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Original Article

Comparison of radiation-induced DNA damage between conventional and computed tomography coronary angiography

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Abstract

Objective: Conventional coronary angiography (CCA) and coronary computed tomography angiography (CCTA) are the most frequently used imaging modalities to diagnose coronary artery disease (CAD). The amount of radiation and genotoxic damage of these imaging methods showed variation with the improved technology. Thus we sought to compare the ionizing radiation doses and radiation-induced DNA damage in patients who were performed CCA and CCTA.

Methods: A total of 76 patients (39 in CCA group, 37 in CCTA group) were enrolled. Patients undergoing CCTA were grouped according to the use of the flash technique (22 patients with CCTA-flash, 15 patients with CCTA-other). The effective radiation dose was recorded. Genotoxicity was compared with the chromosome aberration tests before and after imaging methods.

Results: There was a significant difference between the groups in effective radiation doses given to patients. Radiation was lowest in the CCTA-flash group, followed by CCA, and non-flash CCTA group. There was no change in chromosome aberration rate after CCTA-flash group ($p= 0.479$). There was a significant increase in chromosome aberration rates after CCA and CCTA-other groups (CCA: $p= 0.001$; CCTA-other: $p= 0.01$).

Conclusion: CCTA taken with flash technique in dual-energy CT devices delivers lower dose radiation than other groups. Due to this significant difference, radiation-induced genetic damage was significantly less in patients with CCTA undergoing flash technique.

Keywords: Angiography, chromosome aberration test, genotoxicity, ionizing radiation.

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INTRODUCTION

Regardless of a country's level of development, coronary artery disease (CAD) is the leading cause of morbidity and mortality worldwide, and its prevalence is rising (1, 2). Contrary to other modalities that have been suggested, coronary computed tomography angiography (CCTA) and conventional coronary angiography (CCA) are the methods most frequently used to diagnose coronary artery disease (CAD) (3). Due to its high spatial and temporal resolution, CCA continues to be the gold standard diagnosis method. However, there are a number of drawbacks, including the requirement for hospitalization, the possibility of complications, and the high cost (4,5). However, CCTA is a minimally invasive alternative, particularly for those with low and moderate CAD risk (6,7). Recent advances in CCTA have made it possible to provide more accurate anatomical details of coronary arteries, providing information that is helpful for the diagnosis of CAD (8,9). Both imaging techniques share the use of ionizing radiation, which may have mutagenic effects (5,10). Dual-energy technology significantly reduced the radiation dose, which was previously reported to be higher in CCTA than CCA (11). The radiation dose has also been minimized by using the flash technique, a feature available in recent devices (11-13).

Ionizing radiation affects tissues in a variety of somatic and genetic ways. Observational studies have previously shown the most feared effect, an increase in cancer risk, particularly in those exposed to radiation (14). DNA damage is the most significant contributor to the risk of developing cancer from radiation exposure. There are various techniques for identifying the genotoxic effects of radiation. Various structural chromosomal abnormalities caused by mutagens can be found using the standard technique known as the Chromosome Aberration Test (CAT) (15-17).

Thus, we sought to compare ionizing radiation doses of CCA and CCTA and radiation-induced DNA damage by chromosome aberration test caused by these imaging techniques.

MATERIALS AND METHODS

Study population

The study was designed in Gazi University Faculty of Medicine Department of Cardiology and Radiology. This study included totaly 76 patients who were older than 18 ages. Thirty nine patients underwent CCA for the diagnosis of CAD, and 37 patients underwent CCTA. Patients with signs of active infection as well as those with a history of malignancy, chemo-radiotherapy, coronary artery anomalies, and radiological procedures other than chest radiography within the previous year were excluded. Additionally, patients who underwent ventriculography percutaneous coronary intervention in the same session were not included because our goal was to compare CCTA with diagnostic CCA. Patients were informed about the research before participating, and written consent was obtained. All the methods in the study were approved by the Clinical Research Ethical Committee of Gazi University Faculty of Medicine (Date: 11/09/2017#400). The study was carried out in accordance with the statement of Helsinki Declaration.

Study protocol

Patients who underwent CCTA were split into two groups based on whether they underwent scanning with a dual-energy CT device using a prospective ECG-triggered high-pitch spiral technique (CT-flash). In the end, three patient groups—CCA, CCTA-flash, and CCTA-other—were created. From imaging tools, baseline characteristics and effective radiation doses were calculated and recorded. Blood samples were taken before and after the imaging protocol, respectively, by one hour.

