Why We Lower LDL but Still Miss Heart Attacks

The Case for Serial Imaging in Atherosclerosis

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Disclosures

KOL: Arineta, Cleerly, Novartis, Amgen

Objectives

11-year case presentation **Tracking CAD**

RCT's answer narrow questions — *"what works on average"*

Serial CCTA + AI - *"is it working in this person?"*

Residual risk is expected in CAD

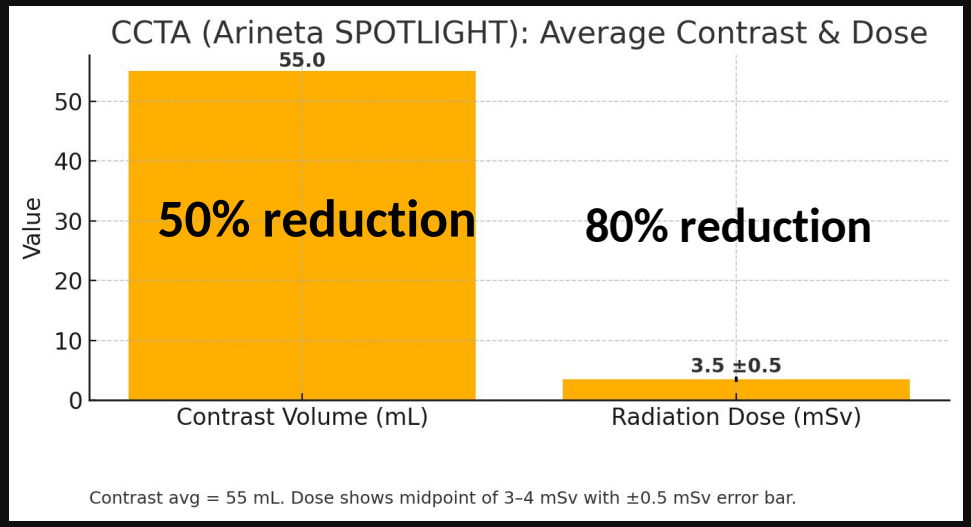
ARINETA SpotLight™
Duo High-Performance Cardiac CT

Installed 12/2022

Images the entire heart in one heartbeat
→ *14 cm* whole-heart coverage, *560 slices*

Freezes motion with ultra-fast rotation
→ *0.24 s* rotation speed, *120 ms* temporal resolution

Visualizes plaque at sub-millimeter detail
→ *0.28 mm* spatial resolution with ***0.5 mm*** detector



From Reactive to Proactive CAD Prevention

Personal shift: waiting for symptoms → monitoring plaque biology with serial CCTA + AI ("See → Treat → See")

Reactive approach:

- **Wait** for Symptoms or Events:
- Imaging mostly answers, **"Is there stenosis?"**
- Cath/stent/Bypass **pathway**
- Treatment **after** an event (late in the disease course)

Proactive approach:

- **Prevent** events by tracking disease
- **SEE**: detect plaque biology before symptoms
- **TREAT**: personalize intensity + adherence
- **SEE AGAIN**: "Is plaque changing?"

SEE → TREAT → SEE AGAIN

Goal: risk reduction by changing the disease trajectory (not "prove cure").

CCTA: Beyond Stenosis — Plaque Phenotypes + High-Risk Biology

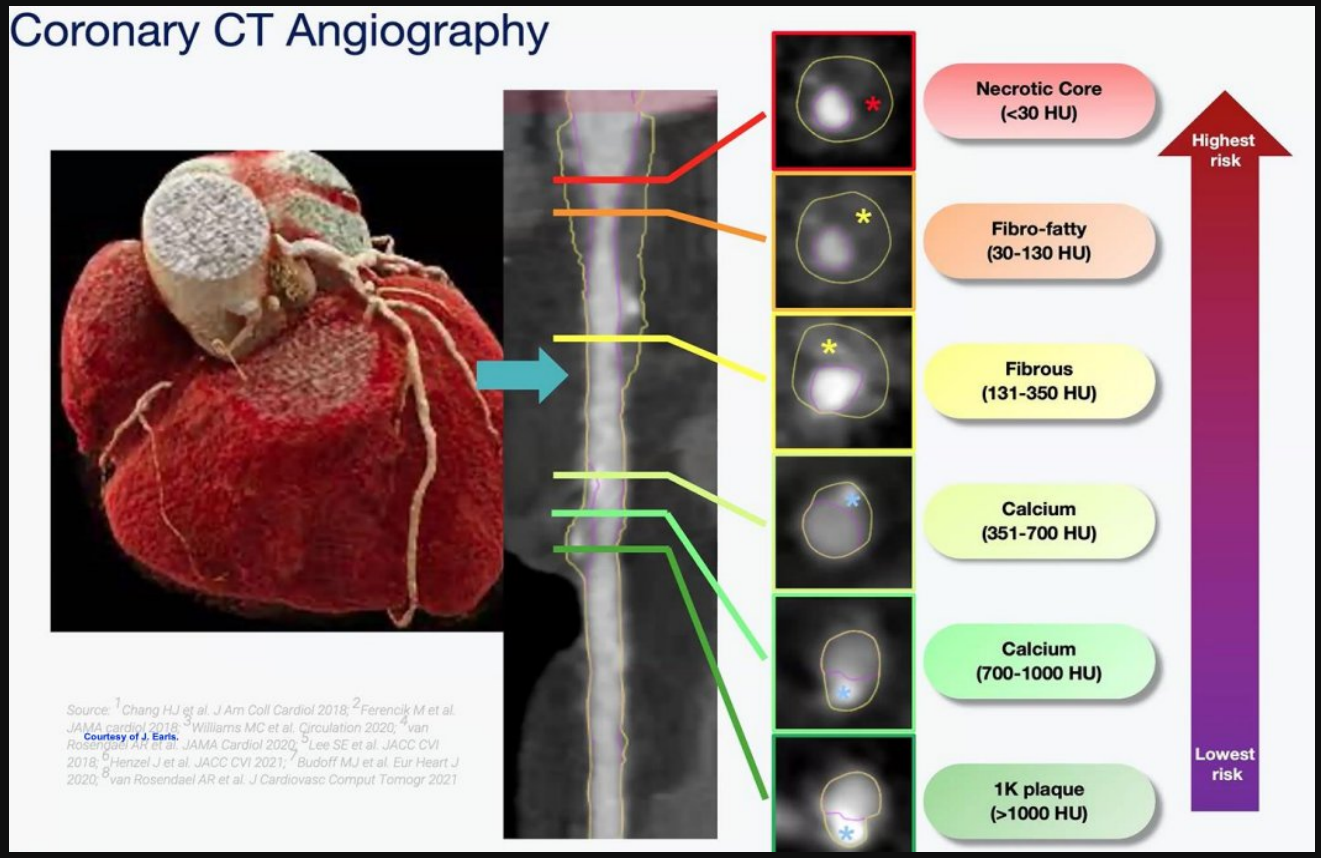
What CCTA can measure

Total plaque burden — RISK
"How much disease overall?"

Plaque composition — RISK
Calcified vs non-calcified vs mixed

High-risk plaque features — RISK
"vulnerable biology" Low attenuation, positive remodeling, etc.

Stenosis involvement — Symptoms
"Where and how tight?"



Take-home CCTA quantifies burden + composition + high-risk features → enables treat-to-plaque (not just treat-to-LDL).

11 year Case Overview

Patient Profile

- **Age:** 55–66 (2014–2025)
- **Risk factors:** Hyperlipidemia; no diabetes; normotensive
- **Lifestyle:** Highly active (former Navy SEAL)

Imaging & Workup

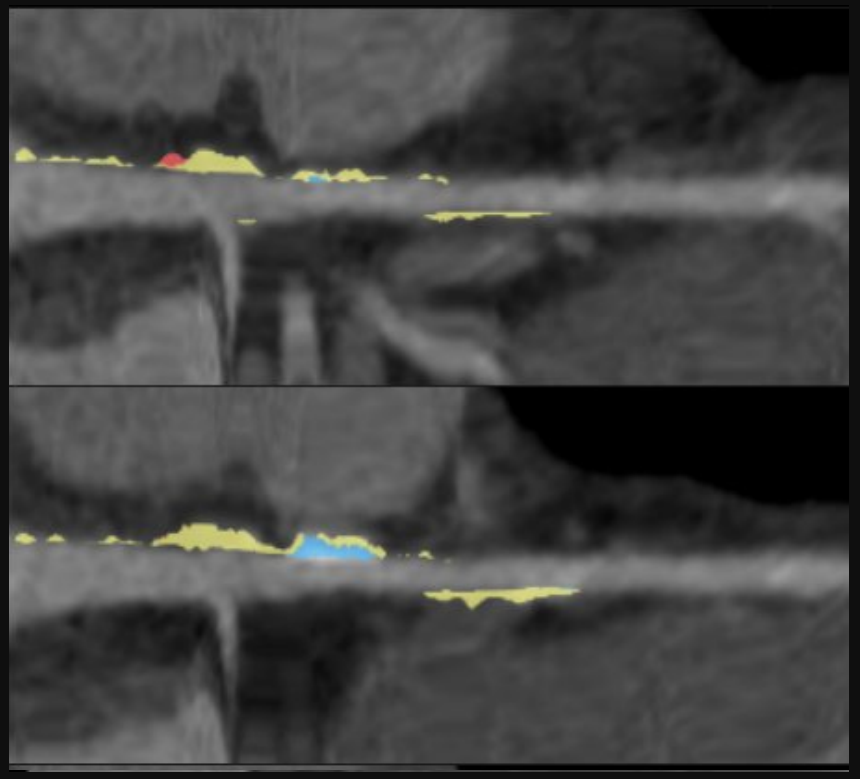
- **Trigger:** Initial evaluation for abnormal CAC score
- **8/15/2014 CCTA:**

LM	LAD
<25%	<50%

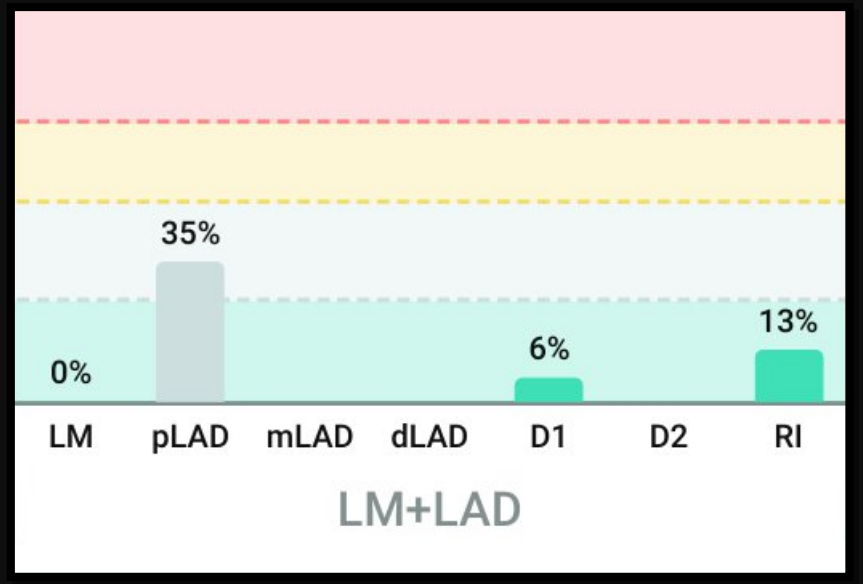
Clinical course (2014–2025): No angina or dyspnea over 11-year follow-up

Abbreviations: CAC = coronary artery calcium; CCTA = coronary CT angiography; LM = left main; LAD = left anterior descending

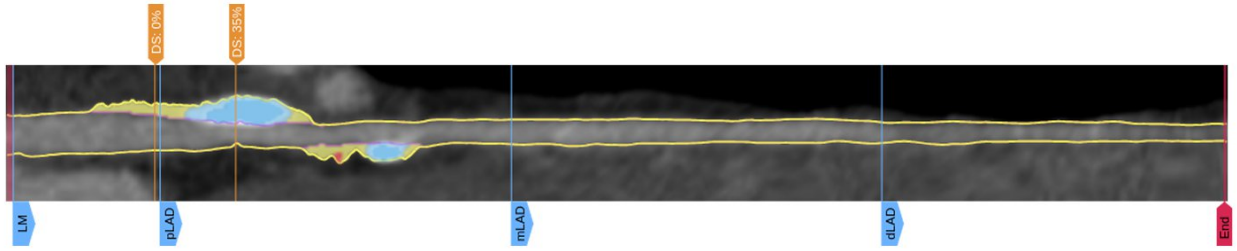
Case



8/15/14 CCTA: LM/LAD



Left Main and Left Anterior Descending (LM+LAD)



318.4 mm^3 23.8% PAV
Total Plaque Volume

8 mm^3 0.6% PAV
Low-Density - Non-Calcified Plaque Volume

216.6 mm^3 16.2% PAV
Total Non-Calcified Plaque Volume

101.8 mm^3 7.6% PAV
Total Calcified Plaque Volume

35% Greatest Diameter Stenosis

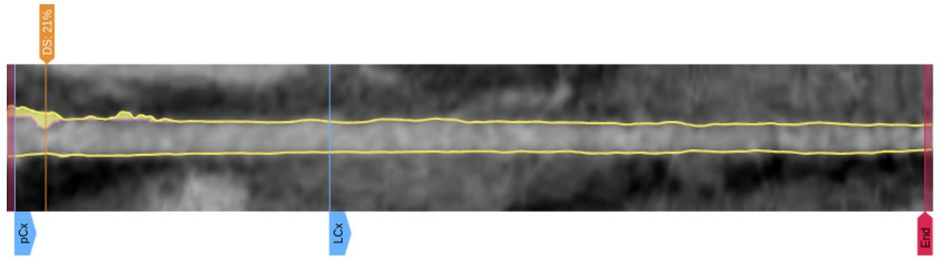
1.4 Highest Remodeling Index

ⓘ A lesion spans the LM, pLAD, D1, pCx and RI with 0% in LM and 35% in pLAD and 6% in D1 and 21% in pCx and 13% in RI.

Case

8/15/14 CCTA: RCA & LCX

Circumflex (Cx)



50.1 mm³ 5.6% PAV
Total Plaque Volume

0.1 mm³ < 0.1% PAV
Low-Density - Non-Calcified Plaque Volume

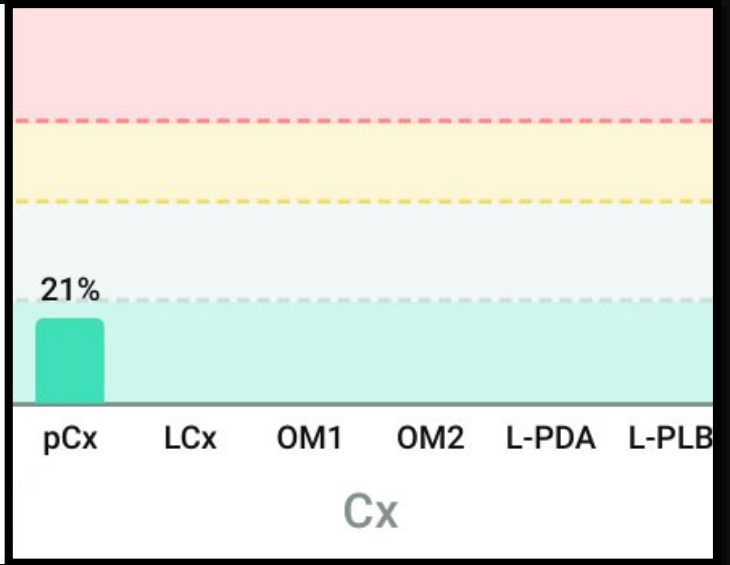
50.1 mm³ 5.6% PAV
Total Non-Calcified Plaque Volume

0 mm³ 0% PAV
Total Calcified Plaque Volume

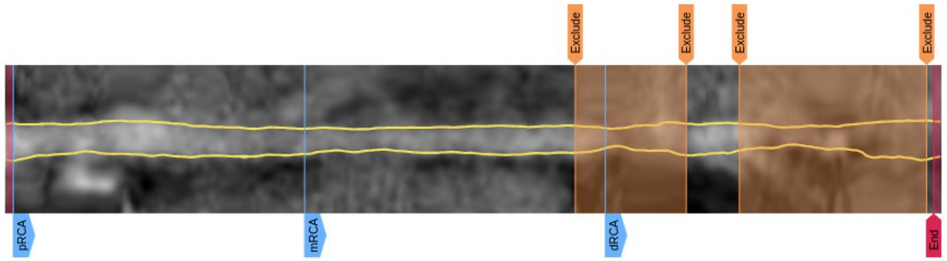
21% Greatest Diameter Stenosis

1.3 Highest Remodeling Index

ⓘ A lesion spans the LM, pLAD, D1, pCx and RI with 0% in LM and 35% in pLAD and 6% in D1 and 21% in pCx and 13% in RI.



