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Histopathological Study of the Gastrointestinal Tract in CT Radiation Exposed Rats

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Authors' contributions

This work was carried out in collaboration among all authors. Authors EKM, KCO and EOM designed the study, performed the statistical analyses, wrote the protocol, and first draft of the manuscript. Author EKM managed the analyses of the study. Authors TON and IGA managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Aims: To investigate the histopathologic impact of low and high doses of CT ionizing radiation on the gastrointestinal tract of albino rats following whole-body irradiation.
Study Design: Randomized controlled experiments.
Place and Duration of Study: Department of veterinary surgery and radiology, University of Nigeria, Nsukka, Nigeria, between July 2023 and Jan 2024.

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Methodology: Thirty healthy male Wistar albino rats aged 9-10 weeks, weighing 180-200g were randomly assigned -into five groups (A, B, C, D, and E) of six rats each. Rats in groups A and B were irradiated with low dose radiation of 74.74 mGy/cm and 352.38 mGy/cm dose length product (DLP) respectively. Group C and D rats were irradiated with high dose radiation of 628.6 mGy/cm and 1,388.42mGy/cm dose length product (DLP) respectively. Group E rats were not irradiated and served as control.
Results: CT radiation at the dose length product (DLP) of 74.74 mGy/cm, 352.38 mGy/cm,628.6mGy/cm and 1,388.46 mGy/cm induced histopathologic changes on the small intestine of the irradiated rats while these radiations did not induce any change in the stomach.
Conclusion: Cell-level microscopic lesions in the gastrointestinal tract of the irradiated rats indicate that the small intestine is more radiosensitive than the stomach. From the cellular structural changes observed in the small intestine of the irradiated rats, it be concluded that CT radiation at a DLP of 628.6mGy/cm is inimical to the vital organs. These findings could suggest that there could be serious microscopic structural changes that go unnoticed during diagnostic and therapeutic CT irradiation in both animals and humans, and emphasizes the need to adhere strictly to as low as reasonably achievable (ALARA) principle in the dispensing of CT radiation.

Keywords: CT radiation; radiobiology; gastrointestinal tract; intestine; stomach.

1. INTRODUCTION

Computed tomography (CT) imaging in recent times has revolutionized diagnostic medicine by providing succinct cross-sectional images of the body's internal structures. However, the high demand for CT scans in clinical practice with consequent ionizing radiation exposure brings up the serious concerns about the associated potential health risks [1]. Although CT scans are invaluable in making prompt diagnosis of different gastrointestinal (GI) disorders, they expose patients and health workers to radiation, which can trigger cellular damage and increase the risk of deleterious health hazard [2]. It is therefore imperative that proper understanding the histopathological effects of CT radiation on the gastrointestinal system is very important for reducing patient and health workers risk as well as optimize imaging protocols.

When it comes to identifying and treating gastrointestinal conditions such as inflammatory bowel disease, gastrointestinal cancers, and gastrointestinal bleeding, computed tomography (CT) imaging is an indispensable tool. CT scans can identify anomalies including tumors, strictures, and inflammation by providing comprehensive anatomical information. Furthermore, improvements in GI imaging sensitivity and specificity, such as multi-detector CT (MDCT) and CT enterography, have led to more precise diagnosis and better patient outcomes [3,4].

CT imaging exposes patients to ionizing radiation, which carries some health hazards, including the possibility of tissue damage and cancer, despite its benefits for diagnosis [5]. The patient's age, underlying medical conditions, the imaging technique, the radiation dose, and other factors all affect the chance of radiation-induced side effects. Although attempts have been made to reduce radiation exposure through techniques for dose reduction and optimized imaging protocols, there is still worry about the possible biological consequences of CT radiation on the gastrointestinal tract [6,7,8].

