Halo and Eluvia

Analysis from EMINENT and IMPERIAL

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Disclosures

. Gouëffic reports:

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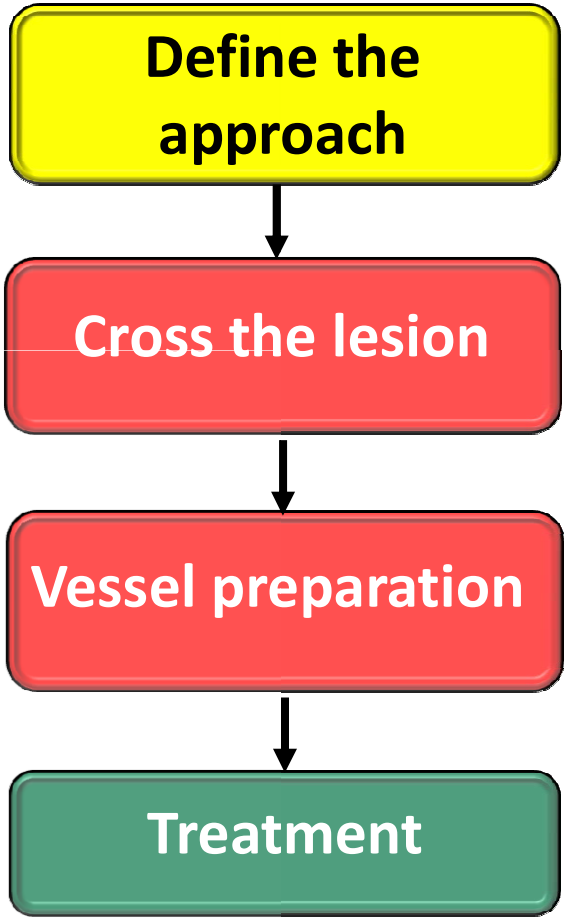
Endovascular femoropopliteal treatment algorythm



Halo in femoropopliteal stenting: no definitive explanation

Bisdas **J Am Coll Cardiol Intv. 2018**

In 2018, investigators for a registry based in Münster, Germany, reported finding dark areas around polymer-DESs in cross-sectional duplex ultrasonography (DUS) images from 5 patients

Other reports

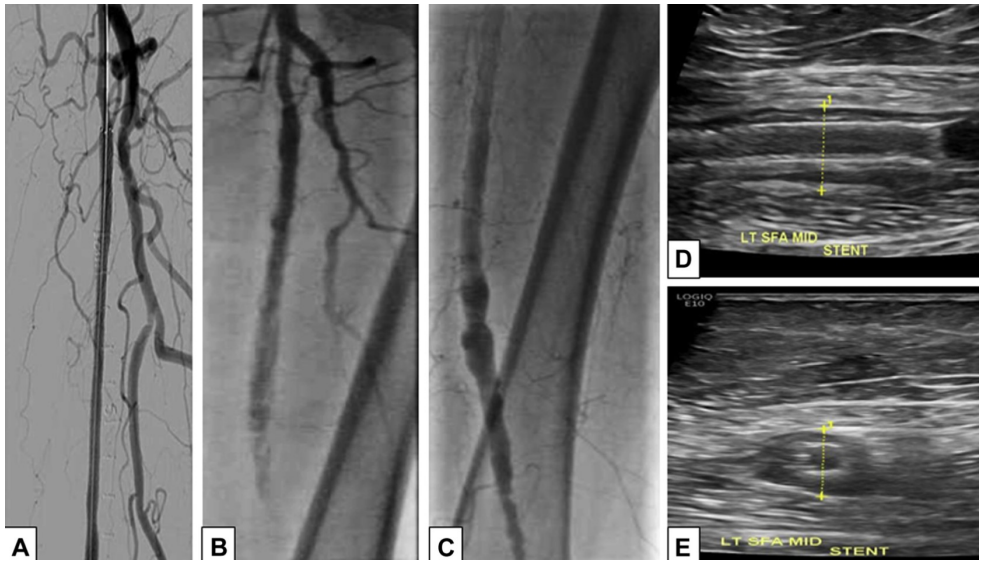
Kum S, Vasc Med. 2021

Tsujimura T, CVIR Endovasc. 2021

Sriya A. Avadhani, JACC Case Report, 2021*

Stavroulakis J Am Coll Cardiol Intv. 2021

Iida O, J Am Coll Cardiol Intv. 2022



Hypo-echogenic area – Aneurysm degeneration - Dark areas

Main Objectives

To investigate:

- the halo prevalence
- the halo development and regression
- the risk factors
- the safety implications of hypoechoic halos identified with DUS

In:

- polymer-based drug-eluting stent (drug eluting stent)
- nonpolymer drug-coated stent (drug coated stent)
- bare metal stent treatment arms

Holden A, Gouëffic Y, Gray WA, et al, J Am Coll Cardiol Intv 2023.