Conventional coronary angiography

Conventional coronary angiography procedures were performed on the Innova IGS 320, General Electric Healthcare (Milwaukee, USA) device by physicians experienced in interventional cardiology. The number of images was left to the initiative of the interventional cardiologist, provided that all coronary imaging were performed (Figure 1).

Coronary computer tomography angiograph

384 slice (2x192), dual energy, 3rd generation tomography device Somatom Force CT, Siemens Healthcare (Siemens AG, Erlangen, Germany) was used for CCTA. All patients had coronary calcium scoring before angiography procedure. No negative chronotropic agents were given to patients to reduce pre-procedure pulse. The imaging protocol was determined by the radiologist according to the pulse rate of the patients during the procedure

(Figure 2). Flash mode shooting (prospective ECG-triggered high-pitch spiral technique with dual-energy) was performed for eligible patients.

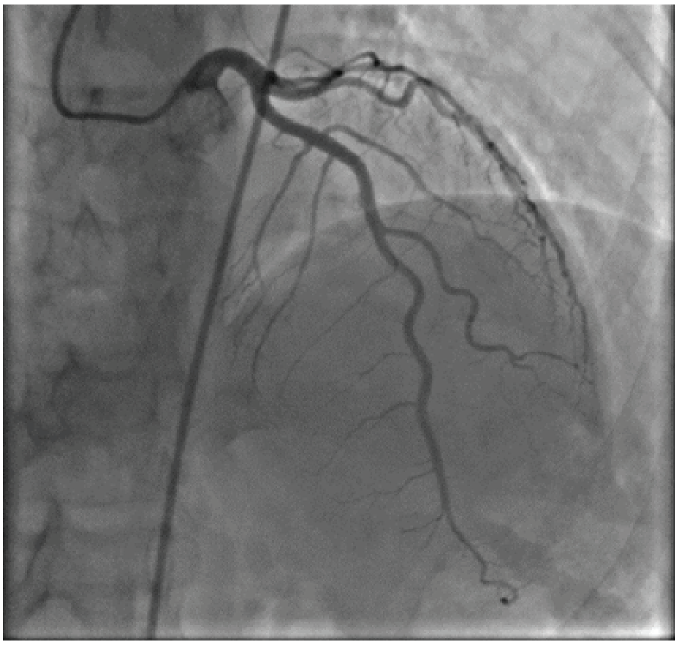

Figure 1. Conventional coronary angiography image of a study patient.

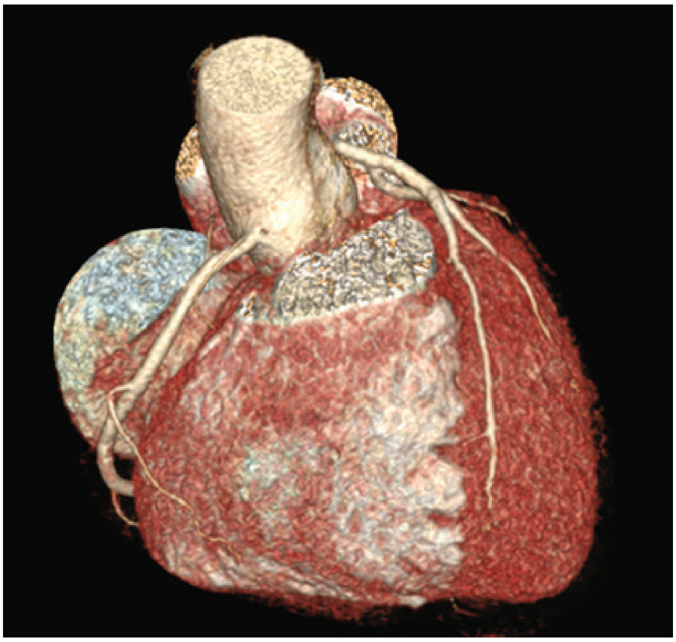

Figure 2. Coronary computed tomography angiography image of a study patient.

Radiation dose measurements

There are different parameters to calculate the radiation doses of the patients. In our study, we used the effective dose (ED) which is more frequently used among these parameters. The dose-area product (DAP) values of the patients who underwent CCA automatically measured by the device after the procedure and were converted to ED unit (mSv) by multiplying the converting factor for diagnostic CCA by 0.12 mSv / Gy.cm2. In CCTA, the dose-length product (DLP) values given by the device were converted to ED by multiplying the conversion factor 0.014 mSv x (mGy x cm) -1 for the chest region.