Right Coronary Artery (RCA)



0 mm³ 0% PAV
Total Plaque Volume

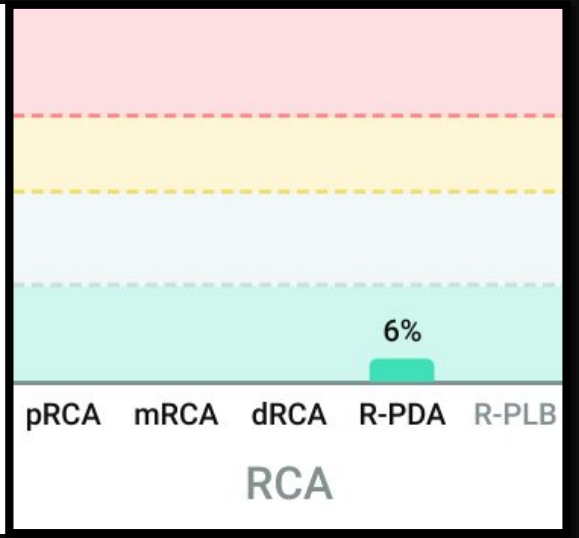
0 mm³ 0% PAV
Low-Density - Non-Calcified Plaque Volume

0 mm³ 0% PAV
Total Non-Calcified Plaque Volume

0 mm³ 0% PAV
Total Calcified Plaque Volume

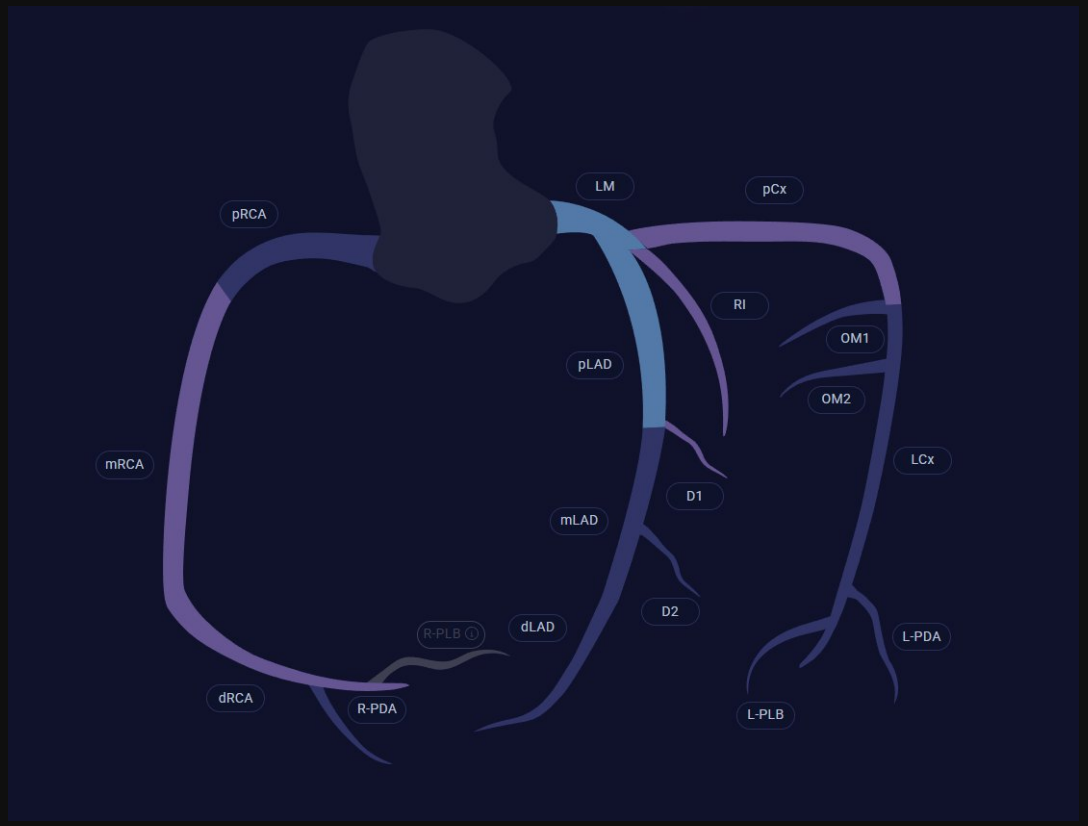
N/A Greatest Diameter Stenosis

1 Highest Remodeling Index



Case

Cleerly Ischemia



Ischemia	Analyzed - No vessels are likely ischemic

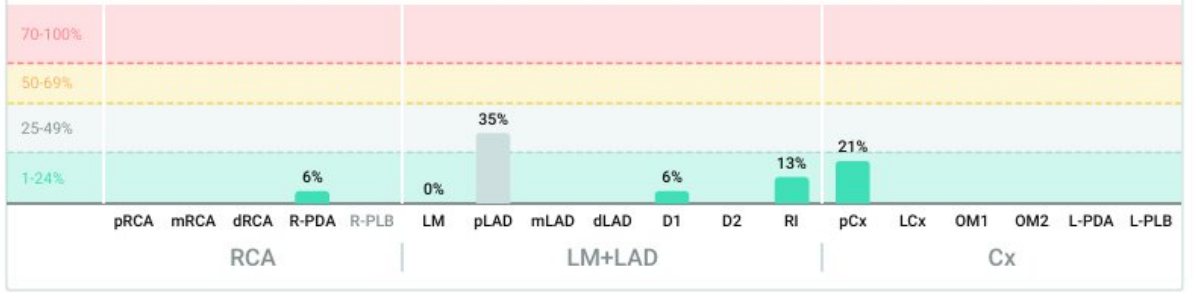
Cleerly Atherosclerosis

Atherosclerosis

Territory	Plaque Volume (mm^3)				Percent Atheroma Volume
	TOTAL	Low-Density - Non-Calcified	Non-Calcified	Calcified	
RCA	9.6	0	9.6	0	1.1%
LM+LAD	349.2	8.1	235.9	105.2	16.7%
Cx	50.1	0.1	50	0	3.8%
TOTAL	408.9	8.2	295.5	105.2	9.5%

Stenosis

Severe	Moderate	Mild	Minimal
≥70% or ≥50% LM only	50-69%	25-49%	1-24%
0	0	1	4



8/15/14

8/14 Management

Management Plan

- Start ASA 81 mg + Atorvastatin 40 mg
- Annual lipid surveillance
- lipid goal LDL ≤ 100 mg/dL
- Lifestyle optimization (diet, exercise)

Follow-up (2017)

LDL
92 mg/dL

WEIGHT
210 lb

BMI
27.7

9 year follow up scan: 9/7/2023 CCTA

Case

9/7/2023 CCTA: Progression of CAD

9 years later

CCTA Findings

9/7/2023

LM

<50% (increase)

Left main stenosis

pLAD

50% (increase)

prox LAD stenosis

Others

<15%

all other segments

Clinical Status & Labs

2/2023

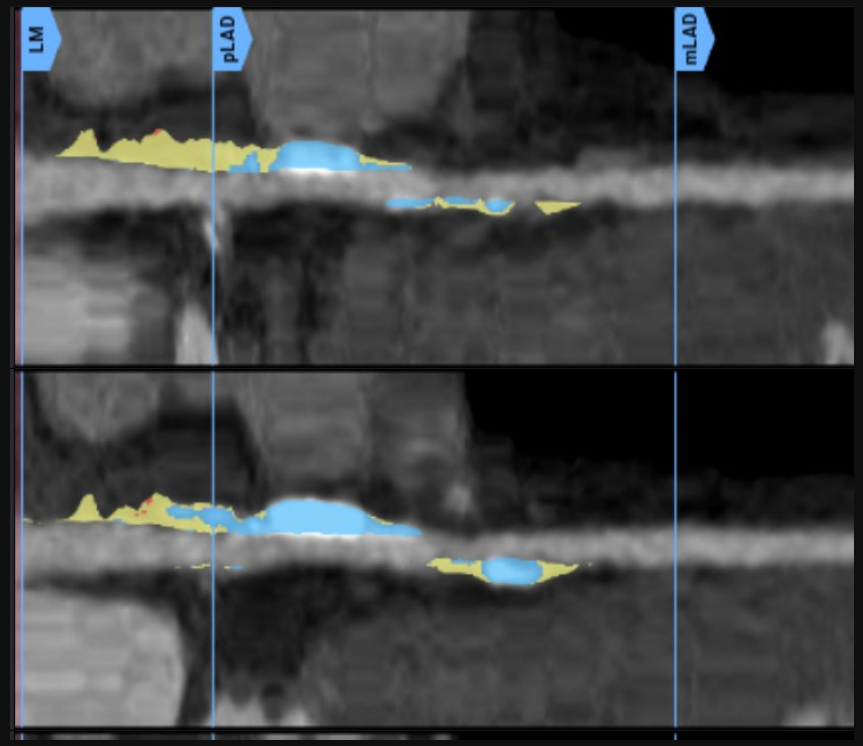
Symptoms: None

LDL	A1c
63 mg/dL	5.0

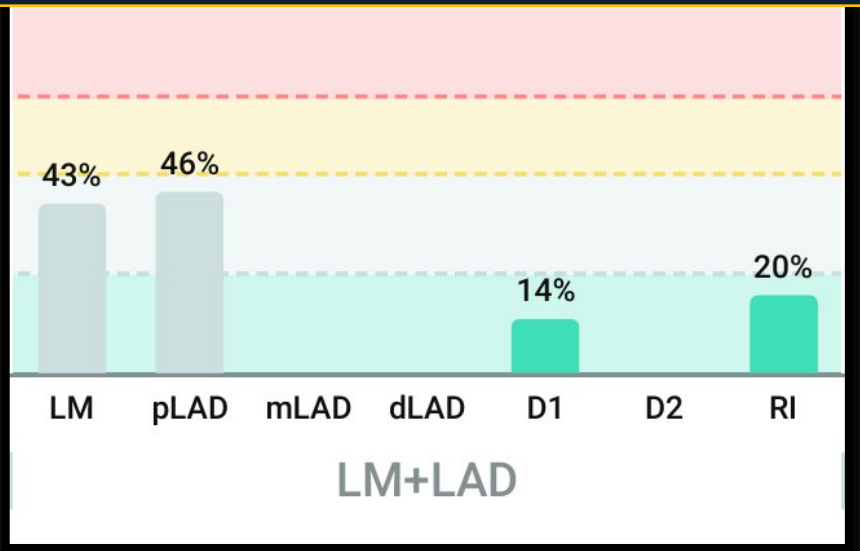
Weight	BMI
219 lb	28.9

LM disease ☾ Refer for cath

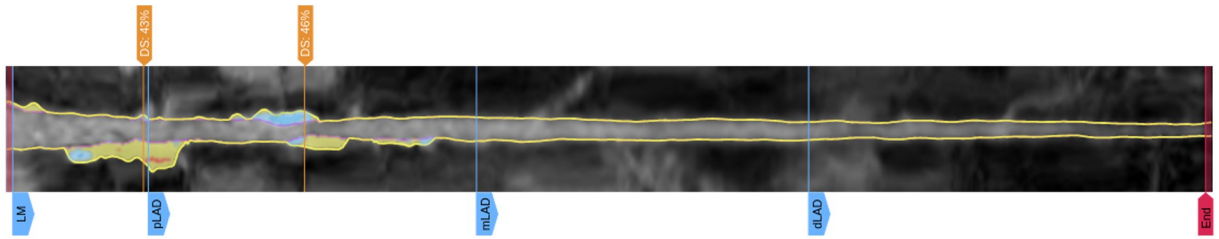
Case



9/7/23 CCTA: LM/LAD



Left Main and Left Anterior Descending (LM+LAD)

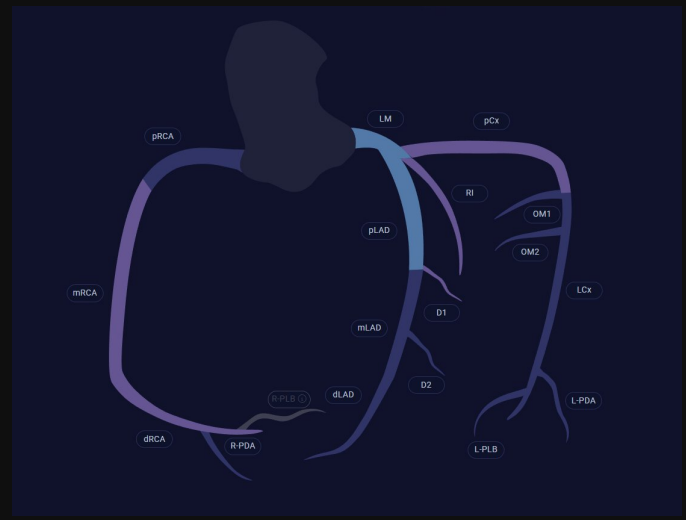


569.5 mm^3 40.5% PAV	19.2 mm^3 1.4% PAV	369.8 mm^3 26.3% PAV	199.7 mm^3 14.2% PAV
Total Plaque Volume	Low-Density - Non-Calcified Plaque Volume	Total Non-Calcified Plaque Volume	Total Calcified Plaque Volume

46% Greatest Diameter Stenosis

1.5 Highest Remodeling Index

ⓘ A lesion spans the LM, pLAD, pCx and RI with 43% in LM and 46% in pLAD and 17% in pCx and 15% in RI.

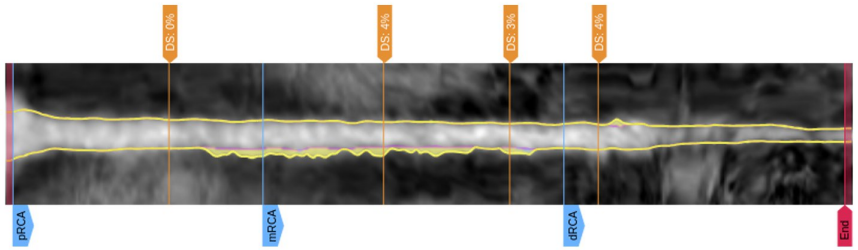


Ischemia	Analyzed - No vessels are likely ischemic

Case

9/7/23 CCTA: RCA & LCX

Right Coronary Artery (RCA)



72.7 mm³ 10.4% PAV
Total Plaque Volume

0 mm³ 0% PAV
Low-Density - Non-Calcified Plaque Volume

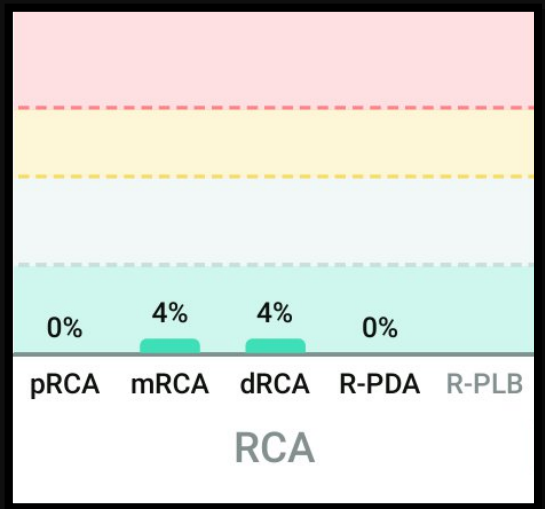
70.7 mm³ 10.1% PAV
Total Non-Calcified Plaque Volume

2 mm³ 0.3% PAV
Total Calcified Plaque Volume

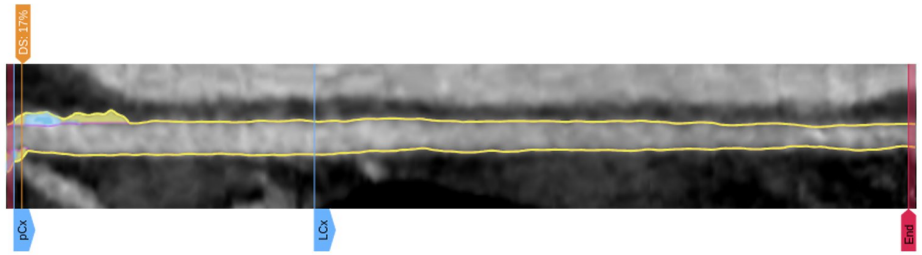
4% Greatest Diameter Stenosis

1.3 Highest Remodeling Index

ⓘ A lesion spans the pRCA and mRCA with 0% in pRCA and 4% in mRCA.



