SciMedCentral

Journal of Radiology & Radiation therapy

Research Article

Cancerogenesis Risk for Coronary CTA Using 64 And 320-Row CT

Boris Nikolic[1], Faisal Khosa[2#], Pei-Jan Lin[4], Atif N. Khan[3], Waqas Shuaib[2]*, Melvin E. Clouse[3] and Mohammad K. Khan[2]

[1]*Department of Radiology, Albert Einstein Medical Center, 5501 Old York Rd, Levy Building, Ground floor, Philadelphia, Pennsylvania 19141*
[2]*Emory University Hospital Midtown, 550 Peachtree St. NE. Atlanta, GA.30308.*
[3]*Department of Radiology, Beth Israel Deaconess Medical Center, Harvard Medical School, 1 Deaconess RD, Boston, MA, 02215*
[4]*Department of Radiology, Virginia Commonwealth University Medical Center, Richmond, VA*
[#]*American Roentgen Ray Society Scholar*

Corresponding author
Waqas Shuaib, Department of Radiology, Emory University Hospital, Midtown, 550 Peachtree Street NE Atlanta, GA 02115; Tel: 404-686-5957; Fax: 404-686-4498; E-mail: waqas.shuaib@emory.edu

Submitted: 20 September 2013

Accepted: 14 November 2013

Published: 19 November 2013

Keywords
- Cancerogenesis
- Coronary CTA
- Screening
- Coronary artery disease
- Risk assessment

Abstract

Purpose: This study compares cancerogenesis risks (CRs) between 64 and 320 row detector CT (RDCT) using coronary CTA (CCTA) decennial screening guidelines for patients between the age of 50 and 70.

Material and Methods: CCTA absorbed radiation dose data for lung, thyroid and female breast was obtained from previous studies for the 64 RDCT and also generated with our own 320 RDCT. Data for the 64 and the 320 RDCT were then used to determine lifetime attributable cancer risks (LAR) based on the BEIR VII report. LAR for thyroid cancer was negligible for both scanners.

Results: The relative LAR (%) reductions for 50, 60 and 70 year old patients using the 320 RDCT were > 30 % lower for lung, and > 50 % lower for female breast compared to the 64 RDCT. The use of 320 RDCT would result in a combined cumulative cancer incidence of less than 1/500 for breast and less than 1/1000 for lung in men; By comparison, this is much lower than other more common risk factors: 16–fold for lung cancer in persistent smokers, 2-fold for breast cancer with a first degree family member history of breast cancer, and 10–fold for thyroid cancer with a family member with thyroid cancer. Decennial screening would benefit at least some of about 355,000 annual sudden cardiac death patients, 94 % of which have at least one stenosis > 75%.

Conclusion: Lung and female breast LAR reductions with 320 RDCT compared to 64 RDCT are substantial, and the benefits would outweigh increased cancer risks with decennial screening from ages 50-70.

INTRODUCTION

The assessment of new medical procedures requires comprehensive evaluation of all conceivable benefits and risks. In the context of coronary computed tomography angiography (CCTA), measurements of the radiation dose have been performed and previously published [1-4]. Despite publication of these earlier studies, radiation risk assessment including secondary cancer risks for CCTA screening guidelines is lacking [5]. Deterministic radiation risk assessment is accomplished by comparing radiation dose measurements associated with CCTA with known threshold numbers, whereas stochastic risk assessment requires more sophisticated calculations that are generally derived from past epidemiological low dose radiation exposures published in the BEIR VII report [6]. Stochastic risk assessments are therefore scarcer and are usually based on data of individual studies, which do not properly account for all available variables in equipment and techniques used in performing CCTA examinations.

We measured absorbed radiation dose to radiosensitive organs using CCTA screening guidelines from our 320 row scanner. The measure absorbed dose was then used to estimate cancerogenesis risks for several radiosensitive organs using stochastic risk assessment models published in the BEIR VII report. Those cancer risks were then compared with the natural

cancerogenesis risk associated with more common risk factors. Finally, a scenario of US wide decennial coronary artery screening from age 50 until age 70 was assumed and the cancerogenesis risk to these radiosensitive organs based on the cumulative absorbed radiation dose associated with such screening was estimated. The estimated cumulative risk was then compared with the potential benefits of detecting clinically occult coronary artery disease within this hypothetically screened population to determine if risks of decennial screening would outweigh the benefits.

