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The influence of ionizing radiation on hematological parameters in patients undergoing CT examinations with or without injection in Congo-Brazzaville

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ABTRACT

The objective of our study is established the diagnostic reference level in the context of CT examinations in the Republic of Congo. This study is carried out in hospitals such as: Pierre MOBENGO Central Armed Forces Hospital, Chino-Congolese Friendship Hospital MFILOU, Net-Care Clinic and Talangai Reference Hospital and Blanche Gomes Hospital; and four types of examination namely: the CT scan of the skull, Thorax-abdomino-pelvic, and the Abdomino-pelvic were carried out. During the collection of information, 350 adult patients and 76 pediatric patients were identified. The age of the patients is between 0 and 78 years old and the sex is 55.3 percent male and 44.7 percent female. At the end of the analysis of our study, we found that the doses delivered to patients during CT examinations without or with injection of contrast product are higher than those of CIPR 60 and CIPR103. These results lead us to affirm that the patients of these medical centers are more exposed to ionizing radiation during CT examinations. A significant decrease in red blood and hemoglobin was observed after 24 h of CT exposure for all patients (p = 0.0002 and p = 0.0004). A significant increase in white blood cells and granulocytes was observed only in adult patients (p=0.0057 and p=0.011). A significant correlation was observed between abdominal CT and Pleven and white blood and granulocyte variation. Interestingly, a decrease in lymphocytes was observed in adult patients and an increase in lymphocytes was detected in young patients.

Recent epidemiological investigations demonstrate an increased risk of cancer in children and adolescents were followed exposure to be lowed dose ionizing radiation from diagnostic CT scans with a cumulative dose of approximately 50 mSv. Peripheral blood lymphocytes from 50 non-cancer patients before and 24 hours after a CT scan were obtained. Chromosomal and telomeric aberrations were performed after fluorescence hybridization staining of telomeres and centromeres. The frequency of these aberrations was compared to the calculated effective radiation dose using a computational dosimetry system and a dose-length product in a scanner. A significant increase in DSB was result from all chromosomal aberrations after CT exposure was observed. A significant increase in telomere aberrations was observed after CT exposure. However, no correlation was observed between the effective radiation dose and the frequency of chromosomal and telomeric aberrations. It should be noted that the increase in chromosomal and telomeric aberrations was age-dependent. We were demonstrated in this study for the first time the significant increase in telomere aberrations after CT exposure. This loss of telomere functionality plays a major role in the continuation of chromosomal instability. These results could be used in the monitoring of populations exposed to low doses.

KEYWORDS: *Influences-Ionizing radiation-Hematological Parameters-Patient*

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I. INTRODUCTION

Ionizing radiation has been many beneficial applications, ranging from power generation to uses in medicine, industry and agriculture (Aldrich *et al*., 2006). Medical exposure remains by far the largest artificial source of exposure to be ionizing radiation and CT scans account for 43% of the total collective effective dose from diagnostic medical radiology (Beauvais-March *et al.,* 2004).The radiological is risked to patients that could be arised from medical exposure in radiology, particularly in CT, must be assessed and, if necessary, controlled. The medical is used of ionizing radiation have been established for a long time and are subjected to the principles of radiation protection resulting from the basic international nuclear safety standards of the International Atomic Energy Agency (Aldrich *et al*., 2006) and the recommendations of the International Commission on Radiological Protection (De González *et al.,* 2004). Because diagnostic procedures are continuously increased, particularly due to the increased use of new high-tech medical imaging equipment such as multi-slice tomography, and because in African countries such as Congo there are very old X-ray generators, it is of paramount importance to regularly assess diagnostic medical exposure and analyze its evolution over time.

Due to the lack of a specific regulatory framework for medical exposure at the national level, patient dosimetry, and consequently the optimization of patient radiological protection, is not implemented in medical structures. In particular, there is no integrated dose optimization practice in the medical diagnostic system, and all the departments using ionizing radiation for medical diagnostic procedures have never been integrated patient radiation protection into their daily clinical practice. The aim of this study is to evaluate the exposure dose of patients in CT scans. The dose of ionizing radiation or "dose" a patient receives during a CT scan examination is considered to have a very low risk of harm when properly was used to gain diagnostic advantage. This is because CT scans are used to create cross sections of the body. This imaging technique is used X-rays and complex computers. It was also formerly known as computed tomography. Each image provides full body anatomy at the location or slice in question. This technology took medicine and diagnosis to an advanced stage, as images provided exceptionally high detail of body structures including soft tissues, brain, organs, bones and blood vessels. It provides information that doctors can be used to helping diagnose medical conditions. The effective dose is currently considered the best dose descriptor available to quantify stochastic risks in diagnostic CT (Brenner *et al.,* 2014). The effective dose takes into account the dose and relative scan-sensitivity of all irradiated organs and can be converted into a corresponding estimate of harm. The medical radiologist or technologist must be skilled in identifying the most appropriate imaging study for a given patient's conditions at a given time. In some situations, other imaging techniques such as ultrasound and magnetic resonance imaging that use non-ionizing radiation may be used instead of CT scans. The introduction of ionizing radiation in the medical field has been revolutionized not only the detection of diseases but also the therapeutic management of patients. The scanner is the most widely used radiological examination in diagnosis allowing greater precision in the detection of diseases. Nevertheless, the CT scan was delivered a low dose of ionizing radiation, approximately 50 mGy. Epidemiological studies and physical dosimetry have been generated sufficient knowledge concerning the absorbed dose after CT and the risks associated with this exposure in the general population and especially in children. In the event of accidental exposure to higher doses, three examinations are recommended: hematological examinations, cytogenetic investigations and biochemical analyses. An abundant literature concerning these three pillars of biological dosimetry after exposure to higher doses is very well established. However, the impact of very low dose exposure such as computed tomography still remains debated and highly controversial.

The impact of low dose exposure on haematological parameters has not been studied so far. In this study, hematological parameters were studied in children and adults before and after 24 hours after exposure to CT-Scan. We were demonstrated for the first time the decrease in hemoglobin and were reed blood in children and adults after CT. In adults, a significant increase in white blood cells and granulocytes has been observed. All of these data clearly demonstrate that CT exposure was induced an inflammatory response.

II. MATERIALS AND METHODS

Plant material collection and preparation

The patients:

We were studied 61 patients who were exposed to CT for diagnosis in three different hospitals (Blanche Gomez, Mfilou, Talangai). These were 27 males and 34 females with male age of female 8a 54 male 7 to 70 (range 7-70 years). None of these patients had been exposed to ionizing radiation. 30 healthy donors with an average age women 8 to 50 men 9 to 55 and 1 M/F ratio were used as controls. Blood samples were obtained before the CT scan and 24 hours after. For healthy donors, similar sampling protocols were performed. Hematological parameters were analyzed using diagnostic protocols. All patients and healthy donors gave their informed consent. This study was carried out in compliance with local ethical rules (N°398/MESRSIT/IRSSA-CERSA).