IMPERIAL Study Overview

Study Design	**RCT (2:1) N=465** **Non inferiority** (effectiveness) – Superiority post-oc analysis **Single-blind** **2 sub-studies**: - *Long Lesion (Eluvia): single arm - lesion length 140 mm-190 mm – N=50* - *Pharmacokinetic (Eluvia): sigle arm – N=13*	
Intervention	Study arm: **Eluvia DES** Control arm: **ZILVER PTX DES**	
Primary Endpoint	**12-Month Primary Patency**	
Investigational Centers	65 study centers: US, Canada, New Zealand, Belgium, Germany, Austria, Japan	
Principal Investigators	Global: William A. Gray, MD	European: Stefan Müller-Hülsbeck

Primary vessel patency is defined as a binary endpoint and will be determined to be a success when the duplex ultrasound (DUS) Peak Systolic Velocity Ratio (PSVR) is ≤ 2.4 at the 12-month ollow-up visit in the absence of clinically-driven TLR or bypass of the target lesion. All DUS readings assessed by an independent core laboratory.DES, drug-eluting stent; PPA, proximal poplitea artery; RCT, randomized controlled trial; SFA, superficial femoral artery.

Gray, Lancet, 2018

EMINENT Study Overview

linicalTrials.gov identifier: NCT02921230

Study Design	**RCT (2:1)** **N=775** **Superiority** (effectiveness) Single-blind	
ntervention	Study arm: **Eluvia DES** Control arm: **Bare nitinol stent**	
Primary Endpoint	**12-Month Primary Patency**	
nvestigational Centers	58 centers in 10 European countries	
Principal nvestigators	Prof. Dr. Yann Gouëffic Groupe Hospitalier Paris St. Joseph, Paris, France	Prof. Dr. Giovanni Torsello Sint-Franziskus-Hospital GmbH, Münster, Germany

Largest industry-sponsored randomized trial of drug-eluting stents for SFA/PPA to date

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Gouëffic, Circulation, 2022

Methodology

DUS image acquisition and analysis were performed prospectively in a blinded fashion by an independent core laboratory (VasCore).

DUS imaging was initially scheduled at:

