Supplementary Table 1: Relevant clinical trials for the treatment of calcified coronary lesions.

Study	Study Arms	Relevant Endpoint(s)	Outcomes/Results*	Conclusions
Cutting Balloon Angioplasty				
GRT[1]	CBA vs. PTCA	Binary restenosis after 6 months	CBA: 31.4% PTCA: 30.4% p=NS	No reduction in restenosis with CBA after 6 months.
RESCUT[2]	CBA vs. PTCA for ISR	Binary restenosis after 7 months	CBA: 29.8% PTCA: 31.4% p=NS	No reduction in recurrent ISR with CBA after 7 months.
CBA before DES[3]	CBA before DES vs. BA	Minimum stent CSA (mm2), Acute lumen gain (mm2)	CBA:6.26±0.4, 3.74±0.38 BA:5.03±0.33, 2.44±0.29 p=0.031, 0.015	CBA achieved larger lumen CSA and larger lumen gain compared to BA.
Mechanisms of Acute Lumen Gain Following Cutting Balloon Angioplasty in Calcified and Noncalcified Lesions[4]	CBA vs. BA in calcified and non-calcified group	ΔEEM CSA (mm2), ΔP+M CSA (mm2), Δlumen CSA (mm2)	<u>Calcified lesions:</u> CBA: 1.4±1.7, -2.3±1.9, 3.7±1.5 BA: 1.2±1.2, -1.8±1.9, 3.0±1.5 p=NS, NS, 0.05 <u>Non-calcified lesions:</u> CBA: 1.0±1.8, -2.9±2.1, 3.9±1.9 BA: 1.6±1.8, -2.0±1.9, 3.6±1.6 p=NS(0.11), 0.03, NS	In calcified lesions, CBA achieves a larger lumen gain vs. BA. In noncalcified lesions, there is larger plaque reduction with CBA but no difference in lumen gain vs. BA.
Scoring Balloon Angioplasty				
Intimal disruption and cobalt-chromium DES[5]	SBA vs. BA	Stent expansion, lumen eccentricity, intimal disruption frequency, extent	SBA: 68%, 0.94, 68%, 122° BA: 62.1%, 0.80, 0.8, 65° p=0.017, 0.18, 0.035, 0.035	SBA achieved increased stent expansion with similar lumen eccentricity when compared with BA. SBA had more frequent and extensive intimal disruption

				when compared with BA.
Rotational Atherectomy				
ERBAC[6]	RA vs. ELCA vs. PTCA	Procedural success$^{\Sigma}$, TVR after 6 months	RA: 89%, 42.4% ELCA: 77%, 46% PTCA: 80%, 31.9% p=0.0019, 0.013	RA achieved superior procedural success when compared with ELCA and PTCA, but both RA and ELCA had unfavorable late outcomes when compared with PTCA.
COBRA[7]	RA vs. PTCA	Binary restenosis after 6 months	RA: 49% PTCA: 51% p=0.35	RA did not reduce restenosis after 6 months when compared with PTCA.
DART[8]	RA vs. PTCA in small vessels (2-3 mm)	TVF after 12 months	RA: 30.5% PTCA: 31.2% p=0.98	RA did not reduce TVF after 12 months when compared with PTCA.
STRATAS[9]	Aggressive RA (B/A 0.7-0.9)] with PTCA (< 1 bar) vs. routine RA (B/A < 0.7) with PTCA (4 bar)	Binary restenosis after 6 months	Aggressive: 58% Routine: 52% p=NS	Aggressive RA debulking did not reduce restenosis after 6 months when compared with routine RA debulking.
CARAT[10]	Aggressive RA (B/A > 0.7) vs. Routine RA (B/A = 0.7)	MACE after 6 months	Aggressive: 36.3% Routine: 32.7% p=NS	Aggressive RA debulking did not reduce MACE after 6 months compared with routine RA debulking.
ROOSTER[11]	RA (B/A = 0.7) vs. PTCA for diffuse ISR with IVUS guidance	TLR after 9 months	RA: 32% PTCA: 45% p=0.04	RA achieved less TLR after 9 months compared with PTCA in diffuse ISR.
ARTIST[12]	RA (B/A = 0.7) vs. PTCA for diffuse ISR with	MACE after 6 months	RA: 80% PTCA: 91% p=0.0052	PTCA achieved a lower MACE when compared to RA in diffuse ISR.