Methods

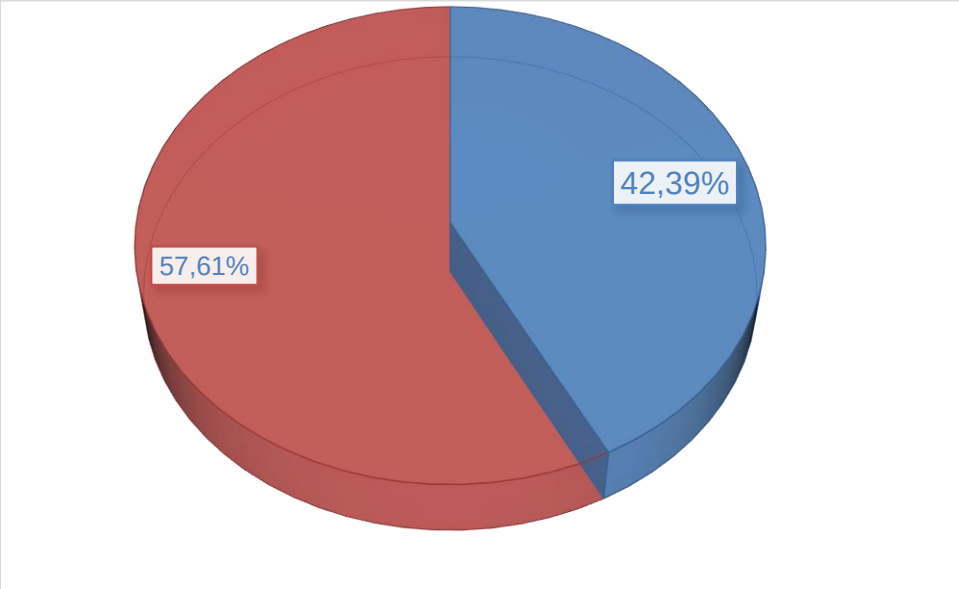
Exposure to scanner:

The patients were exposed to three types of scanner (Siemens and Neusoft) in helical mode with or without contrast medium (OMNIPAQUETM, IOHEXOL). The dose can be quantified by two dosimetric quantities: the computed tomography dose index (CTDI, in Gy) and the dose-length product. In addition, the sensitive dosimeter (RAYSAFE, X2 /Ref.82310106, SWEDEN, SN 283777, calibrated 2021-07-2022) was placed next to the patient to collect the doses absorbed by the patient's skin. Three types of scans were performed according to their availability in the different hospitals: Cerebral, Thoraco-Abdominal, Thoraco-Abdominal-Pelvic.

Analysis of hematological parameters:

The blood study was carried out by the Blood Count technique using EDTA-K3 tubes then passed to the automaton. From this homogenate, 2 to 5µL are aspirated then passed to the analyzer, before the scan. The examination was repeated 24 hours later to confirm the changes in the hematological parameters of the blood cells.

The hematology machine was used to count the number of blood elements. The automated system was used to analyze the blood taken from the patients, allowing the detection of abnormalities of the three blood



lines. Analyzes carried out by the automaton for the collection of hematological parameters: red blood cells or erythrocytes, white blood cells or leukocytes, platelets or thrombocytes. The samples and medical records used in our study were approved by the ethics committee of the Ministry of Hospitals of Congo Brazzaville (n° 0011/MSP/CAB/DGSSa/DH/SH-22) and of the University of Congo Brazzaville (n°398 / MESRSIT/IRSSA-CERSA). Written informed consent was obtained from all participants for the analysis of blood samples. The study involved 50 non-cancer patients (men and women) aged 7 to 70 (mean 58) who underwent medical CT scans.

Declaration of ethics.

The samples and medical records were used in our study were approved by the ethics committee of the Ministry of Hospitals of Congo Brazzaville (n° 0011/MSP/CAB/DGSSa/DH/SH-22) and the University of Congo Brazzaville (No.398/MESRSIT/IRSSA-CERSSA). Written informed consent was obtained from all participants for the analysis of blood samples (Figure1). The study involved 50 non-cancer patients (men and women) aged 7 to 70 (average 58) who underwent medical CT scans. Three hospitals participated in this study. No prior exposure to ionizing radiation or administration of chemotherapy was reported.

Figure1: Distribution according to patients and control cases

A validation cohort of 20 young patients (19 men and one woman; mean age 25 years was added to this study) (Figure2)

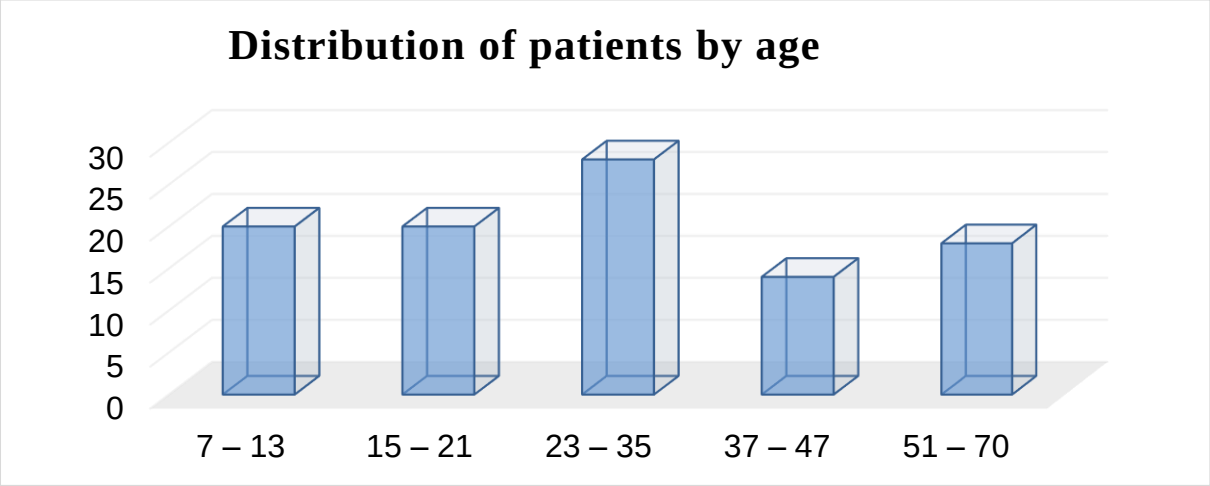


Figure 2: Distribution of patients and healthy donors by age Let m1 be the average age of our sample.

$$\mathbf{m_1} = \frac{73+137+183+257+199+47x3+51x2+70x2}{50} = \mathbf{24,64}$$

Our study sample has an average age of 25 years. Its modal class is: [23-35[.

Our study sample has an average age of 58 years. Its modal class is: While the ages of healthy donors are distributed as follows:

Table: Distribution of healthy donors by age

N°	Ages of healthy donors	Numbers
1	17	01
2	18	01
3	19	03
4	23	02
5	24	02
6	30	01
7	31	01
8	35	02
9	40	01
10	42	01
11	44	01
12	48	01
13	51	01
14	52	02

Let m2 be the average age of our sample.

$$\mathbf{m_2} = \frac{17+18+3x19+2x23+2x24+30+31+35x2+40+42+44+48+51+2x52}{20} = \mathbf{32,3}$$

Our sample of healthy donors has an average age of 32 years.

Statistical analysis:

A script in R® has been developed according to the recommendations of the IAEA. Data were analyzed using the Wilcoxon-Mann-Whitney rank sum test (comparison of two subgroups) or the nonparametric Kruskal-Wallis test (comparison of three subgroups). The null hypothesis was one that considered the subgroups to be identical populations. A value of $p < 0.05$ was considered statistically significant, rejecting the null hypothesis.

III. RESULTS AND DISCUSSION

Distribution of the dose delivered by scanner:
No significant difference was observed between the calculated dose with or without contrast medium. However, a significant difference for the doses delivered was observed between the type of CT scan. Pediatric patients received a reduced dose compared to adult patients (Figure 3).