MATERIALS AND METHODS

A. Absorbed radiation doses associated with CCTA

Previously acquired and published absorbed radiation dose measurements using the 320 row detector scanner were used to estimate cancerogenesis risk assessments for the current study (Table 1) [2]. Previous measurements had been performed with semiconductor field effect transistor detectors calibrated to match the primary beam quality of the CT scanner. Since the CT scanner had beam qualities in the range of 6.5 - 7.5 mmAl half value layer (HVL) at 120 kVp, the detectors were calibrated against a conventional radiographic unit at 118 kVp with beam quality of 7.15 mmAl HVL. This was done by adding 5.5 mm of aluminum to the faceplate of the collimator. The MOSFET detectors were then subjected to radiation doses of 1, 3, 10 and 30 mGy. Individual calibration factors were obtained for all detectors by fitting these four data points with the least-squares fit using XLGENLINE Software (Version 1.0), "Software for Generalized Least-Squares Fitting". The conversion factors were then stored in the MOSFET software (mobileMOSFET® software version 2.0, Revision 7.0, Thomson-Nielsen) for immediate readout after each protocol had been performed. Direct calibration data entry using MOSFET's built-in calibration capability was employed to accommodate multiple tube potential calibrations, the least-square fit method was selected to verify that a given set of calibration factors obtained at 118 kVp with beam quality of 7.15 mmAl HVL may be used for different tube potentials with reasonable accuracy (within 5%).

Calibrated MOSFET detectors were then used to measure absorbed radiation dose for thyroid, mid-breast, breast and mid-lung in an anthropomorphic phantom at 100, 120 and 135 kVp at two different heart rate (HR) settings of 60 and 75 bpm with a scan field of view (S-FOV) of 320 mm, using 400 mA, 320 X 0.5 mm detectors/160 mm collimator width (160 mm range) [2].

Table 1: Protocol and absorbed organs dose measurements for 320 row detector scanner calculating [2] carcinogenesis risk estimates.

Author	# detector rows	Protocol	Breast dose	Lung dose	Thyroid dose
Nikolic et al.	320	320 row detector, S-FOV of 320 mm, 400 mA, 65% to R wave default padding, 0.35 sec rotation, 1.35 sec total scanning time, 0.5 mm scan slice and 160 mm collimator width (160 mm range), half reconstruction, 175 msec time resolution, effective 140 mAs,120 kVp, 60 beats per minute;	33.9 mGy	29.45 mGy	1.09 mGy

B. Cancerogenesis risk estimation

The lifetime attributable risk (LAR) based on organ measurements was adopted from BEIR VII report tabulation (Table 12D-1, page 311), and focused on radiation dose measurements of radiosensitive organs (lung, breast and thyroid exposed to radiation). To provide the most conservative cancerogenesis risk assessment as possible absorbed radiation doses for calcium scoring and contrast enhanced CCTA were added for each study and included in our analysis. Data acquired with 120 kVp tube voltage were selected as being both the average and most frequently used maximum tube voltage used in clinical practice.

C. Lifetime attributable risk (LAR) estimation

The lifetime attributable risk has been described in the BEIR VII report and is expressed by the formula: LAR (D, e) = $\sum$ M (D, e, a) S (a) /S (e) with D being the absorbed dose (in the BEIR VII report set as 0.1 Gy), e is the exposed age of the patient, a being the attained age which is from e+L to 100 (L being the risk-free latent period that equals 5) accounting for remaining lifetime, S (a) being the probability of survival until age a, and S (e) being the probability of survival until age e.

The lifetime attributable cancer risk (LAR) based on absorbed radiation dose for a given organ for each age group of presumed decennial screening was calculated based on linear interpolation of a single time 0.1 Gy radiation exposure data as presented in the BEIR VII report. For instance, the average dose for coronary CTA to the lungs performed with a 320 detector row scanner was 29.45 mGy at 120 kvp and a heart rate of 60 beats per minute. From the BEIR VII report, the lung cancer incidence for 50-year-old women is 230 cases per 100,000. Thus, the LAR from a 29.45 mGy dose is (29.45/100) X (230/100,000), or 0.07 %. This risk estimation methodology has been described and reported as acceptable in prior literature [4].

