### Disclaimer



• These materials are for training, educational and informational purposes only and not for the purpose of providing legal, medical, regulatory or other professional advice. While an effort is made to post only the most accurate available information, Philips does not guarantee that the materials posted or the information contained therein are the most current. Philips does not warrant or make any representations as to the content, accuracy or completeness of the information, text, graphics, links and other items contained in these materials. Philips makes no warranties, express or implied as to the fitness of the information for any purpose, or to results obtained by individuals using the information and is not responsible for any action taken in reliance on the information contained in the materials. The materials available on this website are not intended to be a complete presentation of all information or issues for any topic. Results from any case studies included in the materials are not predictive of future results as results may vary depending on a variety of patient-specific attributes and related factors. Download and use of these materials is at your own risk and responsibility.



# Angiography alone is not enough

**Philips** Image Guided Therapy - Devices



### IVUS benefits patients



- <u>ADAPT-DES 2014</u>
- <u>Meta-Analyses Summary</u>
- <u>Ahn Meta-Analysis 2014</u>
- <u>Elgendy Meta-Analysis 2016</u>
- <u>SCAI Expert Consensus Statement, Guidelines, Appropriate Use Criteria</u>
- <u>IVUS-XPL 2019</u>
- <u>CTO Study 2015</u>
- Mintz review article 2017
- <u>ULTIMATE 2018</u>
- <u>Samsung Medical Center Registry 2019</u>
- <u>Summary of IVUS clinical benefits</u>
- <u>Economic Impact of IVUS</u>

#### Based on a preponderance of data from randomized trials and high quality prospective observational studies



# ADAPT-DES

#### Assessment of Dual AntiPlatelet Therapy with Drug-Eluting Stents

Change in strategy (74%)

No change (26%)

(Assessment of Dual Antiplatelet Therapy with Drug-Eluting Stents)

Results from the Prospective, Multicenter ADAPT-DES<sup>1</sup> study

- Largest study ever conducted with IVUS guidance
- Multi-center global registry with 8583 consecutive patients
- 3349 patients had PCI with IVUS guidance
- 64% Xience / Promus stents

ADAPT-DES

Study data reported IVUS guidance was associated with:



©2019 Koninklijke Philips N.V. All rights reserved. Approved for external distribution. D052685-00 122019

5





#### ADAPT-DES



#### How investigators reported IVUS changed their procedure



\*"Others" category may include a combination of "Higher Pressure", "Under Expansion", "Malapposition", and "Additional Stent". Witzenbichler B. ADAPT-DES: Two-Year Insights from the Largest IVUS Substudy. TCT 2013. Lecture conducted from San Francisco, CA. Graphics adapted from slide presentation.

#### ADAPT-DES



Study data reported IVUS guidance was associated with:



1. Witzenbichler B. ADAPT-DES: Two-Year Insights from the Largest IVUS Substudy. TCT 2013. Lecture conducted from San Francisco, CA

#### Association of IVUS use and MACE

Event rate (n)

4.9% (158) vs. 7.5% (373)

5.0% (2) vs 14.3% (14)-

4.1% (19) vs 8.9% (73)

5.6% (8) vs 10.2% (17)

5.7% (23) vs 9.2% (87)

4.8% (118) vs 6.9% (242)

0.1

Favors IVUS use

IVUS vs Angio

All

Three vessel

Bifurcation

Left main

Two vessel

One vessel

\*Non-left main. non-bifurcation

(Definite/probable ST, cardiac death, MI) in relation to lesion complexity

HR [95%CI]

0.65 [0.54, 0.78]

0.34 [0.08, 1.52]

0.45 [0.27 0.74]

0.54[0.23, 1.26]

0.60 [0.38, 0.95]

0.69 [0.55, 0.86]

Favors angio use

.

-

1. Witzenbichler B et al. Relationship Between Intravascular Ultrasound Guidance and Clinical Outcomes After Drug-Eluting Stents: The ADAPT-DES Study. Circulation

2014 Jan: 129,4;463-470.

# ADAPT-DES

## Study data reported IVUS use benefited even the simplest cases (1 vessel, non-LM/bifurcation, stable CAD)<sup>1</sup>

P-value

< 0.0001

0.14

0.001

0.15

0.03

0.0009

#### Association of IVUS use and MACE

(Definite/probable ST, cardiac death, MI) in relation to index presentation





"The present study... suggests that IVUS guidance may reduce the rates of ST and MI

within 1 year of DES implantation, with the greatest benefits present in patients with