An understanding of the consequences of radiation exposure at the cellular and tissue levels can be gained by histopathological investigation. Radiation-induced DNA damage and cellular stress can result in histological alterations such as inflammation, necrosis, fibrosis, and cellular proliferation. Researchers can determine the underlying mechanisms of radiation-induced injury and quantify the extent and severity of tissue damage by examining histopathological characteristics [9]. This adverse effect results from the direct ionization of cellular structures, especially DNA, or from the indirect effect through free radicals produced by radiolysis of water [10]. Additionally, histopathological evaluation is crucial for determining the efficacy and safety of medical interventions as well as for directing the creation of therapeutic and preventive measures [11,12]. It been assumed that the response to low doses of ionizing radiation may be loci-specific and have both beneficial and detrimental consequences [13,14].

It is crucial to comprehend how different CT radiation dosages affect the gastrointestinal tract's histological integrity in order to evaluate the safety of CT imaging procedures and guide therapeutic decision-making. In order to gain important insight into the biological effects of radiation on gastrointestinal tissues, this study intends to evaluate the histopathological characteristics of the gastrointestinal system in albino rats subjected to various doses of CT radiation.

By evaluating histopathological changes in response to CT radiation exposure, this study seeks to contribute to our understanding of the potential risks and benefits of CT imaging in gastrointestinal diagnostics, ultimately improving patient care and safety.

2. MATERIALS AND METHODS

2.1 Experimental Animal

Thirty healthy male Wistar albino rats, weighing between 180 and 200 grams and aged 9-10 weeks, were procured from the Department of Veterinary Medicine, University of Nigeria, Nsukka. Throughout the investigation, the rats were housed in a standard laboratory setting with 12 hours of light and 12 hours of darkness, and a temperature of 24 ± 3°C. The rats were fed water and standard pellet diet as needed. The rats were randomly assigned into five groups (groups A, B, C, D, and E) of six rats each after a week of acclimatization.

2.2 Equipment

Irradiation was carried out using a GE 16 Slice (General Electric) Revolution ACTs CT scanner (GE Hangwei Medical Systems Co. Ltd, China) with adaptive statistical iterative reconstruction (ASiR) features that allow manual entry of diagnostic exposure parameters to achieve the desired radiation dose.

2.3 Radiation Protocols

There were four irradiated groups (A, B, C, and D) and one unirradiated control group (group E) of six rats each. The six rat per group were immobilized with a customized fixator in supine position with head first. Centering laser beam was at the mid sagittal plane and mid neck before axial beam total body irradiation was acquired from the tip of the nose to the tail. Two (2) scout images, anterior-posterior (AP) and lateral for each group of the irradiated groups were first acquired with the same kV(80) and mAs (20) so as to prevent x-ray beam wastage and to ensure centering accuracy. Tube current (mAs) and tube potential (kv) were manually selected. Radiation dose for each group were automatically estimated by scanner software and displayed in the CT scanner screen as volume weighted computed tomography dose index (CTDIvol) and dose-length product (DLP) values, which are standardized measures of radiation dose during CT examination [15]. A non-contrast helical scan was carried out for each of the irradiated groups once a week for two weeks. Rats in group A were irradiated with exposure factors of 80 kV and 100 mAs and dose length product (DLP) of 74.74 mGy/cm DLP. Rats in group B were irradiated with exposure factors of 100 kV and 140 mAs and dose length product (DLP) of 352.38 mGy/cm. Group C rats were irradiated with exposure factors of 120 kV and 150 mAs and DLP of 628.6 mGy/cm, while group D rats were irradiated with exposure factors of 140 kV and 160 mAs and DLP of 1388.42mGy/cm. Group E rats were not irradiated and served as control.

2.4 Histopathological Studies

Five animals of each group were sacrificed a day after the last irradiation. The stomach and intestine were immediately and carefully dissected and fixed in 10% buffered formalin solution for 24 hours followed by dehydration in ascending series of ethyl alcohol, clearing in xylene, and embedding in paraffin wax and then sectioned at 4 microns thickness by sledge microtome. The sections were mounted on glass slides and stained with hematoxylin and eosin (H & E) according to the method described by Bancroft and Stevens [16]. The stained sections were examined by oil immersion light microscopy and several digital images were taken using Kodak digital camera.

