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Case Study

Advancements in Biological Dosimetry Techniques for Surge Response to Radiation Emergencies in Ghana

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Abstract

The awareness of the use of biodosimetry to estimate external radiation doses received by individuals and in radiation oncology, nuclear medicine, diagnostic, and interventional radiology has gained traction in recent years. At present Ghana is poised to integrate about 1GW of nuclear power into its electricity mix by 2034. The increased awareness of biodosimetry is probably due to increased radiological threats and incidents, medical and forensic applications, the quest to strengthen emergency response to unplanned radiation exposures such as radiological accidents, and the malevolent use of radioactive sources. Biodosimetry capabilities would play an effective role during public health management of radiation emergencies for rapid dose estimation and help to medically categorize the exposures for the purpose of prioritizing treatment of the affected persons. Moreover, it will also serve to provide reassurance and psychological support for the "worried-well". Biodosimetry methods and infrastructure can also be utilized for various applications, including molecular research, medical cytogenetics, and forensics.

This write-up assesses the status of biodosimetry methods and infrastructure capabilities available at the Ghana Atomic Energy Commission (GAEC), which could be leveraged during radiological or allied scenarios.

Introduction

Background

There is increasing interest in nuclear technology for various beneficial purposes worldwide. Nuclear technology finds application in medicine, research, and development, industry, construction of wells, agriculture, and for electricity generation (NPP) [1].

Nuclear technology is essential to modern medicine and scientific progress, with diverse applications ranging from diagnostic imaging and cancer treatment to fundamental research [2].

In medicine, nuclear technology is utilized in diagnostic imaging, specifically in nuclear medicine, where radioactive isotopes are used for imaging and diagnostic purposes. For example, Positron Emission Tomography (PET) scans detect metabolic activity, making them a common tool in cancer diagnosis. Additionally, Single-Photon Emission Computed Tomography (SPECT) is employed to image blood flow in organs such as the heart and brain [2].

In radiation therapy, external beam radiotherapy delivers high-energy radiation to treat cancer, with linear accelerators used to precisely target tumors. Another treatment approach, brachytherapy, involves placing radioactive sources inside or near the tumor. This technique is commonly used in prostate cancer treatment, where radioactive seeds are implanted directly into the prostate [2].

Nuclear technology is used in the sterilization of medical equipment, with gamma radiation being a common method. Gamma irradiation allows for sterilization without the need for

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heat or chemicals, making it ideal for sensitive materials. It is typically used to sterilize items such as syringes, catheters, and surgical tools.

In research and development, nuclear technology plays a crucial role in radiobiology and cancer research, where it is used to study the effects of radiation on biological tissues. Research in radiation biology, for instance, helps to understand cancer progression and contributes to the development of therapies.

Nuclear technology is also employed in nuclear physics research to investigate fundamental particles and forces through the use of particle accelerators. For example, cyclotrons are utilized in this field to better understand atomic structures and their medical applications, such as the production of radioisotopes.

In materials testing, nuclear technology is applied non-destructively to evaluate material properties, such as through neutron activation analysis for detecting trace elements in samples. In agriculture and food science research, radiation-induced mutation breeding is utilized to enhance crop varieties, including the development of drought-resistant crops. Additionally, nuclear technology is employed for food preservation, where irradiation is used to extend the shelf life of products like spices and meat. Small-scale reactors are also used for experimental purposes and to produce radioisotopes for medical applications, such as Technetium-99m.

Radiotracers are employed in Environmental Monitoring and Management to detect pollutants in air, water, and soil. They are also used to study ocean currents and track the spread of pollution. Nuclear technology is essential in modern medicine and scientific progress, with applications ranging from diagnostic tools to cancer therapy and fundamental research.

Radioisotope therapy uses radioactive isotopes to treat various diseases, such as radioiodine (I-131) therapy for thyroid cancer and hyperthyroidism. In addition to therapeutic applications, radioisotopes are also used diagnostically in bone scanning and imaging. Radioactive tracers help detect bone metastases or fractures, with Technetium-99m being commonly employed in bone scans. Radiotracers are also used in Environmental Monitoring and Management to track pollutants in air, water, and soil. Studying ocean currents using radioisotopes to monitor pollution spread. Nuclear technology plays a critical role in modern medicine and scientific advancement through its varied applications, from diagnostic tools to cancer treatment and fundamental research.