Additive lifetime attributable risk estimation for decennial generalized screening from age 50 to 70

For a hypothetical US nationwide generalized CCTA screening for coronary artery disease, the following assumptions were made: screening would be performed decennially for each individual for the ages 50, 60 and 70. Consequently, LARs for female and male lung, female and male thyroid, and female breast were added for CCTAs for the age 50 (LAR_{50}), 60 (LAR_{60}), and 70 (LAR_{70}) to obtain the cumulative LAR for female and male lung, female and male thyroid, and female breast cancer, respectively for such screening guidelines. For ages between 50-60, and 60-70, linear interpolation of the BEIR VII data was used. Our approach is similar to the one used by Einstein et al. , and can be utilized to determine different cumulative LARs [4]. The population size that would be subjected to such screening was assumed to be 18.8 million people and the annual incidence of occurrence of sudden cardiac death was assumed to be 355.000, 94 % of which have at least one stenosis > 75% [7].

RESULTS

LAR calculations for radiosensitive organs for ages 50, 60 and 70 in males and females are tabulated in (Table 2) and figure 1 (a)

and 1 (b). Thyroid LAR is negligible for all ages and both genders regardless of which scanner is used. Amongst radiosensitive organs, all evaluated ages and both genders, LAR is otherwise lowest for female breast at age 70 (0.002 %) and highest for female lung at age 50 (0.068 %).

Cumulative cancerogenesis risk calculation and cancer specific mortality based on the BEIR VII report for men and women assuming decennial screening between ages 50 and 70 are shown in (Table 3). These risks are likewise negligible for the thyroid gland for both genders. Cumulative cancerogenesis risk for the recommended CCTA screening assumption using the 320 row detector scanner is 0.17 % for the female lung and 0.026 % for the female breast. Similarly, the cumulative cancerogenesis risk for CCTA screening assumption is 0.079% for male lung using the 320 row detector scanner. By comparison, common risk factors which increase cancer risks are as follows: 16–fold for lung cancer in persistent smokers [8], 2-fold for breast cancer with a first degree family member history of breast cancer [9] and 10–fold for thyroid cancer with family member history of thyroid cancer [10]. By way of comparison, CCTA screening in a population assumed to be 18.8 million in size would prevent occurrence of sudden cardiac death in at least some of estimated 355.000 patients, 94 % of which have at least one stenosis > 75%.

DISCUSSION

In our study we estimated specific organ cancerogenesis risks using 320 detector row scanners and similar organ absorption dose measurement methodologies. This is an improvement to prior organ cancerogenesis estimates that solely relied on respective "in house" absorbed radiation dose measurements in association with CCTA and are therefore more anecdotal in nature. In several previously published studies, radiation absorbed dose was calculated based on the volume CT dose index ($CTDI_{vol}$) and dose length product (DLP) as proposed by the European Working Group for Guidelines on Quality Criteria for Computed Tomography [11-19]. Although these studies have withstood and passed peer review scrutiny, it should be noted that the CTDI is not meant to be used for dose calculations of individual patients, but rather as a quality assurance and an improvement tool that allows for dose comparisons for different types of CT scanners when the same protocol is applied, or for the same scanner if different protocols are evaluated. As such, it has no role in the calculation of absolute absorbed dose related to deterministic and stochastic risk assessment models.

In this study we focused on absorbed dose measurements of radiosensitive organs that are either directly within the CT radiation beam (lung, breast and skin tissue) or exposed to nearby scattered radiation (thyroid gland). Only one study that had been previously performed with a 320 row detector scanner could be included in this analysis. Yet, the stark differences of cancerogenesis risk reduction of > 30 % for the lung and > 50 % for the female breast for the 320 compared to 64 row CT

Table 2: Lifetime attributable risk (LAR) for cancer induction based on prior organ dose measurements.