Comparison with ICRP 60 or 103.

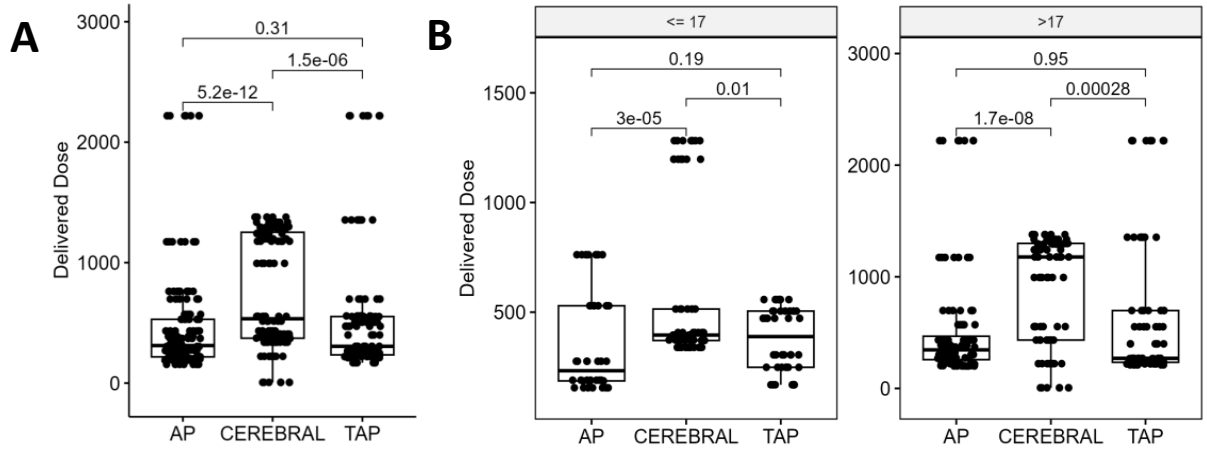


Figure 3: DPL and CTDI delivered by CT-Scan.

Variation in hematological parameter after CT scan

Figure 3 shows the variation in hematological parameters in patients 24 hours after exposure to CT-Scan compared to the control population sampled under the same conditions. A significant decrease in red blood cells and hemoglobin was observed in all patients compared to controls (p=0.00028 and p=0.00042 respectively). Nevertheless, a significant increase in white blood cells and granulocytes were observed in patients compared to controls. Moreover, no significant difference was observed in the lymphocyte count between patients and controls. However, greater interindividual variation was observed (Figure 4).

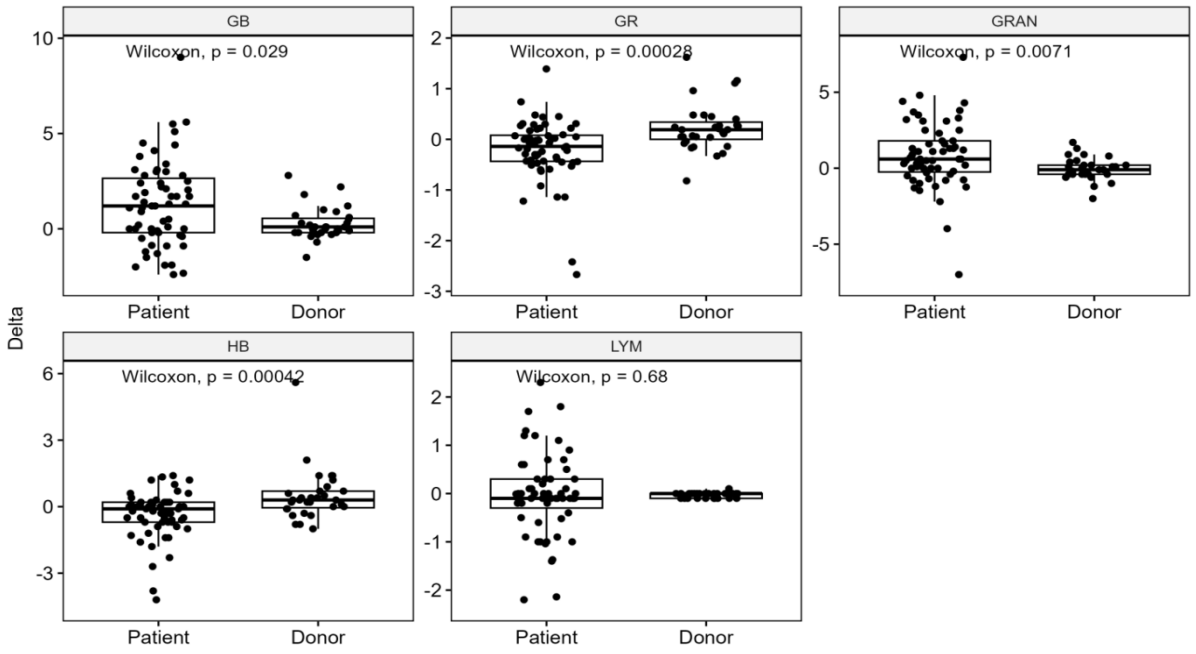


Figure 4: Lymphocyte counts between patients and controls

Then, we analyzed the impact of the type of CT-Scan for these hematological examinations. A significant decrease in red blood cells and hemoglobin was observed after different types of CT-Scan. A similar correlation was obtained for increases in granulocytes and all CT-Scan types. However, only a significant correlation was obtained between AP CT Scan and white blood.

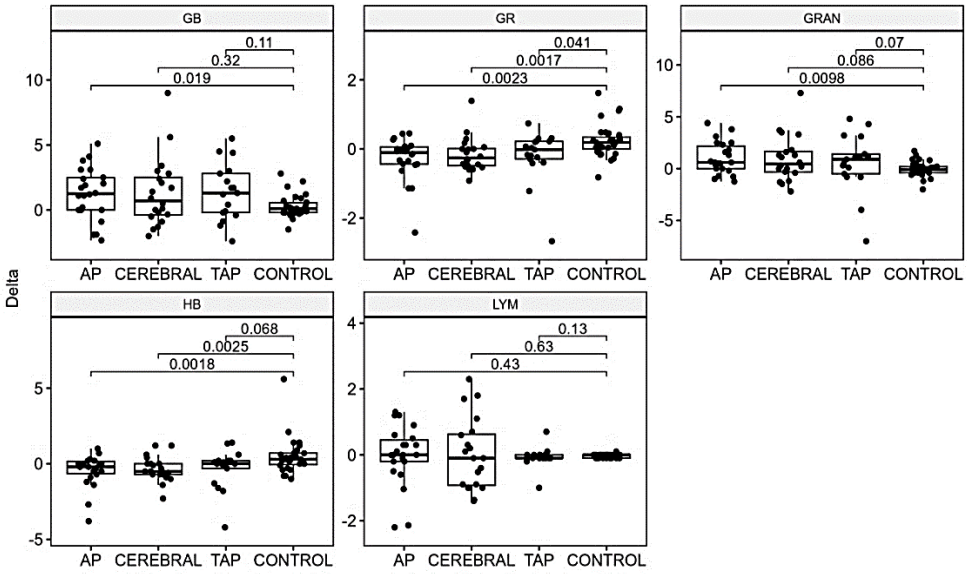


Figure 5: Correlation between the type of scanner and the variation of hematological parameters.

The variation of the haematological parameter depends on the age: Regarding the higher interindividual variation, we analyzed the variation of hematological parameters in young patients (<17 years) and adult patients (>17 years).

