Coronary Atherosclerotic Plaque Imaging with ECG-gated CT

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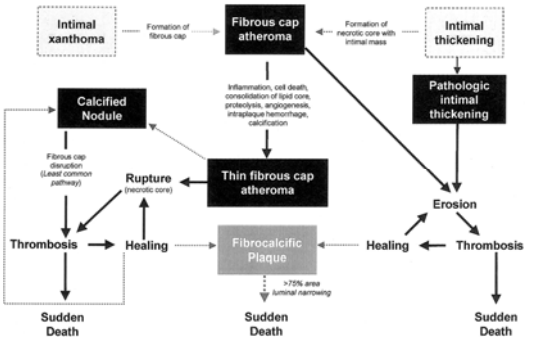
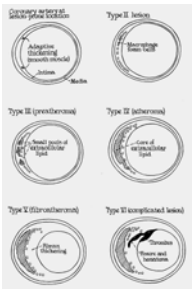
ECG-gated MDCT

1. Detection of coronary artery stenosis / occlusion
2. Coronary calcium scoring
3. Evaluation of atherosclerotic plaque
4. Evaluation of stent patency
5. Postoperative evaluation of bypassed vessels
6. Myocardial imaging
7. Evaluation of myocardial function
8. Coronary artery anomalies

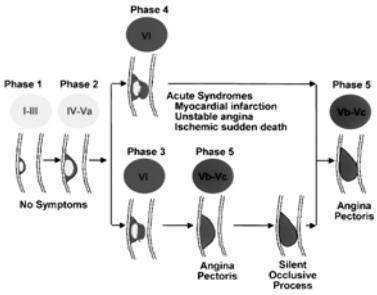
Coronary Atherosclerosis



Coronary Atherosclerosis



Stary, Circulation 1995

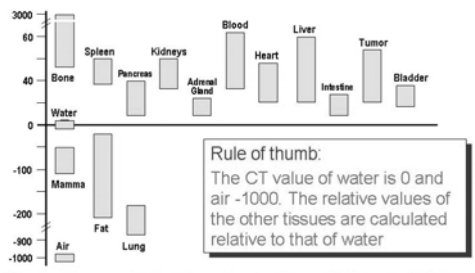


Fayad, Circ Res 2001

Imaging Modality

- IVUS: Clinical gold standard
  - Characterization: soft, fibrotic, calcified
- Angioscopy
- MRI
  - Coronary MRA, Wall imaging
  - New contrast media: ex. USPIO (macrophage)
- CT
  - Coronary calcium scoring
  - Coronary CTA

CT Density



This is the so-called CT number in Hounsfield unit (HU)

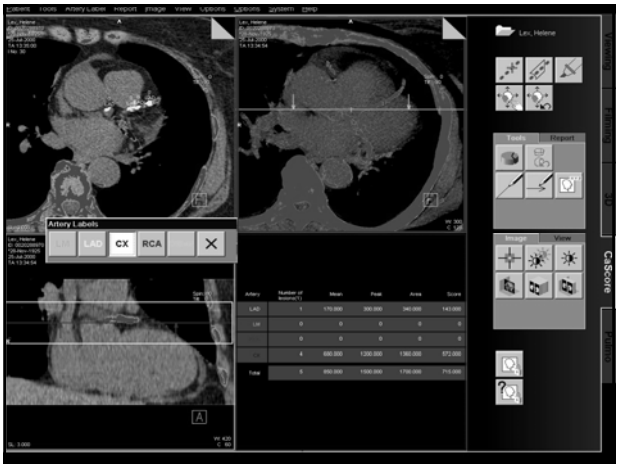
CT for Coronary atherosclerosis

- Coronary Calcium Scoring
  - EBCT method (since 1990)
  - Relatively large data
  - No contrast agent / low radiation
  - Indirect assessment of noncalcified plaque
- Coronary CT angiography
  - New technique
  - Lumen + wall change
  - Contrast-enhanced / high radiation
  - Limited data available

Coronary Calcium Scoring

Clinical impact

- Evidence of coronary atherosclerosis
- Correlates with total plaque burden
- Possible indicator for future myocardial events in asymptomatic high risk persons



