Is computed tomography angiography really useful in screening patients with high risk of coronary artery disease?

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Background

- **Coronary artery disease (CAD) and its complications are the primary cause of mortality, morbidity, and healthcare expenditures in leading countries.**
- **Noninvasive stress testing can provide useful and often indispensable information to establish the diagnosis and estimate the prognosis in patients with chronic stable angina.**

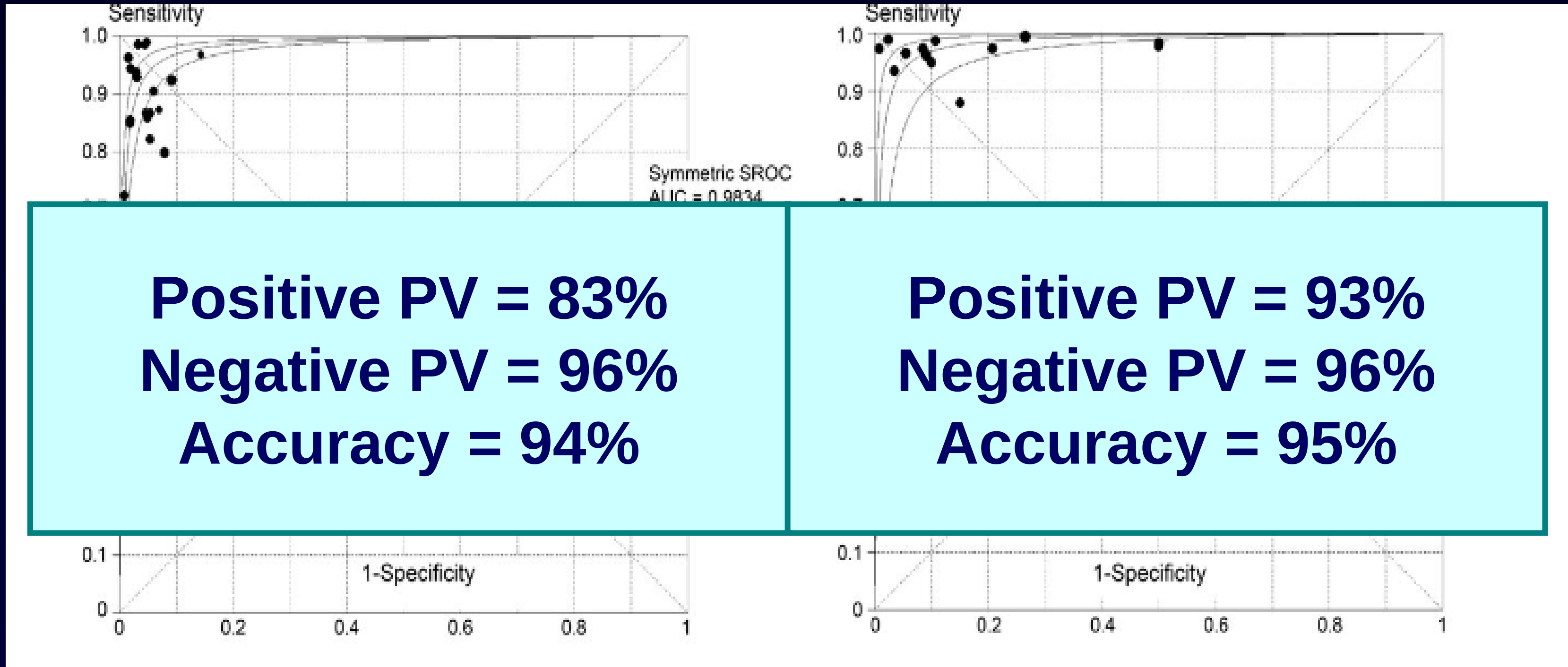
Lloyd-Jones D et al. Circulation 2009
Rosamond W et al. Circulation 2008
Gibbons RJ et al. Circulation 2002

Background

- Noninvasive stress testing include exercise electrocardiography, stress myocardial perfusion imaging, pharmacological nuclear stress testing, and stress echocardiography.
- In addition, the introduction of multi-slice-computed tomography coronary angiography (CTA) has changed the field of non-invasive imaging.

How good is CTA?

64-slice CT vs. coronary angiography (meta-analysis)



Positive PV = 83%
Negative PV = 96%
Accuracy = 94%

Positive PV = 93%
Negative PV = 96%
Accuracy = 95%

Per-segment (19 studies)

Per-patient (13 studies)

Abdulla J et al. European Heart Journal 2007.

64-slice CT vs. coronary angiography (Meta-analysis)

- **The results of this study show that 64-slice CT angiography can be used to rule out or detect the presence of CAD in *carefully selected populations suspected for CAD*.**

Abdulla J et al. European Heart Journal 2007.

Diagnostic accuracy of CCTA for obstructive CAD

- 64-detector row CCTA (2005):
  > 50 studies have been published
  CCTA vs Conventional coronary angiography (CCA)

- ACCURACY, CORE64, Meijboom et al

ACCURACY trial

- Prospective multicenter trial of stable chest pain patients without known CAD
- N=230 subjects, both CCTA and CCA
- Prevalence of CAD: 25%
- sensitivity, specificity, positive predict value (PPV), negative predictive value (NPV) to detect ≥ 50% or ≥ 70% stenosis

Budoff MJ, et al., JACC 2008

ACCURACY trial

Table 2 Patient-Based Analysis

	Estimate, %	95% CI, %	Subjects in Group, n	Subjects Correct by CCTA, n
≥50% stenosis				
Sensitivity	95	85–99	55	52
Specificity	83	76–88	172	142
PPV	64	53–75	81	52
NPV	99	96–100	143	142
≥70% stenosis				
Sensitivity	94	79–99	31	29
Specificity	83	77–88	196	162
PPV	48	35–62	60	29
NPV	99	96–100	164	162

CCTA = coronary computed tomographic angiography; CI = confidence interval; NPV = negative predictive value; PPV = positive predictive value.