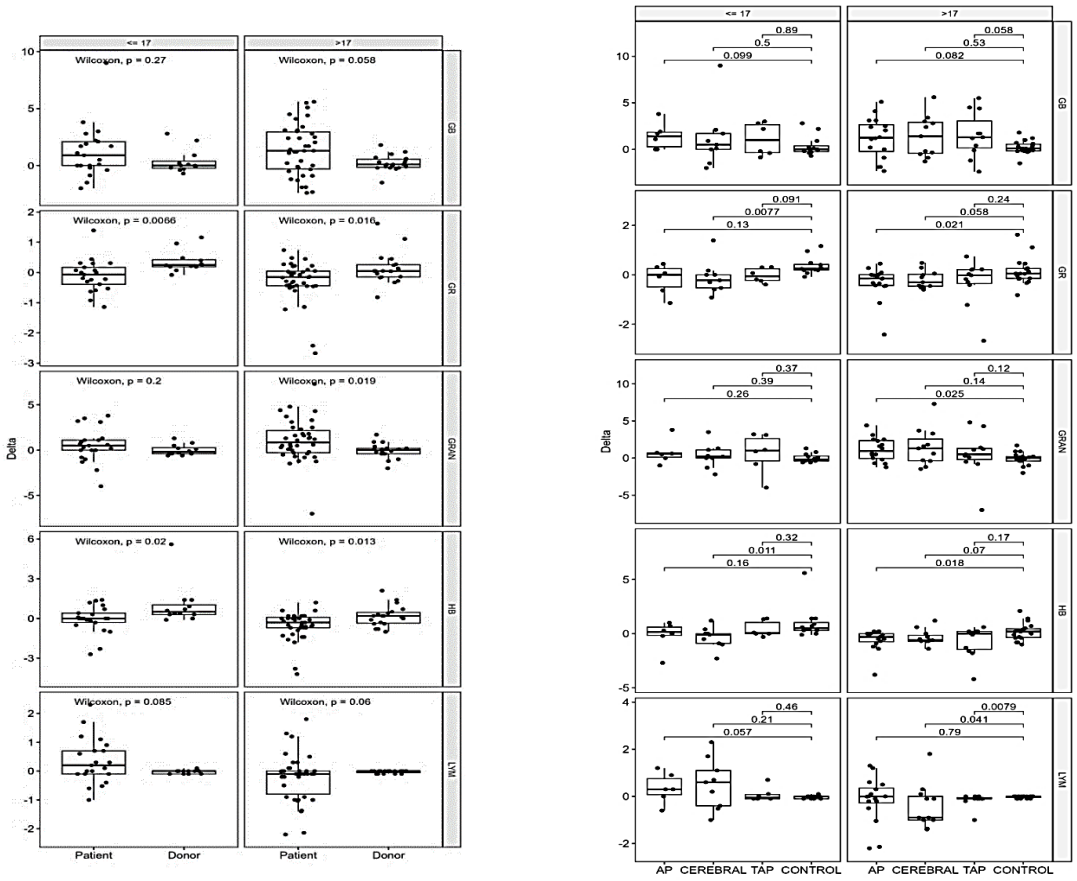
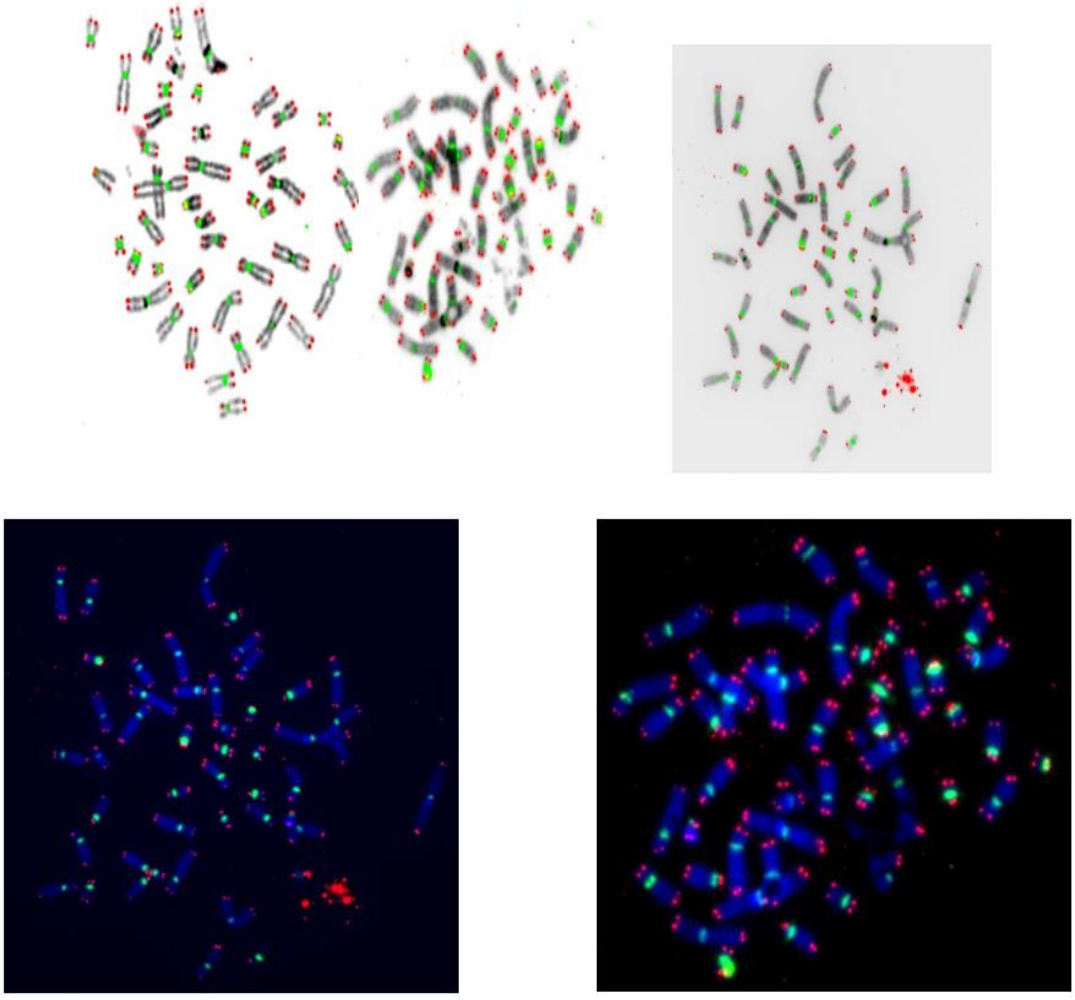


Figure 6: Impact of CT on hematological parameters for these two groups

We were confirmed the significant decrease in red blood cells and hemoglobin in young and adult patients. However, significant increases in the number of white blood cells and granulocytes were observed only in adult patients. Regarding the variation of lymphocytes, we were observed the different variation between young and adult patients. Increases in lymphocyte counts were detected in young patients and decreases in adult patients. Then, we analyzed the impact of age and type of CT-Scan on hematological parameters. A significant difference was observed between the variation of white blood, granulocytes and hemoglobin and CT-Scan AP in adult patients. For young patients, only white blood was correlated with the TAP CT Scan. Regarding the variation of lymphocytes, a significant correlation was observed between the CEREBRAL CT scan in adults and the AP CT scan in young patients.