The threat of dirty bomb deployment in Africa cannot be completely ruled out in the light of past experiences in Nairobi and Dar es Salaam in 1998 and Mombasa in 2002, [3-5]. In this regard, capacities and capabilities in biodosimetry will be essential to help in the medical management of acutely exposed victims in case of a radiological event which is integral to triage and management processes and for reassurance of the worried well. Moreover, Ghana has significant activities in industries like industrial radiology (mining and oil refinery), radiotherapy, medical radiology, and military deployments. In consonance with the global collective commitment to the sustainable availability of power, and the peaceful exploitation of nuclear energy to enhance rapid industrialization, and propel economic growth the Government of Ghana is poised to integrate up to 1GW of nuclear power into its electricity mix by 2034 [6-8]. In this regard, the Government of Ghana officially transitioned into Phase 2 of her Nuclear Power Programme with an official declaration made by the President of the Republic H.E. Nana Addo Dankwa Akufo-Addo on 31 August 2022. Moreover, the terrorist attack of September 11, 2001, mandated government authorities to rigorously prioritize radiation protection and safety procedures more than ever [9]. This obliges healthcare systems to develop and apply a preparedness plan to mitigate the consequences of radiological terrorism.

Up until now, competencies in biological dosimetry in Ghana and Africa remain a gray area thus, establishing capacity and capabilities in cytogenetic biodosimetry infrastructure in Ghana will be a major milestone and a big boost to all of Africa. It will help Ghana close a critical gap in the nation's ability to respond to a mass casualty radiation incident and afford it the opportunity to offer training in this area to sister countries [6]. The utility of biological dosimetry in industry, occupational medicine, epidemiology, toxicology agriculture, and related disciplines for human biomonitoring programmes cannot be over-emphasized

Well-established capabilities in biological dosimetry in Ghana when realized will enhance its ability to safely manage nuclear energy programmes. Besides it will ensure the health and safety of its population, meet international regulatory standards, and foster economic growth and scientific knowledge. For Ghana, building a robust biodosimetry capability is a critical component of national preparedness for radiological emergencies, especially as Ghana plans to incorporate 1 GW of nuclear power into its electricity mix by 2034 [7].

This write-up situates the position of biodosimetry capabilities being harnessed and nurtured at the Applied Radiation Biology Centre (ARBC) of the Radiological and Medical Sciences Research Institute (RAMSRI) of the Ghana Atomic Energy Commission (GAEC), the sole organization mandated to undertake nuclear research in Ghana and concludes with the future perspectives of biodosimetry in Ghana.

The applied radiation biology centre

The ARBC, a center within the Radiological and Medical Sciences Research Institute of the Ghana Atomic Energy Commission, aspires to become a leading comprehensive radiation biology, cancer, and biodosimetry center in Ghana and West Africa. Utilizing innovative diagnostic techniques in clinical laboratory research, it aims to provide precise research information to physicians to deliver effective patient care and to make life-saving decisions. The center seeks recognition as a center of excellence in biodosimetry in Ghana and West Africa.

Biological dosimetry

Biodosimetry uses established biological techniques to

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measure doses of ionizing radiation received by individuals suspected of being exposed to ionizing radiation [10-12]. It is an internationally approved method used to quantify exposures, also to perform radiation dose assessments following radiation accidents, a biological estimate of the dose received by victims provides an independent means of obtaining information otherwise based solely on computer modelling, dose reconstruction, or physical considerations and assumptions. As opposed to biological dosimetry, physical dosimetry can furnish the total dose at specific points at any time after exposure with immediate readout but lacks the ability to indicate the biological implications of the exposure or variation in the dose rate. In biological dosimetry, the dose is not recorded but its effects at the cellular level are investigated to determine the dose received by the individual and the associated health risks of the dose receive [13]. Different individuals react differently to radiation; therefore, biological dosimetry considers inter-individual variations in radiation sensitivity when assessing the effects of radiation in humans [14]. On the 15th of June 2007, a revised International Health Regulation (IHR) came into force, where potential threats to public health were extended to include other types of public emergencies such as infectious disease outbreaks, natural disasters, and chemical and radiation emergencies. The inclusion of radiation emergency scenarios in the IHR document mandates countries to strengthen their preparedness for the management of radiation emergencies. One of the main public health management challenges during radiological events is emergency triage management, which permits the evaluation of the number of over-exposed victims and the severity of individual exposure [15]. When done expeditiously, potential patients can be identified, efficiently, and timeously triaged in points of care for better treatment outcomes. The availability of this capability will inure to the benefit of resource-poor settings where hospital and laboratory facilities are limited, permitting efficient allocation of scarce resources and timely assessment of radiation dose in order for critical "life-saving" clinical decisions to be made especially for those with exposures to moderate and high doses of radiation [16].