Circumflex (Cx)



42.5 mm³ 4.8% PAV
Total Plaque Volume

0 mm³ 0% PAV
Low-Density - Non-Calcified Plaque Volume

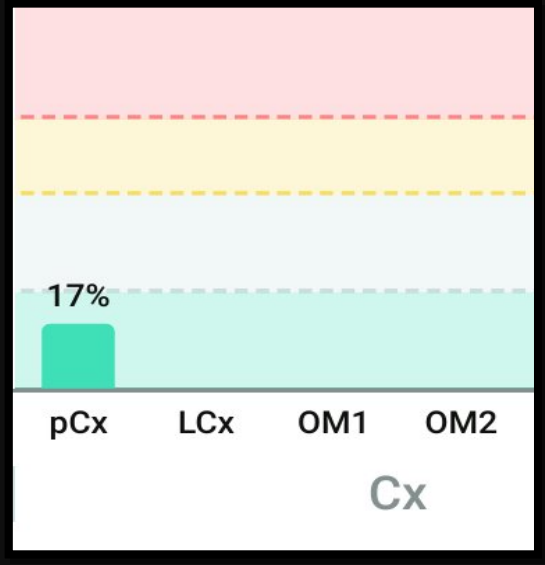
26 mm³ 2.9% PAV
Total Non-Calcified Plaque Volume

16.5 mm³ 1.9% PAV
Total Calcified Plaque Volume

17% Greatest Diameter Stenosis

1.3 Highest Remodeling Index

ⓘ A lesion spans the LM, pLAD, pCx and RI with 43% in LM and 46% in pLAD and 17% in pCx and 15% in RI.

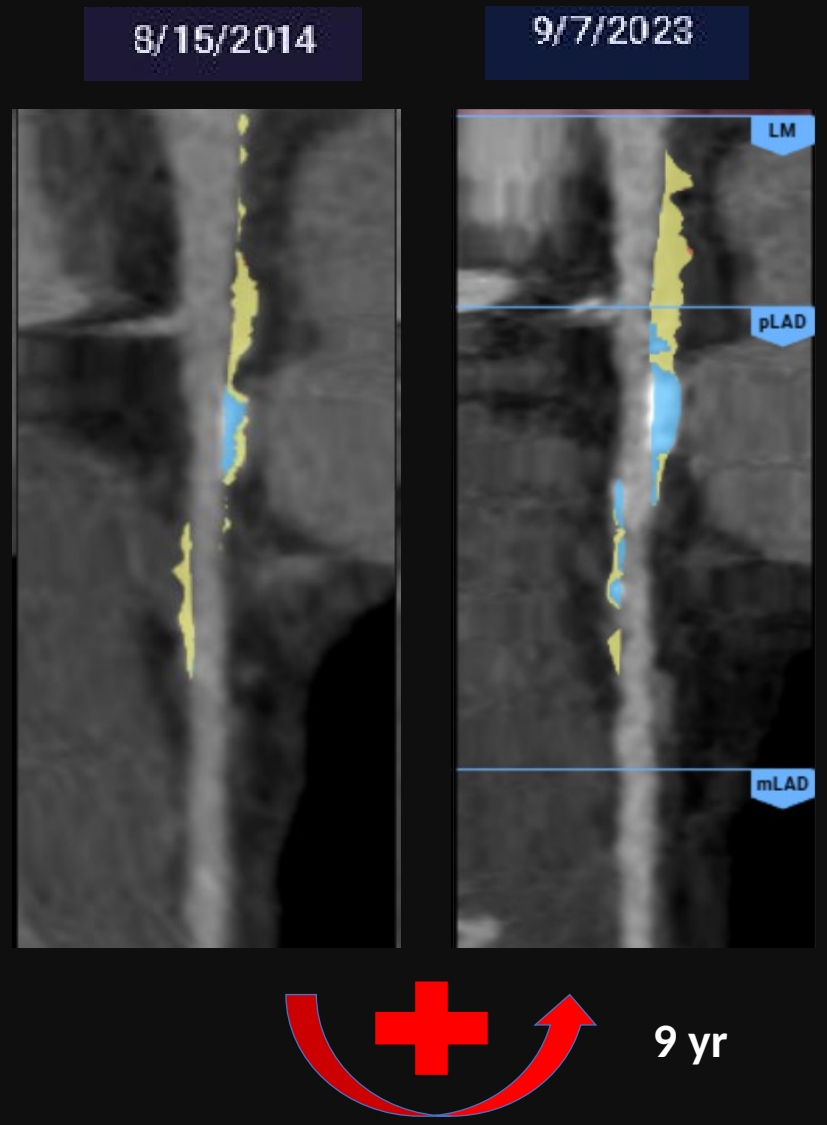


Case

9/7/23 Cleerly Compare

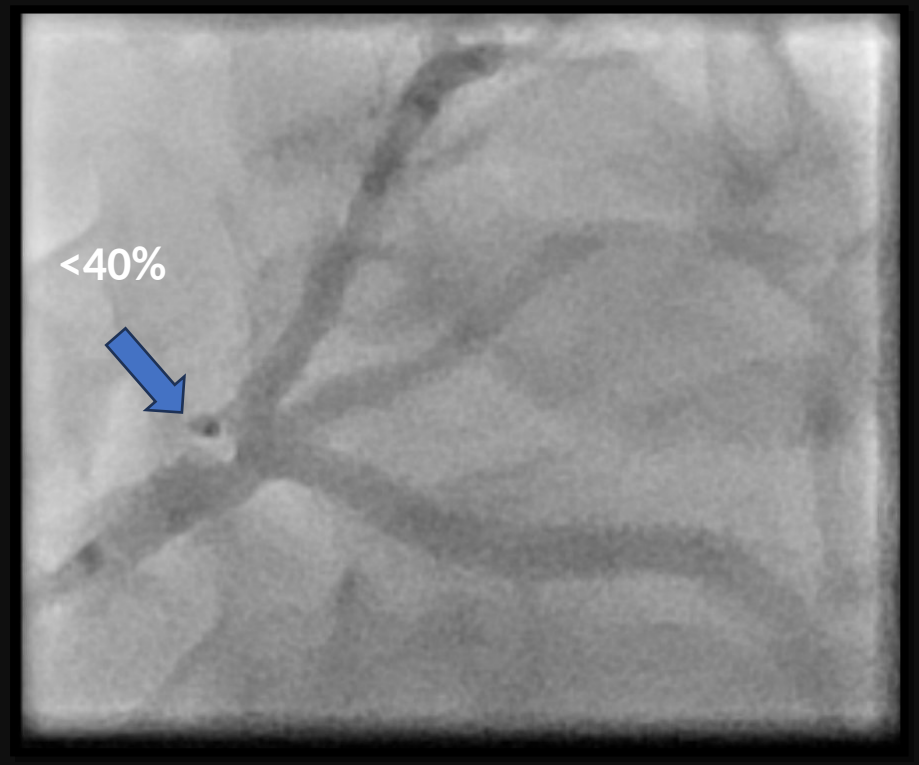
TPV +35/yr

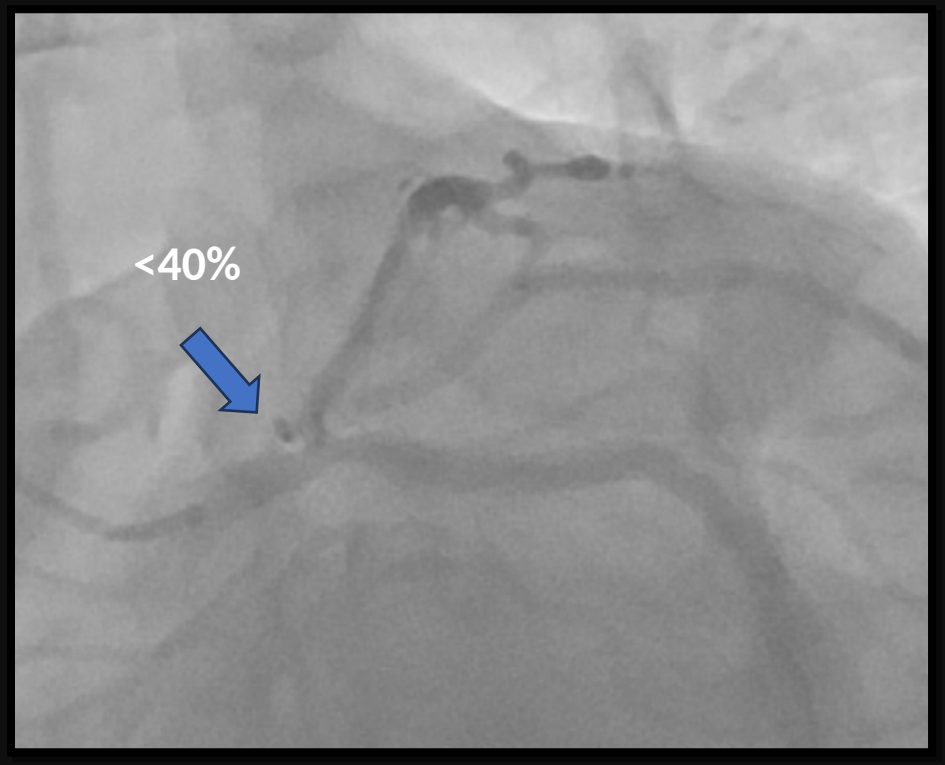
ALL (mm³ / PAV)	Compared Cleerly ID: HLTTNDLL 8/15/2014	(# / %)	Current Cleerly ID: 3C1972CB 9/7/2023
Total Plaque Volume (mm³)	408.9	▲ +318.9	727.8
Total Non-Calcified Plaque Volume (mm³)	303.7	▲ +195.5	499.2
Low-Density - Non-Calcified Plaque Volume (mm³)	8.2	▲ +11	19.2
Total Calcified Plaque Volume (mm³)	105.2	▲ +123.4	228.6
# of Severe Stenosis	0	=	0
# of Moderate Stenosis	0	=	0
Highest Remodeling Index	1.6	▼ -0.1	1.5
Greatest Diameter Stenosis (%)	35	▲ +11	46
Greatest Area Stenosis (%)	61	▲ +13	74
Length (mm)	660.3	▼ -1.8	658.5



9/7/2023 CCTA

- 10/26/2023 Cath: Distal LM 30–39%, mLAD 30–39%, RCA 10–19%.
  - Recommendations: no PCI, No CABG, aggressive management:





Case

11/9/2023 Post Cath visit:

Post-cath follow-up

Symptoms: Asymptomatic

Management:

- **Continue: Atorvastatin 40 mg + ASA 81 mg**
- **Add PCSK9 inhibitor (Repatha 140 mg q2wk)**
- lipid goal **LDL ≤55 mg/dL**; monitor LDL response to PCSK9i.
- Emphasize BP <130/80 and exercise adherence.

Follow-Up Labs

2/2024 labs

LDL	A1c
11 mg/dL	5.2

Weight	BMI
227 lb	29.9

Repeat CCTA in 12 months to assess biological and structural response to therapy

RCTs answer a narrow question

“Trials count events. They don’t directly measure plaque stability or regression.”

A 3–5 year trial can’t fully answer lifetime questions.

Interpret results within the observed window — and ask what happens after.

?

RCT

Outcome trials (RCTs)

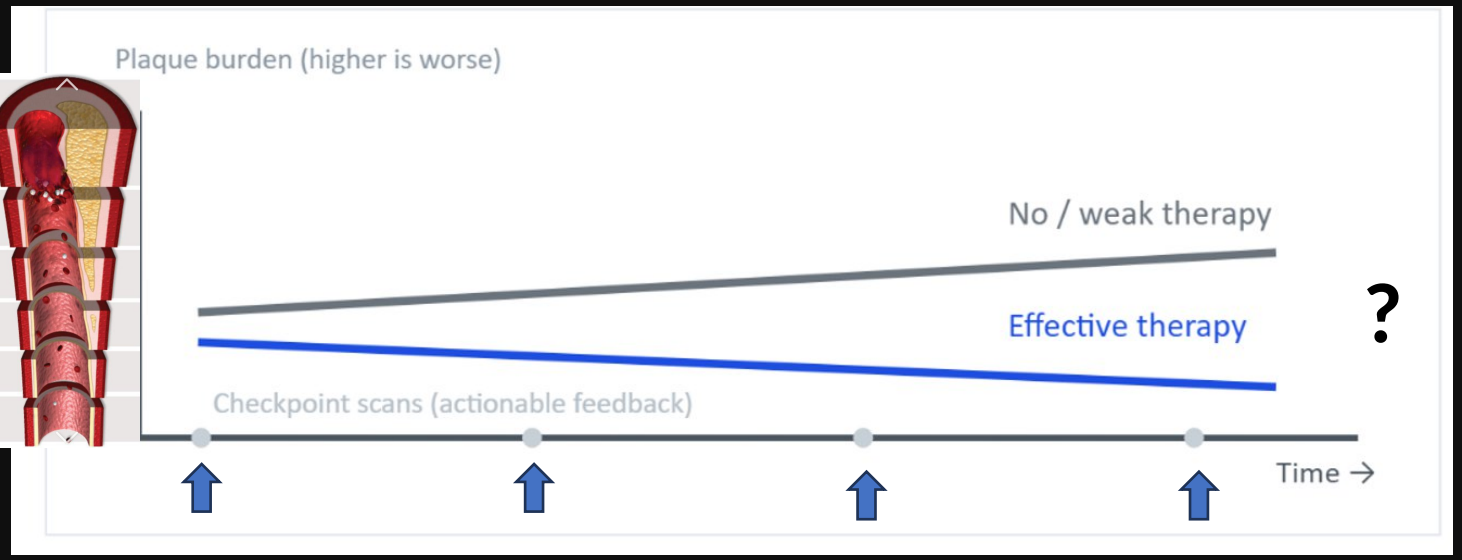
- **Best for:** net clinical benefit (events + safety)
- **Answers**: “On average, does A beat B over X years?”
- **Guideline-grade evidence** (population average)

Not proof of plaque regression or “cure” in CAD. *Population truth is not personal truth*

Serial Imaging asks a different question than trials:

"Is plaque burden and phenotype improving over time in THIS patient?"

CCTA can quantify plaque burden + composition and estimate a progression slope — a more direct readout of whether biology is changing.



Checkpoint scans

IMG

Disease "readout"

- **Best for**: tracking atherosclerosis (burden + composition)
- **Answers:** "Is plaque stable, regressing, or progressing?"
- Can show ***trajectory* before** events accrue

Doesn't prove fewer events without outcomes evidence.

Statins evidence : benefit ≠ cure

(secondary prevention Trials)

Even in landmark placebo-controlled trials, many patients still had events and deaths.

Trial (population)	Comparator	Follow-up	N (Statin)	N (Placebo)	Trial "MACE" definition	MACE — Statin	MACE — Placebo	All-cause deaths — Statin	All-cause deaths — Placebo
4S (CHD: angina and/or prior MI)	Simvastatin vs placebo	5.4 y (median)	2221	2223	"Major coronary events"	**431 (19%)** 32% RRR	**622 (28%)**	**182 (8%)** 33% RRR	**256 (12%)**
LIPID (prior MI or unstable angina)	Pravastatin vs placebo	6.1 y (mean)	4512	4502	CHD death or nonfatal MI	**557 (12.3%)** 23% RRR	**715 (15.9%)**	**498 (11.0%)** 22% RRR	**633 (14.1%)**
CARE (post-MI; average cholesterol)	Pravastatin vs placebo	5.0 y (median)	2081	2078	CHD death or nonfatal MI	**212 (10.2%)** 23% RRR	**274 (13.2%)**	**180 (8.6%)** 9% RRR	**196 (9.4%)**

Take-home

- Statins reduced MACE vs placebo—but over 5–6 years, ***hundreds still had MACE and many still died***.
- When you hear "works," mentally add "***works on average***, not perfectly, and not forever."

Statins (Secondary Prevention): benefit ≠ cure

Pooled placebo-controlled trials (4S, LIPID, CARE): ~17,600 patients • ~5–6 years

Compared to placebo, statins reduce both major events and death — but substantial residual risk remains.