#### Association of IVUS use and MACF

acute coronary syndromes and complex target lesions."<sup>1</sup>

HR [95%CI]

0.65 [0.54, 0.78]

0.34 [0.08, 1.52]

0.45 [0.27 0.74]

(Definite/probable ST, cardiac death, MI) in relation to lesion complexity

Left main 5.6% (8) vs 10.2% (17) Two vessel 5.7% (23) vs 9.2% (87) One vessel 4.8% (118) vs 6.9% (242) 0.69 [0.55, 0.86] 0.1 Favors IVUS use \*Non-left main, non-bifurcation

Event rate (n)

4.9% (158) vs. 7.5% (373)

5.0% (2) vs 14.3% (14)

4.1% (19) vs 8.9% (73)

IVUS vs Angio

All

Three vessel

Bifurcation

#### Association of IVUS use and MACE

(Definite/probable ST, cardiac death, MI) in relation to index presentation



P-value

<0.0001

0.14

0.001

0.15

0.03

0.0009









# **Overview of Meta-analyses**

### Summary of Meta-Analyses



Meta-analyses with a preponderance of data from randomized clinical trials and high quality prospective longitudinal observational studies reported IVUS outcomes<sup>1,2,3,4,5,6</sup>

- Includes 39 studies covering over 36,000 patients
- 15,469 patients had PCI with IVUS Guidance
- Comprehensive analysis reflecting DES studies over the last decade

<sup>1.</sup> Ahn JM, Kang SJ, Yoon SH, et al. "Meta-Analysis of Outcomes After Intravascular Ultrasound - Guided Versus Angiography-Guided Drug-Eluting Stent Implantation in 26,503 Patients Enrolled in Three Randomized Trials and 14 Observational Studies" Am J Cardiol. 2014;113:1338-1347.

<sup>2.</sup> Elgendy IY et al. Outomes with Intravascular Ultrasound-Guided Stent Implantation: A Meta-Analysis of Randomized Trials in the Era of Drug-Eluting Stents. Circ Cardiovasc Interv. 2016;9:e003700

<sup>3.</sup> Jang JS, et al. Intravascular Ultrasound-Guided Implantation of Drug-Eluting Stents to Improve Outcome, A Meta-Analysis. J Am Coll Cardiol Intv. 2014;7(3):233-243

<sup>4.</sup> Zhang YJ, et al. Comparison of intravascular ultrasound versus angiography-guided drug-eluting stent implantation: a meta-analysis of one randomized trial and ten observational studies involving 19,619 patients. EuroIntervention. 2013;9:891-892

<sup>5.</sup> Klersey C, et al. Use of IVUS guided coronary stenting with drug eluting stent: A systematic review and meta-analysis of randomized controlled clinical trials and high quality observational studies. Int J Cardiol. 2013 Dec 5;170(1):54-63.

<sup>6.</sup> Mintz GS. Intravascular ultrasound and outcomes after drug-eluting stent implantation. Coronary Artery Dis. 2017 Jun; 28(4):346-352

# 39 distinct studies enrolling more than 36,000 patients



A large body of evidence from randomized trials, observational studies, and metaanalyses reports that IVUS guidance is associated with reduced MACE, MI, ST and death.<sup>1,2,3,4,5,6</sup>

Author	Ahn JM	Elgendy IY	Klersey C	Zhang YJ	Jang JS	Total*
IVUS patients	12,499	1,593	9,965	8,102	11,793	15,469
DES patients	26,503	3,192	18,707	19,619	24,849	36,831

1. Ahn JM, Kang SJ, Yoon SH, et al. "Meta-Analysis of Outcomes After Intravascular Ultrasound - Guided Versus Angiography-Guided Drug-Eluting Stent Implantation in 26,503 Patients Enrolled in Three Randomized Trials and 14 Observational Studies" Am J Cardiol. 2014;113:1338-1347.

2. Elgendy IY et al. Outomes with Intravascular Ultrasound-Guided Stent Implantation: A Meta-Analysis of Randomized Trials in the Era of Drug-Eluting Stents. Circ Cardiovasc Interv. 2016;9:e003700

3. Jang JS, et al. Intravascular Ultrasound-Guided Implantation of Drug-Eluting Stents to Improve Outcome, A Meta-Analysis. J Am Coll Cardiol Intv. 2014;7(3):233-243

4. Zhang YJ, et al. Comparison of intravascular ultrasound versus angiography-guided drug-eluting stent implantation: a meta-analysis of one randomized trial and ten observational studies involving 19,619 patients. EuroIntervention. 2013;9:891-892

5. Klersey C, et al. Use of IVUS guided coronary stenting with drug eluting stent: A systematic review and meta-analysis of randomized controlled clinical trials and high quality observational studies. Int J Cardiol. 2013 Dec 5;170(1):54-63.