Aside from emergency and radiation protection considerations, biodosimetry methods are becoming increasingly significant in radiation oncology, nuclear medicine, diagnostic, and interventional radiology where they contribute to the improvement of radiation-associated healthcare quality assessments [17]. Furthermore, the harrowing threat of malevolent use of radiation sources in the wrong hands lends serious credence to the need to develop competencies in medical countermeasures for managing large-scale population exposures to radiation. In this context, it is advisable for national security authorities to review their emergency plans to incorporate biodosimetry practice in National policy documents and to ensure that these laboratories are capable of conducting recommended tasks, either domestically or through international collaborative efforts, and establish intercomparison programmes to meet internationally recommended standards across different laboratories [18-20].

Existing biodosimetry methods at the GAEC

Dicentric Chromosome Assay (DCA): The DCA has been touted as the "gold standard" used in biological dose estimation and remains the most used biodosimetry technique worldwide. It is an *in vitro* technique performed on peripheral blood lymphocytes after radiation exposure. In this assay dicentrics, centric rings, acentric fragments, or translocations have long been used as the reliable endpoint for radiation-induced damage in cases of exposure or suspected overexposure to ionising radiation [17]. Figure 1 below indicates metaphase spreads of non-irradiated and irradiated lymphocytes, where DNA damage is illustrated in the irradiated cells. Cytogenetic dosimetry is an important method for measuring external whole-body radiation doses and assessing the dose distribution within an irradiated individual and can help provide useful information to diagnostic and prognostic physicians.

For a country planning to incorporate nuclear power into its energy mix, it is of essence to ensure that laboratory staff are proficient in performing the DCA with high accuracy and reproducibility given that the DCA remains the gold standard. The basic requirements for a laboratory undertaking blood lymphocyte culture for cytogenetic biodosimetry are listed elsewhere [17,22] and must be considered critically in the establishment of capabilities in biodosimetry. Towards building capacity in biological dosimetry in Ghana, our group established in-house dose-response calibration curves for photons at the GAEC [23]. Since then, Owusu has evaluated chronic exposure to low-dose radiation in diagnostic and interventional radiology workers in a Ghanaian hospital essentially employing the DCA and micronucleus assays [24]. To meet IAEA standards and be able to acquire ISO certification, further validation work is required by our team to achieve our ambition of producing sound and trustworthy results and eventually establishing a Centre of Excellence Laboratory in Biological Dosimetry in Africa.

The cytokinesis block-micronucleus (CBMN) Assay: Another tool of biological dosimetry that has been installed in the laboratories of the Ghana Atomic Energy Agency is the *in vitro* CBMN assay. The micronucleus test has been recognized as a straightforward, non-invasive, and cost-effective method for assessing the effects of genotoxins and carcinogens [25,26]. IR induces the formation of micronuclei which include whole chromosomes or chromosome fragments not incorporated into the daughter nuclei during cell division and enveloped by a nuclear membrane outside the cell [13]. In our laboratory, this method has been used by Owusu [24] and Agbenyegah [21] to

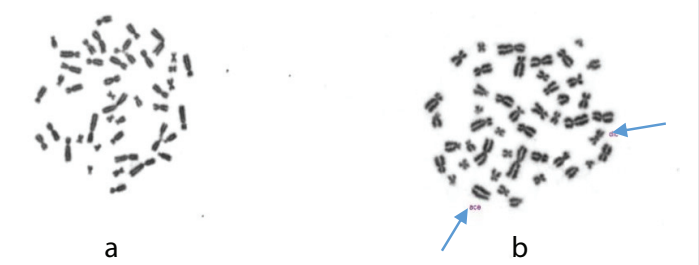

Figure 1: (a) is a representation of non-irradiated metaphase spread with all 46 chromosomes appearing normal. (b) show one metaphase spread from irradiated 1Gy sample with an abnormal chromosome indicating radiation damage in the form of a dicentric chromosome and an acentric fragment [21].

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monitor hospital workers exposed to low-dose radiation. In this method, dose is estimated using the correspondence between micronucleus yields and dose-effect curves. Figure 2 displays some MN results obtained from these studies. Characterized by high inter-individual variability due to age and gender, the MN assay is further limited by its ability to detect only acentric fragments. Furthermore, it does not allow the detection of partial-body exposures, is not radiation-specific, and may be induced by many genotoxic agents [27].

For surge management, the micronucleus assay has numerous limitations, including its laborious and time-consuming nature, low sensitivity (insensitive to doses below 0.1 Gy), high inter-individual variability, need for highly skilled personnel, and lack of specificity.