	IVUS guidance in a subset			
ROTAXUS[13]	RA with DES vs. DES	Late lumen loss (mm) after 9 months	RA with DES: 0.31±0.52 DES: 0.44±0.58 p=0.04	RA before DES achieved increased late lumen loss when compared to DES alone.
Prepare-CALC[14]	RA vs. modified CSA	Successful stent delivery and expansion, late lumen loss (mm) after 9 months	RA: 98%, 0.22±0.41 CSA: 81%, 0.16±0.40 p=0.001, 0.21	RA achieved greater success at stent delivery and expansion than CSA and had similar late lumen loss rates after 9 months.
Orbital Atherectomy				
ORBIT I[15]	OA single arm	Device success∫ Procedural success∫∫ TLR, MACE after 6 months	Device success: 98% Procedural success: 94% TLR, MACE (6 months): 2%, 8%	OA successfully facilitated stent delivery with a low cumulative TLR and MACE after 6 months.
ORBIT II[16]	OA single arm	Safety endpoint Ω (95% CI) Efficacy endpoint Ψ (95% CI)	Safety endpoint: 89.6% (86.7%-92.5%) Efficacy endpoint: 88.9% (85.5%-91.6%)	OA significantly exceeded the primary safety and efficacy endpoints of 83% and 82% respectively. OA also improved in-hospital and 30-day outcomes compared to historic controls with severe CAC.
Laser Atherectomy				
LAVA[17]	ELCA vs. PTCA in native vessels or SVG	MACE after 6 months	ELCA: 28.9% PTCA: 23.5% p=0.55	ELCA did not reduce MACE after 6 months compared with PTCA in native vessels or SVG.

AMRO[18]	ELCA vs. PTCA in native vessels	MACE after 6 months	ELCA: 33.3% PTCA: 29.9% p=0.55	ELCA did not reduce MACE after 6 months compared with PTCA in native vessels.
Intravascular Lithotripsy				
DISRUPT CAD I[19]	Coronary IVL single arm	Safety endpoint Ω Effectiveness endpoint Ψ	Safety endpoint: 95% Effectiveness endpoint: 98.5%	Coronary IVL safely and effectively aided stent placement with minimal perioperative complications.
DISRUPT CAD II[20]	Coronary IVL single arm	Safety endpoint Ω Effectiveness endpoint Ψ Calcium fractures measured by OCT Mean stent expansion	Safety endpoint: 100% Effectiveness endpoint: 94.2% Calcium fractures: 67.4% Mean stent expansion: 101.7%	Coronary IVL safely and effectively aided stent placement with minimal perioperative complications. OCT demonstrated that calcium fractures were an underlying mechanism for IVL. Coronary IVL allowed for excellent stent expansion.
DISRUPT CAD III[21]	Coronary IVL single arm	Safety endpoint Ω (lower-bound of 95% CI) Effectiveness endpoint Ψ (lower-bound of 95% CI)	Safety endpoint: 92.2% (89.9%, p=0.0001) Effectiveness endpoint: 92.4% (90.2%, p=0.0001)	Coronary IVL safely and successfully assisted with stent delivery. The lower bounds of the 95% CI for the safety and effectiveness endpoints exceeded the performance goal of 84.4% and 83.4%, respectively.
DISRUPT CAD IV[22]	Coronary IVL single arm	Safety endpoint Ω: CAD IV cohort vs. propensity matched	Safety endpoint: 93.8% vs. 91.2%, p=0.008	Coronary IVL safely and effectively aided stent placement with minimal perioperative complications.

		historical IVL control group Effectiveness endpoint Ψ: CAD IV cohort vs. propensity matched historical IVL control group	Effectiveness endpoint: 93.8% vs. 91.6%, p=0.007	The results from coronary IVL in the Japanese CAD IV cohort were non-inferior to those from a study of patients treated with IVL in the USA and Europe.

Abbreviations: ΔEEM, change in external elastic membrane; ΔP+M, change in plaque plus media; Δlumen, change in lumen or acute lumen gain; B/A, burr/artery ratio; BA, balloon angioplasty; BMS, bare-metal stent; CABG, coronary artery bypass surgery; CAC, coronary artery calcification; CBA, cutting balloon angioplasty; CI, confidence interval; CSA, cross-sectional area; DES, drug-eluting stent; ELCA, excimer laser coronary angioplasty; ISR, in-stent restenosis; IVL, intravascular lithotripsy; IVUS, intravascular ultrasound; MACE, major adverse cardiac events; MI, myocardial infarction; NS, nonsignificant; NC, noncompliant balloon; OA, orbital atherectomy; OCT, optical coherence tomography; PTCA, percutaneous transluminal coronary angioplasty; PTRA, percutaneous transluminal rotational atherectomy; RA, rotational atherectomy; SBA, scoring balloon angioplasty; SVG, saphenous vein graft; TVF, target vessel failure; TVR, target vessel revascularization.
* In order of relevant endpoints; ∑ Diameter stenosis < 50%, absence of death, non-Q-wave MI, or CABG; ∫ Residual stenosis <50% without device malfunction; ∬ <20% residual stenosis; Ω 30-day freedom from MACE; Ψ residual stenosis <50% without in-hospital MACE

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