3. RESULTS

The intestines sections of rats in the irradiated groups A, B, C and D exposed to CT radiation dose length product (DLP) of 74.74 mGy/cm, 352.38 mGy/cm, 628.6 mGy/cm and 1,388.46 mGy/cm respectively showed loss of villi and distortion of intestinal crypts (Fig. 1A, 1B,1C and 1D). However, the intestinal section of the rats in the non irradiated E showed apparently normal histological features of mucosa with intact and tall villi (Fig. 1E).

Microscopic examination of the stomach sections of rats in the irradiated groups A, B, C, and D showed apparently normal features of the mucosa with no histological variation compared to the sham-irradiated control group E (Fig. 2A-2E).

4. DISCUSSION

Our study's histological results highlight the intricate interactions that occur in the GI system between radiation dose, tissue sensitivity and biological response. Radiation-induced gastrointestinal toxicity is complex, involving direct cellular effects, inflammatory cascades and vascular perturbations. This is reflected in the reported mucosal damage, inflammatory changes, and vascular abnormalities.

Because histopathological alterations are dose-dependent, it is imperative to minimize radiation doses while preserving diagnostic efficacy in order to minimize potential GI tract injury [17,18].

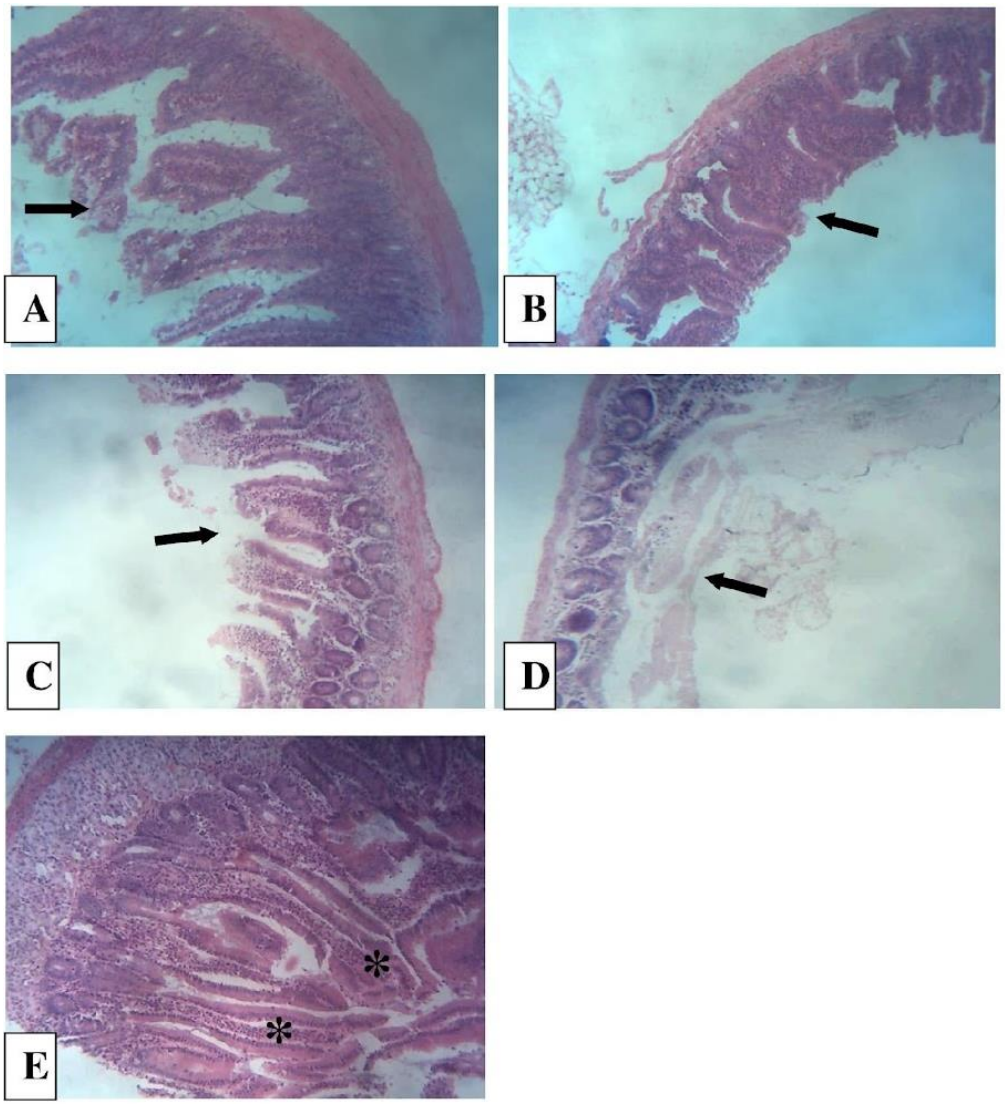

Fig. 1. Photomicrograph of the intestine of rats from the experimental groups. (A) intestine of rats exposed to radiation dose of 74.74mGy/cm, (B) intestine of rats exposed to radiation dose of 352.38mGy/cm, (C) intestine of rats exposed to radiation dose of 628.6mGy/cm and intestine of rats exposed to radiation dose of 1,388.46 mGy/cm (D) showing loss of villi and distortion of intestinal crypts (arrows) while the intestine of non-irradiated control rats (E) shows apparently normal histological features of mucosa with intact and tall villi (asteriks). H and E stain × 100

