Impact of bone scintigraphy and exposure dose on red blood cells with proposed solutions

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Received - 22 December 2020 Initial Review - 12 January 2021 Accepted - 30 January 2020

ABSTRACT

Background: Nuclear medicine (NM) technology is as indispensable field, is being widely used in research as well for diagnostic/ staging purposes. However, it is also associated with potential hazards of radiation especially among radiation practitioners. **Objective:** The objective of the study was to determine the effects of NM exposure doses of bone scintigraphy in red blood cells and to propose a recent technology to be incorporated in NM and radiology technologies. **Materials and Methods:** A retrospective study was carried out among 75 patients who underwent bone scintigraphy between 2014 and 2018. A blood sample of these patients was characterized using transmitted light microscope and obtained data were analyzed using SPSS. **Results:** There was a decrease in the RBCs% and hemoglobin (HGb) count with the increment of interval time of bone scintigraphy ($p=0.3$). The average applied radioactive (Methylene Di-phosphate/Technetium-99m) dose of 15±2.9 mCi reduces RBCs and HGb count insignificantly by 3.56% and 3.1%, respectively. With an increased dose of 20±5.8 mCi and after interval time of bone scintigraphy, the histological changes in RBCs such as loss of biconcavity, increased diameter (10±0.4 μm), developed spikes (anisocytosis and poikilocytosis) were observed. **Conclusion:** The proposed robotic intelligent system can be utilized partially while performing NM and other radiological examinations under supervision of specialists to prevent stochastic and non-stochastic effects among radiation practitioners.

Key words: *Blood, Dose, Effects, Exposure, Histology, Radiation*

The field of nuclear medicine (NM) has been extensively used for diagnostic/staging purposes as well as in research including isotopes dilution analysis, radioimmunoassay, brain physiology, and behavioral science. NM as a diagnostic modality shows the morphology, anatomy, physiology, and information on metabolic process of the living organs [1]. Therefore, is widely used in advanced researches in pharmacology (testing new inventing drugs/medicine to determine it is efficiency to treat diseases and to determine it is side effects), biomedical engineering (Testing of synthesized organs compatibility with human tissue as in case of man made organs implantation/transplantation), and behavioral science (Testing and assessment of creatures behavior after being exposed to radiation, or injected with specific hormone). Bone scintigraphy is a type of NM aids in detection of microscopic metastasis of cancer cells, volumetric assessment, cancer staging, or assessment of organs/tumor physiology. The general applied radiation dose ranges from 10 to 30 mCi and this complies with the radiation protection guidance such as "as low as reasonably achievable" principle and the justification end (overwhelming benefits compared with hazards) [2-4]. In USA, the mean effective dose of NM examinations is 3.0 mSv and the mean cumulative effective dose for patient subjected to cardiac radiologic examination is 23.1 mSv. Similarly a dose of 0.05 Sv/year has been standardized as a reference dose for the workers internationally [5].

However, the diagnostic and therapeutic procedures with NM are accompanied by potential hazards to patients as well as the attending staff, either at circulatory system level and/or organs level. The consequences after exposure to ionizing radiation implies nausea, diarrhea, fatigue, vomiting, infection, and internal hemorrhage within few minutes after exposure and further effects as obvious drop in WBCs within 24 h and the platelets decreases gradually following the time [6]. Prolonged radiation exposure has shown significant tissue damage in experimental animals [7]. Female patients who underwent bone scintigraphy showed a higher incidence of breast cancer in a study at Sudan [8]. Previous studies have shown that patients who underwent radiotherapy of the head and neck region showed reduction of T4/T3 hormones and increased TSH levels, irradiation of breast has shown increased respiratory rate in patients [9]. However, these effects are dependent on some factors and parameter such as: The amount of dose, dose rate, quality of radiation, dose fractionation, and the condition of the irradiated host [10,11].

Effect of gamma radiation on blood components has been studied previously. Exposure to gamma radiation has shown significant decrease in most of blood components, prolonged clot formation, increased levels of thrombin-antithrombin III complex, and increased circulating nucleosome/histone [12-17]. Irradiation results in non-homogenous stain distribution within the erythrocytes, contracted hemoglobin (HGb) at the periphery of the cell, pale stain central regions, and clumping appearance in smear examinations [13]. With an increased dose, the proportions of echinocytes, sphero-echinocytes, and erythrocytes with a degenerated shape increases, suggesting that the changes of ultra-structure of RBCs are dose and storage time dependent [18]. Radiation exposure to human immortalized Jurkat cells and peripheral blood lymphocytes results in oscillations of cytosolic Ca^{2+}, an upregulation of CD25 surface expression, interleukin-2, and interferon-γ synthesis, elevated expression of Ca^{2+} sensitive K^{+} channels and an increase in cell diameter [19]. The aim of the current study was determine the effects of NM exposure doses of bone scintigraphy in red blood cells and to propose a recent technology to be incorporated in NM and radiology technologies.