6. Mintz GS. Intravascular ultrasound and outcomes after drug-eluting stent implantation. Coronary Artery Dis. 2017 Jun; 28(4):346-352

\* All the numbers of patients participated in the studies are deduplication.



# Ahn Meta-Analysis Study



# Ahn Meta-Analysis builds on a large body of evidence



# 2005-2014 IVUS in Clinical Research

17 STUDIES (14 OBSERVATIONAL AND 3 RANDOMIZED) INCLUDED IN THE AHN META-ANALYSIS OF OUTCOMES AFTER INTRAVASCULAR ULTRASOUND-GUIDED VERSUS ANGIOGRAPHY-GUIDED DRUG-ELUTING STENT IMPLANTATION



Ahn JM, Kang SJ, Yoon SH, et al. "Meta-Analysis of Outcomes After Intravascular Ultrasound - Guided Versus Angiography-Guided Drug-Eluting Stent Implantation in 26,503 Patients Enrolled in Three Randomized Trials and 14 Observational Studies" Am J Cardiol. 2014;113:1338-1347.

#### Study data reported IVUS-guided DES implantation was associated with a significant reduction of MACE

#### Major adverse cardiovascular events

Author name (year)	Statistics f	or each stuc	ly			Odds ratio	and 95% Cl				
	Odds ratio	Lower limi	t Upper limi	Z-Value	p-Value						
Ahn JM et al. (2013)	0.555	0.400	0.772	-3.499	0.000						
Ahn SG et al. (2013)	0.174	0.050	0.604	-2.755	0.006						
Chen SL et al. (2012)	0.759	0.503	1.146	-1.312	0.190						
Chieffo A et al. (2013)	0.673	0.374	1.211	-1.321	0.186						
Claessen BE et al. (2011)	0.755	0.566	1.009	-1.900	0.057						
Hur SH et al. (2012)	0.851	0.706	1.026	-1.689	0.091			•			25% reduction in
Jakabcin J et al. (2010)	0.906	0.388	2.118	-0.227	0.820				_		(composite of de
Kim JS et al. (2011)	0.889	0.599	1.318	-0.587	0.557						MI, and repeat
Kim JS et al. (2013)	0.598	0.287	1.247	-1.370	O.171						revascularization
Kim SH et al. (2010)	0.436	0.223	0.852	-2.430	0.015						
Park KW et al. (2012)	1.434	0.872	2.358	1.421	0.155				<b>-</b>		
Park SJ et al. (2009)	0.466	0.271	0.802	-2.755	0.006						
Roy P et al. (2008)	0.877	0.677	1.137	-0.991	0.322						
Witzenbichler B et al. (2013)	0.649	0.514	0.819	-3.631	0.000			•			
Yoon YW et al. (2013)	1.097	0.556	2.167	0.268	0.789				_		
Youn YJ et al. (2011)	0.664	0.354	1.246	-1.276	0.202						
Random effect model	0.735	0.637	0.849	-4.197	<0.001			•			
Test for heterogeneity	Q=27.9, df	=15, p=0.02,	l <sup>2</sup> =46.2			0.01	0.1	1	10	10	00
						Fa	vors IVU	S	Favors CA	٩Ġ	

Ahn JM, Kang SJ, Yoon SH, et al. "Meta-Analysis of Outcomes After Intravascular Ultrasound - Guided Versus Angiography-Guided Drug-Eluting Stent Implantation in 26,503 Patients Enrolled in Three Randomized Trials and 14 Observational Studies" Am J Cardiol. 2014;113:1338-1347.

©2019 Koninklijke Philips N.V. All rights reserved. Approved for external distribution.