Chromosome aberration test

To identify various structural and numerical chromosomal abnormalities brought on by mutagens, the standard technique known as CAT is frequently used. A biomarker of cancer risk, chromosome aberration frequency is determined in individuals and measures both the early biological effects and a person's sensitivity to exposure to genotoxic chemicals (17). Human lymphocyte metaphase chromosomal aberration analysis is still regarded as the gold standard method for radiation biodosimeters (18). Blood samples collected from patients before and after the CAT imaging procedures were processed according to standard procedures in our study. After spreading the metaphase stage of lymphocytes onto slides, each person had 100 metaphases examined by skilled researchers (Figure 3). For each patient in our study, the total aberration rate was calculated before and after the procedure, and the structural aberration types, including chromosome-chromatid gap, chromosome-chromatid fracture, ring chromosome, dicentric, and asentric chromosomes, were identified. It was agreed that radiation's genotoxic effects were manifested in a relative change in chromosome aberration rates.

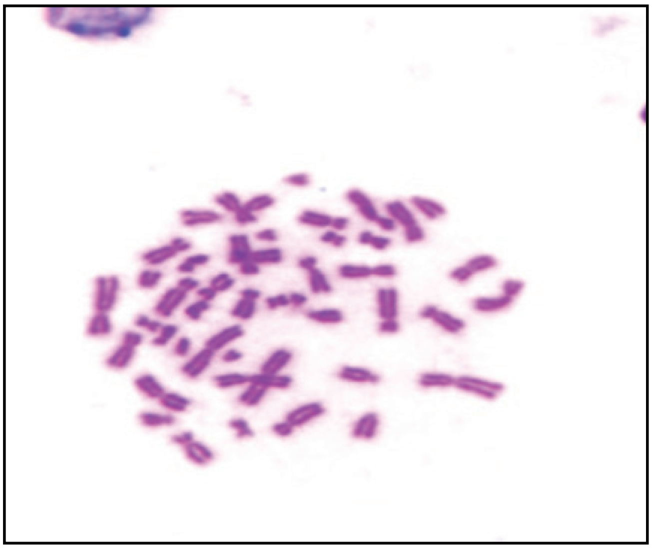

Figure 3. Chromosome aberration test of lymphocyte chromosomes at the metaphase stage with light microscopy