Major coronary / MI-type events

Statin	14%
Placebo	18%

22% RRR

≈ 4 fewer events per 100

ARR: 4.0%/NNT 25

All-cause death

Statin	10%
Placebo	12%

17% RRR

≈ 2 fewer deaths per 100

ARR: 2.0%/ NNT 50

Residual risk remains (even on statin):

- ~14/100 still have a major coronary/MI-type event
- ~10/100 still die over ~5–6 years

Secondary prevention populations (CHD / prior MI / unstable angina). Rates shown are crude pooled percentages from trial counts.

High Intensity Statins evidence: benefit ≠ cure

(secondary prevention Trials)

Largest CAD trials comparing intensive statin strategies

Trial (population)	Comparator	Follow-up	N (Statin)*	N (Control)*	Trial "MACE" definition	**MACE — Statin**	**MACE — Control**	**All-cause deaths — Statin**	**All-cause deaths — Control**
TNT (stable CAD)	Atorva 80 vs 10 mg	4.9 y (median)	4,995	5,006	Major CV events	**435 (8.7%)** 20% RRR	**546 (10.9%)**	**285 (+5.7%)** INCREASE	**280 (5.6%)**
IDEAL (prior MI)	Atorva 80 vs Simva 20–40	4.8 y (median)	4,439	4,449	Major coronary event	**411 (9.3%)** 11% RRR	**463 (10.4%)**	**366 (8.2%)** NEUTRAL	**374 (8.4%)**
PROVE-IT TIMI-22 (recent ACS)	Atorva 80 vs Prava 40	~2 y (mean)	2,099	2,063	Death, MI, UA, revasc, stroke	**464 (22.1%)** 15% RRR	**537 (26.0%)**	**46 (2.2%)** 31% RRR	**66 (3.2%)**
MIRACL (early post-ACS)	Atorva 80 vs placebo	16 w	1,538	1,548	Death, MI, cardiac arrest, UA	**228 (14.8%)** 15% RRR	**269 (17.4%)**	**64 (4.2%)** NEUTRAL	**68 (4.4%)**

Take-home

Intensive statin strategies lower MACE, yet deaths and events persist

Refs: (1) TNT — ACC trial summary (% used to derive counts). (2) IDEAL — counts; % derived from counts/N. (3) PROVE-IT — ACC (% for deaths) + JACC analysis for primary events. (4) MIRACL — counts; % derived from counts/N.
Note: Endpoints differ across trials. TNT/PROVE-IT counts for some outcomes were derived by rounding N×reported %.

High-Intensity Statins (Secondary Prevention): benefit ≠ cure

Pooled CAD trials comparing high-intensity strategies (TNT, IDEAL, PROVE-IT, MIRACL): ~26,100 patients • 16 weeks–~5 years

Compared to control, high-intensity strategies modestly reduce major CV events; mortality difference is small.

Major CV events (MACE*)

High-intensity	12%
Control	14%

14% RRR

≈ 2 fewer events per 100

ARR: 2.1/ NNT 48

All-cause death

High-intensity	5.8%
Control	6.0%

3% RRR

≈ 0.2 fewer deaths per 100

ARR: 0.2%

Residual risk remains (even on high-intensity):

- ~12/100 still have a major CV event (MACE*)
- ~6/100 still die over 16 weeks–~5 years (NO DIFFERENCE)

Secondary prevention (stable CAD / prior MI / ACS). Comparators vary (moderate statin or placebo). Rates shown are crude pooled percentages from trial counts.

PCSK9 inhibition evidence: Lower LDL <55 (APoB <55)

fewer events, but not zero

With very low LDL levels, event rates fall—but patients still have MACE and deaths.

Trial (population)	Comparator	Follow-up	N (Tx) **(n; LDL)**	N (Placebo) **(n; LDL)**	Trial "MACE" definition	**MACE — Tx**	**MACE — Placebo**	**All-cause deaths — Tx**	**All-cause deaths — Placebo**
FOURIER (stable ASCVD)	**Evolocumab + statin** vs **placebo** + statin	2.2 y (median)	**13,784** **(LDL 30 mg/dL/ apoB ~38)**	**13,780** **(LDL 92 mg/dL)**	CV death, MI, stroke	**816** **(5.9%)** 20% RRR	**1,013** **(7.4%)**	**444** **(3.2%)** NEUTRAL	**426** **(3.1%)**
ODYSSEY OUTCOMES (recent ACS)	**Alirocumab + statin** vs **placebo** + statin	2.8 y (median)	**9,462** **(LDL 53 mg/dL apoB 39)**	**9,462** **(LDL 101 mg/dL)**	CHD death, MI, ischemic stroke, UA hosp	**903** **(9.5%)** 15% RRR	**1,052** **(11.1%)**	**334** **(3.5%)** 15% RRR	**392** **(4.1%)**
VESALIUS-CV (high-risk ASCVD, no prior MI/stroke)	Evolocumab vs placebo (on statin)	4.6 y (median)	6,106 **(LDL 45 mg/dL)**	6,110 **(LDL 109 mg/dL)**	CV death, MI, stroke	**336** **(6.2%)** 23% RRR	**443** **(8.0%)**	**434** **(7.9%)** 19% RRR	**539** **(9.7%)**

Take-home

- Achieving LDL <55 lowers MACE, but events and deaths persist
- "Better" therapy moves risk down; it rarely moves risk to zero.

Refs: (1) FOURIER NEJM 2017. (2) ODYSSEY OUTCOMES NEJM 2018. (3) VESALIUS-CV (TIMI 66) NEJM 2023.
Note: Endpoints differ (ODYSSEY uses 4-pt composite incl. UA hospitalization). For apples-to-apples, present hard 3-pt MACE across trials.

PCSK9 inhibitors (LDL <55 & ApoB <50): benefit ≠ cure

Pooled outcomes trials (FOURIER, ODYSSEY OUTCOMES, VESALIUS-CV): ~58,700 patients • ~2–4.6 years

Compared to placebo + statin, PCSK9 inhibition lowers MACE; mortality difference is small — residual risk remains.

Major CV events (MACE*)

PCSK9i	7.0%
Placebo	8.5%

18% RRR

≈ 1.5 fewer events per 100

Absolute difference: 1.5%

All-cause death

PCSK9i	4.1%
Placebo	4.6%

11% RRR

≈ 0.5 fewer deaths per 100

Absolute difference: 0.5%

Residual risk remains (even on PCSK9i):

- ~7/100 still have MACE
- ~4/100 still die over ~2–4.6 years

High-risk ASCVD / ACS populations on background statin therapy. Rates shown are crude pooled percentages from trial counts.

Blind spot in RCTs: Is CAD prevented — or just postponed?

Observed during the trial (≈2–5 years)

What MACE tells you

- **Endpoints** are counted only until follow-up ends *(the trial "**stops the clock**").*
- **Lower MACE** at 4y can reflect **prevention** (fewer lifetime events) *or* **postponement** ?(events shifted later).

TAKE-HOME: **"Trials stop the clock; biology doesn't."**

After the trial ends (4 → 10+ years)

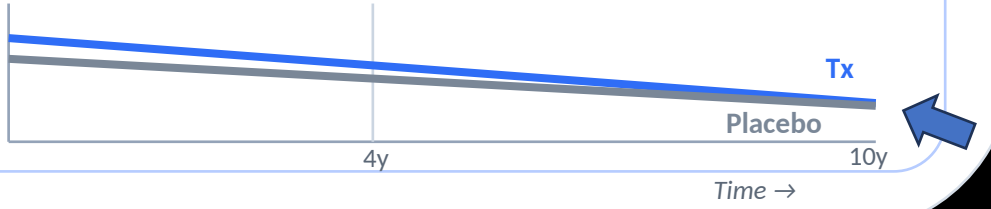
Key question: Are "good outcomes" at 4 years **still** good at 10 years ?

Scenario A — Prevention: curves stay separated

Therapy reduces lifetime event count; separation persists at 10y.

Scenario B — Delay: curves converge after 4y

If mostly postponement, placebo "catches up" and long-term differences shrink.



Illustrative concept (not long-term trial data). Pair outcomes with a CAD "disease readout" to test durability.

Why residual risk persists

Mechanisms

Common reasons patients still have events

Serial CT trackable

CAC/CTA: plaque burden • phenotype • progression

Undiagnosed disease / missed screening

No imaging → disease stays “invisible” until first event.

High starting plaque burden

More disease → more “dice rolls” over time.

Active plaque biology

Lipid-rich core, inflammation, FAI, remodeling → higher-risk phenotype.

Other drivers

Thrombosis • comorbidity • treatment gaps • adherence

Thrombosis + platelets

Endothelial dysfunction + triggers → clot events.

Aging + comorbidities

HF, AF, CKD, frailty, cancer, systemic inflammation, etc.

Treatment gaps

Dose, tolerability, cost, access, “therapeutic inertia”.

Adherence + lifestyle

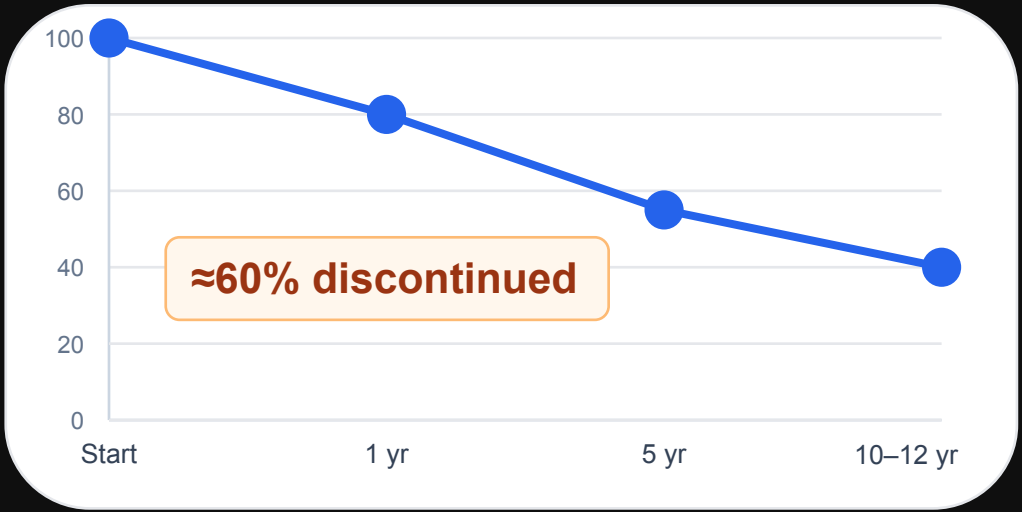
The best plan fails if it isn’t lived (time × persistence).

Clinical framing: “CT-trackable” ≠ fully controllable — it’s one bucket. Residual risk persists via multiple pathways.

Discontinuation rises over ~10 years

Without reinforcement, persistence erodes over time

Persistence decays without reinforcement



>50% discontinue by ~10–12 years.

Why persistence erodes

- Low symptoms → urgency fades
- Perceived need declines after the initial “trigger” visit
- Friction: side effects, cost/access, regimen complexity
- Competing priorities: comorbidities, life events

Reinforcement levers that sustain persistence

- Schedule “re-trigger” touchpoints (serial imaging/ feedback)
- Use results to set shared goals + next step

Sources (examples): Kalia et al., Atherosclerosis (2006); Rozanski et al., JACC (2011) (EISNER); Chowdhury et al., Eur Heart J (2013)

Case

11/7/2024 CCTA: PROGRESSION + Clot

LM

50% (increase)

pLAD

50–69% (increase)

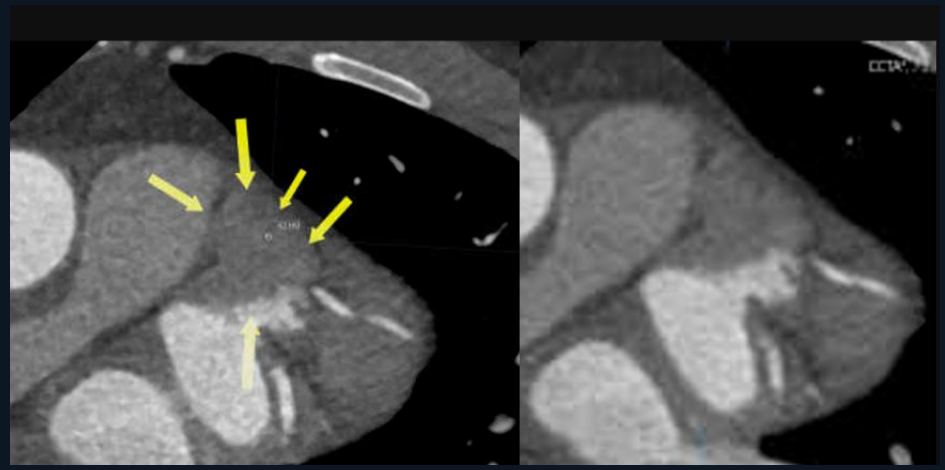
LAA

Thrombus

Symptoms & monitoring

- **Symptoms:** Asymptomatic. No palpitations.
- **Zio monitor:** Schedule 2-week monitor.
- **Outcome:** No AF detected on Zio.

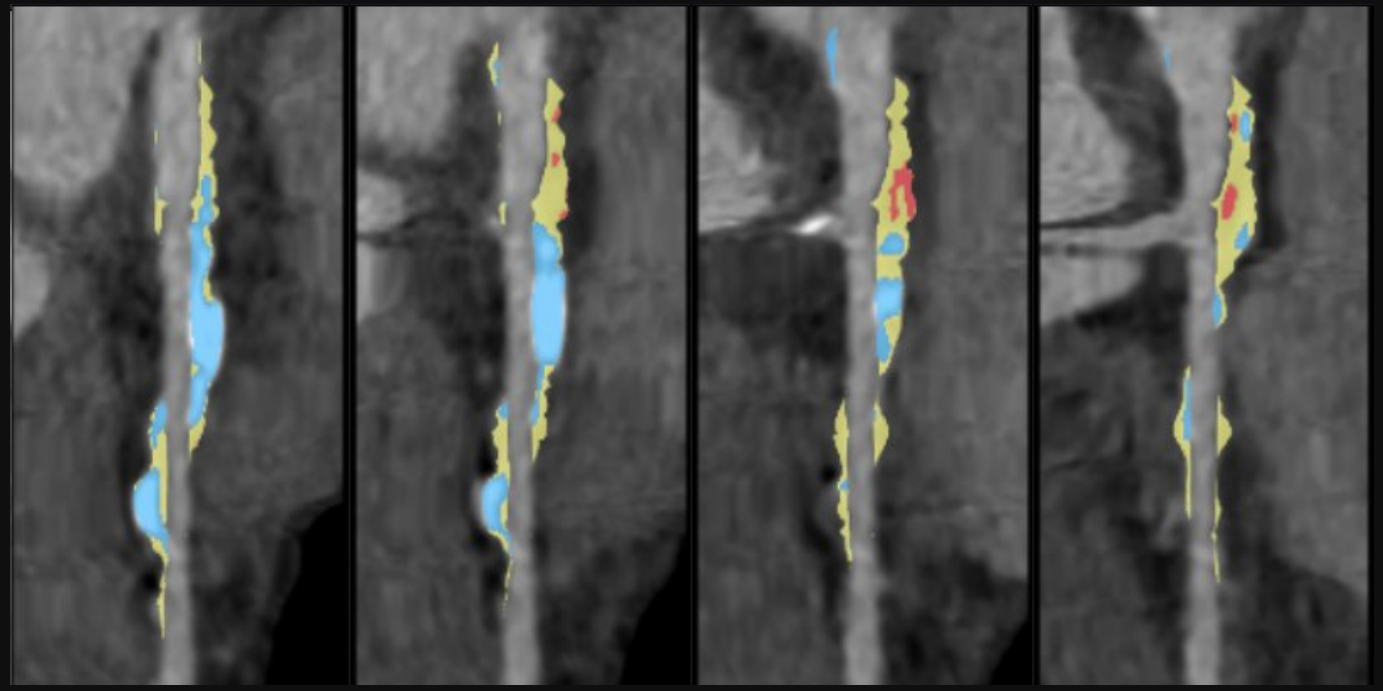
LAA thrombus (arrows)