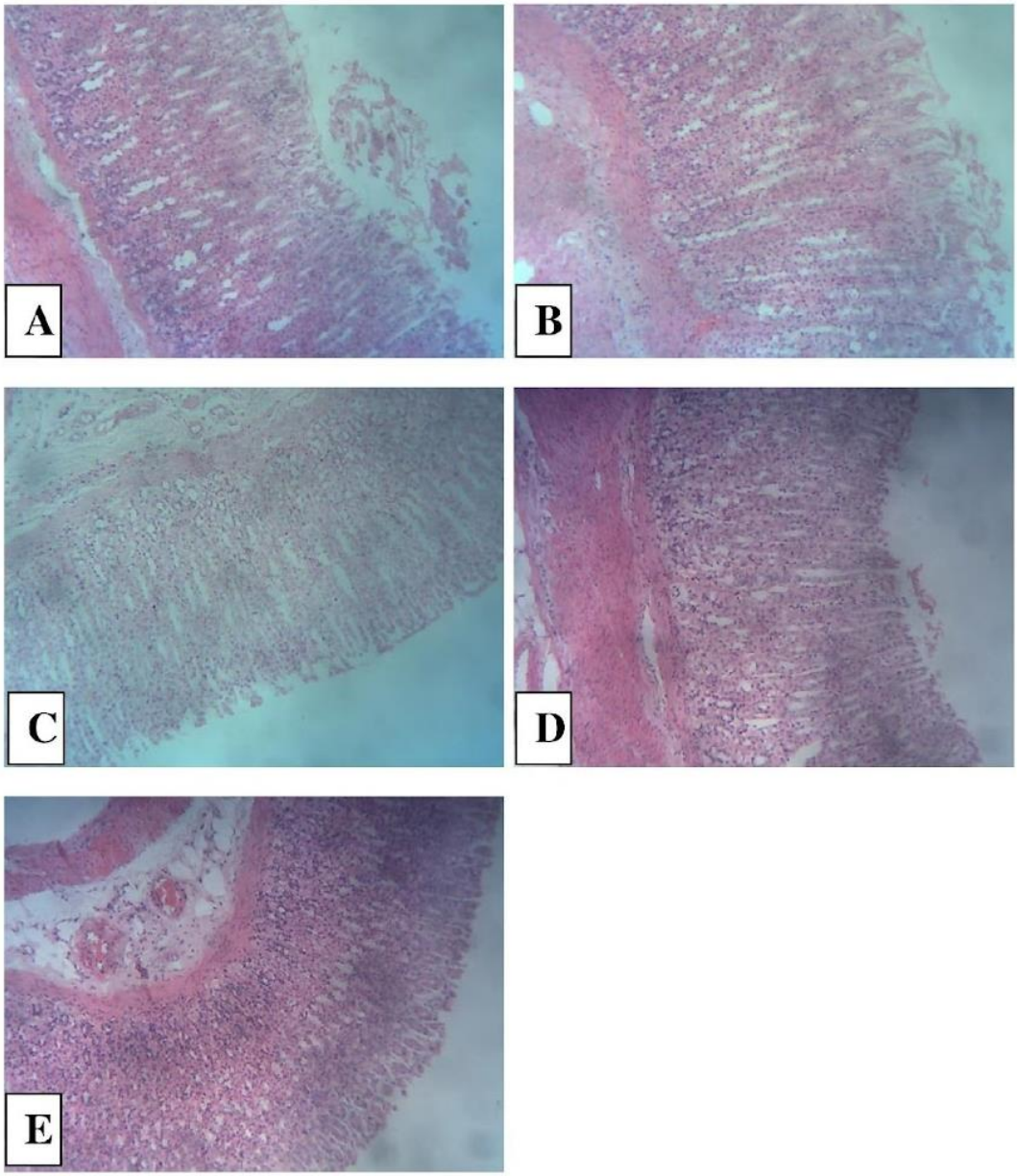

Fig. 2. Photomicrograph of the stomach from the experimental groups. (A) stomach of rats exposed to radiation dose of 74.74mGy/cm, (B) stomach of rats exposed to radiation dose of 352.38 mGy/cm), (C) stomach of rats exposed to radiation dose of 628.6 mGy/cm, (D) stomach of rats exposed to radiation dose of 1,388.46 mGy/cm and (E) stomach of non-irradiated control rats showing normal histological features. H and E stain × 100

Dose optimization solutions, including customized imaging protocols, patient-specific dose modulation and sophisticated radiation dose-reduction techniques must be put into practice as a result. Clinicians can limit the risk of radiation-induced gastrointestinal damage without sacrificing diagnostic accuracy by minimizing needless radiation exposure and implementing evidence-based dosage guidelines.

Furthermore, our results emphasize how crucial it is to be watchful.

In spite of the known medical benefits of radiation, high doses of ionizing radiation have been shown to have detrimental biological effects on various body organs [1,5,19,20]. The objective of the current study is to assess the histopathologic changes of different CT ionizing radiation dosages on the gastrointestinal system

of albino rats exposed to weekly total-body irradiation for two weeks.

There are several studies that indicate radiosensitivity of the gastrointestinal tract [21,22]. A study done by Li et al. [23] on effect of age on radiation induced GI damage showed histologic changes in the crypts base columnar cells of small intestine being more pronounced in the older mice(28months) compared to younger mice (3 month) which falls into the age group of this study.

Janru et al. and Hua et al. [24,25] also corroborates early histologic changes in the intestines of rat exposed to radiation as changes included loss of mucosal surface area, inflammation, intestinal wall thickening even though sensory nerve ablation exacerbated the rate of progression of these changes.

