposure and estimation of dose up to 96 hours post-exposure to radiation, and with the ability to detect partial-body exposures through distribution analysis [9, 42, 43]. The primary advantage of the assay is the speed at which samples can be processed and analysed, within 4 – 5 hours upon receipt. However, the assay is less sensitive than other cytogenetic approaches but can assist in initial trial and categorisation of samples to identify the critically exposed from those unexposed individuals, aiding in the prioritisation of individuals for more accurate follow up dosimetry techniques whilst relieving anxiety in the ‘worried-well’ through quick indications of low-or-no dose exposures. The assay was first demonstrated in 2015 as an appropriate tool approach for triage during the EC-funded RENEB intercomparison [8] of 8 laboratories, whereby the assay was able to identify and categorise radiation dosed blood samples successfully. A second intercomparison of the assay further supported the applicability of the assay as a useful triage tool that can be applied and followed by multiple laboratories, increasing surge capability across Europe if needed [23].

The DCA is widely regarded as the gold standard for biological dosimetry due to its specificity to IR with a low and stable background dicentric frequency [44] and a well-established dose response curve(s). A notable strength of the DCA is its reliability for detecting recent exposures, with a lower detection limit of 0.1 Gy. Although scoring for routine analysis requires 1000 scored cells which is time-consuming, for cytogenetic triaging only approximately 50 cells need to be scored (roughly 1 hour of staff effort compared to 20 hours for routine testing). However, in the instance of a mass-casualty event, extremely high chromosome analysis efforts would be required. Therefore, the intercomparison exercises alongside many efforts to establish and maintain national or international biodosimetry networks of mutual assistance are vital to remain prepared [44, 45].

Various ILCs have validated the effectiveness and reproducibility of results for the DCA, as seen in the RENEB 2021 ILC where 33 laboratories from 22 countries received 3 samples each to blindly analyse [46], though it can be noted that there was a slight observed systematic

shift of dose estimates perhaps as the samples were irradiated with X rays rather than γ rays (which some laboratories had dose effect curves based on). However, this slight overestimation of DEs may be better tolerated in the instance of a large-scale RN event as this would lead to prompt medical intervention alongside more in-depth testing. Conversely, false-negative classifications or underestimated DEs may lead to a delayed medical response and associated adverse patient outcomes. Regular exercises are essential for training in the logistics of sample shipment and processing, assessing and enhancing the ability of network members to deliver accurate dose estimates, and identifying potential weaknesses in the overall response system.

A further study [47] investigated the suitability of semi-automated scoring as a method of high throughput biological dosimetry technique to rapidly triage individuals in the instance of a mass-casualty event. Promising results had previously confirmed the validity and strength of the DCA and γH2AX assays [48] in previous studies as part of the MULTIBIODOSE project. Beginning to introduce the applications of semi-automated scoring among ILCs show this may be a useful tool, enabling high throughput and heavily reduced staff effort.

The recent development of *FDXR* gene expression analysis and its applicability during large-scale radiation exposure events has been tested during an intercomparison exercise within the RENEB network in 2021 with all unexposed samples correctly identified and categorised by all participating institutions [2]. Doses above 1 Gy were correctly triage categorised in only half of the participating laboratories. However, the applicability of gene expression analysis to identify unexposed from exposed persons is nevertheless and extremely valuable tool for triage of samples to support medical management decisions. An earlier RENEB interlaboratory comparison exercise in 2015 further validated the effectiveness of *FDXR* as a suitable gene for dose estimation. This study also confirmed that *FDXR* gene expression was able to discriminate blood samples from patients prior to radiation exposure to those post- exposure [49].

To represent the capacity of IR dose estimation at UKHSA, approximate reporting times per method have been calculated taking into consideration number of staff and equipment limitations (Table 11). The table below summarises the approximate reporting times for five samples as well as extrapolated times for 100 samples for each assay. These should not be viewed in isolation, as factors such as staff availability, technical expertise, number of specialised equipment and transporting of materials can significantly impact throughput. Therefore, in an emergency scenario, where rapid triage is essential, the balance between assay accuracy, scalability, and practicality factors must be greatly considered.

Table 11 *- Approximate triage reporting times by assay*

Assay	**Approximate Rapid Dose Estimation reporting time for this exercise (5 samples)**	**Approximate Rapid Dose Estimation reporting time for 100 samples**	**Notes**
DCA Manual	4 days	Once all the samples have been processed (3 days) 100 samples could	This is for triage of 50 cells only to categorise individuals –

		be scored, and a dose estimate reported in 7 days. Assumes 2 scores working an 8 h day at the microscope.	Routinely, 1000 cells are analysed to warrant accurate DE.
Automated DCA	4 days	Once all the samples have been processed (3 days) and are ready to score 100 samples can be image captured (150 cells per sample), scored and a dose estimate reported in 3 - 4 days. Assumes 1 scorer, but the Metafer capturing images overnight.	Scoring will start on day 4. Scoring faster than manual DCA as only involves 3 minutes. staff effort for scoring. Image capture and running DCScore software takes ~30 minutes for 150 cells
γ-H2AX	4-5 hr	3 days	Useful for initial triage to determine who needs immediate healthcare.
Gene Expression	5 hr	16 hr	Proves to be an accurate and valuable tool for categorising potentially overexposed individuals. Multiplexing up to 6 genes at a time possible.
Tachyon	5 hr	5 hr	Can be used at the point-of-care by non-trained personnel

Logistical Requirements and Limitations

In the event of a radiation emergency, there are significant logistical challenges that need to be overcome in order to ensure samples are effectively collected and their integrity maintained so that dosimetry can be accurately performed. The specific nature of any given incident will be unique; however, the key concerns remain for each of the methods of dosimetry being used.