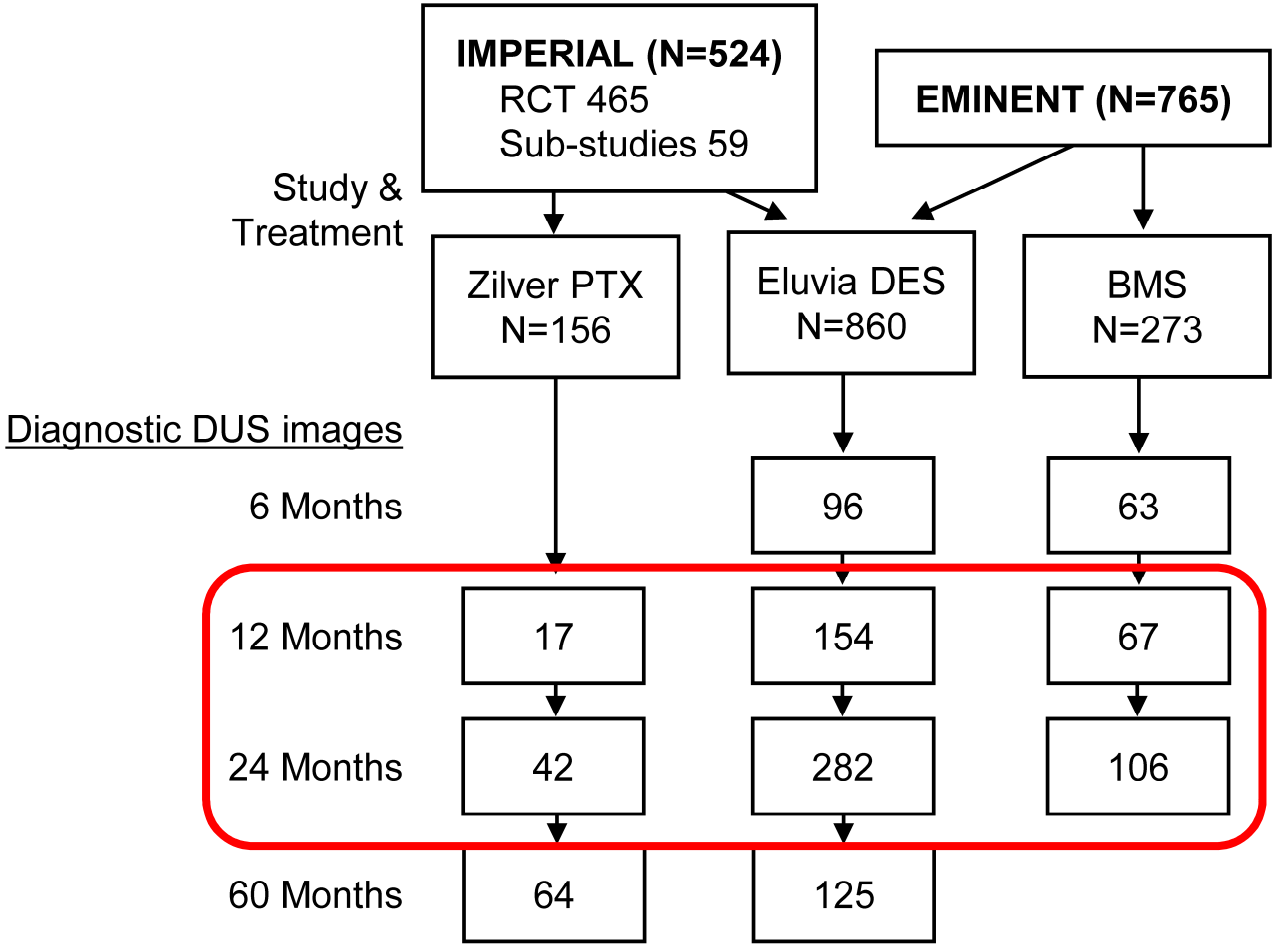
- ***6, 12 and 24 months in EMINENT***
- ***12, 24 and 60 months in IMPERIAL***

Systematic halo DUS identification protocol began in July 2018 for IMPERIAL and May 2019 for EMINENT

Holden A, Gouëffic Y, Gray WA, et al, J Am Coll Cardiol Intv 2023

agnostic DUS Availability

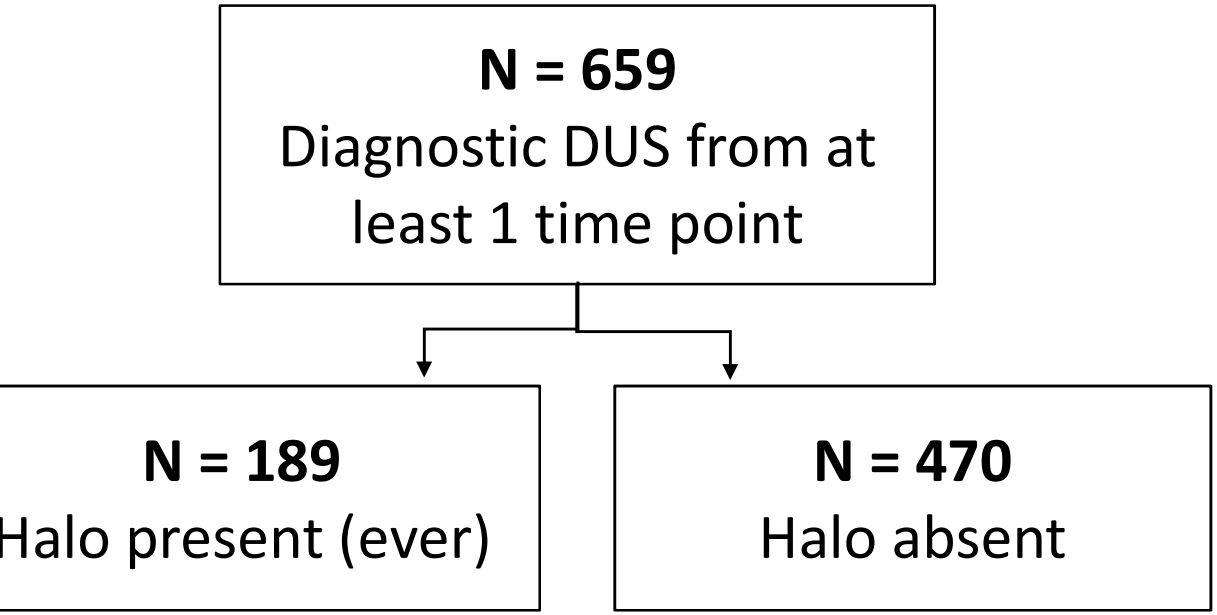
Time points ranging from 6 months to 5 years post–stent implantation.