γ-H2AX Assay: Double and single-strand breaks in DNA are indicated by the DSB biomarker γ-H2AX, a sensitive, specific, and reliable dose-dependent method for the detection and quantification of radiation-induced DNA damage. Detection γ H2AX phosphorylation is an indicator of DNA damage with foci formation. In terms of inhomogeneous exposures or partial body irradiation that can be visualized by immunofluorescence, due to the redistribution of lymphocytes in blood, the γ-H2AX assay can be used to estimate the dose delivered to the whole body even if only a part of the body was irradiated. An advantage of using the γ-H2AX assay is its high sensitivity and ability to detect DNA damage induced by radiation doses as low as 1.2 mGy [25,28]. Our team has demonstrated that foci yields increase linearly with dose increase and its main disadvantage is the absence of stability over time. Cellular images displayed in Figure 3 show some γ-*H2AX Foci*. A close correlation between γ H2AX foci and DSB numbers and between the rate of foci disappearance and DSB repair has been established, providing a sensitive assay to monitor DSB repair in individual cells at low doses.

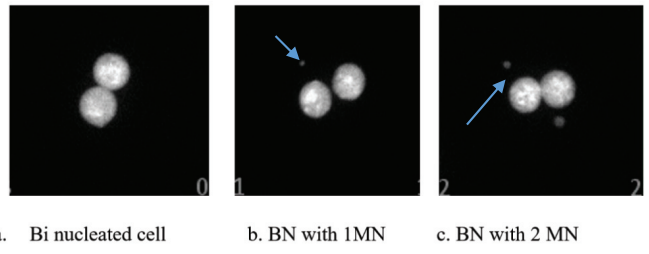

Figure 2: (a) bi-nucleated cell; (b) bi-nucleated cell with 1 micronucleus; (c) bi-nucleated cell with 2 micronuclei [21].

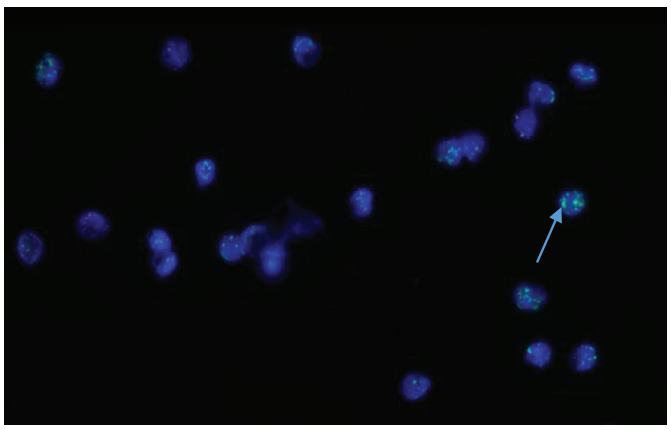

Figure 3: Shows the image obtained of cells with FOCI (bright dots in the middle of the cells) irradiated at 1Gy and analysed 20mins after irradiation [21].

Using flow cytometry-based γH2AX Assay we demonstrated the potential utility of this tool for high throughput biodosimetry in blood samples of human volunteers exposed to up to 5 Gy. In this study, there was a significant emergence of inter-individual differences in γH2AX expression [29]. It is instructive to enhance this technique for quick and sensitive detection of DNA damage as well as develop protocols for high throughput screening. Perhaps the work of Achel and coworkers sets the tone for the ARBC/GAEC to consider integrating flow cytometry-based γ-H2AX assay for high-throughput capabilities [29].

Gene expression analysis

IR provokes alterations in gene, protein, and metabolite expression. These biomarkers *may* be used to elucidate cause-*effect* and dose-*effect* relationships in the assessment of health risks associated with exposure to radiation [30] such as the severity of the acute radiation syndromes [31]. Comparing the gene expression levels in the potentially exposed individuals to a baseline or reference cohort helps distinguish those in need of medical attention from the worried well as well as avoid misclassification of the exposed or the unexposed individuals during a large-scale radiological or nuclear scenario [31-33]. Gene expression analysis is a rapid, sensitive, reliable method that requires only small amounts of DNA or RNA and holds promise for application in high throughput scenarios due to the possibility of automation. This makes it possible to analyse the expression of hundreds to thousands of genes from numerous people or samples. Gene expression analysis, for instance, might be an adequate methodology for large-scale scenarios [28] providing a shortcut for effect prediction. With individuals ranging from tens to thousands being affected; diagnosis obviously becomes a problem due to the large numbers [30]. Gene expression automated equipment and devices for high throughput analysis will be useful for processing these large numbers of samples. e.g. The QI symphony by Qiagen enables the processing of a large number of samples in high throughput studies for a short period of time [34].