Male lung				
Age at exposure	Author	Reported Dose	LAR	LAR in %
50	Nikolic et. al.	29.45	0.000297445	0.0297445
60	Nikolic et. al.	29.45	0.000262105	0.0262105
70	Nikolic et. al.	29.45	0.000191425	0.0191425
Female lung				
Age at exposure	Author	Reported Dose	LAR	LAR in %
50	Nikolic et. al.	29.45	0.00067735	0.067735
60	Nikolic et. al.	29.45	0.000591945	0.0591945
70	Nikolic et. al.	29.45	0.000432915	0.0432915
Female breast				
Age at exposure	Author	Reported Dose	LAR	LAR in %
50	Nikolic et. al.	22.8	0.0001596	0.01596
60	Nikolic et. al.	22.8	0.00007068	0.007068
70	Nikolic et. al.	22.8	0.00002736	0.002736
Female thyroid				
Age at exposure	Author	Reported Dose	LAR	LAR in %
50	Nikolic et. al.	1.09	0.000000436	0.0000436
60	Nikolic et. al.	1.09	0.000000109	0.0000109
70	Nikolic et. al.	1.09	3.27E-08	0.00000327
Male thyroid				
Age at exposure	Author	Reported Dose	LAR	LAR in %
50	Nikolic et. al.	1.09	0.000000436	0.0000436
60	Nikolic et. al.	1.09	3.27E-08	0.00000327
70	Nikolic et. al.	1.09	1.09E-08	0.00000109

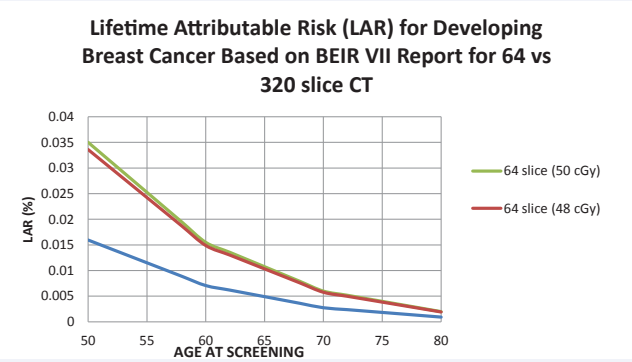

Figure 1a Reduction in Lifetime Attributable Risk (LAR) for Breast Cancer with 320 row CT v.s. 64 row CT.

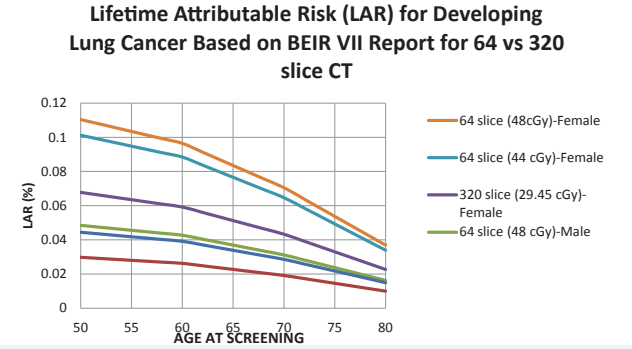

Figure 1b Reduction in Lifetime Attributable Risk (LAR) for Lung Cancer with 320 row CT v.s. 64 Slice CT.

Table 3: LAR for cancer induction/mortality from decennial screening in ages 50-70 for 64/320 row detector scanners.

Author and scanner type	Female lung	Male lung	Female breast	Female thyroid	Male thyroid
Nikolic et. al. (320): LAR	0.00170221	0.000750975	0.00025764	5.777E-07	4.796E-07
Nikolic et. al. (320): LAR in %	0.170221	0.0750975	0.025764	0.00005777	0.00004796
Nikolic et. al. (320): Mortality Risk in %	0.1552015	0.078926	0.007524	0.0	0.0

detector scanners suggest that an epidemiologically meaningful impact is likely due to the padding effects and internal filtration improvements associated with the 320 row detector. These improvements can reduce the stochastic risk with future coronary artery screening, and may cause a paradigm shift when weighing risks and benefits of such a screening program. Specifically, the cancerogenesis estimates data that were calculated based on the 320 row detector CCTA would result in a combined cumulative cancer incidence of less than 1 in 500 for breast and lung cancer in women and a cumulative cancer incidence of less than 1 in 1000 for lung in men. As such, these cancerogenesis risk estimates are magnitudes lower than common risk factors such as persistent smoking for the development of lung (16-fold) or history of breast cancer in a first degree relative for the development of breast cancer (2-fold) [8,9] It should be noted, that cancerogenesis incidence estimates do not equate to cancer induced mortality data. Our data may underestimate the role of other causes of death and also does not account for the capability of CCTA to detect other clinically relevant findings such as clinically occult pulmonary embolism, malignant pulmonary nodules or other undetected cardiopulmonary abnormalities which may also translate into improved patient outcome. In terms of expected benefits of a screening program as the one suggested, the population size that would be submitted to such screening was previously assumed to be 18.8 million people and the annual incidence of occurrences of sudden cardiac death as 355,000, 94 % of which have at least one stenosis > 75% [7]. As such, we believe that CCTA screening along the lines suggested with use of 320 row detector scanning and associated improvements in padding and filtration techniques can be justifiably advocated. This is in contradictory to prior statements that have identified absorbed radiation associated with CCTA as a primary concern to deny CCTA as a screening tool for coronary artery disease [5].