The 99% NPV : CCTA as an effective noninvasive alternative to ICA to rule out obstructive coronary artery stenosis

CORE64 study

- Prospective multicenter trial
- N=291, both with and without known CAD with baseline CACS < 600 Agatston units
- Multidetector CT angiography as compared with conventional coronary angiography
- Prevalence of CAD: 56%

Miller JM, et al. NEJM 2008

Table 4. Diagnostic Accuracy of 64-Row Multidetector CT Angiography (MDCTA) for Patient- and Vessel-Based Detection of Coronary Stenosis of ≥50%.*

Measure of Accuracy	Patient-Based Detection				
	Quantitative MDCTA (N=291)	Visual MDCTA (N=291)			
AUC — median (95% CI)	0.93 (0.90–0.96)	0.93 (0.89–0.95)			
Stenosis by CCA — no.	163	163			
Stenosis by MDCTA — no.	152	146			
False positive — no.	13	11			
False negative — no.	24	28			
Sensitivity — % (95% CI)	85 (79–90)	83 (76–88)			
Specificity — % (95% CI)	90 (83–94)	91 (85–96)			
Positive predictive value — % (95% CI)	91 (86–95)	92 (87–96)			
Negative predictive value — % (95% CI)	83 (75–89)	81 (73–87)			
	Vessel-Based Detection†				
	Three-Vessel Quantitative MDCTA (N=866)	Three-Vessel Visual MDCTA (N=868)	LM–LAD (N=291)	LCX (N=288)	RCA (N=287)
AUC — median (95% CI)	0.91 (0.89–0.93)	0.90 (0.88–0.93)	0.88 (0.84–0.92)	0.92 (0.88–0.95)	0.93 (0.89–0.95)
Stenosis by CCA — no.	269	271	111	82	76
Stenosis by MDCTA — no.	247	243	110	73	64
False positive — no.	44	41	21	13	10
False negative — no.	66	69	22	22	22
Sensitivity — % (95% CI)	75 (69–81)	75 (68–80)	80 (72–87)	73 (63–82)	71 (60–80)
Specificity — % (95% CI)	93 (90–94)	93 (91–95)	88 (83–92)	94 (89–96)	95 (91–97)
Positive predictive value — % (95% CI)	82 (77–86)	83 (78–87)	81 (72–87)	82 (72–89)	84 (73–91)
Negative predictive value — % (95% CI)	89 (86–92)	89 (86–91)	88 (82–92)	90 (85–93)	90 (85–93)

Diagnostic accuracy of CCTA for obstructive CAD

Table 4 Diagnostic Performance of 64-Slice CTCA for the Detection of ≥50% Stenosis on QCA in the Per-Patient Analysis (95% CI)

	Prevalence of Disease, %	n	TP	TN	FP	FN	Sensitivity, %	Specificity, %	PPV, %	NPV, %
Patient-based analysis	68	360	244	73	41	2	99 (98–100)	64 (55–73)	86 (82–90)	97 (94–100)
Stable angina pectoris	63	233	145	56	31	1	99 (98–100)	64 (53–74)	82 (76–88)	98 (95–100)
Non–ST-segment elevation acute coronary syndrome	79	127	99	17	10	1	99 (97–100)	63 (45–81)	91 (85–96)	94 (84–100)
Men	76	245	185	38	20	2	99 (97–100)	66 (53–78)	90 (86–94)	95 (88–100)
Women	51	115	59	35	21	0	100 (100–100)	63 (50–75)	74 (64–83)	100 (100–100)
Typical angina pectoris	70	151	104	31	15	1	99 (97–100)	67 (54–81)	87 (81–93)	97 (91–100)
Atypical angina pectoris	50	82	41	25	16	0	100 (100–100)	61 (46–76)	72 (60–84)	100 (100–100)
Unstable angina pectoris	75	77	57	13	6	1	98 (95–100)	68 (48–89)	90 (83–98)	93 (79–100)

Table 1 Summary of Diagnostic Performance of 64-Detector Row CCTA From Prospective Multicenter Studies

			Patient Type							
	n	CAD Prevalence	Stable	Unstable	No Known CAD	Known CAD	Sensitivity	Specificity	PPV	NPV
ACCURACY (7)	230	25%	X		X		95%	83%	64%	99%
CORE64 (8)	291	56%	X		X	X	85%	90%	91%	83%
Meijboom et al. (9)	360	68%	X	X	X		99%	64%	86%	97%

CAD = coronary artery disease; CCTA = cardiac computed tomography angiography; NPV = negative predictive value; PPV = positive predictive value.

Limitations of CTA

- **Some preclusion criteria restricted the number of eligible patients prior to scanning.**
- **The estimated prevalence of CAD based on per-segment compared per-patient analysis was an expected much lower (19 vs. 57.5%).**
- **Motion artifacts**
  - **Breath holding, stable and slow heart rate.**
  - **90% need beta-blockers.**
  - **<60% achieve adequate heart rate control.**
- **Metallic objects (surgical clip, marker, wire, and stents) and extensive calcification are big issues.**
- **High radiation dose and the risk of cancer.**

Abdulla J et al. European Heart Journal 2007.

What are the current indication of CTA?

AHA scientific statements of CTA

- **Class I Indication**
  - No multivendor trial data are available for coronary CTA (LOE C)
  - CTA results should describe any limitations of technical quality (LOE A)

- **Class IIa Indication**
  - Greatest and reasonable for symptomatic patients who are intermediate risk for CAD after initial risk stratification, including equivocal stress test results (LOE B)
  - Anomalous coronary artery evaluation (LOE B)

Bluemke DA et al, Circulation 2008

AHA scientific statements of CTA

- **Class IIb Indication**
  - The presence of pronounced coronary calcification (LOE B)
- **Class III Indication**
  - No coronary CTA should be used to screen CAD routinely (LOE C)
  - High risk patients who have a very low pretest likelihood of coronary stenoses (LOE C)
  - Patients who have a high pretest likelihood of coronary stenoses and require PCI or angiogram (LOE C)

Bluemke DA et al, Circulation 2008

Inappropriate indications of CTA

- **Chest pain**
  - High pre-test probability of CAD
- **Acute chest pain**
  - High pre-test probability of CAD
  - ST-segment elevation on ECG and/or positive cardiac enzymes
- **Asymptomatic patients**
  - Low CHD risk (Framingham risk criteria)
  - Moderate CHD risk (Framingham risk criteria)
- **General population**
  - Low CHD risk (Framingham risk criteria)
- **Chest pain with prior test results**
  - Evidence of moderate to severe ischemia on stress test (exercise, perfusion, or stress echo)

Hendel RC et al, JACC 2006

Appropriate indications of CTA

- **Chest pain**
  - Intermediate pre-test probability of CAD
  - ECG un-interpretable or unable to exercise
- **Chest pain with prior test results**
  - Un-interpretable or equivocal stress test (Exercise, perfusion, or stress echo)
- **Acute chest pain**
  - Intermediate pre-test probability of CAD
  - No ECG changes and serial enzymes negative
- **Evaluation of intra-cardiac structures**
  - Suspected coronary anomalies

Hendel RC et al, JACC 2006

CTA in Evaluation of ACS

- Advantages
  - CTA can definitively establish or exclude CAD as the cause of chest pain in low-risk (normal ECG and negative cardiac enzymes) acute chest pain patients.
  - CTA evaluation reduced diagnostic time and lowered costs compared with standard of care.
- Limitations
  - Inability to determine the physiological significance of intermediate severity coronary lesions and cases with inadequate image quality are present limitations.

Goldstein JA et al, JACC 2007

Is CTA useful in screening individual high risk patients?

Diabetes Mellitus

- Screening asymptomatic patients remains uncertain, because of limited database and the lack of prospective clinical trials.