Table 1. Baseline characteristics of the participants

<table>
<tr><th rowspan="2">Variables</th><th rowspan="2">Total
(n=76)</th><th rowspan="2">CCA
(n=39)</th><th colspan="2">[*¥#]CCTA (n=37)</th><th rowspan="2">P</th></tr>
<tr><th>CCTA-Flash
(n=22)</th><th>CCTA-Other
(n=15)</th></tr>
<tr><td rowspan="2">Age (year)</td><td rowspan="2">56.9 ± 10.8</td><td rowspan="2">59.2 ± 11.1[#]</td><td colspan="2">54.5 ± 10.0</td><td>0.057</td></tr>
<tr><td>54 ± 9.5</td><td>50.3 ± 10.7[#]</td><td>0.016</td></tr>
<tr><td rowspan="2">Gender (female)</td><td rowspan="2">31 (40.8%)</td><td rowspan="2">16 (%41)</td><td colspan="2">15 (40.5%)</td><td>0.460</td></tr>
<tr><td>6 (27.3%)</td><td>9 (60.0%)</td><td>0.138</td></tr>
<tr><td rowspan="2">SBP</td><td rowspan="2">133.8 ± 12.9</td><td rowspan="2">135.1 ± 13.1</td><td colspan="2">132.3 ± 12.7</td><td>0.342</td></tr>
<tr><td>133.2 ± 10.5</td><td>131 ± 15.7</td><td>0.563</td></tr>
<tr><td rowspan="2">DBP</td><td rowspan="2">80.7 ± 7.7</td><td rowspan="2">79.9 ± 7.8</td><td colspan="2">81.5 ± 7.3</td><td>0.363</td></tr>
<tr><td>81.4 ± 6.9</td><td>81.7 ± 8.6</td><td>0.658</td></tr>
<tr><td rowspan="2">HR</td><td rowspan="2">71.6 ± 10.1</td><td rowspan="2">72.7 ± 10.4[*]</td><td colspan="2">70.3 ± 9.75</td><td>0.304</td></tr>
<tr><td>63 ± 2.8[*¥]</td><td>81.1 ± 4.9[¥]</td><td><0.001</td></tr>
<tr><td rowspan="2">Lenght (cm)</td><td rowspan="2">167 ± 10.4</td><td rowspan="2">167 ± 10.4</td><td colspan="2">166.3 ± 8.1</td><td>0.770</td></tr>
<tr><td>168 ± 8.1</td><td>164 ± 8.0</td><td>0.455</td></tr>
<tr><td rowspan="2">Weight (kg)</td><td rowspan="2">77.7 ± 13.9</td><td rowspan="2">76.9 ± 15.6</td><td colspan="2">78.5 ± 12.1</td><td>0.610</td></tr>
<tr><td>80.6 ± 12.4</td><td>75.5 ± 11.3</td><td>0.493</td></tr>
<tr><td rowspan="2">BMI (kg/m^2)</td><td rowspan="2">28.2 ± 4.3</td><td rowspan="2">27.5 ± 4.2</td><td colspan="2">28.8 ± 4.4</td><td>0.182</td></tr>
<tr><td>28.9 ± 4</td><td>28.8 ± 5.1</td><td>0.413</td></tr>
<tr><td rowspan="2">Diabetes mellitus</td><td rowspan="2">18 (23.7%)</td><td rowspan="2">13 (33.3%)</td><td colspan="2">5 (13.6%)</td><td>0.059</td></tr>
<tr><td>3 (13.6%)</td><td>2 (13.3%)</td><td>0.127</td></tr>
<tr><td rowspan="2">Hypertension</td><td rowspan="2">36 (47.4%)</td><td rowspan="2">21 (53.8%)</td><td colspan="2">15 (40.5%)</td><td>0.262</td></tr>
<tr><td>9 (40.9%)</td><td>6 (40%)</td><td>0.508</td></tr>
<tr><td rowspan="2">Hyperlipidemia</td><td rowspan="2">29 (38.2%)</td><td rowspan="2">18 (46.5%)</td><td colspan="2">11(29.7%)</td><td>0.163</td></tr>
<tr><td>8 (36.4%)</td><td>3 (20%)</td><td>0.204</td></tr>
<tr><td rowspan="2">Smoking</td><td rowspan="2">42 (55.3%)</td><td rowspan="2">21 (53.8%)</td><td colspan="2">21 (56.8%)</td><td>0.786</td></tr>
<tr><td>13 (59.1%)</td><td>8 (53.3%)</td><td>0.104</td></tr>
<tr><td rowspan="2">Alcohol</td><td rowspan="2">17 (22.4%)</td><td rowspan="2">8 (20.5%)</td><td colspan="2">9 (24.3%)</td><td>0.821</td></tr>
<tr><td>4 (18.2%)</td><td>5 (33.3%)</td><td>0.512</td></tr>
<tr><td rowspan="2">CKD</td><td rowspan="2">5 (6.6%)</td><td rowspan="2">4 (10.2%)</td><td colspan="2">1 (2.7%)</td><td>0.359</td></tr>
<tr><td>0 (0%)</td><td>1(6.7%)</td><td>0.300</td></tr>
</table>

Abbreviations*; BMI: Body mass index, CCA: Conventional coronary angiography, CCTA: Coronary computed tomography angiography, CKD: Chronic kidney disease, DBP: Diastolic blood pressure, HR: Heart rate, SBP: Systolic blood pressure.*

Table 2. Total chromosome aberration rates before and after imaging

Groups	Total Chromosome Aberration Rate (%) – Before	Total Chromosome Aberration Rate (%) – After	P
CCA	4.3 ± 2.9	5.3 ± 2.9	0.001
CCTA – Flash	3.4 ± 2.4	3.2 ± 2.3	0.479
CCTA – Other	3.1 ± 2.4	4.7 ± 2.6	0.010

Abbreviations*; CCA: Conventional coronary angiography, CCTA; Coronary computer tomography angiography*

Statistical analysis

IBM SPSS (IBM, Chicago, IL, USA) for Windows Version 19.0 package program was used to conduct the statistical analyses. The means, standard deviations, or medians of the numerical variables were summarized along with the interquartile range. Numbers and percentages were used to represent categorical variables. The Shapiro Wilks test was used to determine whether numerical variables were normal. Utilizing the T-test in dependent groups under parametric test assumptions and the Wilcoxon test under non-parametric test assumptions, the difference between the numerical values prior to and following imaging was analyzed. Using the chi-square test, categorical variable differences were assessed. If parametric test assumptions were met, differences between groups were examined using one-way analysis of variance; otherwise, the Kruskal-Wallis test was used. Post-hoc tests used the Bonferroni correction. The percentage difference between the parameters of the genetic damage assessment before and after imaging. The significance level of 0.05 was accepted.