Interpretation of Ca. Score

Step I		Step II	
EBCT Score (Agatston Method)	Interpretation	Age- and sex-specific (score percentiles)	Risk Assessment
0-11	No/minimal plaque	0-25	Small risk
11-100	Some plaque present	26-50	Moderate risk
111-400	Moderate plaque burden	51-75	Increased risk
401-1000	Severe plaque burden	75-90	High risk
> 1000	Very severe plaque burden	> 90	Very high risk

Prognostic Value of Ca. Score: EBCT Studies

Author	No.	F/U (mo)	CAC in pts with events	CAC in pts without events	RR
Arad	1177	43	764 ± 935	135 ± 432	14.3
Raggi	632	32	303 ± 441	92 ± 240	12.5
Park	967	77	395 ± 571	195 ± 378	4.4-7.5

Prognostic Value of CAC Screening

- 10,377 asymptomatic subjects
- 5 y follow-up, death rate = 2.4%
- CAC was independent predictor of mortality ($p<.001$)
- 5-y risk-adjusted survival was 95% for score > 1,000, 99% for score < 10.
- Risk-adjusted relative risk value for CAC, compared with CAC < 10 : 1.7, 2.5, 4.0 for >100, >400, >1000

Shaw et al. Radiology 2003;228:826-833

ACC/AHA Consensus (2000)

1. A negative EBCT test makes the presence of atherosclerotic plaque, including unstable plaque, very unlikely.
2. A negative test is highly unlikely in the presence of significant luminal obstructive disease.
3. Negative tests occur in the majority of patients who have angiographically normal coronary arteries.
4. A negative test may be consistent with a low risk of a cardiovascular event in the next 2 to 5 years.
5. A positive EBCT confirms the presence of a coronary atherosclerotic plaque.
6. The greater the amount of calcium, the greater the likelihood of occlusive CAD, but there is not a 1-to-1 relationship, and findings may not be site specific.
7. The total amount of calcium correlates best with the total amount of atherosclerotic plaque, although the true "plaque burden" is underestimated.
8. A high calcium score may be consistent with moderate to high risk of a cardiovascular event within the next 2 to 5 years.

Suggested Guidelines for CAC Scoring *(Partner's HealthCare System 2002)*

- Not recommended for asymptomatic low-risk subjects
- Positive test might be valuable in determining actual risk (apparently intermediate → actually high risk)

Ca. Scoring: Problems

- Interscan, interobserver, intraobserver variability
- Is it OK to use EBCT data in interpreting MDCT?
- What is the best score?
  - Agaston vs. Volume vs. Mass
- No standardized imaging technique
- No Korean Reference Data
- Noncalcified vulnerable plaque

CT for Coronary atherosclerosis

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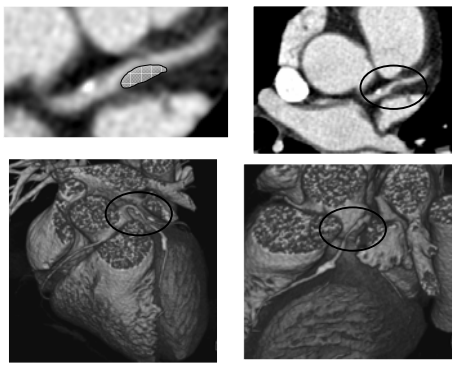
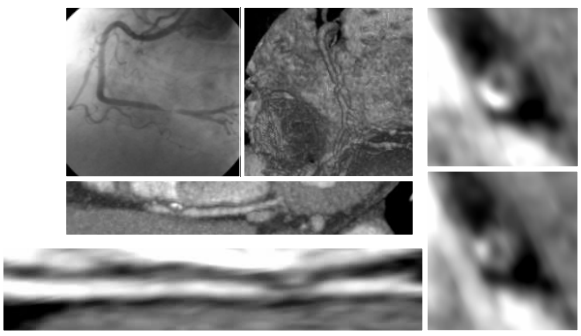
Plaque Imaging

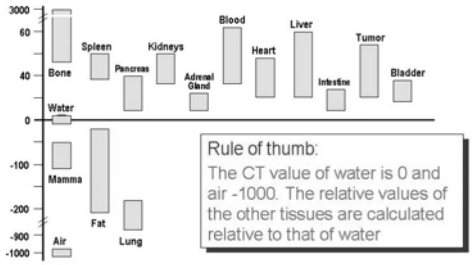


Plaque Imaging



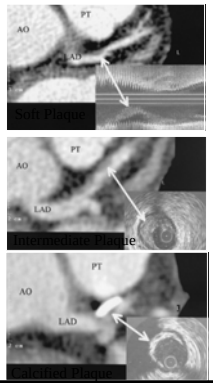
Plaque Characterization

CT Density

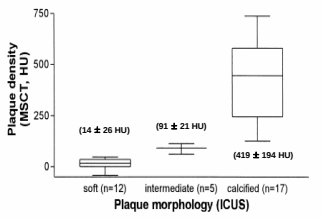


This is the so-called CT number in Hounsfield unit (HU)