- The coronary calcium score
  - An excellent marker for coronary atherosclerotic burden.
  - Identifies asymptomatic individuals at higher risk for inducible ischemia.
  - Should be used with full knowledge of patient's complete cardiovascular risk profile.
  - Not valuable in low Framingham risk.
  - May be useful as screening tool in intermediate risk

Bax JJ et al, Diabetic care 2007

Diabetes Mellitus

- There was only limited support for coronary calcium testing of patients at intermediate risk, with a class IIb recommendation.
- Usefulness of screening asymptomatic intermediate risk populations with CTA is currently unknown.

Bax JJ et al, Diabetic care 2007

Diabetes Mellitus

- **As previous recommendations for stratifying diabetic patients based on risk factors have not proven effective, the question remains whether there are diabetic patients in whom CTA would seem particularly appropriate.**

- **Conventional coronary angiography remains the key technique for diagnosing lesions and is essential for angioplasty, useful for treating diabetics and other patients with new stent devices.**

Bax JJ et al, Diabetic care 2007
Bordier L et al, Diabetics and metabolism 2008

Chronic Kidney Disease and End-Stage Renal Disease

- Patients with CKD and ESRD often die from cardiovascular diseases.
- The AHA has recommended that these patients be placed in the "highest risk" category and receive aggressive prevention.
- The coronary artery calcium
  - High prevalence in patients with ESRD.
  - Not well defined as a marker of cardiovascular risk.
  - Debating results as association with luminal stenosis on CAG or mortality.

Bonow RO et al, circulation 2007

Chronic Kidney Disease and End-Stage Renal Disease

- In summary, the role of coronary calcium scoring in determining risk in patients with CKD and/or ESRD is unclear due to a limited number of clinical studies in these populations.

- Further prospective studies are needed to determine the utility of coronary calcium testing in patients with CKD and ESRD for predicting risk for CVD events.

Bonow RO et al, circulation 2007

Why CTA should not be used for screening asymptomatic high risk patients?

- The risk of CTA may outweigh the potential benefits in asymptomatic patients.
- No study has demonstrated an association between change in coronary plaque burden by CTA and improved outcome.
- Given the prevalence of high risk patients on the basis of risk factors and the high cost of CTA, the cost-effectiveness of screening with CTA is likely to be poor.

Kramer CM, Circulation 2008

Case #1

Patient’s Profile

- 62 year old woman
- Diabetes mellitus, oral hypoglycemic agents for 3 years
- Intermittent atypical chest discomfort