Frequency of unstable chromosomal aberrations after exposure to CT:

Unstable chromosomal aberrations have been noted in circulating lymphocytes of non-cancer patients before and 24 hours after computed tomography examinations. Analysis of unstable chromosomal aberrations was also performed in circulating lymphocytes from healthy donors of similar age and ethnicity. The results obtained for the chromosomal aberrations before and after the CT scan in the patients and in the control group show that some of the typical aberrations founded in the circulating lymphocytes were shown in Figure 6. No dicentric chromosomes were observed in the circulating lymphocytes of the patients before the CT scan as well as in the control group. After computed tomography, a significant increase in the dicentric chromosome rate was observed, but this increase was significant. Interestingly, some radial formations were observed after CT scan in B cells. The frequency was significantly higher after CT compared to that observed before. However, the main chromosomal aberrations noted after CT scan were chromosomal acentricity and chromosomal deletion.



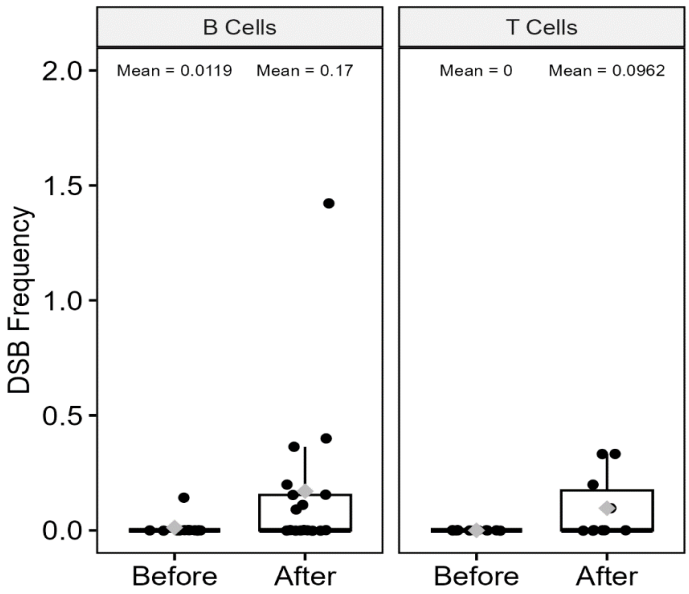


Figure 7: Image captures of chromosomal acentricity and chromosomal deletion

Taking into account all the chromosomal aberrations induced for the calculation of DSBs, the frequency of total DSBs after CT scan increases significantly compared to that estimated before CT scan in B and T lymphocytes (respectively p<2.2 10-16 and p<2.0210-8). Frequency of telomere aberrations after CT exposure: Telomere structural aberrations abolish the presence of a functional telomere leading to chromosomal instability. In this study, we analyzed telomere loss and telomere doublet formation before and after CT exposure.

Note that telomere deletion is considered DSB and their frequency has been introduced into the estimation of total DBS. After CT scan, the rate of telomere loss was significantly higher in B and T cells compared to their rate before exposure to CT scan (Figure 8).

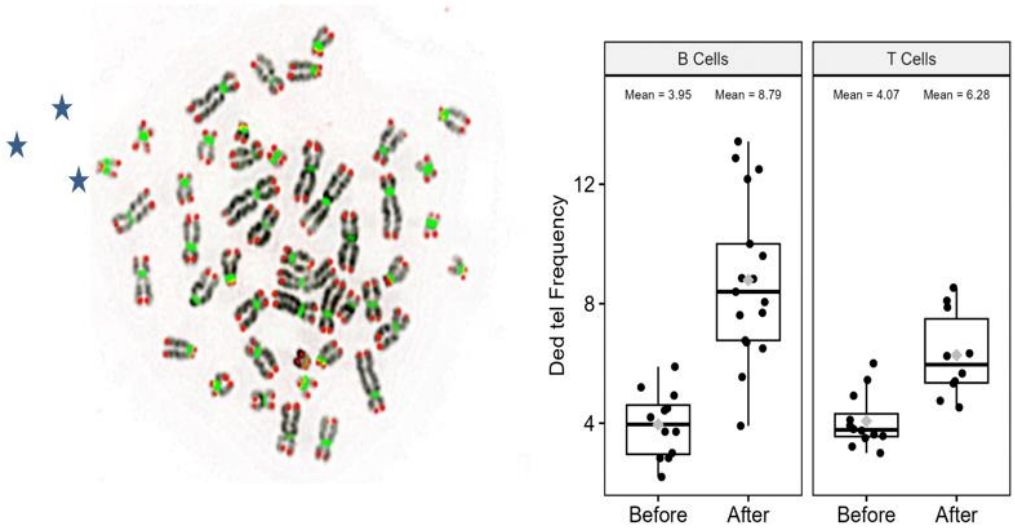


Figure 8: Frequency of telomere aberrations after CT exposure

Similar results were obtained for telomere doublet formation after CT scan compared to that seen before CT exposure (Figure 9).

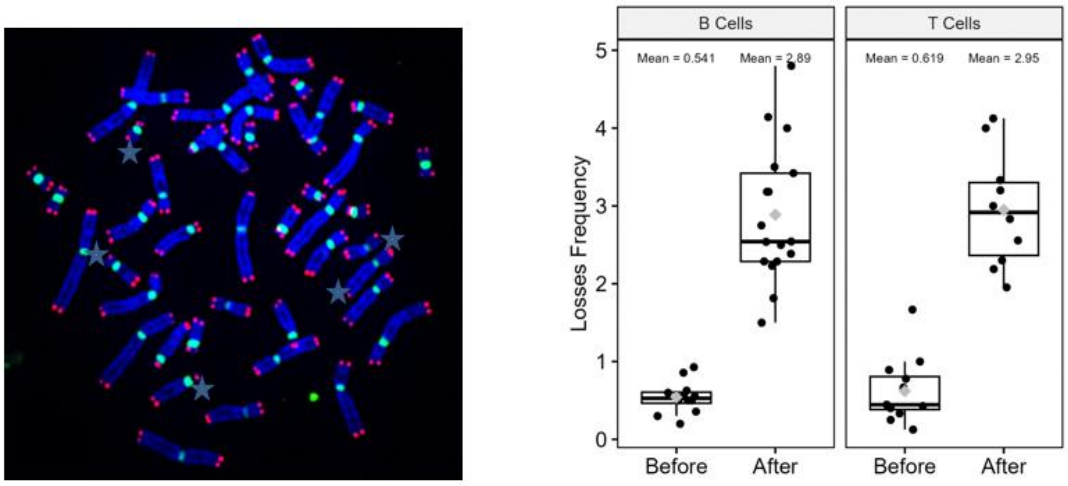


Figure 9: Formation of telomere doublets after computed tomography

It should be noted that the telomere doublet rate in B cells was significantly higher than the rate observed in T cells (p<10-3).