D052685-00 122019



MACE eath,



### Study data reported IVUS-guided DES implantation was associated with a significant reduction of MI

#### Myocardial infarction

Author name (year)	Statistics fo	or each study	/			Odds ratio a	nd 95%	כו		
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value					
Ahn JM et al. (2013)	0.373	0.131	1.061	-1.849	0.064					
Ahn SG et al. (2013)	0.126	0.014	1.154	-1.833	0.067					
Chen SL et al. (2012)	0.494	0.257	0.948	-2.120	0.034					
Chieffo A et al. (2013)	0.810	0.338	1.941	-0.472	0.637					
Claessen BE et al. (2011)	0.399	0.214	0.744	-2.893	0.004			<b>—</b> • <b>—</b>		
Hur SH et al. (2012)	0.497	0.247	1.004	-1.949	0.051					
Jakabcin J et al. (2010)	0.242	0.028	2.094	-1.288	0.198	_				
Kim SH et al. (2010)	0.139	0.017	1.150	-1.830	0.067		,	<u> </u>		
Kim JS et al. (2011)	0.189	0.054	0.665	-2.596	0.009					
Kim SH et al. (2013)	0.209	0.010	4.414	-1.006	0.315				-	
Park SJ et al. (2009)	0.757	0.369	1.550	-0.762	0.446					
Park KW et al. (2012)	3.043	1.125	8.234	2.191	0.028					
Roy P et al. (2008)	0.670	0.369	1.218	-1.313	0.189					
Witzenbichler B et al. (2013)	0.660	0.508	0.858	-3.110	0.002			•		
Yoon YW et al. (2013)	0.666	0.083	5.317	-0.383	0.701			*	_	
Youn YJ et al. (2011)	0.640	0.167	2.458	-0.650	0.516					
Random effect model	0.571	0.435	0.751	-4.011	<0.001			•		
Test for heterogeneity	Q=22.9, df=	=15, p=0.086	, I²=34.5%			0.01	0.1	1	10	100

Favors IVUS Favors CAG

Ahn JM, Kang SJ, Yoon SH, et al. "Meta-Analysis of Outcomes After Intravascular Ultrasound - Guided Versus Angiography-Guided Drug-Eluting Stent Implantation in 26,503 Patients Enrolled in Three Randomized Trials and 14 Observational Studies" Am J Cardiol. 2014;113:1338-1347.



### Study data reported IVUS-guided PCI was associated with a significantly reduced risk of TLR

#### Target lesion revascularization

Author name (year)	Statistics fo	or each study	/			Odds ra	itio and	95% Cl			
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value						
Ahn SG et al. (2013)	0.025	0.001	0.452	-2.501	0.012	-	*		-		
Ahn JM et al. (2013)	0.708	0.449	1.118	-1.481	0.139				<b>.</b>		
Chen SL et al. (2012)	0.603	0.362	1.003	-1.949	0.051			_			
Chieffo A et al. (2013)	0.750	0.350	1.608	-0.739	0.460			-	•		
Hur SH et al. (2012)	1.133	0.881	1.458	0.974	0.330				•		
Jakabcin J et al. (2010)	1.000	0.320	3.124	0.000	1.000			_			
Kim SH et al. (2010)	0.875	0.364	2.105	-0.298	0.765			-			
Kim JS et al. (2011)	1.113	0.681	1.819	0.427	0.670						
Park KW et al. (2012)	0.954	0.462	1.967	-0.129	0.898						
Roy P et al. (2008)	0.693	0.467	1.027	-1.829	0.067						
Witzenbichler B et al. (2013)	0.636	0.457	0.884	-2.696	0.007				•••		
Youn YJ et al. (2011)	1.014	0.449	2.287	0.033	0.974						
Random effect model	0.811	0.660	0.996	-1.998	0.046				•		
Test for heterogeneity	Q=18.7, df=	11, p=0.067,	I²=41.2			0.01		0.1	-	10	100
						0.01		0.1	I	10	100
							Favor	s IVUS	Fav	ors CAG	

Ahn JM, Kang SJ, Yoon SH, et al. "Meta-Analysis of Outcomes After Intravascular Ultrasound - Guided Versus Angiography-Guided Drug-Eluting Stent Implantation in 26,503 Patients Enrolled in Three Randomized Trials and 14 Observational Studies" Am J Cardiol. 2014;113:1338-1347.

 $\ensuremath{\mathbb{C}}$  2019 Koninklijke Philips N.V. All rights reserved. Approved for external distribution.