Number of patients with DUS images appropriate for analysis across studies, treatments, and follow-up time points

Holden A, Gouëffic Y, Gray WA, et al, J Am Coll Cardiol Intv 2023.

Halo Prevalence Ranged from 20% to 35% of Patients with Diagnostic DUS at all FU Time Points



Halo Prevalence among Patients with Diagnostic DUS Images

Month	Halo Present
6	20.1% (32/159)
12	20.6% (49/238)
24	26.7% (115/430)
60	35.4% (67/189)

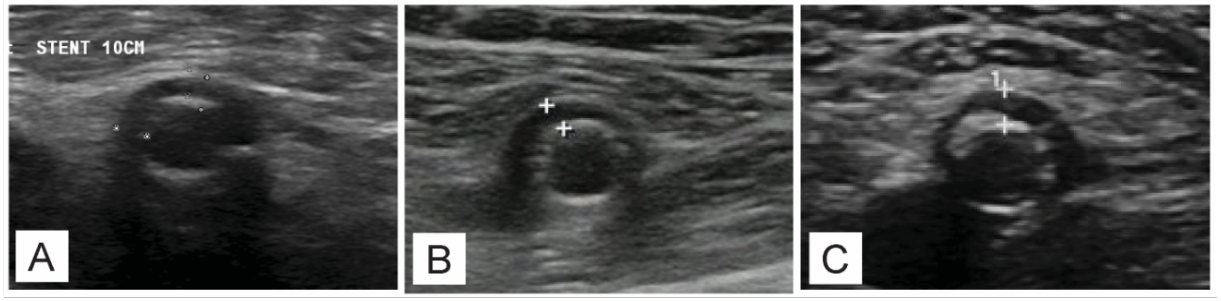
Prevalence among patients with diagnostic DUS at the specified time point.

Holden A, Gouëffic Y, Gray WA, et al, J Am Coll Cardiol Intv 2023; in press.

alos Observed Around All Stent Types

No statistically significant difference in odds of halo between stent types

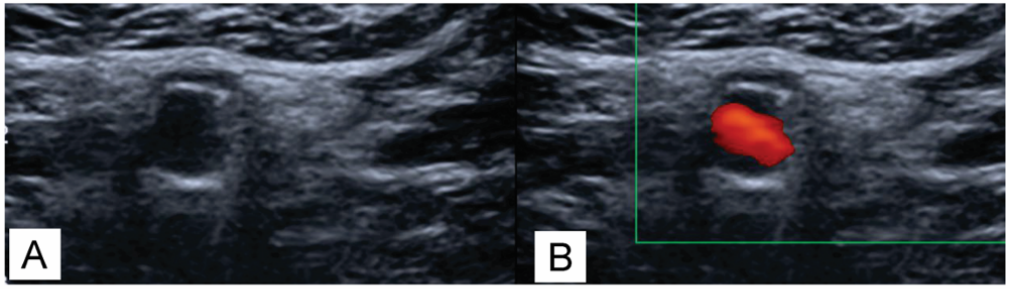
No abnormal findings were detected in the lumen or walls of stented patent arteries



BMS **Eluvia DES** **Zilver PTX DCS**

BMS, bare metal stent; DES, drug-eluting stent; DCS, drug-coated stent.

Flow within the halo or beyond the stent was not seen in any case



Grayscale and color-flow views of an artery with a halo.

Holden A, Gouëffic Y, Gray WA, et al, J Am Coll Cardiol Intv 2023

alo Development & Regression

	Time 1[a]	Time 2[b]
Halo	25.6% (61/238)	31.5% (75/238)
No Halo	74.4% (177/238)	68.5% (163/238)

[a]Median time 363 days (IQR: 185-671 days) following stent implantation.
[b]Median time 744 days (IQR: 729-1,804 days) following stent implantation.