Confounding factors in the formation of chromosomal aberrations after CT Many confounding factors were tested such as age, sex, dose was delivered and changed in hematological parameters. Telomere dysfunction is being one of the hallmarks of aging and used as a biomarker in the prognosis of several age-related chronic diseases. The intimate link between telomere length and male and female infertility has been previously reported (Laurier *et al.,* 2013).Telomere length has been proposed as a new and important biomarker to elucidate the formation of chromosomal and telomeric aberrations in patients after CT examinations in Congo-Brazzaville. Indeed, chromosomal and telomeric aberrations were realized after staining by fluorescence hybridization of telomeres and centromeres. Thus, the frequency of these aberrations is compared to the effective radiation dose calculated using a computational dosimetry system and a dose-length product in a scanner. This made it possible to first deduce a significant increase in DSB resulting from all chromosomal aberrations after CT exposure. Then, the results of the analyzes also show a significant increase in telomere aberrations after exposure to the scanner. However, no correlation has been inferred between the effective radiation dose and the frequency of chromosomal and telomeric aberrations. It is urgent to note that the increase in chromosomal and telomeric aberrations depended on age. Here, we demonstrated, for the first time, the presence of telomere aberrations after CT exposure, in addition to telomere shortening, in patients and that telomere loss and/or telomere short ratio is less of a diagnostic tool for identifying damaged cells than conventional measurements of telomere length. This loss of telomere functionality plays a major role in the continuation of chromosomal instability. Considering all the chromosomal aberrations induced for the calculation of DSBs, the frequency of total DSBs after CT scan increases significantly compared to that estimated before CT scan in B and T lymphocytes (respectively p<2.2 10-16 and p<2.0210-8). What explains telomere dysfunction can affect B and T cells and compromise chromosome pairing, causing recombination defects. These events will ultimately lead to very low frequencies of unstable chromosomal aberrations. As a logical next step, we used circulating lymphocytes to study telomere shortening and aberrations in patients as part of the analysis of chromosomal aberrations, a standard test used in the medical care of these patients. The primary outcome of this study was the identification of increased telomere aberrations. However, studies of telomere dysfunction in these patients are limited. Quantification of telomere length from a control cohort, with ages ranging from 17 to 52 years, shows that telomere length is age-dependent and decreases at a rate of 79 bp/year. This rate of telomere loss, linked to natural aging, is consistent with previous reports.

The length of the telomeres varies (Gilson *et al.,* 2007; Hernandez *et al.,* 2015) according to the different cellular types in a single individual, but also on the arms of chromosomes in a single given cell (Pommier *et al.,* 2002)) decreases continuously to each cycle of cellular replication (Harley et al., 1990). This telomere shortening can be accelerated either by exposure to ionizing radiation or by an increase in cell proliferation with the aim of replacing dead cells after exposure, or even by radiation-induced telomeric damage thus preventing telomere maintenance. Accelerated telomere shortening will be prolonged by continued exposure to other endogenous and exogenous DNA-damaging agents over the life of the cell (d'Adda di Fagagna *et al.,* 2003; Jackson *et al.,* 2009; Lin *et al.,* 2012; Price *et al.,* 2013). Considering that heterogeneity in telomere length on each arm of individual chromosomes is maintained during telomere shortening at each cell cycle, the shorter telomeres will eventually become critical and dysfunctional. In normal cells with intact cell cycle checkpoints, these dysfunctional or unprotected telomeres are detected as DNA damage; DNA damage response

mechanisms are activated thus forming TIFs (Takai *et al.,* 2003). A major study suggested that normal human cells are able to tolerate a small number of dysfunctional telomeres and continue to proliferate until a threshold of five TIFs per cell is reached. In normal cells with intact cell cycle checkpoints, senescence or apoptosis is triggered when this threshold of five dysfunctional telomeres is reached. In immortalized cells, which are incapable of senescence due to loss of cell cycle checkpoint proteins (such as p53 or p16), senescence is temporarily bypassed, and cells continue to proliferate while accumulating chromosomal instabilities, TIFs, and telomeric shortening, until a "telomeric crisis" is reached. In cells undergoing this crisis, more than five dysfunctional telomeres were found (Kaul *et al.,* 2012), with massive chromosome fusion and cell death (Counter *et al.,* 1992; Counter *et al.,* 1994; Ducray *et al.,* 1999), probably due to extreme telomere shortening and loss of shelterin proteins. We deduce that this cell death due to "too much" genomic instability stops the process of carcinogenesis, but is responsible for the increased risk of cell death-related diseases. Exposure to ionizing radiation also induces a variety of other DNA and cellular damage, most notably double-strand breaks and mitochondrial dysfunction. Double-strand breaks in DNA can lead to the formation of chromosomal aberrations. Stress signals can be transmitted to progeny of irradiated cells, but also to non-irradiated bystander cells and their progeny, leading to continued oxidative stress, prolonged cell injury, and propagation of genomic instability; telomeres themselves may play a role in the long-term transmission of chromosomal instability (Shim *et al.,* 2014).

As presented in this thesis, there are inter-individual variations in radiosensitivity, measured in terms of radiation-induced double-strand breaks, which may be related to age, gender, and intrinsic telomere lengths and their radiation-induced modifications. In addition, radiation-induced mitochondrial dysfunction produced by an excess of reactive oxygen species may cause further damage to the genome. This mitochondrial dysfunction can also spread into bystander cells and their progeny, leading to be prolonged oxidative stress producing more DNA damage long after exposure. Prolonged oxidative stress can therefore exacerbate genomic instability (Shim *et al.,* 2014). All of these factors can also be related to telomeres, as their dysfunctions can be caused and propagated genetic instability and loss of heterozygosity. Thus, telomeres can be considered as key players in the process of radiation-induced diseases. Several characteristics of telomeres and the mechanisms of their maintenance make telomeres a promising candidate as a predictive biomarker (Shim *et al.,* 2014) presented in Section 6). In agreement with the article (Shim *et al.,* 2014), a recent article (Mirjolet *et al.,* 2015) highlights the potential of telomeres and their maintenance as key players in the prediction of individual radiosensitivity that can be applied to personalize radiotherapy protocols. Key points supporting telomeres as a predictive biomarker of individual radiosensitivity are summarized as follows:

• The length of telomeres varies between individuals and within the same individual, including within a given cell. The length of telomeres in somatic proliferative tissues naturally decreases during each cycle of cell replication, and therefore with age. Natural telomere shortening can be accelerated by endogenous factors and by external environmental and lifestyle stressors that cause DNA double-strand breaks or poor telomere replication. Telomere length can therefore be considered as a prognostic marker taking into account a set of all past events.

• Reduced telomere length reflects the accumulation of previous insults from various damaging conditions and has been associated with many chronic diseases that are generally considered diseases of aging, such as diabetes, cancer, and heart disease (M'Kacher *et al.,* 2015). Telomerase is up-regulated in approximately 85% of human cancers, suggesting its important role in the process of cell immortalization and tumorigenesis. This shows that telomeres and their maintenance mechanisms play important roles at different stages in the initiation and development of cancer and other human pathologies.

• Telomeric regions are particularly sensitive to radiation-induced oxidative stress and are more prone to DNA double-strand breaks, possibly due to their inappropriate processing: the presence of DNA damage in telomere sequences hinders telomere replication, leading to telomere shortening or loss. Impaired repair of DNA double-strand breaks near telomeres has been suggested to play a role in the chromosomal instability associated with human cancers. This makes telomeres more sensitive to exposure to ionizing radiation than the rest of the genome, and therefore to radiotherapy.