Initially, there will be a sample collection phase requiring suitably trained individuals to arrive at the scene or be stationed at a location that potentially irradiated individuals would be able to travel to in the following days. This is more challenging with respect to biological dosimetry, where there will be the need for trained phlebotomists to take blood from those in the affected area and appropriately package them for safe transit. This would also require a potentially large stock of equipment e.g. syringes, needles, EDTA and Lithium-Heparin blood tubes, depending on the scale of the incident. Physical dosimetry is easier to obtain as no special training would be required, only to collect the physical dosimeter from those carrying them. However, it must be noted that depending on the location and nature of the incident, it is less likely that individuals will have TLDs or alanine pellets on their person. Alternatively, mobile phones would be almost ubiquitous and would be a more reliable option for collection in the general population, provided they agree to the loss of their phone for testing purposes.

The next phase would be the transit itself, where samples will have to be delivered to the UKHSA labs in Chilton. The duration of this step is highly dependent on the location of the incident and the number of samples being transported. The most accurate results seen with biological dosimetry methods are at 4 – 24 hours post-exposure, although limitations around transport times make this timeframe more difficult to achieve. γ-H2AX can only provide accurate results up to 48 hours post exposure, while gene expression is reliable up to 3-5 days. The DCA can still provide accurate dose estimations up to one year post-exposure. To ensure integrity of the samples, it is essential that blood samples are stored in either Lithium-Heparin or EDTA blood tubes (assay-dependent) and kept at room temperature. The integrity of the blood is maintained provided there are no extremes in temperature during transit. An exception to this would be the Tachyon device, as it is designed to be used in the field to provide dose estimates at the scene of the incident, therefore minimising and transport or handling complications. Physical dosimeters are very stable, and dose estimation methods often require high energy [50, 51]. This makes them much less sensitive to fluctuations in conditions during transport, as temperatures and humidity are unlikely to reach those that could have any significant effect on the readouts in the short-term. Readouts have however been shown to fade over time due to temperature and humidity, therefore prompt transport is still essential [51, 52].

It is essential that all samples, biological or physical, monitored throughout their transportation. In a nuclear incident, the purpose of dosimetry is to triage as many effected or ‘worried-well' as possible. If time is wasted testing samples that have been compromised before reaching the lab, this could significantly impact the capacity of the emergency response effort. Monitoring can be achieved, if available, using data loggers, recording temperature and humidity throughout the process. Fresh TLDs are also used alongside samples to act as a

control for any additional radiation received from the point the samples have been taken. This may happen, for example, by being put through an x-ray scanner at an airport if the samples are required to travel by plane. In this scenario it is essential that appropriate labelling and requests are carried out so that the samples are not scanned.

8: Conclusion

In summary, this exercise demonstrated the capacity of UKHSA to efficiently categorise individuals potentially exposed to IR exposure according to triage categories (low <1 Gy, medium 1-2 Gy and high >2 Gy) using various biological and physical dosimetry assays/techniques. Although, as doses become higher, difficulties may arise due to smaller number of cells scored for cytogenetic methods such as DCA and γH2AX, however the results demonstrate that these techniques are adequate for categorising irradiated blood into the categories above. All techniques, both biological and physical demonstrate applicability in categorising potentially exposed victims into medically suited broad 1 Gy categories which strengthens UKHSA's emergency response plan and we should aim to implement as many techniques as possible to create an accurate model of the radiation exposure scenario. This practical exercise reinforces the value of a multi-assay approach to radiation biodosimetry, where complimentary methods can provide cross-validation and improved reliability in dose assessment. Future work should focus on consolidating and improving the various assays and the integration and refinement of high-throughput automated systems to establish an organised and collaborative emergency response plan with regards to the use of biological and physical dosimetry as and when needed. UKHSA will seek to implement multi-parametric analytical approaches to build complete models of individual radiation exposure and produce rapid and/or accurate dose estimations to inform on medical management and long-term follow up of exposed populations. UKHSA are also exploring, though various collaborations, the future role of implementing artificial intelligence (AI) approaches to further improve capacity and capability for dosimetry during emergency response.

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Appendix

Dose (Gy)	No. Cells evaluated	Number of dicentrics	Dicentrics per cell	SE	Dicentric distribution						Variance to mean	U
					0	1	2	3	4	5		
0.00	10423	8	0.0008	0.0003	10415	8	0	0	0	0	0.999	-0.052
0.10	4740	23	0.0049	0.0010	4717	23	0	0	0	0	0.995	-0.231
0.25	4301	50	0.0116	0.0016	4251	0	0	0	0	0	0.989	-0.534
0.50	2740	71	0.0259	0.0031	2671	67	2	0	0	0	1.031	1.148
0.75	2989	140	0.0468	0.0040	2853	132	4	0	0	0	1.011	0.4128
1.00	1724	128	0.0742	0.0066	1599	122	3	0	0	0	0.9732	-0.7899
1.40	4753	459	0.0966	0.0045	4322	403	28	0	0	0	1.026	1.252
2.00	3291	673	0.2045	0.0079	2697	523	63	8	0	0	1.054	2.207
3.00	2732	1222	0.4473	0.0128	1777	734	180	36	5	0	1.074	2.719
4.00	2123	1112	0.5238	0.0157	1308	573	194	42	5	1	1.124	4.048

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UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats. We provide intellectual, scientific and operational leadership at national and local level, as well as on the global stage, to make the nation health secure.

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Version 1

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