MATERIALS AND METHODS

A retrospective study was carried out among 75 patients who were referred for bone scintigraphy for metastasis assessment at Department of NM, Radiation and Isotopes Center of Khartoum, Sudan during June 2014–2018. The need of the study was explained to the patients and an informed consent was obtained before the study. Patients were informed about the relative preparation including hydration, hair shaving, and fasting before the day of the study. Patients between the ages of 18 and 28years were included in the study. Body mass index (BMI) was calculated for each patient using the formula "patient weight divided by the square of height in meter" (weight in kg/height in m^2). Based on BMI patients were categorized as underweight (≤18.49 kg/m^2), normal BMI (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), obese (30–39.9 kg/m^2), and morbidly obese (≥40 kg/m^2). Furthermore, based on the radiation dose patients were divided into four groups ("a" = control group 0.0 mCi, group "b" = 15 mCi, group "c" = 20, mCi and group "d" = 25 mCi) with consideration to standard deviation (±STD) for each group. BMI count of RBCs and RBCs histology was tested in individual patients.

On the day of bone scintigraphy, a routine blood check-up was done before radioactive dose administration to record the baseline WBC and RBC counts. Radioactive dose was eluted from Technetium-99m (99mTc) generator based on its daily time activity formula , where I_0 refers to initial activity and I refers to activity after elapsed time t and based on the disintegration constant λ) as total volume for all patients prepared for scan. Individual patient dose was estimated based BMI and further the relative amount was mixed with Methylene Di-phosphate (MDP) for each specific patient. The administrated dose composed of 99mTc/MDP was given intravenously to each patient. Bone scan was performed after 3 h for image acquisition as stated by Collier *et al*. [20] with bladder voiding. At this moment, a 5 cc of blood sample was drawn from each patient and sent to laboratory for further blood analysis. RBCs were counted using automated cell counter (Sysmex KX-21) and HGb was measured. The obtained data were analyzed using SPSS software, t-test was used to calculate the results and presented in the form of a scattered plot.

RESULTS

The results presenting the impact of bone scintigraphy dose is presented in the form of scattered plot for the reduction percentage of RBCs versus interval time in hours together with induced histological effects and the HGb with regards to the BMI as main parameter affecting the administrated radioactive dose in NM. Fig. 1 shows the correlation between the reduction in RBCs and the interval time of bone scintigraphy (2–4 h). The RBCs% decreased insignificantly (p=0.3) at 2–4 h after radiation exposure for bone scintigraphy. The correlation between the exposure and RBC% is calculated using the equation form, y = −0.061 × +5.72, where x refers to interval time of bone scan and y refers to reduction of RBCs% and the correlation was insignificant (R^2=0.06).

After interval time of bone scintigraphy, transient histological changes were observed with the RBCs (Fig. 2). Among patients in group "a" (0.0 mCi) representing the control group, RBCs appeared as normal shape and size. In group "b" (15 mCi), there was loss of biconcavity and increased diameter of RBCs (10±0.4 μm), in group "c" (20 mCi) RBCs developed spikes mimicking *Tribulus terrestrial* (Zygophyllaceae) fruit like which known as anisocytosis and poikilocytosis shape deformity, and in group "d" (25 mCi) RBCs appeared with intensive anisocytosis and poikilocytosis with shrinking size. We observed an insignificant increase in HGb (p=0.31) following the increment of BMI (Fig. 3). Upon administering MDP/Tc-99m dose of 15±2.9 mCi and after interval time of bone scan, the HGb count decreased insignificantly (p=0.3) from the initial count by 3.1% relative to its average normal value.