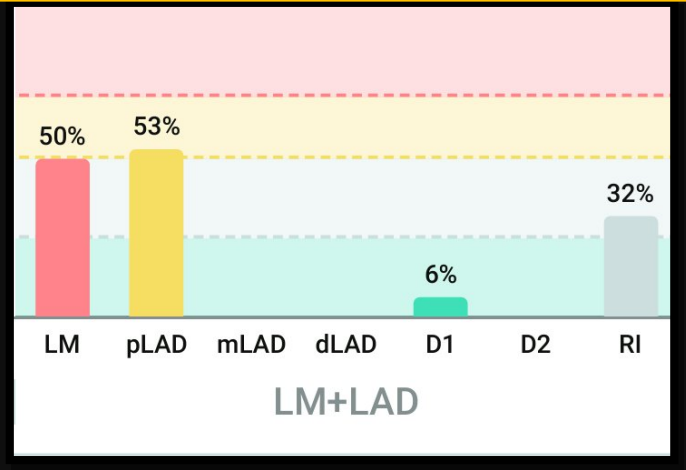


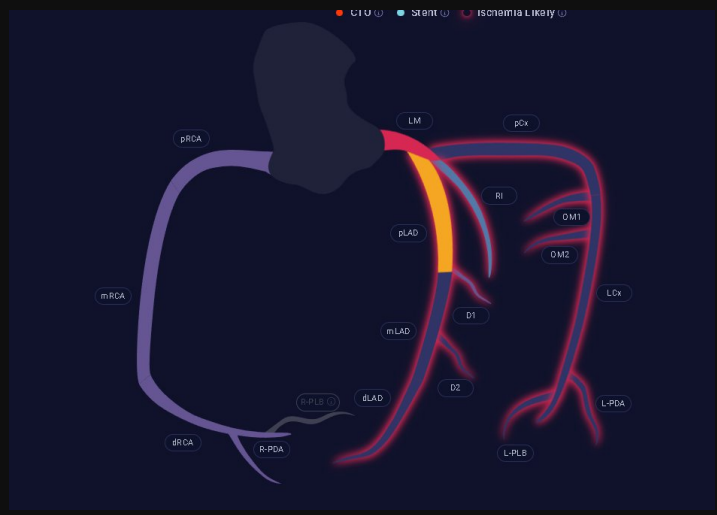
Asymptomatic Afib diagnosed indirectly

Case

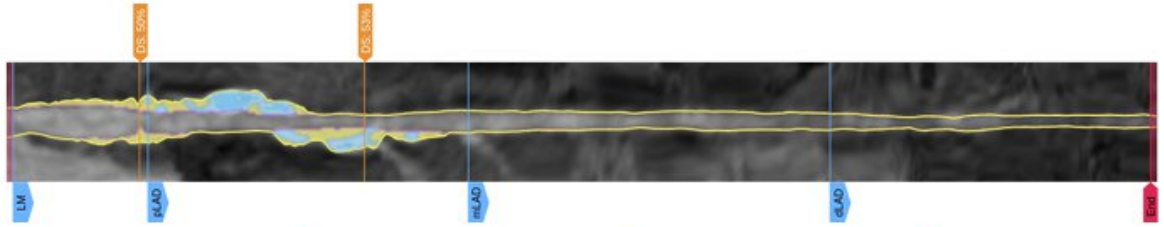
11/7/24 CCTA: LM/LAD







Left Main and Left Anterior Descending (LM+LAD) ISCHEMIA LIKELY Ischemia likely present in LAD only



623.1 mm³ 43.3% PAV
Total Plaque Volume

19.4 mm³ 1.3% PAV
Low-Density - Non-Calcified Plaque Volume

418.9 mm³ 29.1% PAV
Total Non-Calcified Plaque Volume

204.2 mm³ 14.2% PAV
Total Calcified Plaque Volume

53% Greatest Diameter Stenosis

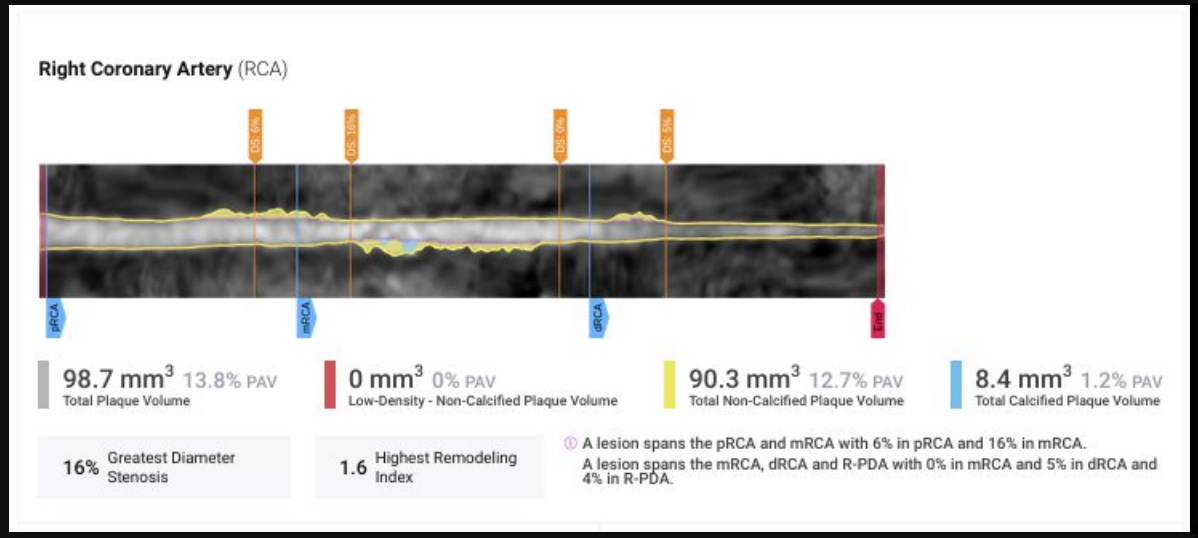
1.6 Highest Remodeling Index

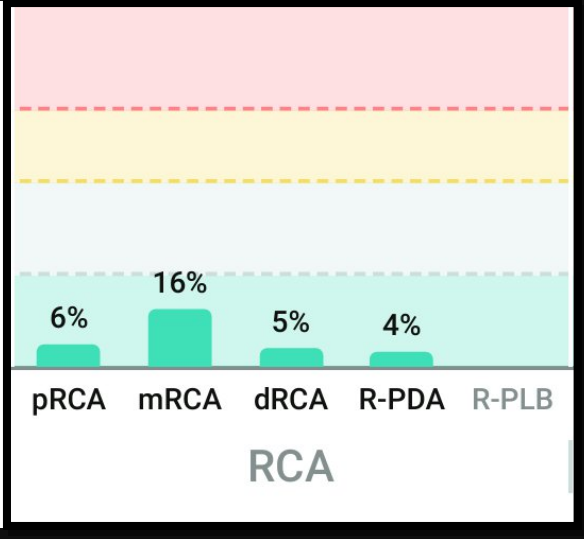
ⓘ A lesion spans the LM, pLAD and RI with 50% in LM and 53% in pLAD and 32% in RI.

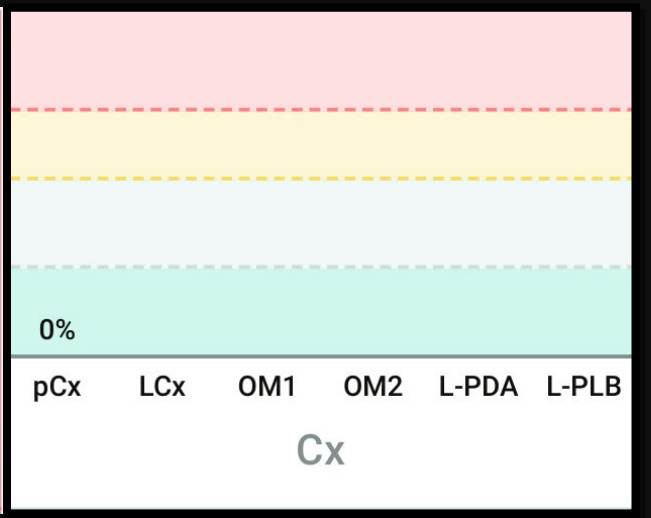
Ischemia Likely present in: LAD D1 D2 Cx OM1 OM2 L-PDA L-PLB RI

Case

11/7/24 CCTA: RCA & LCX





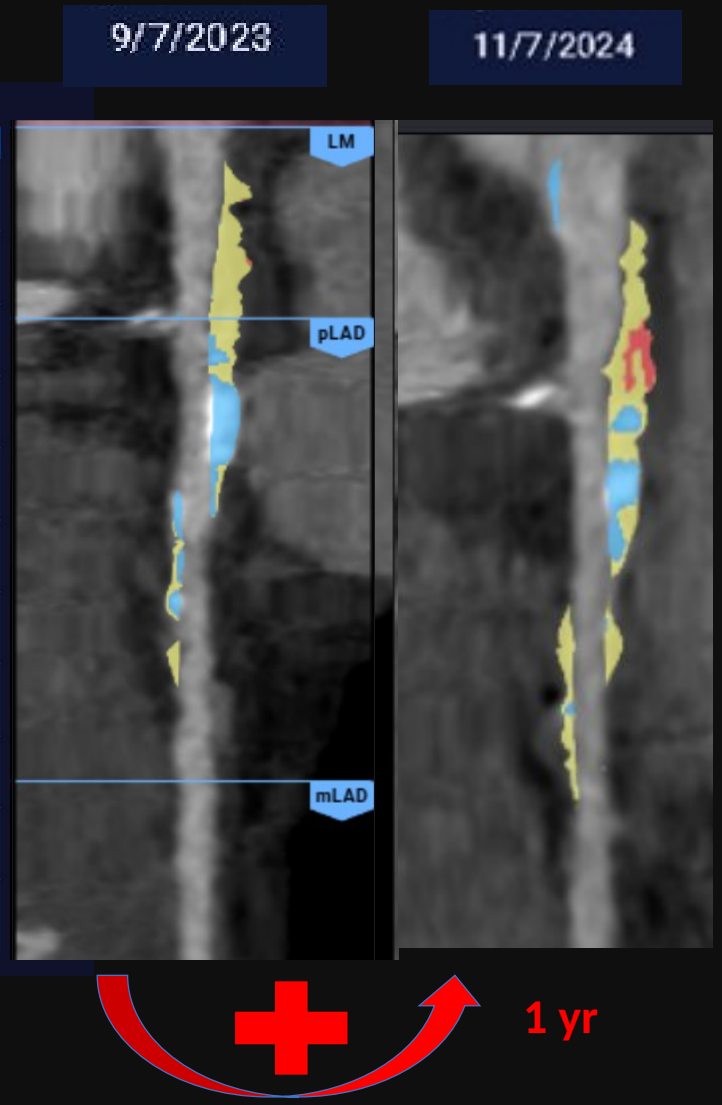


Case

11/7/24 Cleerly Atherosclerosis COMPARE

TPV +35/annualized

ALL (mm³ / PAV)	Compared Cleerly ID: HLTTNDLL 8/15/2014	# / %	Current Cleerly ID: 3C1972CB 9/7/2023	# / %	Current Cleerly ID: 7B90E2A4 11/7/2024
Total Plaque Volume (mm³)	408.9	+318.9	727.8	+172.7	900.5
Total Non-Calcified Plaque Volume (mm³)	303.7	+195.5	499.2	+141.4	640.6
Low-Density - Non-Calcified Plaque Volume (mm³)	8.2	+11	19.2	+0.2	19.4
Total Calcified Plaque Volume (mm³)	105.2	+123.4	228.6	+31.3	259.9
# of Severe Stenosis	0	=	0	+1	1
# of Moderate Stenosis	0	=	0	+1	1
Highest Remodeling Index	1.6	-0.1	1.5	+1	2.5
Greatest Diameter Stenosis (%)	35	+11	46	+7	53
Greatest Area Stenosis (%)	61	+13	74	+4	78
Length (mm)	660.3	-1.8	658.5	+48.5	707



Case

Progression Despite Targets Achieved

Parameter	2017–2025 Trend	% Change / Impact	Target Met
LDL-C	92 → 11 mg/dL	**– 86 % ↓**	●
ApoB	?		●
Lp(a)	?		●
A1c	**5.0 %**	Normoglycemic, Insulin resistance?	●
Weight	219 lb **(BMI ≈ 29)**	Optimal BMI <30	●

Evidence-Based Therapy

- **Atorvastatin 40 mg daily**
- **Repatha 140 mg every 2 weeks**

Progressing Low-density plaque still **HIGH risk** **for rupture**

Case

11/7/24 Management

Lipid & Antithrombotic Optimization

- **Increase Atorvastatin to 80 mg daily**.
- **Continue** Repatha **140 mg** every 2 weeks.
- **Start Xarelto 15 mg nightly + ASA 81 mg daily.**
- **Start low-dose colchicine 0.6 for Inflammation Modulation**.

Advanced Biomarkers

Assess **Lp(a)**, **ApoB**, **hs-CRP**, and **TG, Insulin levels** to evaluate residual risk.

Lifestyle Intensification

- **Weight < 200 lb** (focus on visceral fat reduction).
- **Anti-inflammatory diet**.

Imaging Follow-Up

Repeat CCTA Cleerly in 6 months to assess biological and structural response to therapy and **LAA thrombus resolution**.

Case

5/8/2025 CCTA

CCTA findings

Date: 5/8/2025

Left main (LM)	prox LAD (pLAD)	RCA
>50% (Increase)	50-69%	<25%

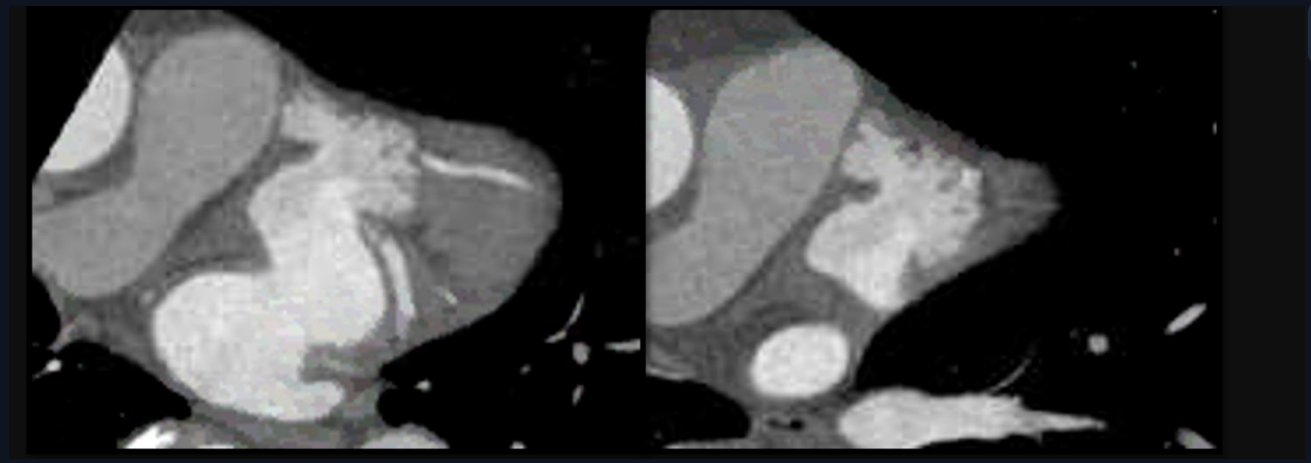
✓ Thrombus resolved

Goals met

Symptoms: none

LDL (mg/dL) 13 (34 → 13)	ApoB (mg/dL) 24
Lp(a) <10	A1c 5.2%
Weight / BMI 205 lb (BMI 27)	hs-CRP <0.3