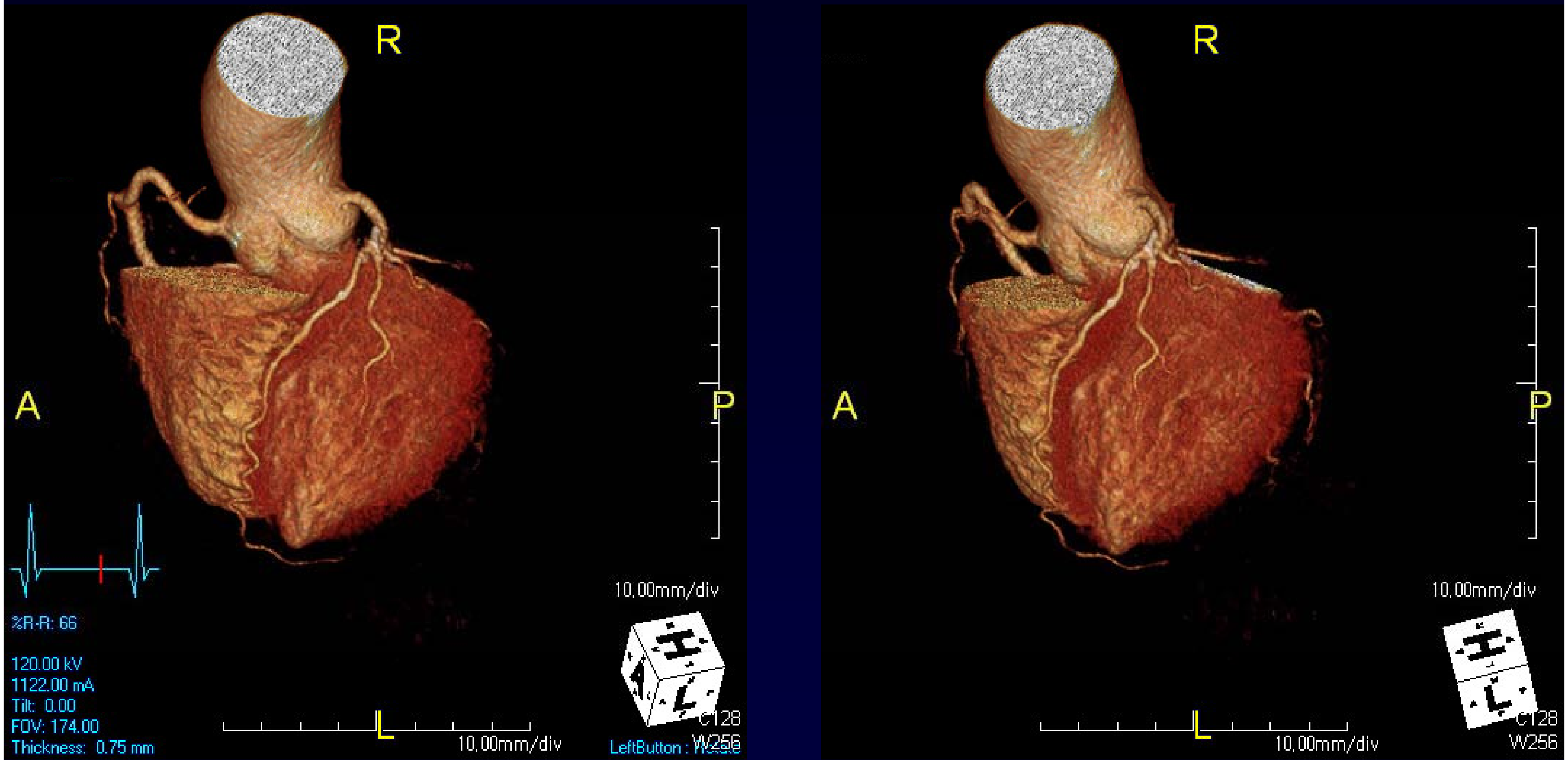
CT angiography

RCA: No significant luminal narrowing at RCA

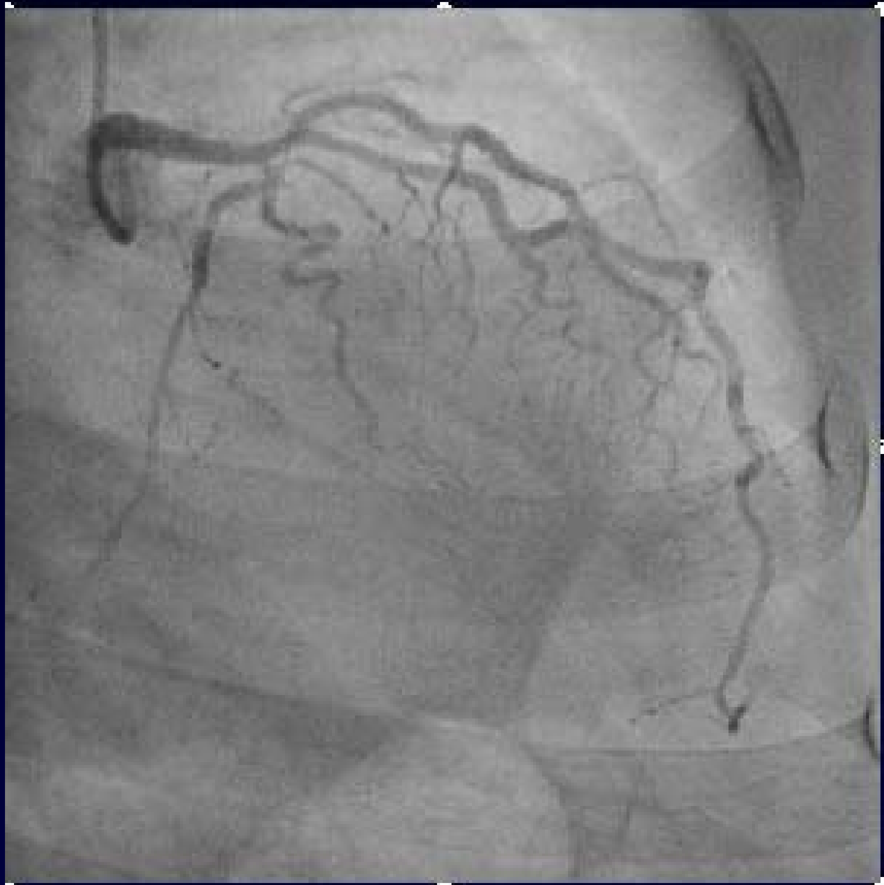
CT angiography

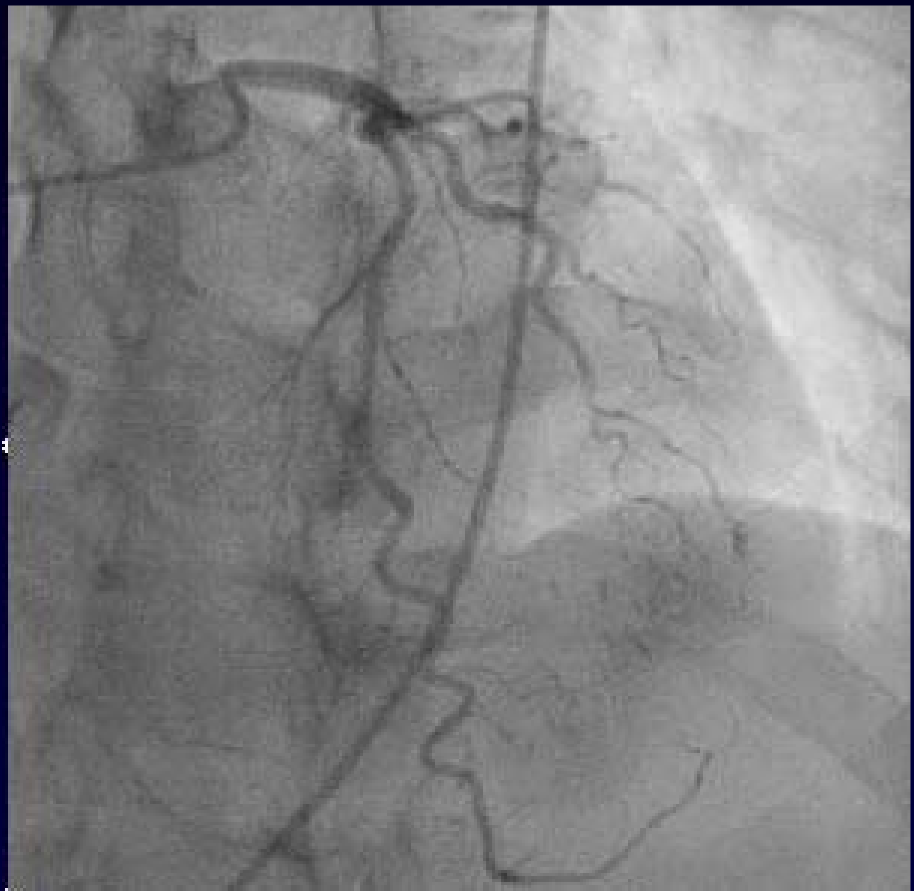
Lt main: mixed plaque(1) at LM with moderate (50-70%) stenosis.
LAD: A mixed plaque at m-LAD with moderate (50-70%) stenosis.
A calcified plaque at m-LAD with minimal (30%) stenosis.

CT angiography



Coronary angiography





Coronary angiography

Coronary angiography

Coronary angiography

Case #2

Patient's Profile

- 70 year old man
- Old pulmonary tuberculosis
- Known hypertension, DM
- Asymptomatic

CT angiography

RCA: Diminitive, one calcified plaque, m-RCA, without significant stenosis.