However, the cost involved in gene expression methods is prohibitive due to the high cost of equipment, consumables, and reagents and the highly skilled manpower requirement. This tool has been employed variously by our team to evaluate its possibility for high throughput biodosimetry for rapid response to radiological scenarios [32,33]. To operationalise the gene expression assay in the context of biodosimetry for surge response, it is essential for the laboratory at the GAEC to equip the laboratory with the needed accoutrements, identify unique radiation response genes, standardize and validate gene expression panels specific to radiation exposure and implement high-throughput real-time PCR or next-generation sequencing platforms for rapid analysis as well as overcome the hurdle of skilled manpower requirement and high cost of equipment, reagents, and consumables.

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Expansion of assay repertoire

Different biodosimetry techniques are available but are not currently being practiced by our group. However, they are worth considering for inclusion in the GAEC biodosimetry assay repertoire, as discussed below.

Premature Chromosome Condensation (PCC) Assay: The premature chromosome condensation (PCC) technique is a sensitive and unique method for detecting interphase chromosome damage caused by exposure to hazardous chemicals and physical agents. This technique provides a useful biodosimetric alternative to evaluate acute whole or partial-body exposures in high-dose radiation emergencies compared with the conventional dicentric assay [35-38].

The unique feature of this method is its ability to detect exposures to low radiation doses as well as to life-threatening acute high doses of low LET [39] and high-LET radiation [40]. Moreover, the PCC assay can discriminate between total- and partial-body exposures [41]. Also, the PCC assay can be performed immediately after irradiation and data can be generated within 3–4 h after setting up the experiment as compared to the other existing assays [35-38]. Usually, after high-dose exposure to ionizing irradiation, obtaining mitotic chromosomes is a huge difficulty, posing a challenge to cytogenetic analysis. The PCC is particularly useful when metaphase spreads are difficult to obtain.

Therefore, to incorporate the PCC as an effective and efficient tool for surge response in the context of a country intending to include nuclear power in its energy mix but also to expand its use of nuclear technology, it is important to invest in training and equipment for PCC, which is valuable for detecting radiation exposure in interphase cells.

Translocation analysis by Fluorescent *in situ* Hybridization (FISH)

One major drawback of both the DCA and the CBMN assays is that the damage is unstable and disappears with time after exposure to ionizing radiation making them unsuitable for retrospective biological dosimetry. Translocations, persist longer in lymphocytes and are thus suited for retrospective measurement of radiation exposure [28]. The FISH technique is used for detecting and quantifying various structural and numerical chromosomal abnormalities employing chromosome-specific probes to detect, localize, and hybridize with specific chromosomes. In this assay, probes that hybridize along an entire chromosome are used to identify the chromosome number, depict translocations, or identify extra-chromosomal fragments of chromatin (whole-chromosome painting).

Figure 4 below depicts the use of two-color FISH to detect DNA aberrancy in metaphase spreads.

There is a need for our laboratory to develop capabilities for FISH to detect specific chromosomal aberrations with the knowledge of hindsight that this technique can be combined with other cytogenetic assays for comprehensive analysis. Although

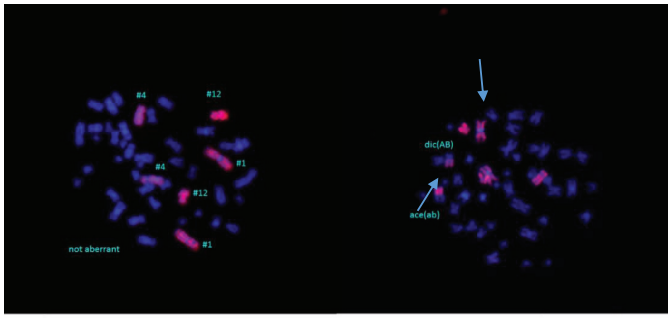

Figure 4: (a) A representative normal 0Gy metaphase spread with no translocations between chromosomes and (b) shows translocations in the chromosomes of cells irradiated with 2Gy radiation dose [21].

FISH analysis is now a well-accepted method for retrospective biodosimetry, the high cost, long and complicated staining protocols have limited its use in emergency biodosimetry.