83.6% of identified halos persisted to later follow-up

Net increase over time due to 24 new cases and 10 cases of regression

Holden A, Gouëffic Y, Gray WA, et al, J Am Coll Cardiol Intv 2023.

Risk Factors for Halo Presence

Adjusted Model

ariable	Adjusted OR (95%CI)	P-value
ial (EMINENT vs IMPERIAL)	**0.49** (0.31-0.79)	0.0034
ex (Male vs Female)	**2.12** (1.30-3.46)	0.0025
eatment		
Non-polymer DCS vs polymer-based DES	0.59 (0.31-1.12)	0.1078
BMS vs polymer-based DES	0.61 (0.33-1.11)	0.1062
edically-treated diabetes mellitus (vs No)	**0.48** (0.31-0.76)	0.0015
edically-treated hypertension (vs No)	**0.35** (0.22-0.57)	<0.0001
rget lesion length (≤100 mm vs >100 mm)	**0.53** (0.35-0.80)	0.0027
alcification (none/mild vs moderate/severe)	**2.16** (1.43-3.27)	0.0003
eference Vessel Diameter (<5 mm vs ≥5 mm)	**0.56** (0.37-0.84)	0.0055
cclusion (vs No)	**1.67** (1.10-2.54)	0.0166
rget lesion crossing (True Lumen vs Subintimal)	1.00 (0.48-2.09)	0.9954

ltivariable logistic regression using stepwise backward selection, while controlling for treatment type and subintimal crossing.
S, bare metal stent; DCS, drug-coated stent; DES, drug-eluting stent; OR, odds ratio.

Holden A, Gouëffic Y, Gray WA, et al, J Am Coll Cardiol Intv 2023

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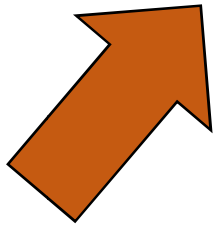

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Hypoechoic Halo & Safety Outcomes

Halo (vs no halo)	OR (95%CI)	P-value
1-Year CD-TLR	1.27 (0.70-2.30)	0.4240
1-Year Primary Patency	0.68 (0.43-1.07)	0.0927

CD-TLR, clinically-driven TLR; OR, odds ratio.

No statistically significant association was found between halo status and 1-year CD-TLR or primary patency

No clinical sequelae or adverse clinical safety events were associated with the halo finding at any time

Holden A, Gouëffic Y, Gray WA, et al, J Am Coll Cardiol Intv 2023

Conclusions

“Aneurysmal degeneration” is not appropriate (flow is not detected outside the stent)

Systematic screening and core lab imaging assessment showed that hypoechoic halos occur in 20%-35% of patients with femoropopliteal stents

Halo presence was not significantly associated with stent features such as polymer or paclitaxel coating

Halo presence is benign with no associated clinical sequelae

Halo and Eluvia

(analysis from EMINENT and IMPERIAL)

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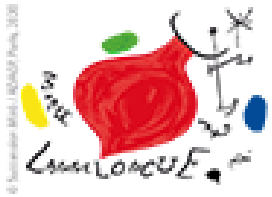
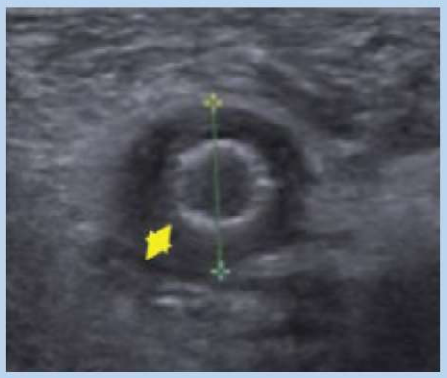


Femoropopliteal Artery Stent Placement in IMPERIAL or EMINENT Trials

IMPERIAL (N = 524)
Paclitaxel-eluting polymer-based nitinol stent
vs
Paclitaxel-coated nitinol stent (2:1)

EMINENT (N = 765)
Paclitaxel-eluting polymer-based nitinol stent
vs
Bare nitinol stents (2:1)