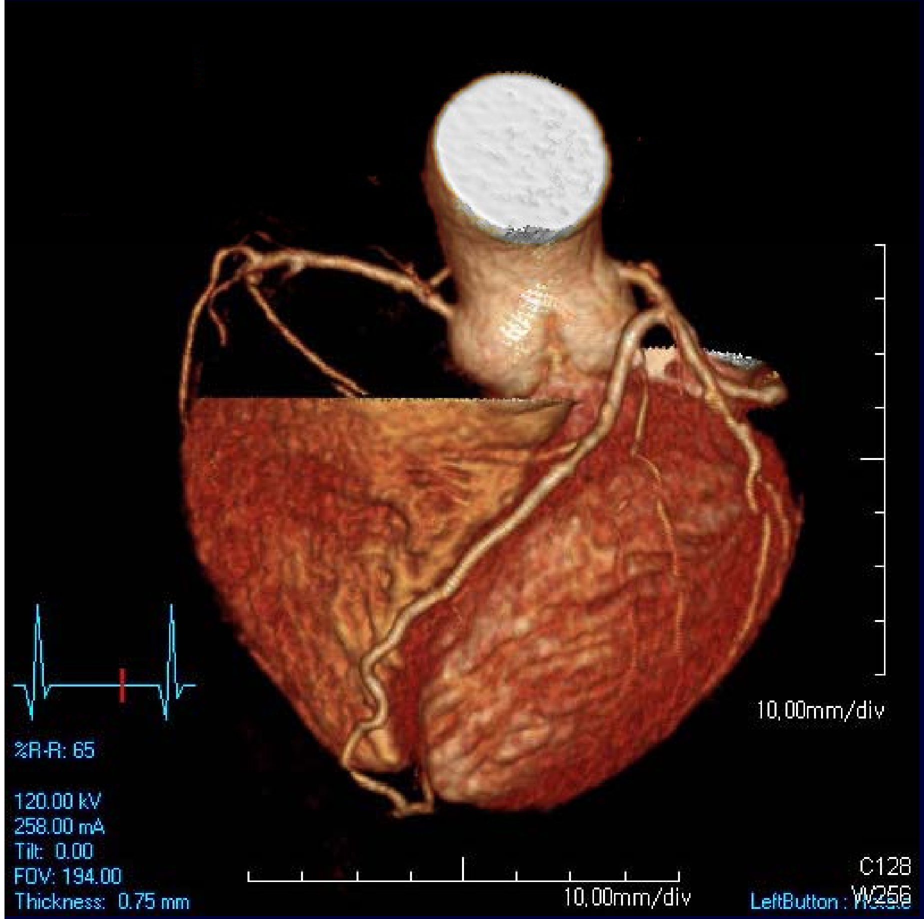
CT angiography

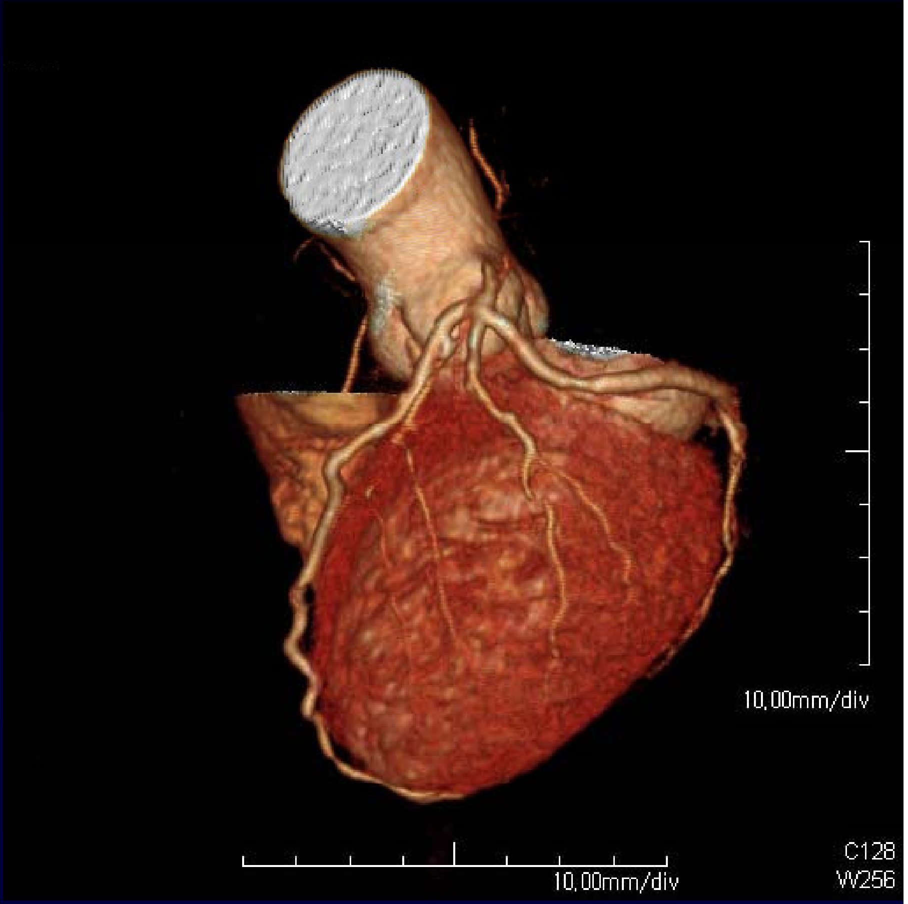
LCx; No evidence of significant luminal narrowing or stenosis.

CT angiography

LM: One non-calcified plaques, moderate luminal stenosis (50-70%)
LAD: One non-calcified plaque, p-LAD, mild stenosis (30-50%),
One mixed plaque, m-LAD, moderate stenosis (50-70%)