Comet assay (single-cell gel electrophoresis)

Another versatile tool used in genotoxicity assays and worth exploring and including in the skills bank of our laboratory is the comet assay. This method for assessing damage in DNA measures single or double-stranded breaks in the DNA produced in response to exposure to chemicals or physical agents such as radiation. In this procedure, damaged strands of DNA lose their compactness migrating out of the cell and into agarose gel during electrophoresis while large undamaged DNA strands remain in the cells. The damaged DNA migrates away from the undamaged DNA containing nucleoid body creating the "comet head" while the damaged DNA which migrates out of the cell under electrophoresis creates a "comet tail". The DNA is then stained using a fluorescent dye and viewed using a fluorescence microscope. The fluorescence intensity in the comet tail indicates the extent of DNA damage. This can be performed by manual scoring or automatically by imaging software. However, the responses obtained from this method are not necessarily radiation-specific, moreover, there is a need for internal reference to avoid variations. Though not currently available in our laboratory are exploring the possibility of installing this assay for detecting radiation-induced DNA strand breaks because of its relative simplicity, cheapness, and sensitivity and its potential for automation and high throughput screening [42].

Lymphocyte depletion kinetics (LDK; hematological analysis)

This tool employs lymphocyte depletion rate to estimate radiation dose received by victims. It has the added advantage of being fast to perform when compared with other traditional cytogenetic assays such as DCA and CBMN assays. In this procedure, blood samples from exposed or potentially exposed individuals can be tested for lymphocyte depletion which occurs hours after exposure to radiation. The kinetics of lymphocyte count can be measured as soon as possible and repeated at short intervals over a given time range and the data points are compared to an established dose-response

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curve to estimate the doses received. In large-scale radiation emergencies, biodosimetry based on lymphocyte depletion kinetics, clinical signs and symptoms, and dose reconstruction from geographic information are likely to be available more rapidly than biodosimetry based on dicentric chromosome assay. It is noteworthy to note that lymphocyte counts in a normal human differ with age, gender, and ethnicity.

Thus, enhancing the capability and capacity in lymphocyte depletion kinetics as a biodosimetry tool may come in handy, especially in contexts of surge response to a radiological emergency. At present frantic efforts are being made to perfect automated flow cytometry-based LDK to facilitate precise and rapid counting of lymphocytes which facilitates efficient and scalable lymphocyte depletion kinetics studies. Moreover, advanced software algorithms are now available to automate data analysis, providing quicker and more accurate interpretation of lymphocyte counts and depletion rates. Also, high-throughput systems have been developed that can process multiple samples simultaneously, improving efficiency in large-scale screening situations, such as radiation emergencies.

For a robust biodosimetry laboratory that focuses on surge management, it is important to expand and upgrade hematological assays at the GAEC hospital which currently performs routine hematological analysis to include comprehensive blood panel analyses as this remains the only biodosimetric test that can be performed outside a specialized laboratory.

Emerging Omics-assays

Conventionally, two named cytogenetic methods above i.e. DCA and CBMN are employed for dose estimation in nuclear incidents. However, due to the time-consuming nature of these methods, there is a search for new techniques for dose estimation, particularly in the event of a large-scale radiation accident affecting thousands of individuals. In the context of deploying biodosimetry for large-scale radiation accidents, pre-screening methods are essential to enhance sample throughput for an initial rough dose categorization. The rapid advancement and growing use of omics methods in research and individual applications present new opportunities for biological dosimetry. In addition to the discovery and search for new biomarkers, dosimetry assays based on omics technologies are becoming increasingly interesting and hold great potential, especially for large-scale dosimetry [43]. Omics methods which span the spectrum of genomics through to transcriptomics, epigenomics, proteomics, and metabolomics can potentially contribute to the discovery of new radiation-dependent biomarkers as well as to the development of novel analytical methods for biological dosimetry to fill this research gap. Amongst the lot, changes in gene expression have been found to be highly sensitive to radiation exposure and show some potential exploits for biodosimetry. Moreover, metabolomics, one of the "omic" techniques is also emerging as a strong contender for biodosimetry to qualitatively and quantitatively correlate specific changes in metabolites to the level of radiation exposure. It seems likely that the successful integration of metabolomics and gene expression profiling could be exploited as a strategic tool for biodosimetry and surge management. However, this requires more investigations to understand the power and limitations of these techniques for dosimetry [31,33,44,45]. Applying omics-based techniques to identify radiation response biomarkers offers a promising opportunity to develop high-throughput assays for biological dosimetry, becoming a valuable asset in managing large-scale radiation incidents. However, further research is necessary to integrate omics into future accident management [43].