D052685-00 122019



### Study data reported IVUS-guided PCI was associated with a significantly reduced risk of ST

#### Definite or probable stent thrombosis

Author name (year)	Statistics for each study				Odds ratio and 95% Cl							
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value							
Ahn SG et al. (2013)	0.163	0.017	1.557	-1.575	0.115							
Ahn JM et al. (2013)	0.199	0.037	1.079	-1.872	0.061				<u> </u>	_		
Chen SL et al. (2012)	0.164	0.055	0.489	-3.240	0.001							
Chieffo A et al. (2013)	3.009	0.121	74.609	0.672	0.501			-				
Claessen BE et al. (2011)	0.553	0.149	2.051	-0.885	0.376				×			
Hur SH et al. (2012)	0.855	0.558	1.308	-0.723	0.470				- •	ŀ		
Jakabcin J et al. (2010)	0.653	0.184	2.314	-0.661	0.509				w			
Kim SH et al. (2010)	0.263	0.059	1.179	-1.745	0.081				<u></u>	_		
Kim JS et al. (2011)	0.332	0.033	3.300	-0.941	0.347		-		<u>.</u>			
Kim JS et al. (2013)	1.000	0.070	14.371	0.000	1.000							
Park SJ et al. (2009)	1.000	0.406	2.465	0.000	1.000					•		
Park KW et al. (2012)	0.498	0.091	2.719	-0.804	0.421							
Roy P et al. (2008)	0.583	0.392	0.867	-2.666	0.008				• • •			
Witzenbichler B et al. (2013)	0.497	0.289	0.855	-2.529	0.011				- •			
Yoon YW et al. (2013)	1.000	0.106	9.393	0.000	1.000			-				
Youn YJ et al. (2011)	0.854	0.210	3.468	-0.221	0.825							
Random effect model	0.592	0.468	0.750	-4.358	<0.001				•			
Test for heterogeneity	Q=15.7, df=	15, p=0.40, l <sup>;</sup>	2=4.63%			0.	01	0.1		I	10	100

Favors IVUS Favors CAG

Ahn JM, Kang SJ, Yoon SH, et al. "Meta-Analysis of Outcomes After Intravascular Ultrasound - Guided Versus Angiography-Guided Drug-Eluting Stent Implantation in 26,503 Patients Enrolled in Three Randomized Trials and 14 Observational Studies" Am J Cardiol. 2014;113:1338-1347.

©2019 Koninklijke Philips N.V. All rights reserved. Approved for external distribution.

D052685-00 122019



### Study data reported IVUS-guided PCI was associated with a significantly reduced risk of Death

#### Death

Author name (year) Statistics for each study				Odds rati	o and 95	% <b>C</b> l					
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	1					
Ahn SG et al. (2013)	1.095	0.174	6.898	0.097	0.923						
Ahn JM et al. (2013)	0.477	0.301	0.756	-3.152	0.002				•		
Chen SL et al. (2012)	0.554	0.216	1.422	-1.227	0.220						
Chieffo A et al. (2013)	0.198	0.009	4.170	-1.041	0.298					-	
Claessen BE et al. (2011)	0.656	0.376	1.147	-1.478	0.139			-			
Hur SH et al. (2012)	0.486	0.358	0.661	-4.604	0.000				•		
Jakabcin J et al. (2010)	1.515	0.259	8.874	0.461	0.645						
Kim SH et al. (2010)	0.172	0.050	0.590	-2.802	0.005				-		
Kim JS et al. (2011)	0.857	0.425	1.725	-0.433	0.665						
Kim JS et al. (2013)	1.578	0.254	9.784	0.490	0.624						
Park SJ et al. (2009)	0.259	0.107	0.629	-2.982	0.003			•	_		
Park KW et al. (2012)	1.673	0.506	5.533	0.844	0.399					—	
Roy P et al. (2008)	0.791	0.539	1.160	-1.200	0.230				•••		
Witzenbichler B et al. (2013)	0.875	0.636	1.204	-0.818	0.413				• • •		
Yoon YW et al. (2013)	0.248	0.039	1.587	-1.472	0.141			*			
Youn YJ et al. (2011)	0.210	0.026	1.698	-1.463	0.143			*			
Random effect model	0.613	0.478	0.786	-3.861	<0.001				•		
Test for heterogeneity	Q=25.9, df	=15, p=0.039	, I²=42.2			0.01	0	.1	1	10	100
						Fa	avors	IVUS	Fav	ors CAG	

Ahn JM, Kang SJ, Yoon SH, et al. "Meta-Analysis of Outcomes After Intravascular Ultrasound - Guided Versus Angiography-Guided Drug-Eluting Stent Implantation in 26,503 Patients Enrolled in Three Randomized Trials and 14 Observational Studies" Am J Cardiol. 2014;113:1338-1347.



# Elgendy Meta-Analysis Study

3,192 Patients, 1,593 IVUS Patients

5 Multi-center Studies And 2 Single-center<sup>1</sup>

7 Important Large Studies





#### **Only Randomized Trials**

Previous meta-analysis included predominant observational studies. The present work used stronger methodology because it includes only randomized trials.