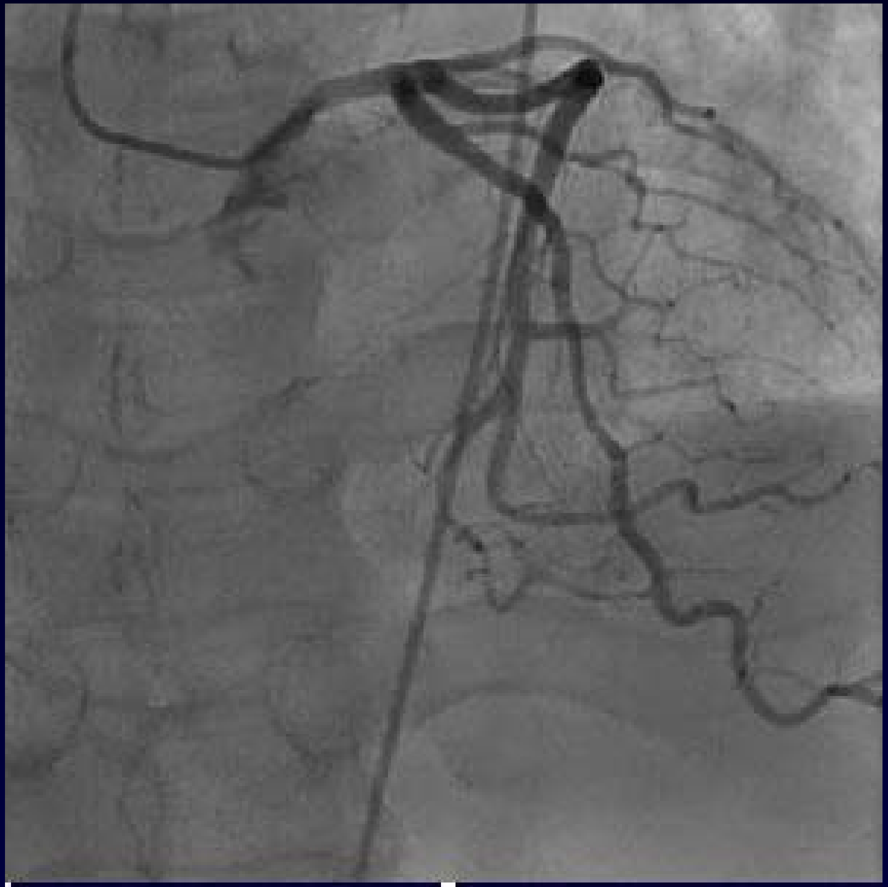
CT angiography

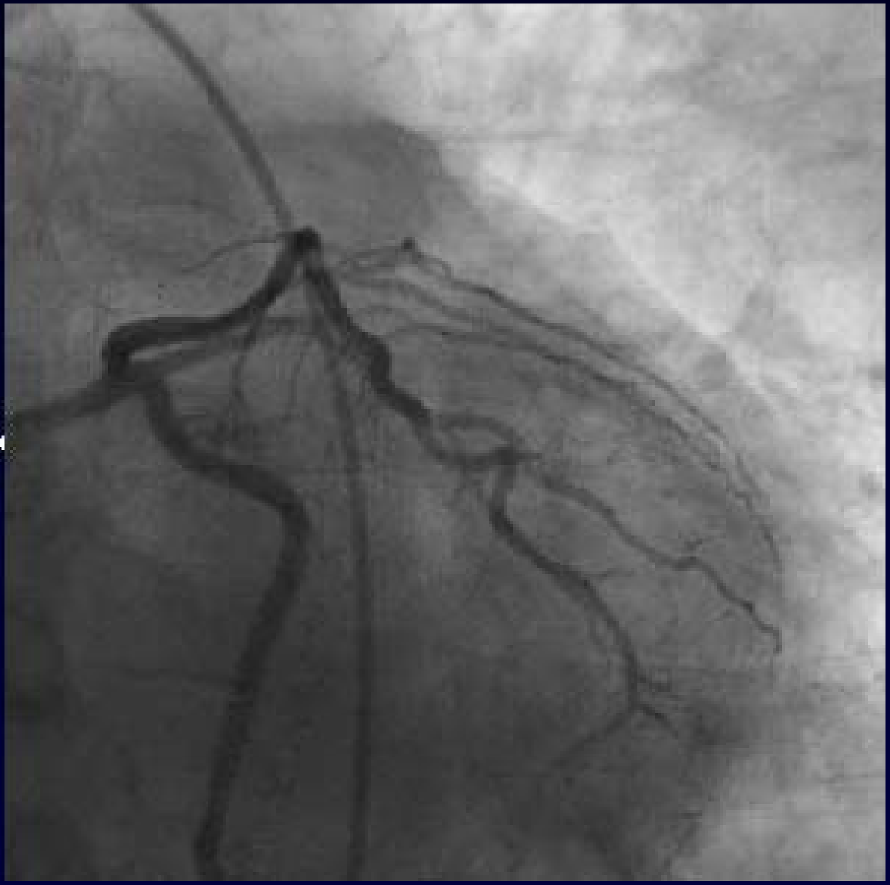




Coronary angiography

Coronary angiography





Case #3

Patient's Profile

- 54 year old woman
- No cardiovascular risk factors
- Intermittent effort-related chest discomfort for 7 months
- Treadmill test: positive at 4th stage in Bruce protocol