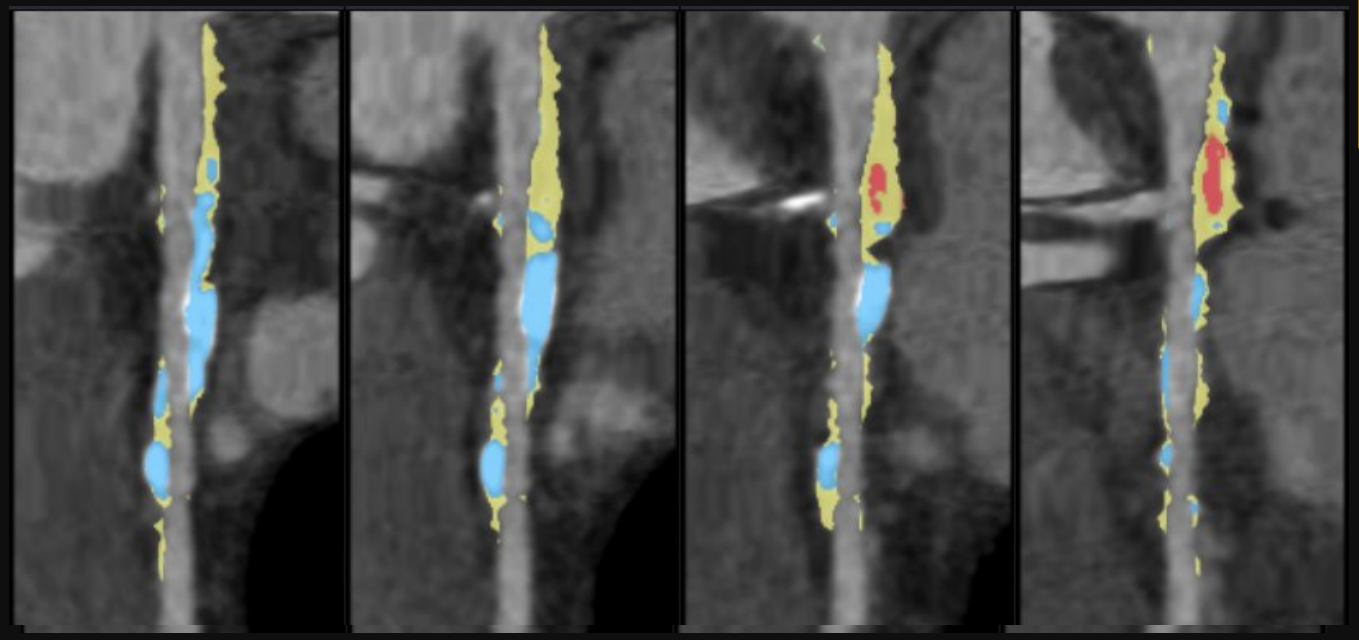
CCTA images

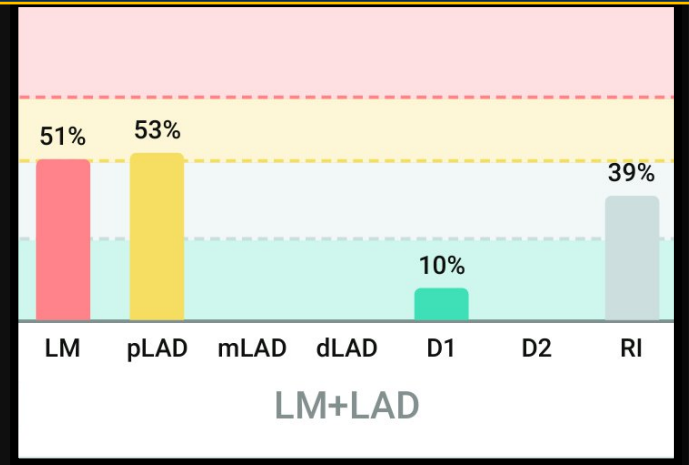


Follow-up: May 2025

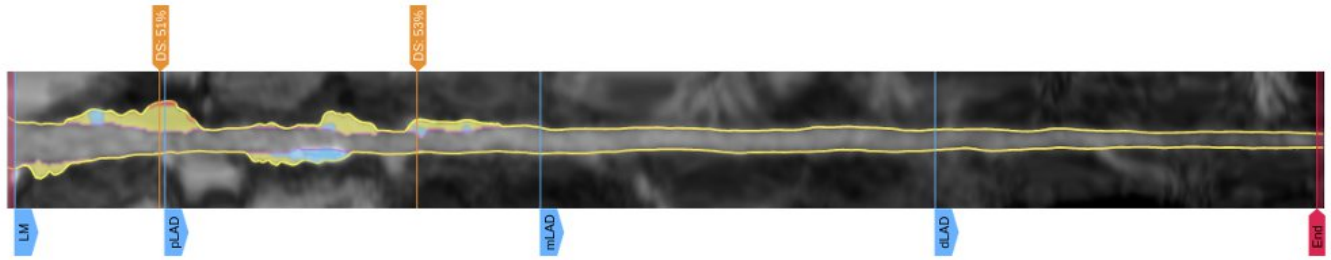
Case

5/8/25 CCTA: LM/LAD





Left Main and Left Anterior Descending (LM+LAD) ISCHEMIA LIKELY Ischemia likely present in LAD only



665.5 mm³ 43.4% PAV
Total Plaque Volume

26.7 mm³ 1.7% PAV
Low-Density - Non-Calcified Plaque Volume

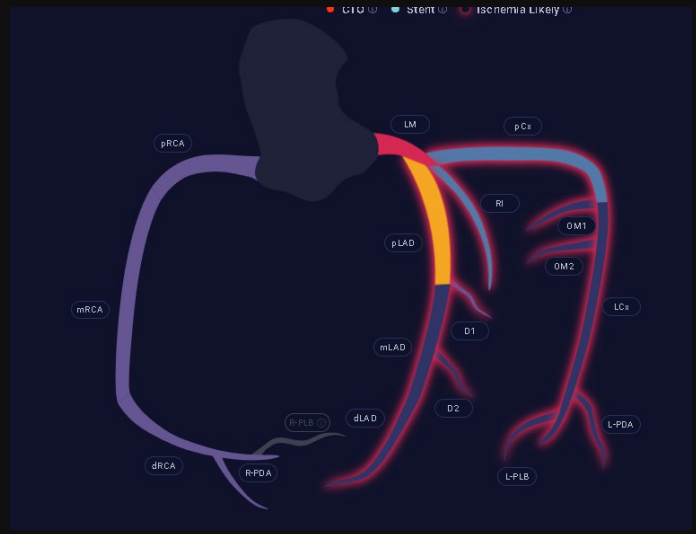
466.5 mm³ 30.4% PAV
Total Non-Calcified Plaque Volume

199 mm³ 13% PAV
Total Calcified Plaque Volume

53% Greatest Diameter Stenosis

1.5 Highest Remodeling Index

A lesion spans the LM, pLAD, D1 and pCx with 51% in LM and 53% in pLAD and 10% in D1 and 28% in pCx.

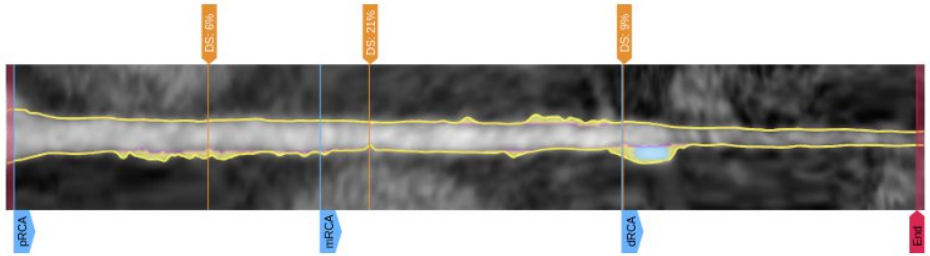


Ischemia Likely present in: LAD D1 D2 Cx OM1 OM2 L-PDA L-PLB RI

Case

5/8/25 CCTA: RCA & LCX

Right Coronary Artery (RCA)

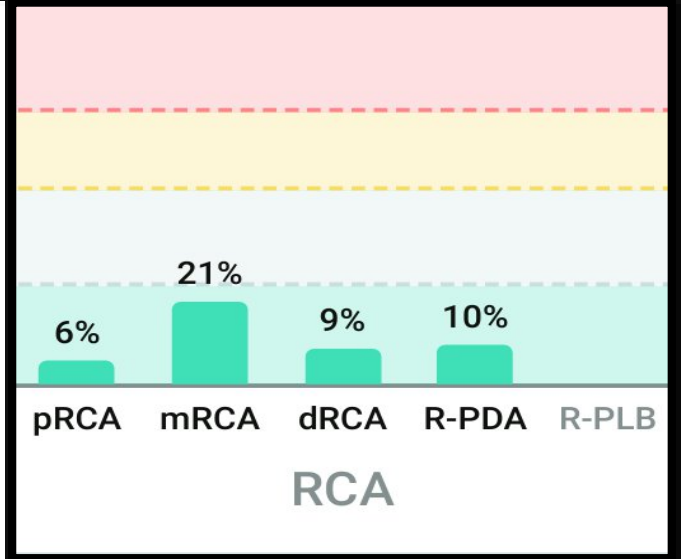


111.2 mm³ 14.1% PAV	0.1 mm³ < 0.1% PAV	100 mm³ 12.7% PAV	11.2 mm³ 1.4% PAV
Total Plaque Volume	Low-Density - Non-Calcified Plaque Volume	Total Non-Calcified Plaque Volume	Total Calcified Plaque Volume

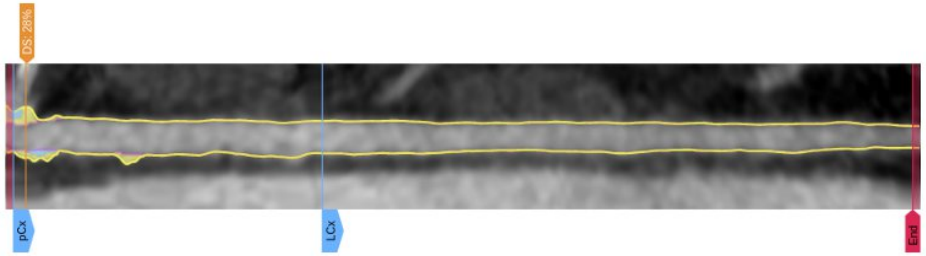
21% Greatest Diameter Stenosis

1.5 Highest Remodeling Index

ⓘ A lesion spans the pRCA, mRCA, dRCA and R-PDA with 6% in pRCA and 21% in mRCA and 9% in dRCA and 10% in R-PDA.



Circumflex (Cx) ISCHEMIA LIKELY

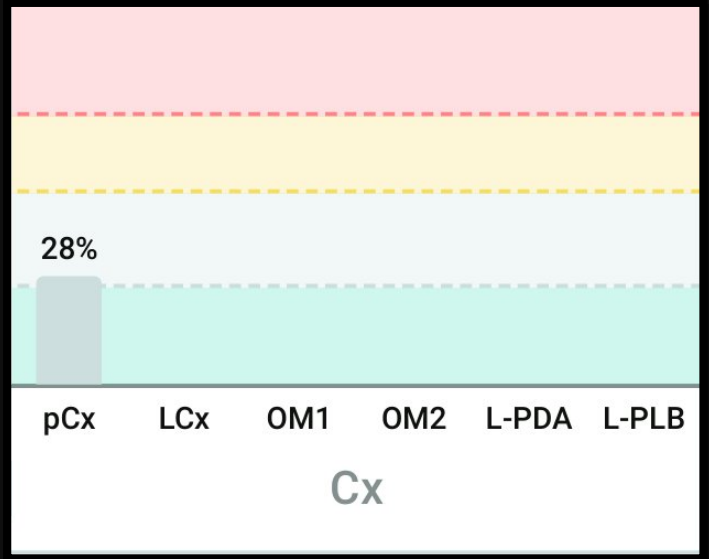


99.9 mm³ 10.5% PAV	0.1 mm³ < 0.1% PAV	74.1 mm³ 7.8% PAV	25.8 mm³ 2.7% PAV
Total Plaque Volume	Low-Density - Non-Calcified Plaque Volume	Total Non-Calcified Plaque Volume	Total Calcified Plaque Volume

28% Greatest Diameter Stenosis

1.3 Highest Remodeling Index

ⓘ A lesion spans the LM, pLAD, D1 and pCx with 51% in LM and 53% in pLAD and 10% in D1 and 28% in pCx.



Case

5/8/25 Cleerly Atherosclerosis COMPARE

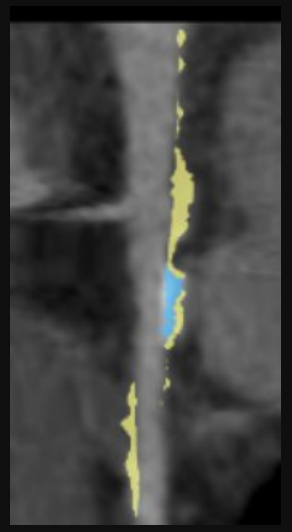
TPV +35/ annualized

ALL (mm³ / PAV)	Compared Cleerly ID: HLTTNDLL 8/15/2014	# / %	Current Cleerly ID: 3C1972CB 9/7/2023	# / %	Current Cleerly ID: 7B90E2A4 11/7/2024	# / %	Current Cleerly ID: 8984FEDE 5/8/2025
Total Plaque Volume (mm³)	408.9	▲ +318.9	727.8	▲ +172.7	900.5	▲ +85.3	985.8
Total Non-Calcified Plaque Volume (mm³)	303.7	▲ +195.5	499.2	▲ +141.4	640.6	▲ +84.6	725.2
Low-Density - Non-Calcified Plaque Volume (mm³)	8.2	▲ +11	19.2	▲ +0.2	19.4	▲ +7.6	27
Total Calcified Plaque Volume (mm³)	105.2	▲ +123.4	228.6	▲ +31.3	259.9	▲ +0.7	260.6
# of Severe Stenosis	0	=	0	▲ +1	1	=	1
# of Moderate Stenosis	0	=	0	▲ +1	1	=	1
Highest Remodeling Index	1.6	▼ -0.1	1.5	▲ +1	2.5	▼ -0.3	2.2
Greatest Diameter Stenosis (%)	35	▲ +11	46	▲ +7	53	=	53
Greatest Area Stenosis (%)	61	▲ +13	74	▲ +4	78	▲ +3	81
Length (mm)	660.3	▼ -1.8	658.5	▲ +48.5	707	=	707

Case

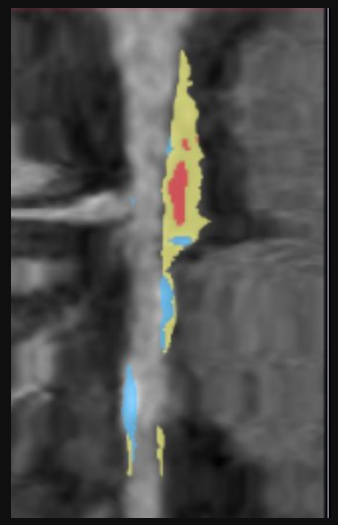
Left Main progression

8/15/2014



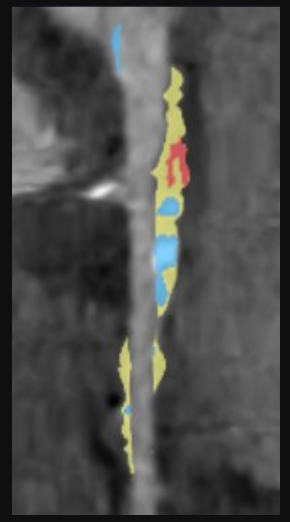
NCPV: 216.6 mm^3
LAP: 8.0 mm^3
LM: 0%
ISCHEMIA: Negative

9/7/2023
9 years



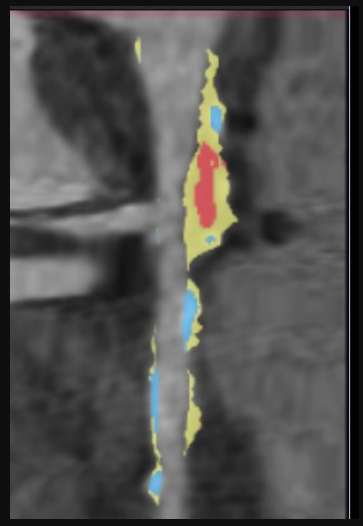
NCPV: 369.8 mm^3 **(+153.2 mm^3)**
LAP: 19.2 mm^3 **(+11.2 mm^3)**
LM: 43% **(+43%)**
ISCHEMIA: Negative

11/7/2024
14 months



NCPV: 418.9 mm^3 (**+49.1 mm^3**)
LAP: 19.4 mm^3 (**+0.2 mm^3**)
LM: 50% (**+7%**)
ISCHEMIA: Positive

5/8/2025
6 months



NCPV: 466.5 mm^3 (**+47.6 mm^3**)
LAP: 26.7 mm^3 (**+7.3 mm^3**)
LM: 51% (**+1%**)
ISCHEMIA: Positive

Case

Progression Despite Targets Achieved

Parameter	2017–2025 Trend	% Change / Impact	Target Met
LDL-C	92 → 13 mg/dL	**– 86 % ↓**	●
ApoB	→ 24 mg/dL	Minimal residual risk	●
Lp(a)	→ < 10 nmol/L	Minimal residual risk	●
A1c	5.0 → 5.2 %	Normoglycemic	●
Weight	219 lb → 205 lb **(BMI ≈ 27)**	**–19 lb ↓** (Optimal BMI <30)	●

Aggressive, Evidence-Based Therapy

- **Atorvastatin 80 mg daily**
- **Repatha 140 mg every 2 weeks**
- **Xarelto 15 mg nightly + ASA 81 mg daily**
- **Colchicine 0.6 mg daily**

Case

Case

5/8/2025 Management

Lipid & Antithrombotic Optimization

- **Continue** Atorvastatin **80 mg daily.**
- **Continue** Repatha **140 mg** every 2 weeks.
- **Continue** low-dose colchicine **0.6.**
- **Reduce** Xarelto to **2.5 mg BID** (per patient preference; risk discussed) + **ASA 81 mg daily.**
- **Start microdosing Semiglutide 0.25→0.5 mg weekly (GLP-1 for metabolic & anti-inflammatory benefit).**

Imaging Follow-Up

Repeat **Cleerly CCTA in** **6 months** to assess biological and structural response to therapy.