RESULTS

Totally 76 patients were included in the study and CCA group consisted of 39 patients. The patients who underwent CCTA were divided into two groups according to the flash mode of the device. Of the 37 patients who underwent CCTA, 22 (59.5%) were in the CCTA-flash group and 15 (40.5%) were in the CCTA-other group. The baseline demographic and clinical characteristics of the participants are shown in Table 1. The mean age of the patients was 56.9±10.8 years. Basal characteristics of the groups were similar except heart rate and age. The mean age of the CCTA-other group was higher compared to others.

The mean effective radiation dose given to all participants was 4.6±2.9 mSv. The mean dose of radiation administered was significantly different between the groups (Figure 4). The highest radiation was observed in the

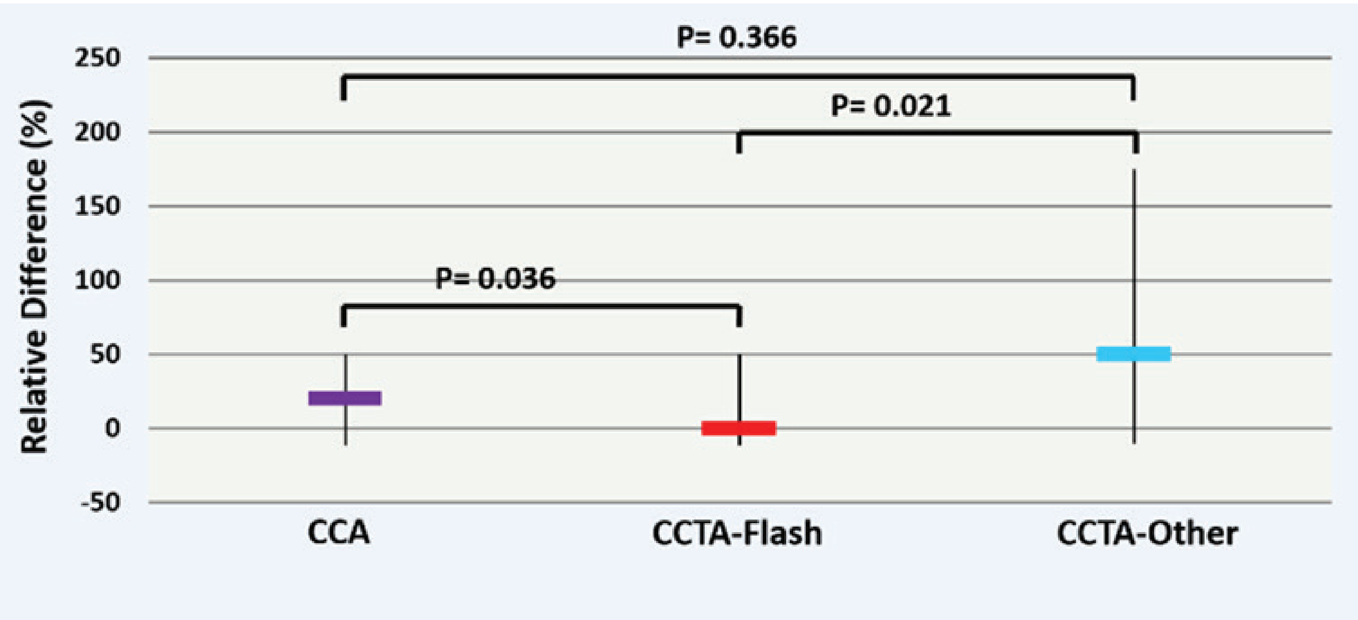

Figure 4. Comparison of mean effective radiation dose among study groups.

(P<0.001 with ANOVA, p values regarding post-hoc tests were presented on the bars) (CCA; conventional coronary anjiography, CCTA-Flash; coronary computed tomographic angiography-flash, CCTA-Other; coronary computed tomographic angiography-other groups)

CCTA-other group with an ED of 7.2±2.4 mSv. The least radiation was seen in the CCTA-flash technique and the mean ED was 1.1±0.2 mSv.

Total chromosome aberration rates measured by CAT before and after imaging methods are shown in Table 2. In the CCTA-flash group with the lowest radiation dose, there was no change in chromosome aberration rate after the study. Chromosome aberration rates increased significantly after imaging protocols for patients in the CCA and CCTA-other groups. The increase in these two groups was found to be similar (p= 0.366).