#### IVUS-XPL, CTO-IVUS, AIR-CTO

Three important large studies namely (IVUS-XPL, CTO-IVUS, AIR-CTO) were recently reported and included in the analysis for a total of 7 trials and 3,192 patients.

#### 15 Months Average Follow-up

It involves patients who underwent implantation of a DES and randomized to either IVUS-guided or angiographyguided procedures with an average follow-up time of 15 months.

1. Elgendy IY et al. Outomes with Intravascular Ultrasound-Guided Stent Implantation: A Meta-Analysis of Randomized Trials in the Era of Drug-Eluting Stents. Circ Cardiovasc Interv. 2016;9:e003700



#### Results

- At a mean of 15 months, routine IVUS-guided percutaneous coronary intervention was associated with a reduction in the risk of major adverse cardiac events (6.5% versus 10.3%; odds ratio, 0.60; 95% confidence interval, 0.46–0.77; P<0.0001), mainly because of reduction in the risk of ischemia-driven target lesion revascularization (4.1% versus 6.6%; odds ratio, 0.60; 95% confidence interval, 0.43–0.84; P=0.003).
- Reduction of Cardiovascular mortality ,reached borderline significance and also appear to be lower in the IVUS guided group
- By including the totality of data to date, this analysis showed the superiority of IVUS-guided PCI compared with angiographyguided PCI in the drug eluting stent era.
- IVUS guidance resulted in more frequent post dilatation, larger post intervention MLD, greater reduction in the diameter stenosis. These results are in line with ADAPT DES showing that IVUS guidance leads to additional optimization of the procedure allowing better stent expansion.

#### Conclusion

 In the era of drug-eluting stents, IVUS-guided PCI is superior to angiography-guided PCI in reducing the risk of major adverse cardiac events (P<0.0001).</li>

Elgendy IY et al. Outomes with Intravascular Ultrasound-Guided Stent Implantation: A Meta-Analysis of Randomized Trials in the Era of Drug-Eluting Stents. Circ Cardiovasc Interv. 2016;9:e003700



#### Summary plot for Major Adverse Cardiac Events



Elgendy IY et al. Outomes with Intravascular Ultrasound-Guided Stent Implantation: A Meta-Analysis of Randomized Trials in the Era of Drug-Eluting Stents. Circ Cardiovasc Interv. 2016;9:e003700



#### Summary Plot For Cardiovascular Mortality, Myocardial Infarction, Target Lesion Revascularization, And Stent Thrombosis

Study	Year	OR (95% CI)	Events IVUS-guided PCI	Events Conventional PCI	% Weight
Cardiovascular m	ortality				
IVUS-XPL	2015	0.61 (0.15, 2.43)	3/700	5/700	31.17
CTO-IVUS	2015	0.13 (0.01, 2.16)	0/201	2/201	7.81
AIR-CTO	2015	0.60 (0.15, 2.44)	3/115	5/115	30.37
Tan et al	2015	0.67 (0.11, 4.00)	2/61	3/62	18.93
Kim et al	2013	0.14 (0.00, 6.95)	0/269	1/274	3.92
AVIO	2013	0.13 (0.01, 2.16)	0/142	2/142	7.80
Subtotal (I–square	ed = 0.0%, p = 0.802)	0.46 (0.21, 1.00)	8/1488	18/1494	100.00
Myocardial infar	tion				
IVUS-XPL	2015	0.14 (0.00, 6.82)	0/700	1/700	3.01
CTO-IVUS	2015 🚽	0.13 (0.01, 2.16)	0/201	2/201	6.01
Tan et al	2015	0.52 (0.05, 5.06)	1/61	2/62	8.88
Kim et al	2013	0.14 (0.01, 2.20)	0/269	2/274	6.01
AVIO	2013	0.82 (0.34, 1.96)	10/142	12/142	61.32
HOME DES IVUS	2010	0.29 (0.05, 1.73)	1/105	4/105	14.77
Subtotal (I–square	ed = 0.0%, p = 0.592)	0.52 (0.26, 1.02)	12/1478	23/1484	100.00
Target lesion rev	ascularization				
IVUS-XPL	2015	0.52 (0.29, 0.91)	17/700	33/700	36.48
CTO-IVUS	2015	0.62 (0.21, 1.87)	5/201	8/201	9.53
AIR-CTO	2015	0.65 (0.26, 1.61)	8/115	12/115	13.87
Tan et al	2015 -	0.39 (0.14, 1.10)	5/61	12/62	11.17
AVIO	2013	0.74 (0.35, 1.58)	13/142	17/142	20.36
HOME DES IVUS	2010	1.00 (0.31, 3.20)	6/105	6/105	8.60
Subtotal (I–squar	ed = 0.0%, p = 0.848)	0.60 (0.43, 0.84)	54/1324	88/1325	100.00
Staat theomhosic					
	2015	1 00 (0 14 7 11)	2/700	2/700	13.20
	2015	0.13 (0.01, 1.30)	0/201	3/201	9.87
	2015	0.21 (0.05, 0.87)	1/115	7/115	25.64
Tan et al	2015	0.52 (0.05, 5.06)	1/61	2/62	9.75
Kim ot al	2013	1.02 (0.06, 16, 33)	1/269	1/274	6.60
Δνιο	2013	7 39 (0 15 372 38)	1/142	0/142	3 31
HOME DESIVUS	2010	0.66 (0.19, 2.34)	4/105	6/105	31.64
Subtotal (I-square	ed = 0.0% n = 0.490)	0.48 (0.24, 0.99)	10/1593	21/1599	100.00
Subtorut (I-squar	eu - 0.0%, p - 0.4507	0.40 (0.24, 0.33)	2221/01	21,1555	100.00
	i				
	.2 1	5			