CT angiography

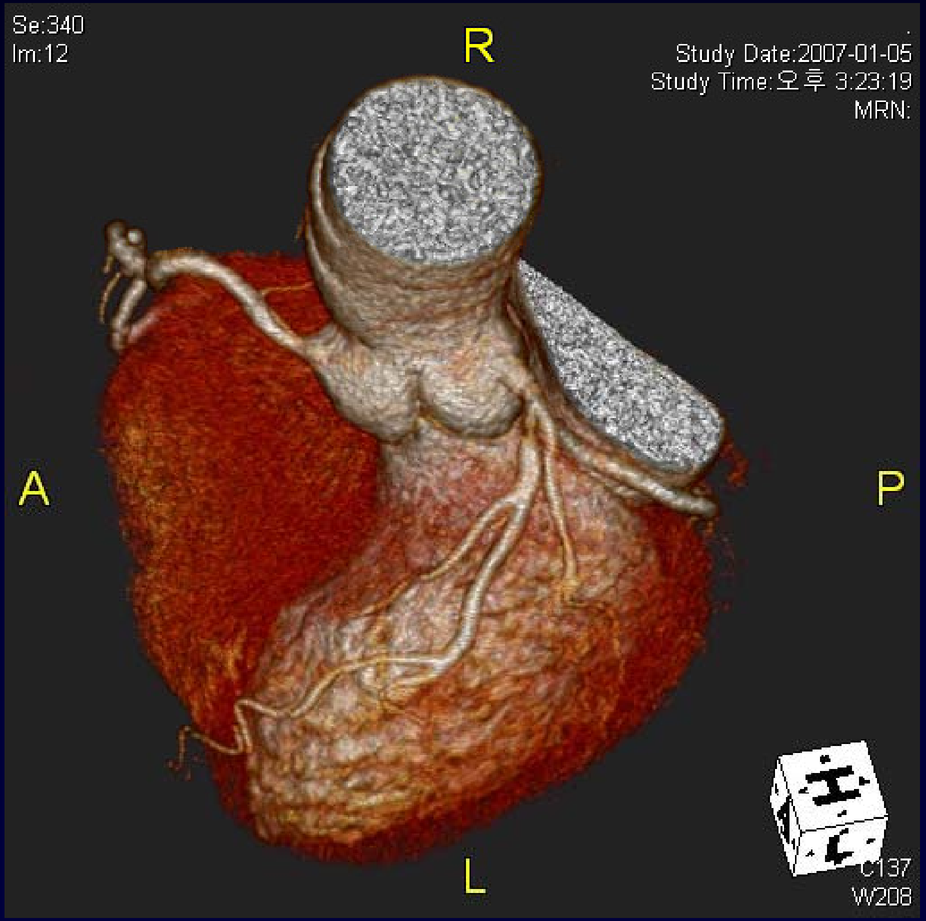
Coronary angiography

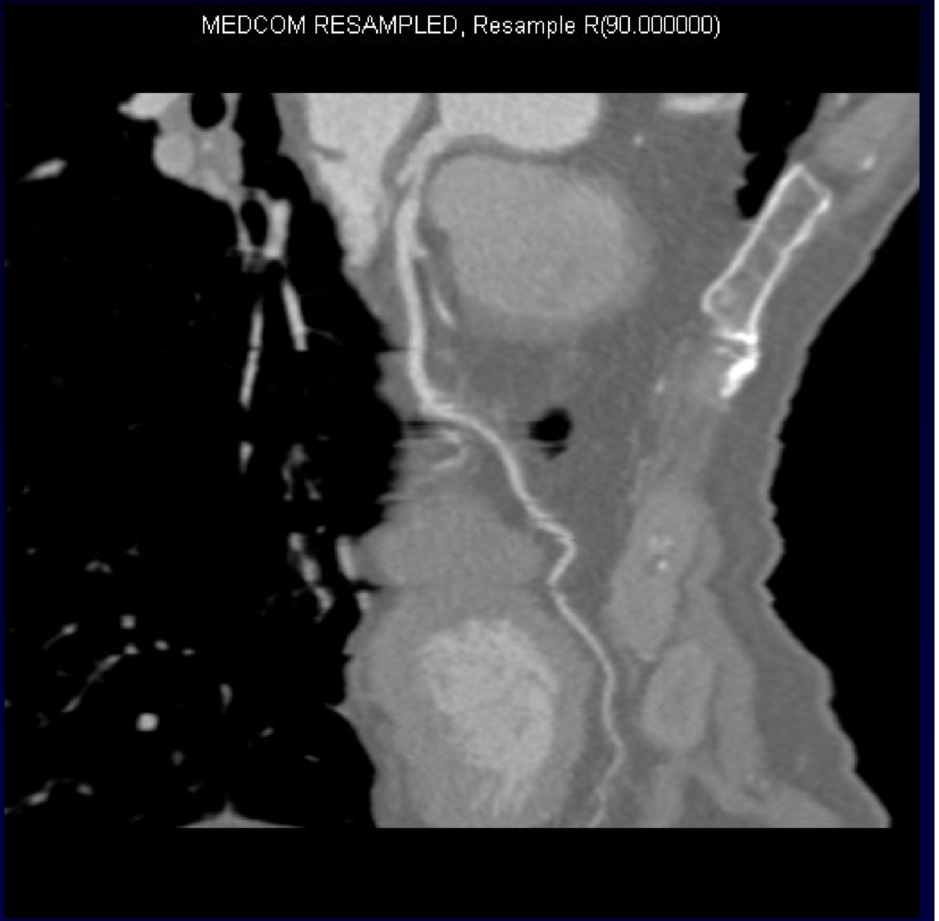
Case #4

Patient's Profile

- 73 year old man
- Hypertension for 8 months
- Effort-related chest pain for 8 months
- Treadmill test: Equivocal at 3rd stage in Bruce protocol

CT angiography

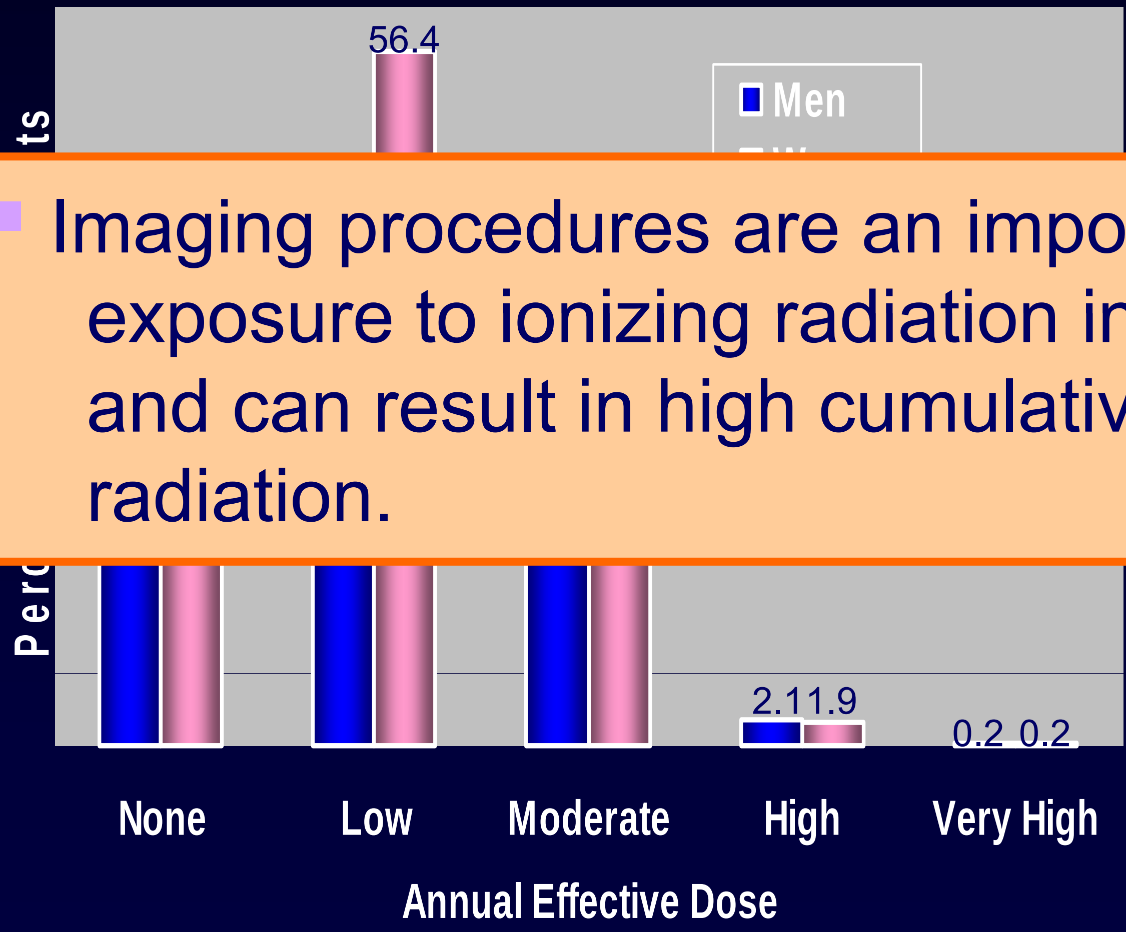




Coronary angiography

Dark side of CTA

Annual Low-dose Ionizing Radiation Exposure from Medical Imaging



- Imaging procedures are an important source of exposure to ionizing radiation in the United States and can result in high cumulative effective doses of radiation.

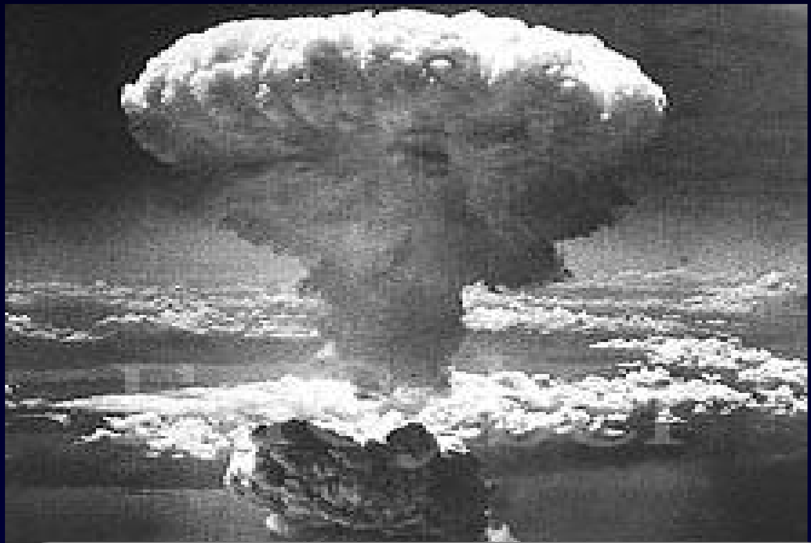
Fazel R et al, NEJM 2009

Effective Doses in Selected Radiological Studies

Imaging mode	Representative effective dose value (mSv)	Range of reported effective dose value (mSv)
Chest x-ray	0.1	0.05-0.24
Coronary angiography	16	5-32
Single source 64-slice coronary CTA	15	12-18
- with tube current modulation	9	8-18
Sestamibi stress/ test	9	
Thallium stress/ test	41	