Case

11/5/2025 CCTA

• IMPROVEMENT / STABILIZATION

CCTA Findings

LM: <50%

pLAD: 50–69%

RCA: <25%

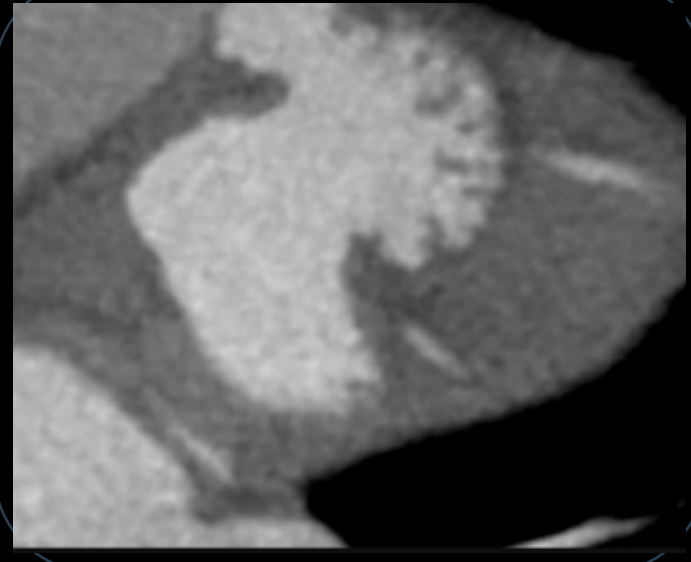
LCX: <25%

Goals Met

LDL	Lp(a)	ApoB
13 mg/dL	<10	24 mg/dL

A1c	Weight
5.2%	200 lb

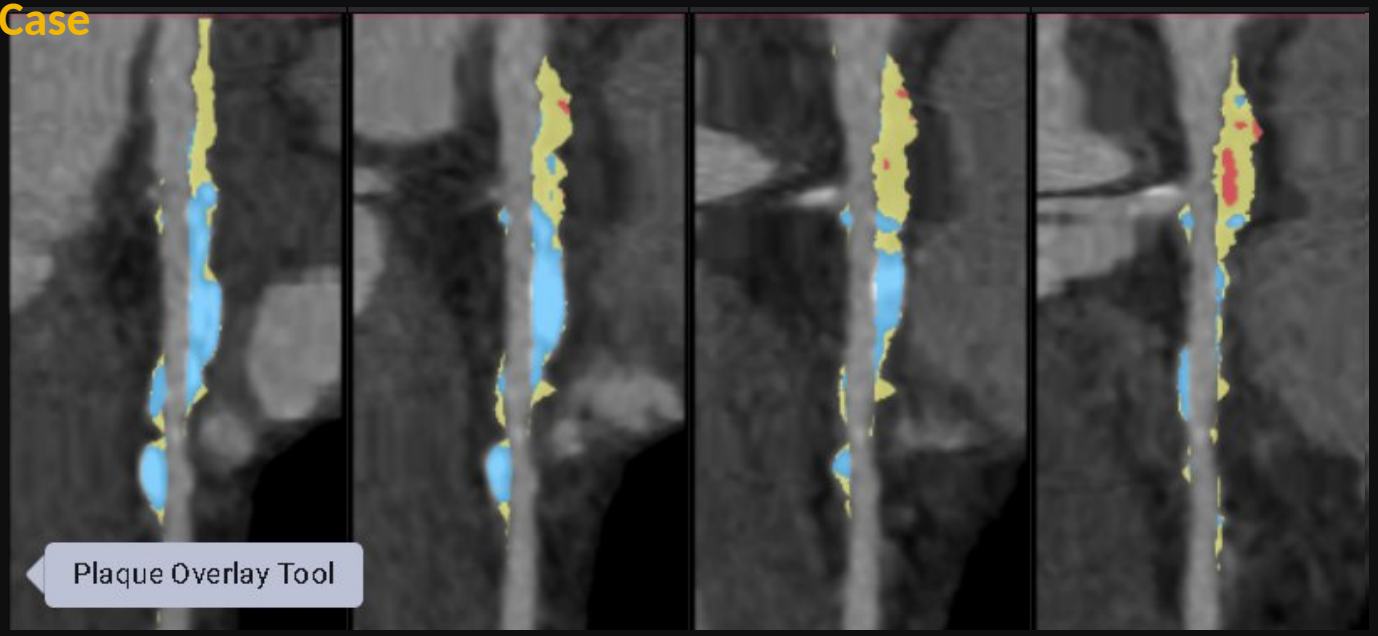
Representative CCTA image



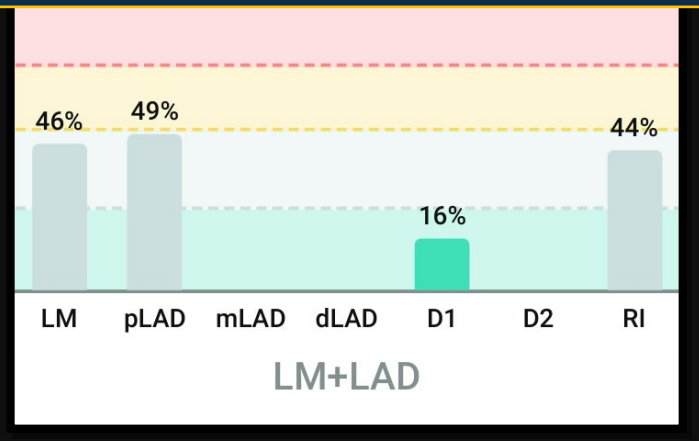
Symptoms: None

Overall: improvement / stability

Case

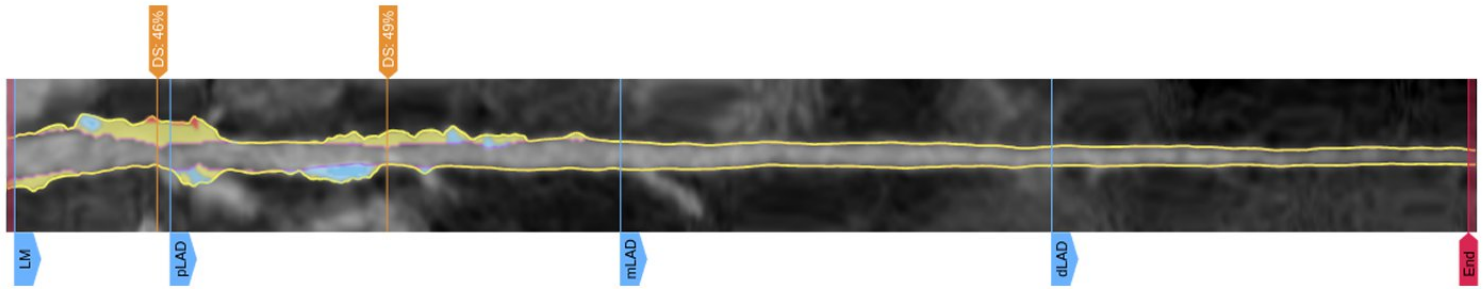


11/5/25 CCTA: LM/LAD



RESOLVED

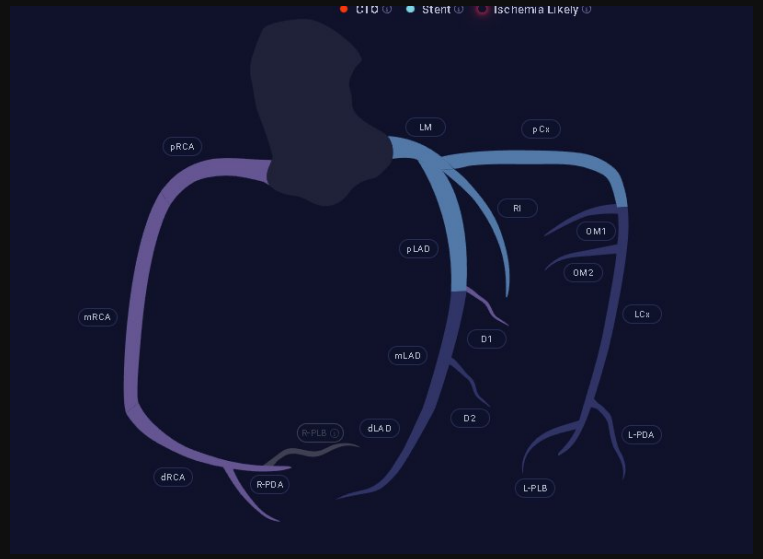
Left Main and Left Anterior Descending (LM+LAD)



678 mm³ 46.5% PAV	21.5 mm³ 1.5% PAV	455.7 mm³ 31.2% PAV	222.3 mm³ 15.2% PAV
Total Plaque Volume	Low-Density - Non-Calcified Plaque Volume	Total Non-Calcified Plaque Volume	Total Calcified Plaque Volume

49%	Greatest Diameter Stenosis
1.6	Highest Remodeling Index

ⓘ A lesion spans the LM, pLAD, D1, pCx, LCx and RI with 46% in LM and 49% in pLAD and 16% in D1 and 29% in pCx and 0% in LCx and 44% in RI.

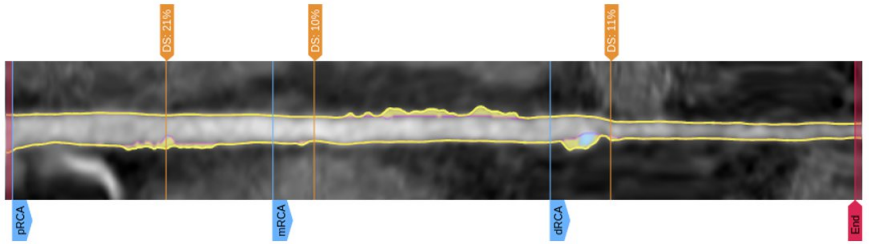


Ischemia	Analyzed - No vessels are likely ischemic

Case

11/5/25 CCTA: RCA & LCX

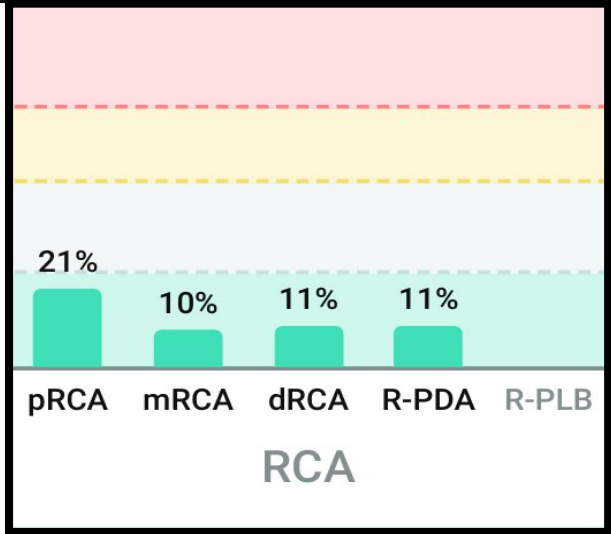
Right Coronary Artery (RCA)



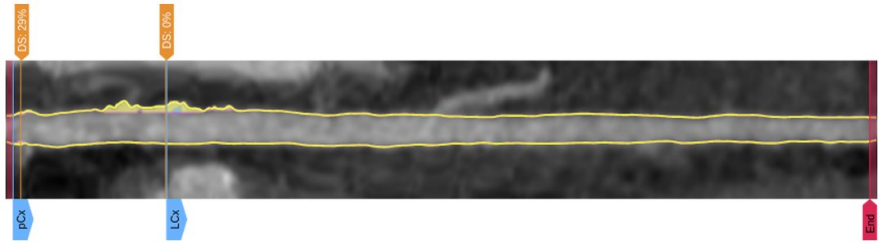
114.3 mm³ 15.8% PAV Total Plaque Volume	0 mm³ 0% PAV Low-Density - Non-Calcified Plaque Volume	101.9 mm³ 14.1% PAV Total Non-Calcified Plaque Volume	12.4 mm³ 1.7% PAV Total Calcified Plaque Volume

21% Greatest Diameter Stenosis	1.6 Highest Remodeling Index

ⓘ A lesion spans the pRCA, mRCA, dRCA and R-PDA with 21% in pRCA and 10% in mRCA and 11% in dRCA and 11% in R-PDA.



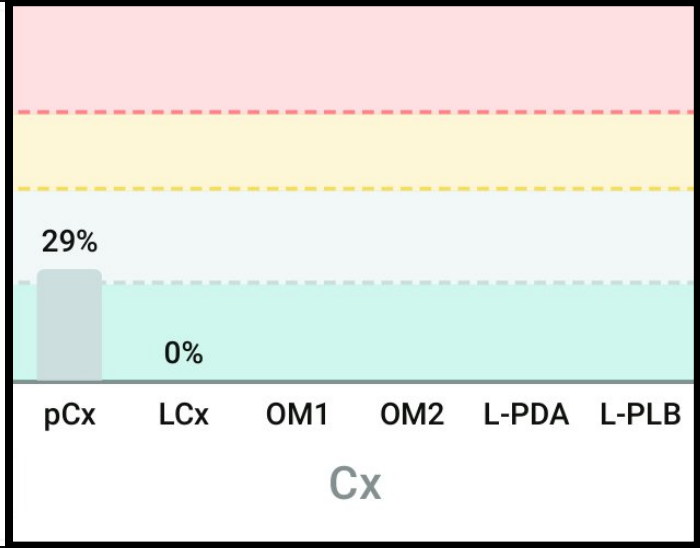
Circumflex (Cx)



73.4 mm³ 7.8% PAV Total Plaque Volume	0 mm³ 0% PAV Low-Density - Non-Calcified Plaque Volume	51.1 mm³ 5.5% PAV Total Non-Calcified Plaque Volume	22.3 mm³ 2.4% PAV Total Calcified Plaque Volume

29% Greatest Diameter Stenosis	1.2 Highest Remodeling Index

ⓘ A lesion spans the LM, pLAD, D1, pCx, LCx and RI with 46% in LM and 49% in pLAD and 16% in D1 and 29% in pCx and 0% in LCx and 44% in RI.