Elgendy IY et al. Outomes with Intravascular Ultrasound-Guided Stent Implantation: A Meta-Analysis of Randomized Trials in the Era of Drug-Eluting Stents. Circ Cardiovasc Interv. 2016;9:e003700



Summary Estimates for the Outcomes of Interest

Outcome	Incidence IVUS-Guided, % /Angiography-Guided, %	Model	OR*	95% CI	<i>P</i> Value	<b>I</b> 2%
MACE	6 5/10 2	Peto	0.60	0.46—0.77	<0.0001	0
MACE	0.3/10.3	DL	0.65	0.52—0.82	<0.0001	0
Cardiovascular	0.5/1.2	Peto	0.46	0.21—1.00	0.05	0
mortality	0.3/1.2	DL	0.51	0.24—1.12	0.09	0
5.41	0.9/1.5	Peto	0.52	0.26—1.02	0.06	0
IVII	0.0/1.5	DL	0.60	0.31—1.17	0.13	0
TID	11/66	Peto	0.60	0.43—0.84	0.003	0
ILN	4. 1/0.0	DL	0.62	0.45—0.86	0.004	0
	5 5/9 7	Peto	0.61	0.41—0.91	0.02	0
	5.5/6.7	DL	0.63	0.43—0.92	0.02	0
Stent	0.6/1.3	Peto	0.49	0.24—0.99	0.04	0
thrombosis	0.0/1.3	DL	0.57	0.26—1.23	0.15	0

Cl indicates confidence interval; DL, DerSimonian and Laird; MACE, major adverse cardiac events; MI, myocardial infarction;

OR, odds ratio; TLR, target lesion revascularization; and TVR. Target vessel revascularization.

\*Risk ratio was reported for DerSimonian and Laird method.

I<sup>2</sup>% is the percentage of total variation across studies that is due to heterogeneity rather than chance

Elgendy IY et al. Outomes with Intravascular Ultrasound-Guided Stent Implantation: A Meta-Analysis of Randomized Trials in the Era of Drug-Eluting Stents. Circ Cardiovasc Interv. 2016;9:e003700



# SCAI Expert Consensus Statement

### SCAI Expert Consensus Statement on IVUS in PCI Guidance:





"...to determine complete stent expansion and apposition and lack of edge dissections or other complications after implantation"



Lotfi A, et al. Focused update of expert consensus statement: Use of invasive assessments of coronary physiology and structure: A position statement of the society of cardiac angiography and interventions. Catheter Cardiovasc Interv. 2018;92:336-347.

### SCAI Expert Consensus Statement on IVUS in PCI Guidance:





"...to determine the size of the vessel undergoing stent implantation"



Lotfi A, et al. Focused update of expert consensus statement: Use of invasive assessments of coronary physiology and structure: A position statement of the society of cardiac angiography and interventions. Catheter Cardiovasc Interv. 2018;92:336-347.

### SCAI Expert Consensus Statement on IVUS in PCI Guidance:



#### Definitely beneficial:

•IVUS is an accurate method to determine complete stent expansion and apposition and lack of edge dissection or other complications after implantation, and the size of the vessel undergoing stent implantation.

#### Probably beneficial:

•IVUS can be used to appraise the significance of LMCA stenosis and, employing a cutoff MLA >6 mm2, to assess whether revascularization is warranted. It is recommended when downstream severe stenosis are present.