• There is a bidirectional and co-dependent relationship between telomeres and DNA damage repair mechanisms. As dysfunctional telomeres are recognized as double-strand breaks and trigger DNA damage repair pathways, proteins of which are also involved in maintaining and protected telomeres. As DNA damage repair processes are also closely related to radiosensitivity, telomere maintenance could also likely be closely related to radiosensitivity. All this evidence indicates that telomeres and their maintenance could be sensitive and reliable biomarkers of ionizing radiation exposure, and could be a new parameter to predict individual radiosensitivity (Shim *et al.,* 2014; Mirjolet *et al.,* 2015). As we found that radiosensitivity could indeed be predicted by a combination of age and gender, as well as the combination of intrinsic telomere length and their radiation-induced changes with TC-FISH analysis. In view of all the above, it would be important for these factors to be able to be adapted in order to establish a clinical method for the identification of radiosensitive

persons. The ability to reliably predict individual radiosensitivity would be allowed the refinement of radiation protection protocols to identify and protect highly radiosensitive individuals in particular. Although the analysis of telomeres and their length using TC-FISH may be too complex to be used to as a biomarker to provide dose estimates for use in biodosimetry, prior knowledge of an individual's radiosensitivity could aid in appropriate medical triage of these individuals. TC-FISH analysis of telomeres and their length to predict individual radiosensitivity could, however, be used ful in the context of radiotherapy.Nevertheless, there remains the question of how to effectively measure and rank individuals according to their radiosensitivity. However, the method we were used to create triage categories in the case of an emergency situation using the global fluorescence of γH2AX at the point of 4 hours post-irradiation allows the creation of these triage categories independent of individual radiosensitivity. It avoids the question of ranking individuals according to their radiosensitivity. Although this method is fast and capable of high-throughput analysis, this analysis is hampered by the time-sensitive nature of the γH2AX measurement. In the context of radiotherapy, as pointed out (Mirjolet *et al.,* 2015), the ability to reliably predict individual radiosensitivity could be allowed the personalization of treatment. Furthermore, since radiosensitivity has been associated with telomere length and telomerase activity, the management of telomere lengths and telomerase could be used ful in radiotherapy.

In general, shorter telomere lengths have been linked to increased radiosensitivity in several in vivo and in vitro studies in mice and telomerase-deficient human cells. Down regulation or inhibition of telomerase has been shown to compromise cancer cell viability while minimizing the effect on normal cells; thus, the use of telomerase inhibitors during chemotherapy or radiotherapy can be made cancer cells more sensitive to treatments. On the other hand, radioresistant cancer cells show upregulation of telomerase activity and longer telomeres (Genesca *et al.,* 2006; Ayouaz *et al.,* 2008). In the context of personalized radiotherapy treatments based on individual radiosensitivity, authors Mirjolet et al propose that telomere lengths and proteins in cancer cells and in normal cells can be used. Telomere length can be used to adjust doses per fraction, which would be improved the efficacy and safety of radiotherapy using pharmacological treatments that interfere with telomere biology in tumor cells (Mirjolet *et al.,* 2015). Long-term exposure to low doses of ionizing radiation can have adverse effects on human cells and tissues of volunteer patients, particularly on peripheral blood cell counts (Deak *et al.,* 2010). New to the research is the examination of hematological effects and susceptibility in people exposed to low-dose ionizing radiation, particularly in patients and controls in Congo-Brazzaville. Thus, this study recruited patients and controls, all volunteers, exposed to ionizing radiation which generally consists of X-rays. The sampling method is being based on a survey of patients and control subjects, all volunteers and is being exposed to radiation in the Mfilou, Branche Gomes and Talangai hospital centers in Congo-Brazzaville, in which we were obtained 61 patients and 31 controls. Indeed, ionizing radiation has been well-documented effects on blood cells and these effects are generally assumed to contribute to the hematopoietic syndrome, were observed in patients and case/control subjects, following exposure to total body irradiation (Billings *et al.,* 2014). Exposure to low doses of IR is being a fact of life in some workplaces. Radiological accidents, while unfortunate at the minimum and devastating at the worst, will be undoubtedly continue to occur. Fortunately, most radiation exposures involve low doses (<1 Gy) and therefore have no immediate fatal effects. However, the long-term effects of low-dose exposures may be real and should be seriously considered (Tucker *et al.,* 2008). Based on the magnitude of the decrease and the time taken to show a significant decrease in blood cell count after irradiation, white blood cells appeared to be the most sensitive to X-ray irradiation among the cell types evaluated (Sanzari *et al.,* 2013a). The damage was caused by IR leads to a significant reduction in the number of blood cells in a dose-dependent manner, which can be considered as a potential health risk during exposure.

However, previously, was reported that long-term exposure to be lowed doses of ionizing radiation can be affect cells and tissues and lead to low blood counts soon after irradiation and recovery within weeks. The decrease in the number of leukocytes confirms the results observed in the blood formula (Rozgaj *et al.,* 1999). Seed et al reported that IR is one of the cytotoxic agents that particularly damage cell renewal systems. They were also demonstrated that lymphocytes and neutrophil granulocytes uniformly showed an early decrease in the first days corresponding to cumulative radiation doses (Seed *et al.,* 2002). A proliferating cell system requires an intact cell type, the stem cell, and early progenitor cells to maintain cell replication and system homeostasis. Following irradiation, whether acute or chronic, all cells can be affected, stem cells and early progenitor cells being among the most radiosensitive. At relatively low doses or dose rates, hundreds of stem and progenitor cell clones can be emerge bearing individual damage, as one would be expected from a 'damaged cell'. Heterogeneity of cell type, proliferative capacity, and cell cycle status in bone marrow, the hypothesis that stem cell subpopulations are selectively resistant to radiation damage was proposed and tested by (Grande *et al.,* 2000). There is an increase in importance with increasing dose. This result was comparable to that of (Thrall *et al.,* 2013) who was detected a statistically significant reduction in leukocyte count 24 h after irradiation for patients at all doses except the 0.25 Gy group. Hematopoietic stem cell damage is the leading cause of death after accidental or intentional exposure to moderate or high dose ionizing radiation. Radiation exposure can be damaged hematopoietic stem cells and generate several types of free radicals in living cells. These free

radicals/reactive oxygen species can be caused apoptosis of hematopoietic cells, decreasing the cells' ability to proliferate. This is very likely to happen because the hematopoietic system is one of the most radiosensitive systems. This system also provides blood clots for whole blood vessels (Muhogora *et al.,* 2010). Figure 3 indicates that levels of red blood cells and hemoglobin were significantly lower in radiation-exposed patients than in controls, while levels of white blood cells and granulocytes were significantly higher in radiation-exposed patients than in controls ($P<0.05$). A previous study by (Shahid *et al.* 2014) stated that levels of red blood cells and lymphocytes were higher in patients exposed to radiation. The possible reason is that the hematological parameters of radiation-exposed patients, with the exception of red blood cells and monocytes, are more sensitive and easily changed due to radiation exposure. For example, although mature platelets are less sensitive to ionizing radiation, stem cells are very radiosensitive. This results in lower platelet levels in patients than in case/control subjects. The platelet count generally is decreased 5 to 10 days after exposure to a mild or moderate IR dose.