Biophysical techniques of dose assessment

Biophysical techniques are based on the measurements of physical parameters in the tissues of exposed individuals, e.g. levels of long-lived radiation-induced free radicals can be detected indirectly by Electron Paramagnetic Resonance (EPR) [46,47] and Optically Stimulated Luminescence (OSL) [48]. Free radicals get trapped in solids and persist long after irradiation, making them suitable for use as integrating, retrospective dosimeters for both acute (accidental) and chronic (lifetime accumulated) radiation exposures. The stable yield of free radicals, which reflects the initial absorbed dose, serves as a biological marker unaffected by post-exposure physiological processes like repair, protection, or renewal, like conventional physical dosimeters. However, physical methods for measuring radiation dose have several limitations, including low sensitivity and difficulty in configuring for high-throughput analysis, necessitating the use of many instruments operating simultaneously to manage large numbers of people [46]. Finally, this dosimetry technique is time-consuming. For long-term monitoring and largely suitable for retrospective dosimetry and dose reconstruction.

Discussion and future perspectives of biological dosimetry in Ghana

Biological dosimetry is crucial for radiation protection, emergency response, and public health, especially in mass casualty situations where high throughput techniques are needed for rapid triage and treatment [49,50]. In recent times, means of predicting health effects including prediction of individual radiosensitivity and suitable tools for understanding radiobiological mechanisms at the cellular and molecular levels have fallen into the realms of biodosimetry. Tools of cytogenetic biodosimetry have been used to evaluate DNA damage in occupational and nonoccupational exposure situations and have provided an estimation of biologically meaningful doses to the body.

Given the current threats of malevolent uses of radioactive materials falling into the wrong hands, it is highly essential to acquire the capacity to assess the absorbed radiation dose received by victims to support treatment decisions. In this regard, biological dosimetry which allows the retrospective determination of absorbed dose using appropriate radiation response biomarkers deserves serious consideration.

The biodosimetric utilities of the DCA and the CBMN assays have long been recognized [46]. However, promising as these

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methods may appear, both suffer from considerable time and expert labor requirements, with no universal methodological harmonization across laboratories making them impractical for use in mass casualty situations. Hence, improvements in the existing techniques and the development of new biodosimetry tools are required for rapid individualized dose estimation. Indeed, recent strategic innovations in biodosimetry have led to the development of new methodologies for quantifying radiation exposure in victims, which can be applied in mass screening settings for triage management. From its application in mass casualty scenarios, biodosimetry can also be applied as a diagnostic tool to provide patient-specific information regarding the amount of radiation-induced tissue damage, which can then be used to guide medical treatment decisions, including field triage and advanced clinical care. Biodosimetry methods are increasingly gaining prominence in radiation oncology, nuclear medicine, diagnostic and interventional radiology, and in the assessment of the quality of health care [14].

Ghana is considering the inclusion of nuclear energy in its electricity mix and expanding its local nuclear content, for which several international contractual agreements have been made [7,51-53]. Equipping and providing adequate resources and training of competent biological dosimetry personnel will be required for a functional capacity to respond to radiation emergencies and to cooperate in regional or international radiation protection networks.

Currently, two cytogenetic methods are being installed in the Biological Dosimetry Laboratory of the ARBC of GAEC namely, the Dicentric chromosome analysis and the Cytokinesis block-micronucleus assay. The International Atomic Energy Agency recommends that each laboratory working with biological dosimetry should create its own dose-response calibration curves. For obvious reasons γ- and X-ray radiation emergency exposures are the most likely to occur, thus it is necessary to establish the dose-response calibration curves for these two types of radiation. In line with this, a previous study was conducted by our group to construct in-house dose-response curves for ^{60}Co γ rays [23]. This study was aimed at setting the pace for establishing a competent biodosimetry laboratory capable of performing cytogenetic analysis for possible use in mass casualty radiation incidents, emergency preparedness, biomonitoring, or supporting medical decision-making and cooperating with international radiation protection networks. It is worth noting that even though the two popular cytogenetic biodosimetry methods have been installed at the ARBC/RAMSRI the equipment currently used to execute this analysis is somewhat outdated. Thus, to improve efficiency, and accuracy, and be able to apply them as a tool in other assays, it is essential to replace them with modern ones. We participated in a WHO survey focused on the development of global biodosimetry laboratory networks (BioDoseNet) which sought to assess the capabilities of countries with biodosimetry capabilities. The study identified the lack of equipment, funding, and training needs as serious gaps that need to be addressed by some of the participating countries [20] and the situation remains unchanged for our laboratory.