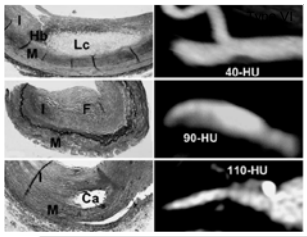
MDCT vs IVUS



- Schroeder, JACC 2001
  - ✓ 15 pts
  - ✓ > 40% stenosis
  - ✓ 34 out of 40 plaque



MDCT vs Histology

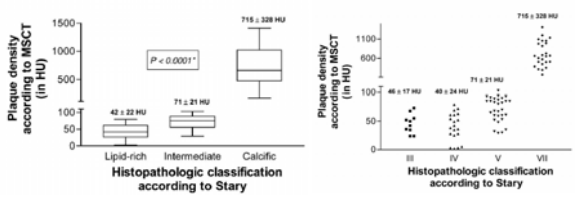


- Becker, Eur Radiol 2003
  - 11 human cadaver heart
  - 50 by macroscopic exam, 40 by CT
  - 33 lesions direct comparison
- CT number
  - Lipid-rich (VI, Va): 47 ± 9 HU
  - Fibrous-rich (Vb, Vc): 104 ± 28 HU
- Failed to detect type I-III lesions

		Macroscopic inspection						
		III	IV	Va	Vb	Vc	VI	Missed
CTA	Non-calcified	0	3	4	3	4	1	0
	Mixed	0	0	2	4	0	0	0
	Calcified	1	5	1	5	0	0	7
	Missed	9	3	3	2	0	0	0
	Sensitivity (%)	10	73	70	86	100	100	–

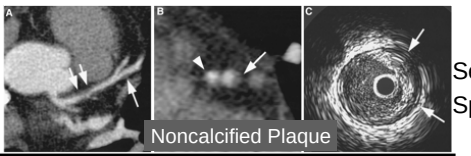
MDCT vs Histology

- Schroeder et al. JCAT 2004
  - 12 human hearts
  - Histology (Stary classification) vs CT (density)



Detection of Nonstenotic Plaque:

Seg. Based Comparison: 16-CT vs IVUS (n = 22)



Sens, 78%;
Spec, 87%.

For Exclusively Noncalcified Plaque:
Sens = 53% (8/15).
Underestimation of plaque volume by MDCT (24 vs 43 mm^3, p <.001)

Sens, 94%;
Spec, 94%.

Achenbach et al. Circulation 2004;109:14-17

Vulnerable Plaque

- By Little (1990) and Muller (1992)
- Lesion prone to thrombosis
- Sudden thrombotic occlusion (Falk, Circulation, 1995)
  - Often occurs in area of moderate pre-existing atherosclerosis
  - Plaque progression: result of episodic thrombosis and organization
  - Risk of plaque rupture correlates only weakly with the degree of stenosis
- Identifying a plaque prone to thrombosis will predict the majority of AMI and sudden death.

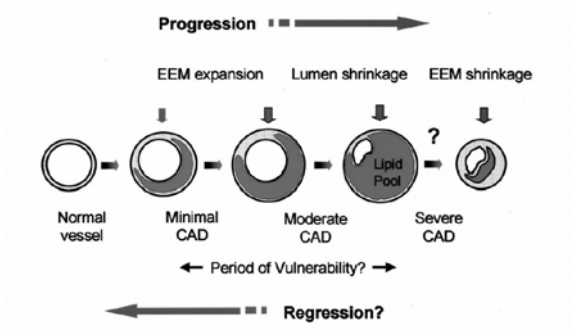
Vulnerable Plaque: Diagnosis

- Major Criteria
  - Active inflammation
  - Thin cap with a large lipid core
  - Endothelial denudation with superficial platelet aggregation
  - Fissured plaque
  - Stenosis > 90%
- Minor Criteria
  - Superficial calcified nodule
  - Glistening yellow on angioscopy
  - Intraplaque hemorrhage
  - Endothelial dysfunction
  - Outward remodeling