DISCUSSION

In our study; we aimed to compare genotoxic damage due to ionizing radiation by assessing CAT in patients who underwent CCA and CCTA. Radiation dose was significantly lower in CCTA-flash group compared to other groups. While chromosomal aberration rate was not increased for CCTA-Flash group, chromosome aberrations were observed in CCTA-Other and CCA groups.

Coronary artery disease is one of the most important health problems worldwide due to its negative consequences and frequency (1,2,19). Although CCA still appears to be the gold standard in diagnosis; use of CCTA has increased considerably with the latest technological advances (10,20). There are two important reasons for this increase: firstly it provides very good anatomical detail in the visualization of coronary arteries with the increase in the number of sections with three-dimensional isometric imaging feature (8,9). Secondly high radiation doses previously feared in CT have been reduced by techniques in the new generation CT devices (11,21,34). The number of patients being scanned by CCA or CCTA is increasing due to higher admissions to hospitals with increased sensitivity to CAD. Moreover, access to mentioned imaging tools has become easier. This makes it more necessary to know the effects of ionizing radiation used in imaging method. Current guidelines emphasize that CCTA should be preferred for the diagnosis of CAD (22). However, adequate protocols should be followed to achiveve low radiation doses to prevent radiation-induced comorbidities. Radiation doses in CCA and CCTA have been compared many times and previous studies observed that patients are exposed to more radiation in CCTA (23,24). However, with the development of CT technology, especially with the emergence of dual energy CT systems, the radiation dose decreased in CCTA scans (25). Flash mode in dual-energy CCTA devices transmits low dose in a single pulse during a certain period of the cardiac cycle (12,13,26). In our study, it was observed that the patients had very low dose of radiation, such as 1.1±0.2 mSv, on flash mode. This result was found to be consistent with previous studies (12,27,33). In order to use flash mode in dual-energy CT devices, patients' heart rates should be low (28,29). Therefore, in our study, it is expected that the heart rates of patients with CCTA-flash group are lower than the other groups. The average ED calculated in the CCA group was found to be similar to previous studies (29). Genotoxicity of ionizing radiation in CCTA has been shown in several studies (30,31). However, there is a few studies comparing CCA and CCTA in this respect (5). Our study provided clinically important results by comparing two methods that expose radiation and whose prevalence is increasing day by day. Chromosomal damage has an important role as a biological indicator of genotoxic carcinogen exposure such as ionizing radiation. Determining the frequency of chromosomal aberration in cultured peripheral blood lymphocytes is one of the most widely used methods in evaluating the biological effects of genotoxic carcinogen exposure (32). In our study, we preferred the CAT because it shows genotoxicity effectively by being reliable for many years. There is no study comparing dual-energy CCTA and CCA using the CAT for the genotoxic effects of radiation. Our results revealed that chromosome aberration increase was lowest in the CCTA-flash group, which has a significantly lower mean radiation dose received. However, the increase in chromosome aberration rate was not higher in CCTA-other group which has the the highest mean radiation dose received compared to CCA group (p=0.366). It could be explained that the number of patients is not enough to provide a statistically significant difference and genotoxic effect may depend not only on radiation dose but also on individual sensitivity. Therefore larger prospective studies should be performed.

Limitations:

The most important limitation of our study was the limited number of patients, however, we believe to explicit relevant results. Another limitation is that evaluation of chromosome aberration can be subjective. Therefore, it was evaluated by the only experienced researchers.

CONCLUSION

The results of this study indicate that coronary imaging with CCTA- flash mode in dual - produces less radiation and radiation-induced genotoxicity than non-flash mode CT scans and CCA. Further studies with a larger patient population are necessary to confirm the results of our study.

Conflicts of interest: The authors declare no conflict of interest.
Financial support and sponsorship: None.
Ethical approval and consent to participate: All the methods in the study were approved by the Clinical Research Ethical Committee of Gazi University Faculty of Medicine (Date: 11/09/2017#400). The study was carried out in accordance with the statement of Helsinki Declaration.
Peer-review: Externally peer-reviewed.
Authorship Contributions: Design of the study; GG,MC,BK,GE - Supervision; MC,BK,NBB,SU - Data collection &/or processing; GG,AE,SU,ACY - Performed data analysis; GG,SU,AE,BK,NBO - Literature search; GG,AE,ACY - Written by; GG,SU,MC,BK,NBO - Critical review; MC,BK,SU.

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