Our study however, disagrees with that done by Breiter et al. [26] in which rat irradiated with 28Gy showed inflammatory changes in the stomach mucosa but our index study showed no histologic change. This may be due to the age of the experimental rodent as older mice are more radiosensitive. Similarly, Francois et al. [27] observed radiation-induced damage to the rectal wall following localized exposure to 27 Gy single dose in the rat with their findings after two weeks of exposure being mucosal / submucosal inflammation, mucosal ulceration evidenced by oedema, reduction in number and distortion in the crypts arrangement. Our own study was however on the stomach and small intestine with similar histopathologic findings in the small intestine which from our study is more radiosentitive to the stomach. This opinion is divergent to the views of other researchers [28-33] which showed the stomach to be more radiosensitive than the intestine due to higher turnover and effective repair mechanisms in the intestines compared to the stomach. However, this discrepancy may be due to the fact that our experimental animals were sacrificed 24hours after the last radiation which may not have given enough time for the manifestation of some of the radiation cellular damage as well as time for repair mechanism differences to be observed.

Additionally, a combined in vivo and invitro effects of irradiation on intestinal epithelial cells by Wróblewski et al. [34] showed reduction in the proliferation of cells of the crypt with increased dose from 1-16Gy. However, at 16 Gy there was complete inhibition of proliferation. This is similar to our study in which there were histological mucosal changes in the small intestine following exposure to various doses of the radiation. Buell et al. [35] also established that acute inflammatory changes in the mucosa of the small intestine starts as early as within the first 24 hours after exposure although our evaluation was done after 1week after first dose and a day after second dose.

5. CONCLUSION

In this study, we investigated the histopathological alterations in the gastrointestinal system of albino rats subjected to varying doses of computed tomography (CT) radiation. Our findings reveal tissue damage to the intestine even at low doses of radiation characterized by loss of villi and distortion of intestinal crypts. However, the stomach showed no histopathological changes with both high and low doses of CT radiation. This therefore infers that the intestines are more radiosensitive compared to the stomach in this study.

These results highlight the need for careful consideration of radiation doses in medical imaging to minimize potential harm. The observed histopathological alterations in the GI tract suggest that even low doses of CT radiation can have measurable impacts, raising important questions about long-term health implications. Future research should focus on elucidating the mechanisms underlying radiation-induced GI damage and exploring strategies to mitigate these effects, such as optimizing imaging protocols and enhancing radioprotective measures.

Overall, this study contributes to the growing body of evidence on the biological consequences of CT radiation, emphasizing the importance of balancing diagnostic benefits with potential risks to ensure patient safety.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

CONSENT

It is not applicable.

ETHICAL APPROVAL

This study was performed in line with the principles of the declaration of Helsinki. All the

study's protocols and the animal care and handling were in accordance with the guidelines set by the university of Nigeria, Nsukka, faculty of veterinary medicine institutional animal care and use committee (IACUC, FVM UNN) with approval number fvm-unn-iacuc-2023-06/105**.**

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. B´alentova´ S, Hnilicov´a P, Kalensk´a D, et al. Effect of wholebrain irradiation on the specific brain regions in a rat model: Metabolic and histopathological changes. Neurotoxicology. 2017;60:70-81.

   DOI:10.1016/j.neuro

2. Brenner DJ, Hall EJ. Computed tomography - An increasing source of radiation exposure. N Engl J Med. 2007; 357:2277-2284.

3. Catherine J Wei, Robin B Levenson, Karen S Lee. Diagnostic utility of CT and fluoroscopic esophagography for suspected esophageal perforation in the emergency department. American Journal of Roentgenology. 215(3).

   Available:https://doi.org/10.2214/AJR.19.22166

4. Brody AS, Frush DP, Huda W, Brent RL. American academy of pediatrics section on Radiology. radiation risk to children from computed tomography. Pediatrics, 2007 120: 677-682.

5. Bora A, Açıkgöz G, Yavuz A, Bulut MD. Computed tomography: Are we aware of radiation risks in computed tomography? Eastern Journal of Medicine. 2014;19:164-168.