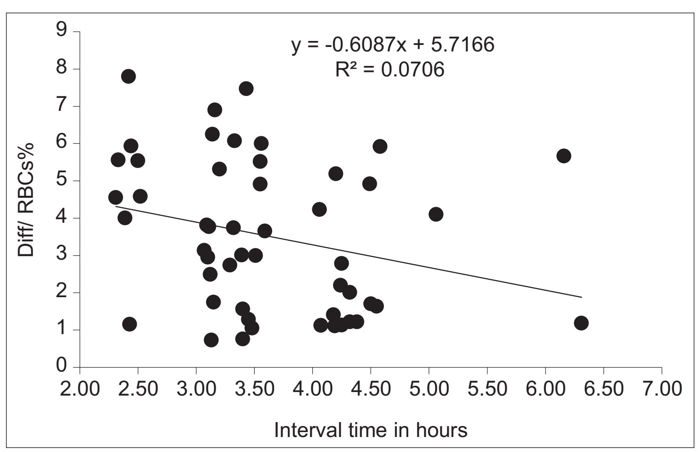
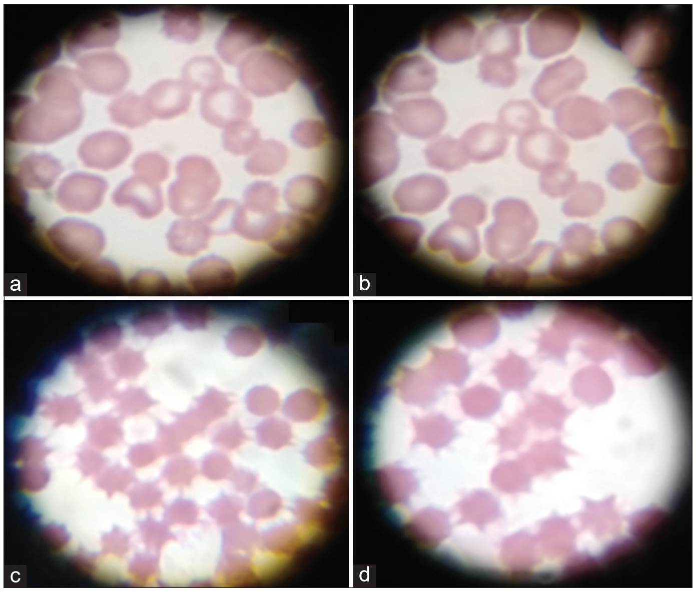


Figure 1: The correlation between the reduction in RBCs and the interval time of bone scintigraphy



Morphological deformities involving RBCs after interval time of bone scan in nuclear medicine (a) control group 0.0 mCi, group (b) 15 mCi, group (c) 20 mCi and group, (d) 25 mCi

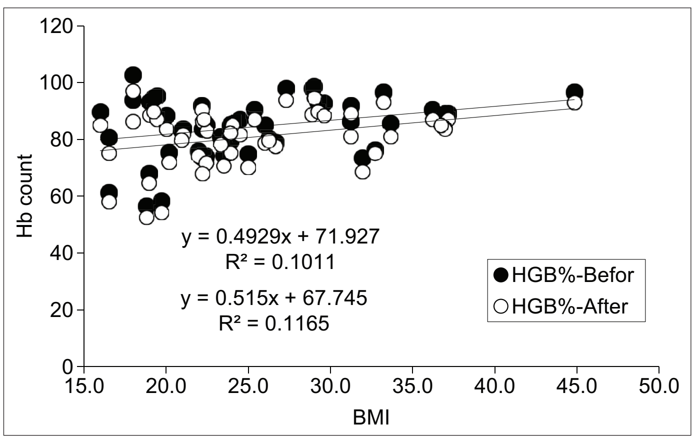


Figure 3: The correlation between hemoglobin and the body mass index before/after interval time of bone scintigraphy

DISCUSSION

Irradiation effects in blood components can occur even at the low-level exposure doses of radiology and NM examinations. Despite the exposure doses being well within the recommended dosage limits such as, mean effective dose of 3.0 mSv [10] and radiation exposure doses received by NM practitioners (0.02–0.05 Sv/year) [21] with exception due to uncooperative patients, emergencies, accidents, and over duties of the staff; potential hazards are still hovering among the radiation practitioners. These include, cell membrane permeability, damage, viscosity increment, pH changes, electrolyte imbalance, reduction in some blood components, and morphological changes and cancer [22].

In our study, with an average applied radioactive dose of 15±2.9 mCi and 20±5.8 mCi, RBCs decreased insignificantly by 3.56% relative to normal count. This could be ascribed to intensive count of RBCs and their small size (small cross-section for interaction probability with radiation). Similarly, the decrease in HGb level is correlated with the insignificant radiation impact in RBCs, while the induction of cell membrane permeability and electrolyte imbalance by irradiation could be blamed for the induction of RBCs histological changes and deformities. These potential effects indeed have relative consequences in the exposed hosts could be as behavioral changes or daily activities. In comparison with the study done Ruano *et al*. [23], when a natural crystal of pyrite (FeS_2) was bombarded by helium ions beam (He^+) at 4.5 keV, multiple ions such as S^{2-2} and S^0, Fe^{2+} and Fe^{3+} ions were generated.