Diagnostic DUS imaging from at least 1 time point (6 months - 5 years)
N = 659



Halo
N = 189

No Halo
N = 470

Prevalence

20%-35% over time

Safety

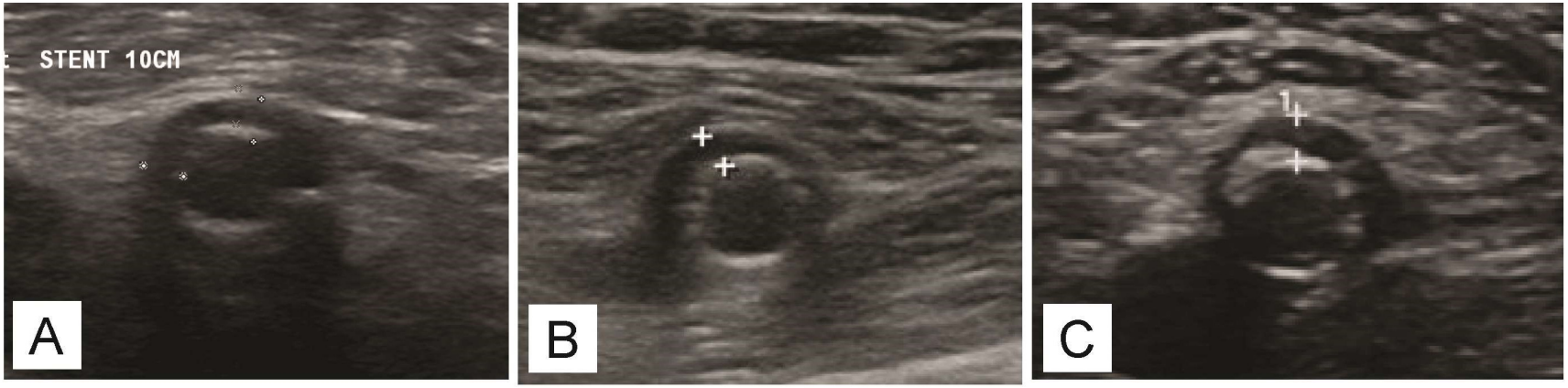
- No statistically significant association between halo and 1-year primary patency or CD-TLR
- No clinical sequelae observed

No significant difference in the odds of halo across stent types

+ Nitinol, polymer, paclitaxel + Nitinol, polymer-free, paclitaxel + Bare nitinol

Gouëffic Y, Gray WA, et al. Hypoechoic Halo Imaging Findings Following Femoropopliteal Artery Stent Implantation: Risk Factors and Clinical Outcomes. J Am Coll Cardiol Intv 2023; in press.

Halos Observed Around All Stent Types



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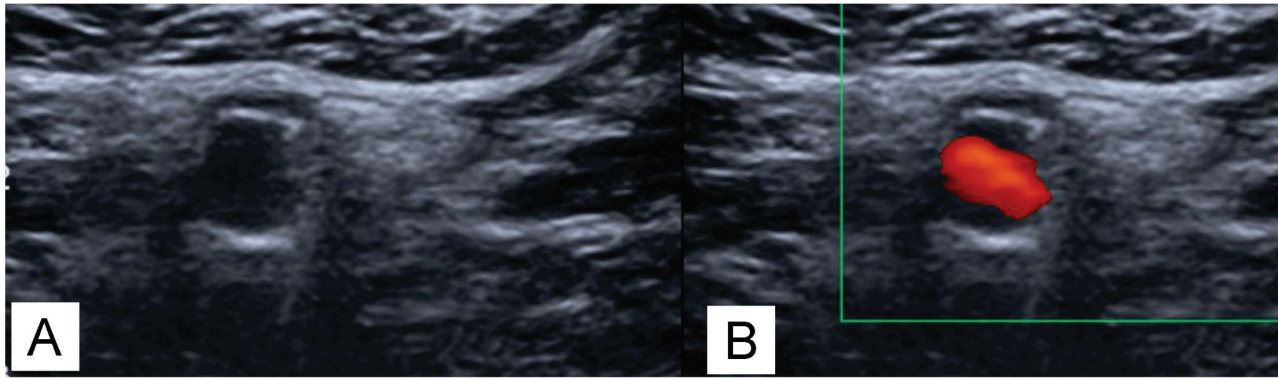

Grayscale and color-flow views of an artery with a halo.

metal stent; DES, drug-eluting stent; DCS, drug-coated stent.

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