The duration of thrombocytopenia is directly correlated with the dose of IR and the utilization of platelets at sites of active bleeding (Krigsfeld *et al.,* 2012) was not being statistically significant compared to the control On the other hand, on the 1st and 2nd day of irradiation, the number of platelets has no obvious change compared to the control for the other doses used In addition, the rate of degradation and the rate of recovery occur at the same time with a net decrease in the number by increasing the dose of irradiation. The red blood cell is not a very radiosensitive cell, so picking it is not a reflection of cell radiation damage on the scan. However, it is a suitable candidate for monitoring the effect of radiation for many reasons. First, it is a representative sample of whole-body exposure, since it circulates throughout the body, second, its accessibility and ease of separation to obtain cells with intact membrane (Shish *et al.,* 2004). But Sanzari *et al.* 2014) found that the differences between the results, following patient exposure to be lowed dose rate and high dose rate radiation for peripheral hematopoietic cell counts, were not statistically significant. In the current study, it was found that the RBCs increased with the gradual increase of the IR dose until it was reached 0.5 Gy, and then was started to decrease until it was reached the maximum at 1 Gy. Thus, the maximum value of the RBC count was reached at the dose of 0.5 Gy 3h after irradiation. Then, the number of red blood cells are decreased exponentially with increasing time. On the contrary, (Goyal *et al.,* 2004) reported that the total red blood cell count showed a significant decrease ($p < 0.001$) throughout the experiment at all radiation dose levels. In addition, radiation exposure significantly ($p < 0.001$) was reduced bone marrow normoblast count and was red blood cell count, hemoglobin, hematocrit, and blood erythropoietin level, but increased myeloid to erythroid ratio. Therefore, the data reported are results obtained at radiation doses of 1 and 2 Gy. Red blood cell, hematocrit, and hemoglobin levels remained within 10% of those of irradiated case/control donors throughout the observation period. Fortunately, red blood cell counts and hematocrit values remained stable after radiation exposure (Billings *et al.,* 2014). Long-term exposure to low doses of ionizing radiation can have been adversed effects on human cells and tissues of volunteer patients, particularly on peripheral blood cell counts (Krigsfeld *et al.,* 2012).New to the research is the examination of hematological effects and susceptibility in people exposed to low-dose ionizing radiation, particularly in patients and controls in Congo-Brazzaville. Thus, this study was recruited patients and controls, all volunteers, was exposed to ionizing radiation which generally consists of X-rays.

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stem cells and early progenitor cells are being among the most radiosensitive. At relatively low doses or dose rates, hundreds of stem and progenitor cell clones can be emerged bearing individual damage, as one would be expected from a "damaged cell". Hypothesis "The consequence would be a large number of cell clones catering to a wide variety of proliferating cells and possibly abnormal cell populations (Kutkov *et al.,* 2011). Given the remarkable degree of heterogeneity in cell type, proliferative capacity, and cell cycle status in bone marrow, the hypothesis that subpopulations of stem cells are selectively resistant to radiation damage has been proposed and tested by (Grande *et al.,* 2000).

In the present study, the significant reduction in white blood cell count was detected 24 h after irradiation at all dose levels compared to the control group and the white blood cell count was started to be affected at the dose of 0.3 Gy. There is an increase in magnitude with increasing dose. This result was comparable to that of Thrall *et al.,* 2013) who was detected a statistically significant reduction in leukocyte count 24 h after irradiation for patients at all doses except the 0.25 Gy group. Hematopoietic stem cell damage is the leading caused of death after accidental or intentional exposure to moderate or high dose ionizing radiation. Radiation exposure can be damaged hematopoietic stem cells and are generated several types of free radicals in living cells. These free radicals/reactive oxygen species can be caused apoptosis of hematopoietic cells, are decreased the cells' ability to proliferate. This is very likely to happen because the hematopoietic system is one of the most radiosensitive systems. This system is also provided blood clots for whole blood vessels (Muhogora *et al.,* 2010). Figure 3 indicates that levels of red blood cells and hemoglobin were significantly lowed in radiation-exposed patients than in controls, while levels of white blood cells and granulocytes were significantly higher in radiation-exposed patients than in controls ($P<0.05$). A previous study by Shahid *et al.,* 2014) was stated that levels of red blood cells and lymphocytes were higher in patients exposed to radiation. The possible reason is that the hematological parameters of radiation-exposed patients, with the exception of red blood cells and monocytes, are more sensitive and easily changed due to radiation exposure. For example, although mature platelets are less sensitive to ionizing radiation, stem cells are very radiosensitive. This results in lower platelet counts in patients than in case/control subjects. The platelet count generally decreases 5 to 10 days after exposure to a mild or moderate IR dose. The duration of thrombocytopenia is directly correlated with the dose of IR and the utilization of platelets at sites of active bleeding (Krigsfeld *et al.,* 2012) were not statistically significant compared to the control. On the other hand, on the 1st and 2nd day of irradiation, the number of platelets has been no obvious change compared to the control for the other doses used. Moreover, the rate of degradation and the rate of recovery occur at the same time with a net decrease in the number by increasing the dose of irradiation. The red blood cell is not a very radiosensitive cell, so picking it is not a reflection of cell radiation damage on the scan. However, it is a suitable candidate for monitoring the effect of radiation for many reasons. First, it is a representative sample of whole-body exposure, since it circulates throughout the body, second, its accessibility and ease of separation to obtain cells with intact membranes.

Previous reports have been shown significant differences in red blood cell count and hemoglobin in patients. But (Sanzari *et al.,* 2014) was found that the differences between the results, following patient exposure to be lowed dose rate and high dose rate radiation for peripheral hematopoietic cell counts, were not statistically significant. In the current study, it was found that the RBCs was increased with the gradual increase of the IR dose until it was reached 0.5 Gy, and then was started to decrease until it was reached the maximum at 1 Gy. Thus, the maximum value of the RBC count was reached at the dose of 0.5 Gy 3h after irradiation. Then, the number of red blood cells was decreased exponentially with increasing time. On the contrary,was reported that the total red blood cell count showed a significant decrease ($p< 0.001$) throughout the experiment at all radiation dose levels. In addition, radiation exposure significantly ($p < 0.001$) was reduced bone marrow normoblast count and red blood cell count, hemoglobin, hematocrit, and blood erythropoietin, but was increased myeloid to erythroid ratio. Therefore, the data was reported, the results were obtained at radiation doses of 1 and 2 Gy. Levels of red blood cells, hematocrit and hemoglobin was remained within 10% of those of irradiated case/control donors throughout the observation period. Fortunately, red blood cell counts and hematocrit values were remained stable after radiation exposure (Billings *et al.,* 2014).

IV. CONCLUSION

A significant decrease in red blood and hemoglobin was observed after 24 h of CT exposure for all patients. A significant increase in white blood cells and granulocytes was observed only in adult patients. A significant correlation was observed between the abdominal CT-Pleven and the variation of white blood and granulocytes. Interestingly, a decrease in lymphocytes was observed in adult patients and an increase in lymphocytes was detected in young patients. During this study, we recorded on the one hand, the loss of telomeres, defined as an end without signal at the level of a single chromatid then an aberration resulting in telomere-end-fusion and rupture-fusion-bridge cycles. On the other hand, it was found the occurrence of telomere doublets or telomere fragility was defined as more of a single arm telomere signal, an aberration

signaling inadequate telomere replication and shelterin protein dysfunction. Indeed, telomeres, long considered the guardians of the genome, can indicate the general state of health of an individual, as they can represent all exposures to various DNA-damaging agents, including ionizing radiation (as they are deficient in repair and therefore lead to accumulation of damage) over a lifetime. Telomeres and the mechanisms for their maintenance could therefore have important implications for long-term human health. As human beings are constantly exposed to ionizing radiation via natural and artificial sources, it is being important to determine if and how telomeres played a role in the mechanisms of direct and indirect radiation-induced biological effects, as well as their role in the transmission of these radiation-induced effects during cell proliferation. These roles are perhaps critical for determining long-term radiation-induced effects on human health, and may contribute to a better understanding of radiation-induced cancers associated with other human pathologies.

Scientific studies have found that a diet high in whole grains, vegetables, fruits, seaweed, seafood, dairy products and coffee is positively associated with good telomere length in white blood cells. This should then be recommended to patients.

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CONFLICT OF INTEREST

The authors here by declare no conflict of interest in this work

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