Naghavi et al. Circulation 2003

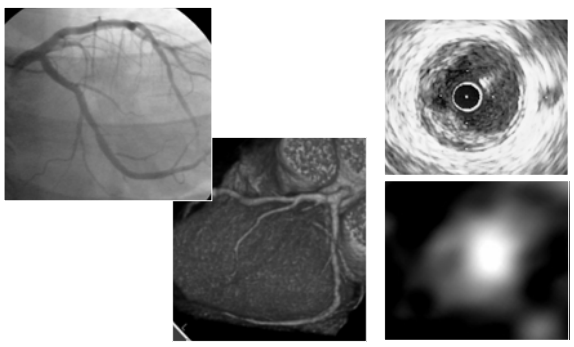
What is Vulnerable Plaque ?

- Large lipid-rich area with thin fibrous cap
- Large lipid core is associated with plaque vulnerability and MI (Virmani, Arterioscler Thromb Vasc Biol 2000)
  - 80% of ruptured plaque: necrotic cores larger than 1.0 mm^2
  - 90%: lipid core greater than 10% of plaque area



Schoenhagen, JACC 2001

Detection of Vulnerable Plaque

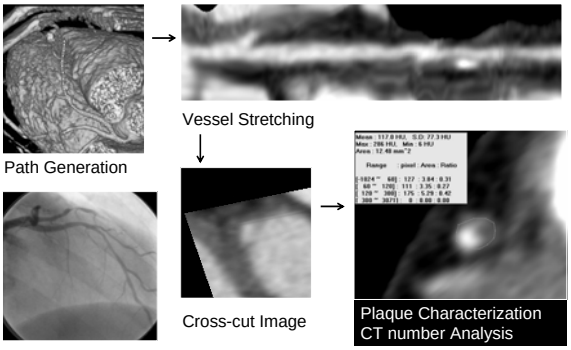


Detection of Lipid-core: AMC

- 30 patients with heart rate < 66/min
- All patients underwent 3 vessel IVUS
- Coronary CTA
  - Reconstructed at mid-diastole, 1mm/0.3mm
  - Cross-sectional MPR image in 0.2mm interval
- Two radiologists blind to the IVUS result, independently
- Lipid Core: low density area in vessel wall
  - CT number <60HU / Area > 5 mm^2
- Nine segment model
  - LM, pLAD, mLAD, dLAD, pLCx, mLCx, pRCA, mRCA, dRCA

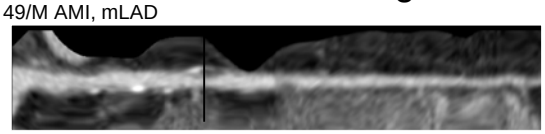
Seo JB 2004 KRS, RSNA

Postprocessing

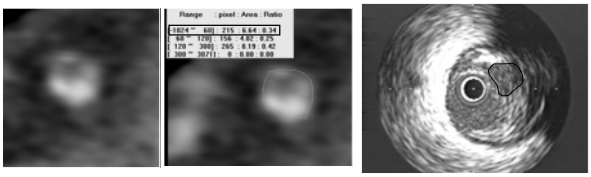


Case 1: Stenotic Segment

49/M AMI, mLAD



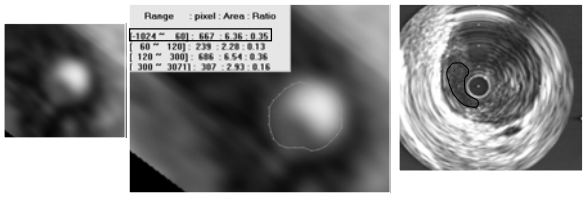
36 mm from LAD-LCx bifurcation



Case 2: Nonstenotic Segment

72/M AMI, pRCA

32 mm from RCA ostium



Results

- Assessable: 230/270 segments
  - 25 segment: poor CT image quality
  - 15 segment: failure of IVUS
- IVUS: 22 lipid cores (13 with stenosis, 9 without)

Detection of hypoechoic (lipid-rich) plaque

	Reader 1	Reader 2
Sensitivity	73%	68%
Specificity	92%	90%

Interobserver agreement: kappa 0.608

* Ten concordant false positive lesions: IVUS misdiagnosis?