At present, building capacities in biodosimetry across the globe and joining the various biodosimetry network groups is becoming all the more important to provide mutual assistance during a mass casualty incident. Moreover, in the wake of the recent COVID-19 pandemic laboratories with capacities and competence in biodosimetry and expertise in conducting rigorous nuclear security and safety protocols, are likely to be called upon to help meet the needs associated with pandemic testing and treatment [54]. During the recent COVID-19 pandemic, particularly in government-funded or affiliated laboratories, biodosimetry specialists i.e. individuals with transferable skills such as project management, emergency response communication, and laboratory techniques-were redeployed to focus on the pandemic response [54,55].

Noting form from these experiences it will be expedient to have a reserve pool of specialized workforce in biological dosimetry to enhance the ability to respond effectively to radiological emergencies (especially a large-scale incident), support public health and safety, and ensure that expertise is readily available when needed [54,55].

When the capacity for a fully-fledged biodosimetry facility is established, it will among other things enable the nation to address various challenges including supporting research initiatives in biological dosimetry specific to Ghana and the African population focused on the development of locally and regionally relevant biomarkers and techniques. Besides, it will be tailored to adapt existing biodosimetry methods to better suit the genetic and environmental diversity in Ghana. In the context of the current threat of malevolent action by terrorists and surge management, strengthening biodosimetry capabilities will enhance Ghana's readiness to respond to radiological emergencies, including natural disasters and incidents involving radiation sources.

Investing in training programs and capacity-building initiatives is likely to enhance local expertise in biodosimetry including training of healthcare professionals, researchers, and emergency responders in the use of biodosimetry tools and techniques as well as boost human biomonitoring studies. Additionally, well developed and established biodosimetry laboratory could complement other groups engaged in human biomonitoring studies. In this wise cytogenetic biodosimetry can be applied for biomonitoring of radiation exposure among occupational workers in industries such as mining, healthcare, and nuclear energy to contribute to maintaining high occupational safety standards and regulations.

Various biodosimetry laboratories worldwide apart from Africa have joined forces and set up regional and/or nationwide networks either on a formal or informal basis. Many of these laboratories are also a part of global networks such as those organized by the World Health Organization, International Atomic Energy Agency, or Global Health Security Initiative. These networks aim to support international cooperation and capacity building in the area of biodosimetry, including the harmonization of protocols and techniques to enable the provision of mutual assistance during mass casualty events [19]. In view of the above-listed benefits that a nation stands to gain

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by establishing capabilities and competencies in biodosimetry, it is essential that Ghana strengthens its biodosimetry capacity and capabilities.

Currently, our literature search indicates that Ghana lacks a biodosimetry policy, which is likely due to low awareness, limited utilization of nuclear technology, and low activity in the biodosimetry fraternity. Nevertheless, it is crucial to establish policies and regulatory frameworks that integrate biodosimetry into the national radiation protection strategic plan. This will ensure the acceptance of biodosimetry as a valuable tool for assessing radiation risks, planning emergency responses, and management of healthcare.

Recently the field of biological dosimetry has seen significant growth in Ghana, indicating a promising future for this promising "new" area in the country. However, its growth hinges largely on the development of a national policy document on biological dosimetry, strategic investments in capacity building, research, collaboration, and consolidating the current gains by integrating it into healthcare systems. These efforts when realized can enhance the ability to mitigate risks associated with radiation exposure in consonance with the IHR regulations, protect public health, and support sustainable development in various sectors. This will be the first-of-its-kind biodosimetry Service in Ghana capable of assessing accidental radiation exposures among others with a possibility of inching into the forensic industry.

Conclusion and recommendations

The document highlights significant efforts made by our group to install biological dosimetry capabilities in our laboratories here at the ARBC/RAMSRI of the GAEC. However, the lack of equipment, funding, and training needs to be addressed to help establish a functional biodosimetry facility. Currently, even though time-consuming, laborious, and impractical for mass casualty scenarios, our staff possess the skills employed for the two main assays used to determine radiation dose i.e. the MN and DCA. Some staff also possess basic skills in the γH2AX and gene expression assays. Since mass surge management is intended, significant machine learning skills are needed by the current staff to enable rapid automated biodosimetry which will be achieved by increasing sample processing through automation and technology integration. The development of automatable assays like gene expression profiles for radiation biodosimetry and/or chromosome-aberration-based dicentric assays for use in mass-casualty events is recommended. Additionally, there is a call for more biodosimetry labs in Ghana and increased international collaboration to improve medical preparedness for radiation emergencies.

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