We assume that same effect could be induced in the exposed RBCs to X-radiation leading to dissociate of HGb to ions. Moreover, the increasing concentration of ions in RBCs will lead to increase the osmolality of RBCs leading to more polarized water molecules which at an intracellular level increase the RBCs size which may persist till RBCs ruptures. In addition, Voos *et al*. [19] and Karmakar *et al*. [24] observed that surfaces of different initial roughness have been generated chemically and bombarded by 16.7 keV oxygen ions (O^{2+}) ions at an oblique angle, the expose to O^{2+} induced regular nanostructures at the surface. Similarly, presence of RBCs morphological change although is transient at low radiation doses, may open up the platform for more researches to end up the debate in the field.

The foresee era of radiology has to be incorporated with recent technology such as robotic intelligent system (RIS) as suggested by Hosny *et al*. [25] and Pakdemirli [21]. As the radiologic imaging has been indispensable for mankind with benefits such as diagnosis, treatment, forensic field and researches, forces the scholars and scientists to adapt the interdisciplinary sciences, and combat the potential hazards. The adoption of RIS, a reprogrammable, multifunctional manipulator designed to move materials, parts, tools, or other specialized devices through various programmed motions for the performance of a variety of tasks is a boon to nuclear imaging [26]. Application of RIS has been reviewed in in orthopedic arthroplasty [27], laparoscopic surgery (prostatectomies and hysterectomies) using Da Vinci surgical robot system developed by Frederick Moll as well as in interventional radiology [28-30].

The role of intelligent robotic system has been highlighted by Erin *et al*. [31] for the service of MRI as well. RIS can be applied in the field of fluoroscopic radiology, radiation therapy, NM, and the control of nuclear reactors where there is considerable radiation exposure may exceed the permissible limits. Despite these benefits, the lack of onset feedback in cases of emergency or un-expected side effects which needs an expert's skills and psychomotor actions are few of the drawbacks. In radiation field, the triggering of feedback actions could be stimulated based on the radiation dose level (radiation detection), patient movement, and general radiologic system orientation (tube, gantry, couch, laser orientation beams, and light intensity).

CONCLUSION

Radiation exposure received by the staff has potential radiation stochastic effects that would appear after certain incubation period. Incorporation of RIS to perform diagnostic and therapeutic tasks in NM will play effective role in preventing or reducing the radiation dose received by practitioners in field.

ACKNOWLEDGMENTS

The authors would like to acknowledge the patients, colleagues, and Laboratory technologists at radiation and isotopes center of Khartoum (RICK) for assisting in histological examination.