Seo JB 2004 KRS, RSNA

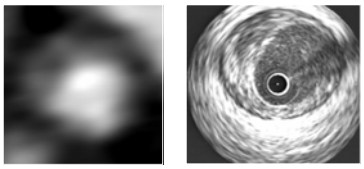
CT Detection of Lipid Core

	Prevalence	Sensitivity R1	Sensitivity R 2	Specificity R1	Specificity R2
All seg.	10% (22/230)	73%	68%	92%	90%
Stenotic seg.	31% (13/42)	85	69	69	76
Nonstenotic seg.	5% (9/188)	56	67	96	92
Left main	7% (2/30)	100	100	89	86
LAD segments	10% (9/87)	100	78	92	86
LCx segments	8% (4/50)	25	50	89	94
RCA segments	11% (7/63)	57	57	95	95

* Interobserver agreement (Kappa): 0.608

False Positive Lesions

- 17 FP lesions in reader 1 / 21 in reader 2 results
- 10 false positive lesions on CT are concordant between two readers



- IVUS: gold standard but subjective
- False positive on CT or IVUS misdiagnosed lesion?
- No histopathologic correlation

Conclusion

- When compared with IVUS, ECG-gated CT with dedicated postprocessing method showed reasonably high accuracy and interobserver agreement in detecting lipid-rich plaque.
- ECG-gated cardiac CT may be used as a noninvasive tool to detect vulnerable, lipid-rich, necrotic core in coronary arterial wall.

Plaque Characterization

- Leber AW, JACC, 2004
  - 37 patient with HR < 65/min
  - 58 vessels analyzable on MDCT / 68 IVUS

IVUS	Accuracy	CT Number (HU)
Hypoechoic (lipid-rich)	62/80 (78%)	49 ± 22
Hyperechoic (fibrous)	87/112 (78%)	91 ± 22
Calcified	150/158 (95%)	391 ± 156
Exclude plaque	484/525 (92%)	

Detection of Vulnerable Nonstenotic Plaque

- Caussin et al. Am J Cardiol 2004
  - 21 patients with ACS
  - CT detection of vulnerable components
    - Rich ripid area / plaque disruption / eccentricity, arterial remodeling, calcification
  - Goldstandard; IVUS

TABLE 3 Intravascular Ultrasound (IVUS) Versus Computed Tomography (CT)

	IVUS*	CT*	Sensitivity	Specificity	p Value
Positive remodeling	7 (41%)	8 (47%)	100%	90%	<0.01
Eccentricity	18 (86%)	18 (86%)	100%	100%	<0.01
Calcium	7 (33%)	8 (38%)	100%	93%	<0.01
Complex plaque	9 (43%)	6 (29%)	67%	100%	<0.01
Disruption	8 (38%)	9 (43%)	57%	71%	NS
CT hypodensity vs IVUS echolucent area	16 (71%)	14 (67%)	81%	80%	<0.05

Plaque in Mildly-Stenotic Seg.

- 46 LCA segments in 14 pts.
- 37 segments (80.4%) assessable
- Plaque presence / calcification / distribution / positive remodeling
- ROC analysis

Table 1 Accuracy of multi-slice computed tomography in comparison to intravascular ultrasound

Descriptors of mildly stenotic coronary atherosclerosis	AUC (95% CI) MSCT reader 1	AUC (95% CI) MSCT reader 2
Presence/absence of plaque	0.996 (0.990–1.00)	0.868 (0.798–0.938)
Calcified/non-calcified plaque	0.927 (0.845–1.00)	0.884 (0.821–0.947)
Symmetric/asymmetric plaque distribution	0.966 (0.934–0.998)	0.969 (0.944–0.994)
Positive remodeling/no remodeling	0.903 (0.862–0.944)	0.868 (0.788–0.948)

AUC, area under the receiver operating characteristic (ROC) curve; CI, confidence interval; MSCT, multi-slice computed tomography.