6. Chen G, Han Y, Zhang H, Tu W, Zhang S. Radiotherapy-induced digestive injury: Diagnosis, Treatment and Mechanisms. Front Oncol. 2021 Nov 5;11:757973.

   DOI: 10.3389/fonc.2021.757973

   PMID: 34804953;

   PMCID: PMC8604098.

7. Araujo IK, Muñoz-Guglielmetti D, Mollà M. Radiation-induced damage in the lower gastrointestinal tract: Clinical presentation, diagnostic tests and treatment options. Best Pract Res Clin Gastroenterol. 2020;48-49:101707.

   DOI: 10.1016/j.bpg.2020.101707

8. Wei J, Wang B, Wang H, Meng L, Zhao Q, Li X, et al.. Radiation-Induced Normal Tissue Damage: Oxidative Stress and Epigenetic Mechanisms. Oxid Med Cell Longev. 2019;2019:3010342.

   DOI: 10.1155/2019/3010342

9. Rusin A, Seymour C, Mothersill C. Chronic fatigue and immune deficiency syndrome (CFIDS), cellular metabolism, and ionizing radiation: A Review of Contemporary Scientific Literature and Suggested Directions for Future Research. Int J Radiat Biol. 2018;94(3):212–28.

   DOI: 10.1080/09553002.2018.1422871

10. Abdel-Aziz N, Moustafa EM, Saada HN. The impact of citicoline on brain injury in rats subjected to head irradiation. Environ Sci Pollut Control Ser. 2021;28:9742-9752.

    DOI: 10. 1007/s11356-020-11101-7

11. Douglass M Eric, J Hall, Amato J Giaccia. Radiobiology for the radiologist. Australas Phys Eng Sci Med.; 201841:1129–1130.

    Available:https://doi.org/10.1007/s13246-018-0684-1

12. Sanders CL. Radiobiology and Radiation Hormesis: New Evidence and its Implications for Medicine and Society. Cham, Switzerland: Springer; 2017.

13. Bernal AJ, Dolinoy DC, Huang D, Skaar DA, Weinhouse C, Jirtle RL. Adaptive radiation-induced epigenetic alterations mitigated by antioxidants. Faseb J. 2013; 27(2):665-671.

    DOI: 10.1096/fj.12-220350

14. Cuttler JM. Application of low doses of ionizing radiation in medical therapies. Dose-response. 2020;18(1):1-17.

    DOI:10. 1177/1559325819895739

15. Bryll A, Krzys´ciak W, Jurczak A, et al. Changes in the Selected antioxidant defense parameters in the blood of patients after high resolution computed tomography. Inter J Environ Res Public Health. 2019;16:1476.

16. Bancroft JD, Stevens A. Theory and practice of histological techniques,3rd edition, Churchill livingstone. Edinburg, London, Melbourne and New York; 1992.

17. Yang L, Yang J, Li G, Li Y, Wu R, Cheng J, Tang Y. Pathophysiological responses in rat and mouse models of radiation-induced brain injury. Mol Neurobiol. 2017;54:1022–1032.

18. Parker GA, Li N, Takayama K, Booth C, Tudor GL, Farese AM, MacVittie TJ. Histopathological features of the development of intestine and mesenteric lymph node injury in a nonhuman primate model of partial-body irradiation with minimal bone marrow sparing. Health Phys. 2019 Mar;116(3): 426-446.
DOI: 10.1097/HP.0000000000000932

19. Zhou D, Huang X, Xie Y, Deng Z, Guo J, Huang H. Astrocytesderived VEGF exacerbates the microvascular damage of late delayed RBI. Neuroscience. 2019;408: 14-21.
DOI:10.1016/j. neuroscience

20. Larrey EK, Pathak R. Radiation-induced intestinal normal tissue toxicity: Implications for Altered Proteome Profile. Genes (Basel). 2022 Nov 2;13(11): 2006.
DOI: 10.3390/genes13112006
PMID: 36360243; PMCID: PMC9689954.