Case

11/5/25 Cleerly COMPARE

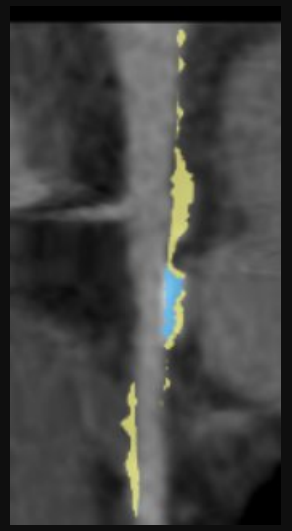
TPV +35/ annualized

ALL (mm³ / PAV)	Compared Cleerly ID: HLTTNDLL 8/15/2014	# / %	Current Cleerly ID: 3C1972CB 9/7/2023	# / %	Current Cleerly ID: 7B90E2A4 11/7/2024	# / %	Current Cleerly ID: 8984FEDE 5/8/2025	# / %	Current Cleerly ID: RPNFHB5F 11/5/2025
Total Plaque Volume (mm³)	408.9	▲ +318.9	727.8	▲ +172.7	900.5	▲ +85.3	985.8	▼ -7.7	978.1
Total Non-Calcified Plaque Volume (mm³)	303.7	▲ +195.5	499.2	▲ +141.4	640.6	▲ +84.6	725.2	▼ -52	673.2
Low-Density - Non-Calcified Plaque Volume (mm³)	8.2	▲ +11	19.2	▲ +0.2	19.4	▲ +7.6	27	▼ -5.4	21.6
Total Calcified Plaque Volume (mm³)	105.2	▲ +123.4	228.6	▲ +31.3	259.9	▲ +0.7	260.6	▲ +44.3	304.9
# of Severe Stenosis	0	=	0	▲ +1	1	=	1	▼ -1	0
# of Moderate Stenosis	0	=	0	▲ +1	1	=	1	▼ -1	0
Highest Remodeling Index	1.6	▼ -0.1	1.5	▲ +1	2.5	▼ -0.3	2.2	▲ +0.2	2.4
Greatest Diameter Stenosis (%)	35	▲ +11	46	▲ +7	53	=	53	▼ -4	49
Greatest Area Stenosis (%)	61	▲ +13	74	▲ +4	78	▲ +3	81	▼ -7	74
Length (mm)	660.3	▼ -1.8	658.5	▲ +48.5	707	=	707	▲ +0.5	707.5

Case

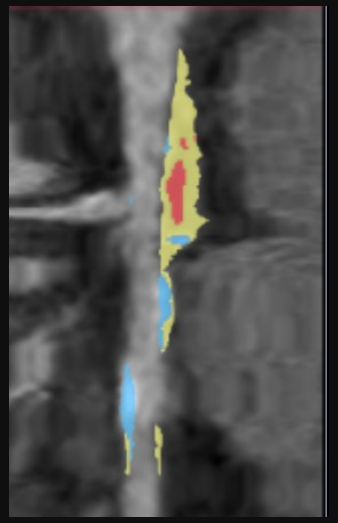
Left Main progression

8/15/2014



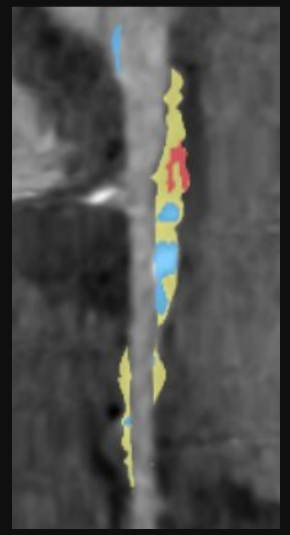
NCPV: 216.6 mm³
LAP: 8.0 mm³
LM: 0%
ISCHEMIA: Negative

9/7/2023
9 years



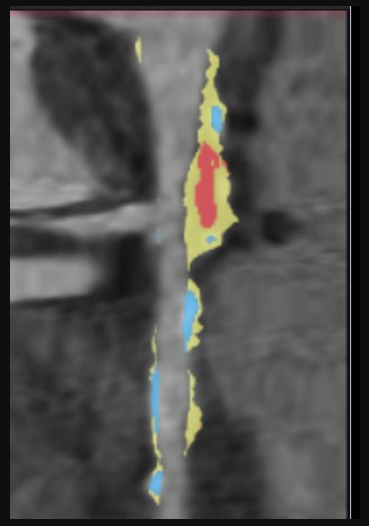
NCPV: 369.8 mm³ **(+153.2 mm³)**
LAP: 19.2 mm³ **(+11.2 mm³)**
LM: 43% **(+43%)**
ISCHEMIA: Negative

11/7/2024
14 months



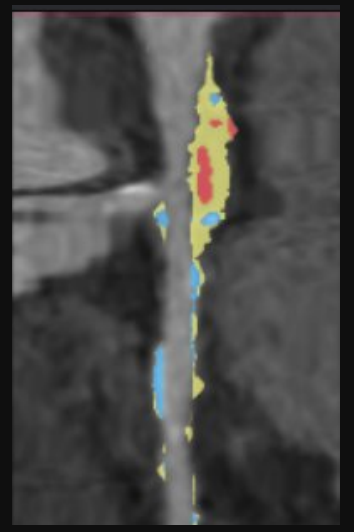
NCPV: 418.9 mm³ **(+49.1 mm³)**
LAP: 19.4 mm³ **(+0.2 mm³)**
LM: 50% **(+7%)**
ISCHEMIA: Positive

5/8/2025
6 months



NCPV: 466.5 mm³ **(+47.6 mm³)**
LAP: 26.7 mm³ **(+7.3 mm³)**
LM: 51% **(+1%)**
ISCHEMIA: Positive

11/5/2025
6 months



NCPV: 455.7 mm³ **(−10.8 mm³)**
LAP: 21.5 mm³ (−5.2 mm³)
LM: 46% **(−5%)**
ISCHEMIA: Negative

Take-Home Points

Trials (RCT's) answer narrow questions — *"what works on average"*

- MACE tells us who had events—not what happened to plaque ("trials stop the clock; biology doesn't").

Serial CCTA + AI - *"is it working in this person?"*

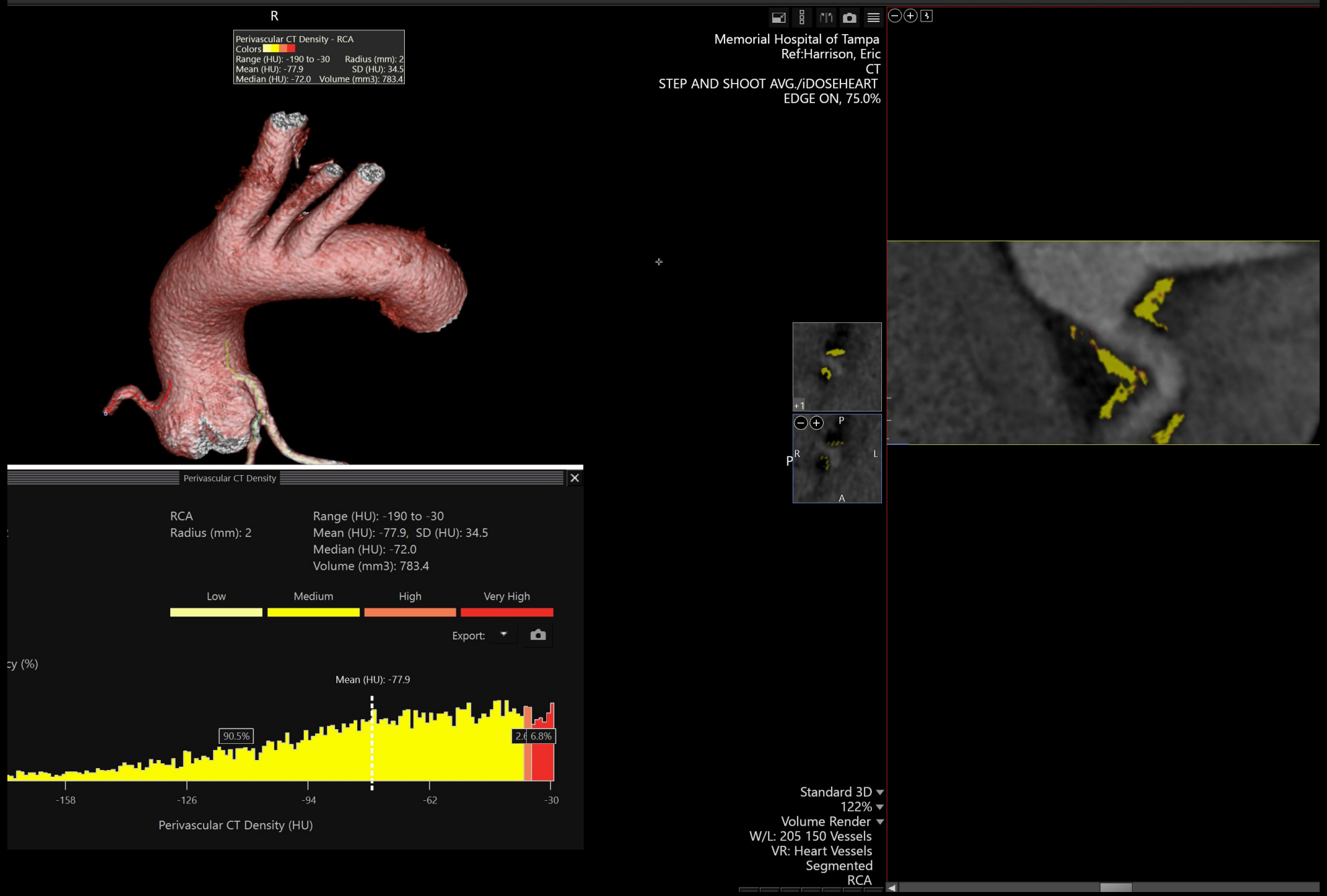
- SEE → TREAT → SEE AGAIN: reveal plaque before symptoms, personalize escalation, spot non-responders early.

Residual risk is expected in CAD

- Atherosclerosis is multi-pathway (lipids + inflammation + cardiometabolic + thrombosis + aging + adherence).
- Plaque progression is **not linear → trajectories vary.**
- Statins & PCSK9 shift the curve—rarely flatten it; risk doesn't go to zero.

We treat heart attacks.
But we don't cure heart disease


R
Perivascular CT Density - RCA
Colors
Range (HU): -190 to -30
Radius (mm): 2
Mean (HU): -65.5
SD (HU): 28.0
Median (HU): -59.0
Volume (mm3): 597.3
SOUTH TAMPA CARDIOLOGY
CT
SCPT Seed
CCTA, 75%, AF2 Low E, CV 70, CardiacCTA
Perivascular CT Density
RCA
Radius (mm): 2
Range (HU): -190 to -30
Mean (HU): -65.5, SD (HU): 28.0
Median (HU): -59.0
Volume (mm3): 597.3
Low
Medium
High
Very High
Export:
uency (%)
Mean (HU): -65.5
85.5%
11.1%
-158
-126
-94
-62
-30
Perivascular CT Density (HU)
+1
P
R
L
A
-1
Standard 3D
122%
Volume Render
W/L: 205 150 Vessels
VR: Heart Vessels
Segmented

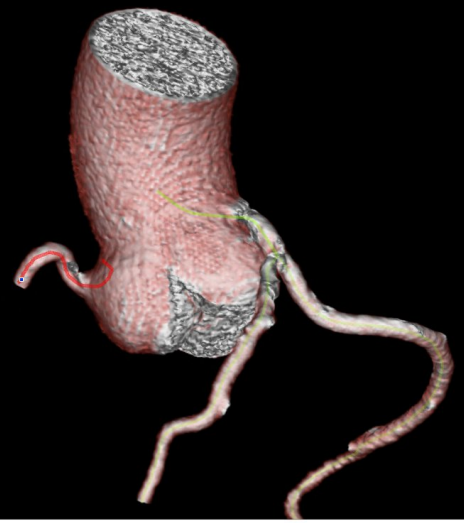

R
Perivascular CT Density - RCA
Colors
Range (HU): -190 to -30
Radius (mm): 2
Mean (HU): -77.9
SD (HU): 34.5
Median (HU): -72.0
Volume (mm3): 783.4
Memorial Hospital of Tampa
Ref:Harrison, Eric
CT
STEP AND SHOOT AVG./iDOSEHEART
EDGE ON, 75.0%
+1
P
R
L
A
Perivascular CT Density
RCA
Radius (mm): 2
Range (HU): -190 to -30
Mean (HU): -77.9, SD (HU): 34.5
Median (HU): -72.0
Volume (mm3): 783.4
Low
Medium
High
Very High
Export:
Mean (HU): -77.9
90.5%
6.8%
-158
-126
-94
-62
-30
Perivascular CT Density (HU)
Standard 3D
122%
Volume Render
W/L: 205 150 Vessels
VR: Heart Vessels
Segmented
RCA

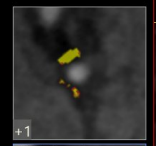

R
Perivascular CT Density - RCA
Colors
Range (HU): -190 to -30
Radius (mm): 2
Mean (HU): -67.0
SD (HU): 29.7
Median (HU): -60.0
Volume (mm3): 562.4
SOUTH TAMPA CARDIOLOGY
Ref:MACDILL AFB
CT
CCTA
CCTA*, 70%, AF2 Medium E, CV 90, CardiacCTA
Perivascular CT Density
RCA
Radius (mm): 2
Range (HU): -190 to -30
Mean (HU): -67.0, SD (HU): 29.7
Median (HU): -60.0
Volume (mm3): 562.4
Low
Medium
High
Very High
Export:
Mean (HU): -67.0
85.6%
11.1%
-158
-126
-94
-62
-30
Perivascular CT Density (HU)
+1
P
R
L
A
Standard 3D
122%
Volume Render
W/L: 205 150 Vessels
VR: Heart Vessels
Segmented
1 of 2

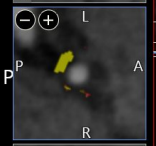
S

Perivascular CT Density - RCA
Colors
Range (HU): -190 to -30 Radius (mm): 2
Mean (HU): -60.0 SD (HU): 23.1
Median (HU): -55.0 Volume (mm3): 573.5

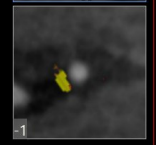
SOUTH TAMPA CARDIOLOGY
Ref:MACDILL AFB
CT
CS-CCTA
CCTA, 75%, AF2 Medium E, DLIR, CardiacCTA

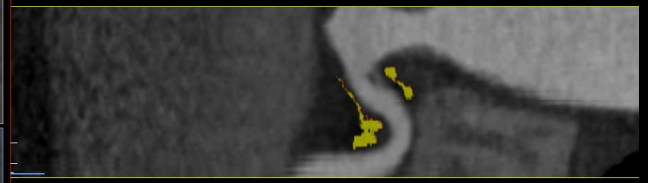






P





Perivascular CT Density

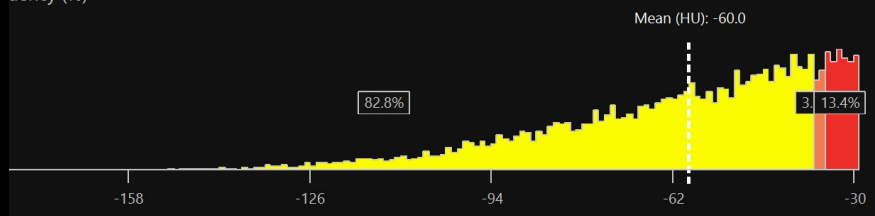
RCA
Radius (mm): 2

Range (HU): -190 to -30
Mean (HU): -60.0, SD (HU): 23.1
Median (HU): -55.0
Volume (mm3): 573.5

Low Medium High Very High

Export:

uency (%)



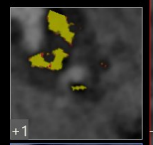
Perivascular CT Density (HU)

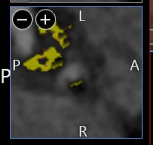
Standard 3D
122%
Volume Render
W/L: 205 150 Vessels
VR: Heart Vessels
Segmented

R

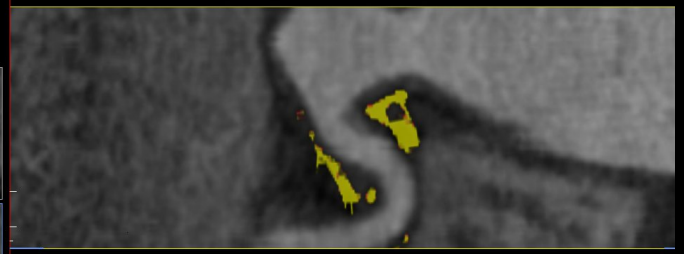
Perivascular CT Density - RCA
Colors
Range (HU): -190 to -30 Radius (mm): 2
Mean (HU): -69.6 SD (HU): 27.3
Median (HU): -66.0 Volume (mm3): 680.5

SOUTH TAMPA CARDIOLOGY
Ref:MACDILL AFB
CT
CCTA
CCTA*, 75%, AF2 Medium E, DLIR, CardiacCTA





P



Perivascular CT Density

RCA
Radius (mm): 2

Range (HU): -190 to -30
Mean (HU): -69.6, SD (HU): 27.3
Median (HU): -66.0
Volume (mm3): 680.5

Low Medium High Very High

Export:

uency (%)

Mean (HU): -69.6

88.8%

2.8 8.4%

-158 -126 -94 -62 -30

Perivascular CT Density (HU)

Standard 3D
122%
Volume Render
W/L: 205 150 Vessels
VR: Heart Vessels
Segmented