Gerber TC, Circulation 2009

Cancer and Radiation



Japanese Atomic-bomb survivors
→ cancer risk (5-150 mSv)
Mean dose 40 mSv

Radiation workers in the nuclear industry
→ Cancer risk ↑
Mean dose 20 mSv

Single chest CT scan
Equivalent of 3 years of background radiation

1.5-2% of all cancers in United States may be attributable to the radiation from CT studies

Brenner DJ et al, NEJM 2007

Safety of CCTA

- Among the numerous methods of performing CCTA, radiation doses can vary by an order of magnitude

- In PROTECTION I, 120 sites reported radiation dose estimates from CCTA
- Average Radiation dose : 12 mSv (4~30 mSv)
- approximately 4 times that derived from the annual background radiation from radon, twice amount of diagnositc coronary angiography

Safety of CCTA

- In an effort to minimize radiation dose from CCTA:
  Automated tube current modulation,
  Electrocardiographic modulation
  Prospective axial triggering
  Reduced tube voltage
  Iterative reconstruction techniques

→ more than a 90% radiation dose reduction to < 1mSv

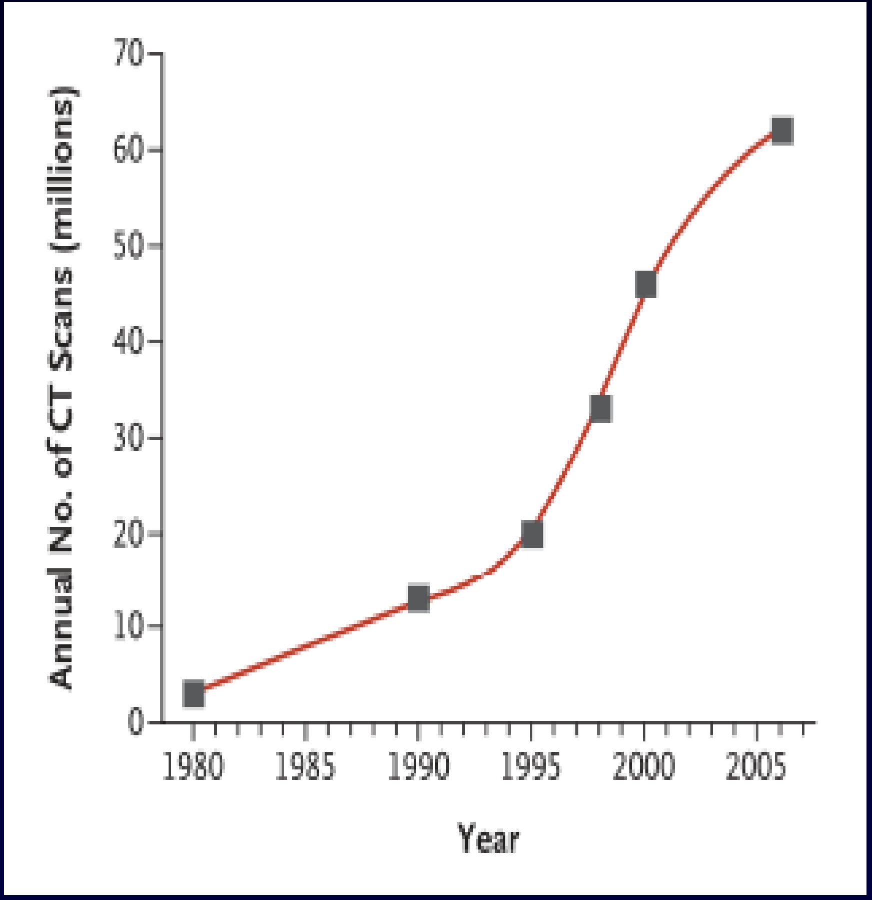
- Advance of CT technology can reduce radiation dose

Risks of Radiation with CTA

- CTA involves much higher doses of radiation, resulting in a marked increase in radiation exposure in the population.
- CTA imaging can result in high cumulative doses of radiation.
- Use of CTA is associated with a nonnegligible lifetime attributable risk of cancer.
- This risk varies markedly and is considerably greater for women, younger patients.

Brenner DJ et al, NEJM 2007
Einstein AJ et al, Circulation 2007
Fazel R et al, NEJM 2009

CT scans in the United States



Estimated number of CT scans performed annually in the United States.

The most recent estimate of 62 million CT scans in 2006.

Brenner DJ, NEJM 2007

Use of CTA according to Risk

Low risk patients

- Risk outweigh potential benefits
- CTA is not recommended for low risk patients

Intermediate risk patients

- Appropriate in chest pain
- Equivocal stress test
- Inconclusive in ACS patients

High risk patients

- Concerns regarding radiation dose limit the use of coronary CTA
- CTA is not recommended for these individuals

Noninvasive Coronary Artery Imaging

Magnetic Resonance Angiography and Multidetector Computed Tomography Angiography

A Scientific Statement From the American Heart Association Committee on Cardiovascular Imaging and Intervention of the Council on Cardiovascular Radiology and Intervention, and the Councils on Clinical Cardiology and Cardiovascular Disease in the Young

David A. Bluemke, MD, PhD, FAHA, Chair; Stephan Achenbach, MD; Matthew Budoff, MD, FAHA; Thomas C. Gerber, MD, FAHA; Bernard Gersh, DPhil, MD, FAHA; L. David Hillis, MD; W. Gregory Hundley, MD, FAHA; Warren J. Manning, MD, FAHA; Beth Feller Printz, MD, PhD; Matthias Stuber, PhD; Pamela K. Woodard, MD, FAHA

Concerns regarding radiation dose limit the use of coronary CTA in high-risk patients who have a very low pretest likelihood of coronary stenoses; patients with a high pretest likelihood of coronary stenoses are likely to require intervention and invasive catheter angiography for definitive evaluation; thus, CTA is not recommended for those individuals. (**Class III, level of evidence C**)

(*Circulation*. 2008;118:586-606.)

Conclusions

- Use of CTA is not as good as coronary angiography.
- CTA should not be used for routine screening.
- CTA is not recommended in high risk patients.
- Patients with chest pain, intermediate risk for CAD, and equivocal stress test results are beneficial.
- ACS Patients with low to intermediate risk need more data.
- Large potential risks for radiation and costs.

Thank you for your attention !!