Unlike for lung and female breast, higher absorbed thyroid doses and resulting stochastic risks were found for the 320 detector row scanner compared to with a 64 row detector scanner. This discordance can be explained by differences in measurement technique. Specifically, measurements with the 320 row detector scanner were performed with the MOSFET detectors on top of the phantom surface, whereas Hurwitz et. al. obtained measurements within the phantom and more closely simulated the anatomic position of the thyroid gland, thus resulting in less scatter and more dose absorption of interposed tissue and hence lower absorbed dose readings of the detectors [3]. However, thyroid dose absorptions are negligibly low in both studies, and the dose that is absorbed by the thyroid gland in association with CCTA can be safely considered as clinically inconsequential as the likelihood of cancer induction is close to zero based on BEIR VII data for patients between the ages of 50-70.

LIMITATIONS

The studies that were selected for comparative purposes used either an anthropomorphic phantom or an anthropomorphic mathematical phantom to measure the absorbed dose. Thus, this provided a certain degree of methodological measurement consistency for a greater transparency in inter-study comparisons of the combined equipment and CCTA protocol effects. Yet, the body mass index of the average patient as well as a potential screening subject may be greater than that of the phantom which may result in underestimation of the scatter radiation dose associated with CCTA. At the same time it should be noted that there are natural limitations to performing direct organ measurements in vivo and that internal organ point measurements in cadavers (the main conceivable alternative to a phantom) also has inherent inaccuracies due to tissue density differences between an actual patient and a bloodless cadaver fixated in formalin.

In addition, the use LAR to estimate cancerogenesis risk was based on the BEIR VII data, which has its own inherent limitations. A “subjective 95 % confidence interval” is assigned to the LAR in the BEIR VII report in acknowledgment of the uncertainties associated with data extrapolated from the Japanese survivors to the U. S. population.

CONCLUSION

Among radiosensitive organs, LAR is highest to the lung but relatively small compared with other more common cancerogenetic risk factors such as smoking. Compared to the 64 row detector, CCTA padding effects and internal filtration improvements associated with the 320 row detector scanner reduce absorbed dose to lung and female breast by > 30% and > 50 %, respectively. Corresponding epidemiologic cancerogenesis risk reduction to radiosensitive organs compared with the 64 row detector CCTA would help at least some of about 355,000 annual sudden cardiac death patients, 94 % of which have at least one stenosis > 75%, and would shift the risk to benefit ratio favorably towards the consideration of routine CCTA screening for patients between age 50-70.

REFERENCES

1. Hollingsworth CL, Yoshizumi TT, Frush DP, Chan FP, Toncheva G, Nguyen G, et al. Pediatric cardiac-gated CT angiography: assessment of radiation dose. AJR Am J Roentgenol. 2007; 189: 12-18.

2. Nikolic B, Khosa F, Lin PJ, Khan AN, Sarwar S, Yam CS, et al. Absorbed radiation dose in radiosensitive organs during coronary CT angiography using 320-MDCT: effect of maximum tube voltage and heart rate variations. AJR Am J Roentgenol. 2010; 195: 1347-1354.

3. Hurwitz LM, Reiman RE, Yoshizumi TT, Goodman PC, Toncheva G, Nguyen G, et al. Radiation dose from contemporary cardiothoracic multidetector CT protocols with an anthropomorphic female

phantom: implications for cancer induction. Radiology. 2007; 245: 742-750.

4. Einstein AJ, Henzlova MJ, Rajagopalan S. Estimating risk of cancer associated with radiation exposure from 64-slice computed tomography coronary angiography. JAMA. 2007; 298: 317-323.

5. Gerber TC, Carr JJ, Arai AE, Dixon RL, Ferrari VA, Gomes AS, et al. Ionizing radiation in cardiac imaging: a science advisory from the American Heart Association Committee on Cardiac Imaging of the Council on Clinical Cardiology and Committee on Cardiovascular Imaging and Intervention of the Council on Cardiovascular Radiology and Intervention. Circulation. 2009; 119: 1056-1065.