21. Merritt AJ, Potten CS, Kemp CJ, Hickman JA, Balmain A, Lane DP, Hall PA. The role of p53 in spontaneous and radiation-induced apoptosis in the gastrointestinal tract of normal and p53-deficient mice. Cancer Res. 1994;54:614–617.

22. Potten CS, Merritt A, Hickman J, Hall P, Faranda A. Characterization of radiation-induced apoptosis in the small intestine and its biological implications. Int J Radiat Biol. 1994;65:71–78.

23. Li H, Kucharavy HC, Hajj C, et al. Radiation-induced gastrointestinal (GI) syndrome as a function of age. Cell Death Discov. 2023;9(31).
Available:https://doi.org/10.1038/s41420-023-01298-0

24. Wang J, Zheng H, Kulkarni A, Ou X, Hauer-Jensen M. Regulation of early and delayed radiation responses in rat small intestine by capsaicin-sensitive nerves. Int J Radiat Oncol Biol Phys. 2006 Apr 1;64(5):1528-36.
DOI: 10.1016/j.ijrobp.2005.12.035
PMID: 16580503.

25. Hua G, Thin TH, Feldman R, Clevers H, Fuks Z, Kolesnick R. Crypt base columnar stem cells in small intestines of mice are radioresistant. Gastroenterology. 2012 Nov;143(5):1266-76.
DOI: 10.1053/j.gastro.2012.07.106.

26. Breiter N, Trott KR, Sassy T. Effect of X-irradiation on the stomach of the rat. Int J Radiat Oncol Biol Phys. 1989 Oct;17(4): 779-84.
DOI: 10.1016/0360-3016(89)90066-7
PMID: 2777667.

27. François A, Milliat F, Guipaud O, Benderitter M. Inflammation and immunity in radiation damage to the gut mucosa. Biomed Res Int. 2013;2013: 123241.
DOI: 10.1155/2013/123241
Epub 2013 Mar 19. PMID: 23586015; PMCID: PMC3614034.

28. Potten CS, Loeffler M. Stem cells: Attributes, cycles, spirals, pitfalls and uncertainties. Carcinogenesis. 1990 Jan; 11(1):17-28.
DOI: 10.1093/carcin/11.1.17.

29. Van der Meer R, Dijkgraaf MW. Intestinal stem cells and their roles in cancer and therapy. Cellular and Molecular Life Sciences. 2012 Nov;69(22):3791-802.
DOI: 10.1007/s00018-012-1157-6.

30. Clevers H. The intestinal crypt, a prototype stem cell compartment. Cell. 2013;154(2): 274-84.
DOI: 10.1016/j.cell.2013.07.004.

31. Shalapour S, Karin M. Immune cells in liver cancer: A complex relationship. Cell. 2015; 161(1):99-111.
DOI: 10.1016/j.cell.2015.03.025.

32. Kim J, Alvarez E. Cellular mechanisms of mucosal repair and regeneration. Front Physiol. 2009;2:41.
DOI: 10.3389/fphys.2011.00041.

33. Takeuchi H, Lichtenberger LM. Mechanisms of epithelial repair. Gastroenterol Clin North Am. 2005;34(2): 341-56.
DOI: 10.1016/j.gtc.2005.02.006.

34. Wróblewski R, Jalnäs M, Van Decker G, Björk J, Wroblewski J, Roomans GM. Effects of irradiation on intestinal *cells in vivo* and *in vitro*. Histol Histopathol. 2002 Jan;17(1):165-77.

DOI: 10.14670/HH-17.165.
PMID: 11813866.

35. Buell MG, Harding RK. Proinflammatory effects of local abdominal irradiation on rat gastrointestinal tract. Dig Dis Sci. 1989 Mar;34(3):390-9.
DOI: 10.1007/BF01536261
PMID: 2920645.

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