REFERENCES

1. Sanchez JR, Devis M, Sanz R, *et al*. Whole-body PET/CT studies with lowered 18F-FDG doses: The influence of body mass index in dose reduction. J Nucl Med Technol 2014;42:62-7.
2. Squillaro T, Galano G, de Rosa R, *et al*. Concise review: The effect of low-dose ionizing radiation on stem cell biology: A contribution to radiation risk. Stem Cells 2018;36:1146-53.
3. American College of Radiology and Society of Pediatric Radiology. Guidelines and Standards Committee of the ACR Commission on Nuclear Medicine in Collaboration with the SPR. ACR-SPR Practice Guideline for the Performance of Adult and Pediatric Skeletal Scintigraphy; 2012.
4. Donohoe KJ, Brown ML, Collier BD, *et al*. Procedure Guidelines for Skeletal Scintigraphy, Version 3.0. Society of Nuclear Medicine and Molecular Imaging Practice Guidelines; 2003.
5. Chen J, Einstein AJ, Fazel R, *et al*. Cumulative exposure to ionizing radiation from diagnostic and therapeutic cardiac imaging procedures: A population-based analysis. J Am Coll Cardiol 2010;56:702-11.
6. Maks CJ, Wan XS, Ware JH, *et al*. Analysis of white blood cell counts in mice after gamma-or proton-radiation exposure. Radiat Res 2011;176:170-6.
7. Ismail AH, Jaafar MS, Mustafa FH. Histological study to estimate risks of radon inhalation dose on a lung cancer: In vivo. In: Osman NA, Abas WA, Wahab AK, *et al*., editors. Kuala Lumpur International Conference on Biomedical Engineering 2011. IFMBE Proceedings. 5th ed., Vol. 35. Berlin, Heidelberg: Springer; 2011. p. 312-4.
8. Rahman SH, Youdif MA. Self-examination of the breast for early detection of breast cancer. Sudan J Public Health 2006;1:36-42.
9. Ali Omer MA, Alsayyari AA, Aldokhail AM, *et al*. Estimation of thyroid hormones levels and lung function in conventional radiotherapy of breast, head and neck cancer's. Open J Radiol 2019;9:194-205.
10. Sanzari JK, Wan XS, Krigsfeld GS, *et al*. The effects of gamma and proton radiation exposure on hematopoietic cell counts in the ferret model. Gravit Space Res 2013;1:79-94.
11. Billings PC, Romero-Weaver AL, Kennedy AR. Effect of gender on the radiation sensitivity of murine blood cells. Gravit Space Res 2014;2:25-31.
12. Sakin GA, Gar-Elnabi ME, Omer MA, *et al*. Assessment of effects induced by bone scintigraphy dose in red and white blood cells relative to ageing and obesity. MOJ Public Health 2020;9:160-4.
13. Diez-Silva M, Dao M, Han J, *et al*. Shape and biomechanical characteristics of human red blood cells in health and disease. MRS Bull 2010;35:382-8.
14. Abojassim AA, Jaffat HS, Hassan AB. Effects of gamma radiation on some hematological parameters in female rats. ISJ Theor Appl Sci 2015;5:101-9.
15. Kennedy AR, Maity A, Sanzari JK. A review of radiation-induced coagulopathy and new findings to support potential prevention strategies and treatments. Radiat Res 2016;186:121-40.
16. Selim N. Comparative study on the effect of radiation on whole blood and isolated red blood cells. Rom J Biophys 2010;20:127-36.
17. Mohamed MA, El Saeid AA, Ahmed MA. Cellular response of blood and hepatic tissue to gamma irradiation author links open overlay panel. J Radiat Res Appl Sci 2016;9:242-8.
18. Xu D, Peng M, Zhang Z, *et al*. Study of damage to red blood cells exposed to different doses of γ-ray irradiation. Blood Transfus 2012;10:321-30.
19. Voos P, Fuck S, Weipert F, *et al*. Ionizing radiation induces morphological changes and immunological modulation of Jurkat cells. Front Immunol 2018;9:922.
20. Collier BD, Hellman RS, Krasnow AZ. Bone SPECT. Semin Nucl Med 1987;17:247-66.
21. Pakdemirli, E. Artificial intelligence in radiology: Friend or foe? Where are we now and where are we heading? Acta Radiol Open 2019; 8(2): 1-5.
22. Fazel R, Krumholz HM, Wang Y, *et al*. Exposure to low-dose ionizing radiation from medical imaging procedures. N Engl J Med 2009;361:849-57.
23. Ruano G, Pomiro F, Ferrón J. Surface chemical reactions induced on pyrite by ion bombardment. Surf Sci 2018;667:138-47.
24. Karmakar P, Mollick SA, Ghose D, *et al*. Role of initial surface roughness on Ion induced surface morphology. Appl Phys Lett 2008;93:103102-3.
25. Hosny A, Parmar C, Quackenbush J, *et al*. Artificial intelligence in radiology. Nat Rev Cancer 2018;18:500-10.
26. Schoellnast H, Solomon SB. Imaging of interventional therapies in oncology: Image guidance, robotics, and fusion systems. In: Dupuy DE, Fong Y, McMullen WN, editors. Image-Guided Cancer Therapy-A Multidisciplinary Approach. New York: Springer; 2013. p. 277-91.
27. Bargar WL, Bauer A, Borner M. Primary and revision total hip replacement using the Robodoc system. Clin Orthop Relat Res 1998;354:82-91.
28. Marohn MR, Hanly EJ. Twenty-first century surgery using twenty-first century technology: Surgical robotics. Curr Surg 2004;61:466-73.
29. Paul S, McCulloch P, Sedrakyan A. Robotic surgery: Revisiting "no innovation without evaluation". BMJ 2013;346:f1573.
30. Kassamali RH, Ladak B. The role of robotics in interventional radiology: Current status. Quant Imaging Med Surg 2015;5:340-3.
31. Erin O, Boyvat M, Tiryaki ME, *et al*. Magnetic resonance imaging system-driven medical robotics. Adv Intell Syst 2020;2:1-18.

Funding: None; Conflicts of Interest: None Stated.

How to cite this article: Sakin GA, Omer MA, Gar-Elnabi ME, Bakry AH, Elamin BA. Impact of bone scintigraphy and exposure dose on red blood cells with proposed solutions. Eastern J Med Sci. 2021;6(1):23-26.

Doi: 10.32677/EJMS.2021.v06.i01.005