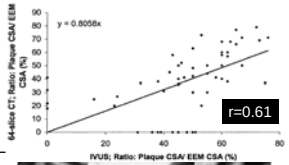
Schoenhagen et al. Coronary Artery Disease 2003

Plaque Quantification

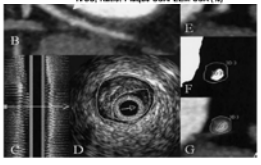
Quantification of Obstructive and Nonobstructive Coronary Lesions by 64-Slice Computed Tomography

A Comparative Study With Quantitative Coronary Angiography and Intravascular Ultrasound

- *Leber et al. 2005 JACC*
- IVUS comparison: 32 vessels / 18 pts



	IVUS	CT	r
Plaque CSA	8.1 mm^2	7.3	0.73
Lumen CSA	8.4 mm^2	9.4	0.81
EEM CSA	16.4 mm^2	16.7	0.88
% vessel obstruction	50.4 %	41.1	0.61



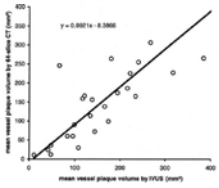
Accuracy of 64-Slice Computed Tomography to Classify and Quantify Plaque Volumes in the Proximal Coronary System

A Comparative Study Using Intravascular Ultrasound

- *Leber et al. 2006 JACC*
- 19 pts / 36 vessel
- Correct detection
  - 54/65 (83%) noncalcified
  - 50/53 (94%) mixed
  - 41/43 (95%) calcified
  - 7/10 (70%) lipid pool
- Plaque volume
  - $r^2 = 0.69$
  - Underestimation of mixed/nonca++ plaque
  - Overestimation of ca++ plaque

Table 1. Consensus Table of 64-Slice CT and IVUS to Detect and Classify Coronary Plaques

	IVUS			
64-Slice CT	None	Calcified	Mixed	Noncalcified
None	192	2	3	11
Calcified	1	34	8	0
Mixed	1	7	38	4
Noncalcified	10	0	4	50

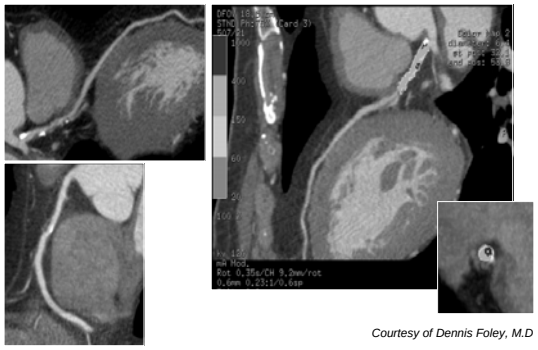


Limitations of CT Angiography

- Limited data available
- Limited temporal resolution
  - motion artifact (RCA)
  - heart rate control
- Limited spatial resolution
  - One pixel: 0.3x0.3x0.4-6mm
- Time consuming: dedicated software
- Influence of intracoronary attenuation on coronary plaque measurement *(Cademartiri, Eur Radiol, 2005)*

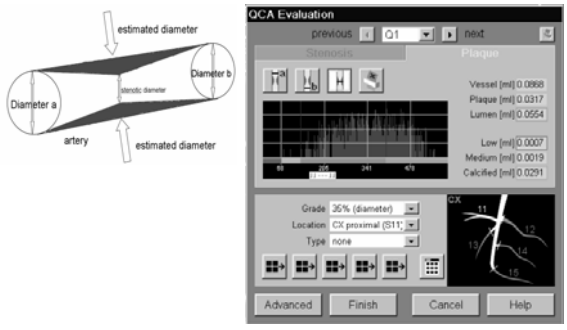
New Software for Plaque Characterization of Quantification

Plaque Characterization



Courtesy of Dennis Foley, M.D

Quantification



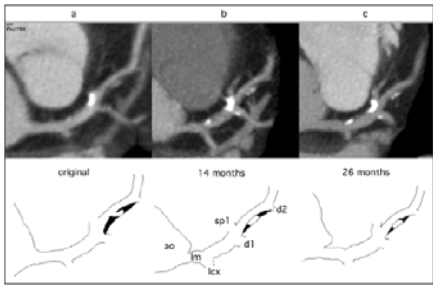
CT Angiography for Plaque Imaging

- Non-invasive / repeated study
- Lumen + wall
- Objective assessment
  - Software dependent
- Ongoing technical improvement

Perspective

- Future studies
  - Accuracy / limitation
  - Clinical impact
  - Research
    - Pathogenesis
    - Monitoring of drug effect

Plaque Monitoring



- 53/M / Regression of plaque (avostatin therapy)
- Johnson KM, AJR, 2006