6. Monson Richard R AH, Bingham E, Buffler PA, Cox R et al. Health risk from Exposure to low levels of ionizing radiation: BEIR VII-Phase 2. In, 2006.

7. Zanzonico P, Rothenberg LN, Strauss HW. Radiation exposure of computed tomography and direct intracoronary angiography: risk has its reward. J Am Coll Cardiol. 2006; 47: 1846-1849.

8. Peto R, Darby S, Deo H, Silcocks P, Whitley E, Doll R. Smoking, smoking cessation, and lung cancer in the UK since 1950: combination of national statistics with two case-control studies. BMJ. 2000; 321: 323-329.

9. Mun S, Ernst RD, Chen K, Oto A, Shah S, Mileski WJ. Rapid CT diagnosis of acute appendicitis with IV contrast material. Emerg Radiol. 2006; 12: 99-102.

10. Pal T, Vogl FD, Chappuis PO, Tsang R, Brierley J, Renard H, et al. Increased risk for nonmedullary thyroid cancer in the first degree relatives of prevalent cases of nonmedullary thyroid cancer: a hospital-based study. J Clin Endocrinol Metab. 2001; 86: 5307-5312.

11. Pflederer T, Jakstat J, Marwan M, Schepis T, Bachmann S, Kuettner A, et al. Radiation exposure and image quality in staged low-dose protocols for coronary dual-source CT angiography: a randomized comparison. Eur Radiol. 2010; 20: 1197-1206.

12. Rixe J, Conradi G, Rolf A, Schmermund A, Magedanz A, Erkapic D, et al. Radiation dose exposure of computed tomography coronary angiography: comparison of dual-source, 16-slice and 64-slice CT. Heart. 2009; 95: 1337-1342.

13. Takakuwa KM, Halpern EJ, Gingold EL, Levin DC, Shofer FS. Radiation dose in a "triple rule-out" coronary CT angiography protocol of emergency department patients using 64-MDCT: the impact of ECG-based tube current modulation on age, sex, and body mass index. AJR Am J Roentgenol. 2009; 192: 866-872.

14. Tatsugami F, Husmann L, Herzog BA, Burkhard N, Valenta I, Gaemperli O, et al. Evaluation of a body mass index-adapted protocol for low-dose 64-MDCT coronary angiography with prospective ECG triggering. AJR Am J Roentgenol. 2009; 192: 635-638.

15. Hosch W, Heye T, Schulz F, Lehrke S, Schlieter M, Giannitsis E, et al. Image quality and radiation dose in 256-slice cardiac computed tomography: comparison of prospective versus retrospective image acquisition protocols. Eur J Radiol. 2011; 80: 127-135.

16. Bischoff B, Hein F, Meyer T, Krebs M, Hadamitzky M, Martinoff S, et al. Comparison of sequential and helical scanning for radiation dose and image quality: results of the Prospective Multicenter Study on Radiation Dose Estimates of Cardiac CT Angiography (PROTECTION) I Study. AJR Am J Roentgenol. 2010; 194: 1495-1499.

17. Arnoldi E, Johnson TR, Rist C, Wintersperger BJ, Sommer WH, Becker A, et al. Adequate image quality with reduced radiation dose in prospectively triggered coronary CTA compared with retrospective techniques. Eur Radiol. 2009; 19: 2147-2155.

18. Hausleiter J, Meyer T, Hadamitzky M, Huber E, Zankl M, Martinoff S, et al. Radiation dose estimates from cardiac multislice computed tomography in daily practice: impact of different scanning protocols on effective dose estimates. Circulation. 2006; 113: 1305-1310.

19. Horiguchi J, Kiguchi M, Fujioka C, Shen Y, Arie R, Sunasaka K, et al. Radiation dose, image quality, stenosis measurement, and CT densitometry using ECG-triggered coronary 64-MDCT angiography: a phantom study. AJR Am J Roentgenol. 2008; 190: 315-320.

Cite this article

Nikolic B, Khosa F, Lin PJ, Khan AN, Shuaib W, et al. (2013) Cancerogenesis Risk for Coronary CTA Using 64 And 320-Row CT. J Radiol Radiat Ther 1(3): 1019.