#### Possibly beneficial:

- •IVUS imaging may be used to characterize plaque morphology (i.e., calcification), which may alter the PCI technique chosen
- •IVUS has been shown in meta-analyses to decrease major adverse events in PCI
- •In long lesion/long stents, IVUS guided PCI is associated with significantly reduced MACE

#### No proven value/should be discouraged

•IVUS measurements for determination of non-LMCA lesion severity should not be performed to determine stenosis significance.

Lotfi A, et al. Focused update of expert consensus statement: Use of invasive assessments of coronary physiology and structure: A position statement of the society of cardiac angiography and interventions. Catheter Cardiovasc Interv. 2018;92:336-347.

### ACC/AHA/SCAI Guidelines



Use of IVUS (actual wording)	Class	Level of Evidence
For the assessment of angiographically indeterminate left main CAD	lla	В
4 to 6 weeks and 1 year after cardiac transplantation to exclude donor CAD, detect rapidly progressive cardiac allograft vasculopathy, and provide prognostic information	lla	В
To determine the mechanism of stent restenosis	lla	С
For the assessment of non-left main coronary arteries with angiographically intermediate coronary stenoses (50% to 70% diameter stenosis)	IIb	В
For <u>guidance</u> of coronary stent implantation, particularly in cases of left main coronary artery stenting	llb	В
To determine the mechanism of stent thrombosis	IIb	С

Class IIa: "is reasonable", Class IIb: "may be considered."

Levine G et al, 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention, Catheterization and Cardiovascular Interventions 00:000–000 (2011), published online 3 Nov 2011.

### ESC/EACTS Guidelines 2018:



Recommendation (actual wording)	Class	Level of Evidence
IVUS to assess severity and optimize treatment of unprotected left main lesions.	lla	В
IVUS or OCT should be considered in selected patients to optimize stent implantation.	lla	В
IVUS and/or OCT should be considered to detect stent- related mechanical problems leading to restenosis.	lla	С

Class IIa: "should be considered"

Neumann et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. European Heart Journal. August 25, 2018.

### Appropriate Use Criteria



#### Table 1.4. Adjunctive Invasive Diagnostic Testing in Patients Undergoing Appropriate Diagnostic Coronary Angiography

Indica	tion	Ар	propriate Use Score (1	-9)				
		Unexpected Angiographic Finding or No Prior Noninvasive Testing	Prior Testing = No Ischemic Findings	Prior Testing = Concordant* Ischemic Findings				
	IVUS for Lesion Sev	erity						
44.	<ul> <li>Angiographically indeterminate left main stenosis (defined as 2 or more orthogonal views contradictory whether stenosis &gt;50%)</li> </ul>	A (7)	A (7)	A (7)				
45.	<ul> <li>Nonobstructive disease by angiography (non-left main) &lt;50%</li> </ul>	l (3)	l (3)	U (6)				
46.	Angiographically intermediate disease (non-left main) 50% to 69%	U (5)	U (5)	U (6)				
47.	<ul> <li>Angiographically obstructive significant disease (non-left main) ≥70% stenosis</li> </ul>	U (4)	U (5)	l (3)				
	IVUS—Examination of Lesion Artery Morphology							
48.	<ul> <li>Coronary lesions or structures difficult to characterize angiographically (e.g., fracture, stent apposition, stent expansion, dissections) or for sizing of vesse</li> </ul>	aneurysm, extent of calc I before stent placement	ification, stent	A (8)				

\*Concordance refers to noninvasive imaging studies that demonstrate evidence of abnormal myocardial perfusion that is

in the same distribution as a coronary artery stenosis, or degree of valvular disease that is similar to clinical impression.

A = appropriate; I = inappropriate; IVUS = intravascular ultrasound; U = uncertain.

Patel et al. 2012 Appropriate Use Criteria for Diagnostic Catheterization. J. Am. Coll. Cardiol. published online May 9, 2012.



# IVUS-XPL

#### IVUS-XPL



#### Prospective, Multi Center, Randomized Trial



Hong S-J, et al. "Effect of Intravascular Ultrasound-guided Drug-Eluting Stent Implantation: Five-Year Follow-Up of the IVUS-XPL Randomized Trial, *JACC: Cardiovascular Interventions* (2019), doi: https://doi.org/10.1016/j.jcin.2019.09.033

### IVUS-XPL



- 1,400 patients receiving Xience Prime stents ≥28 mm randomized (700 IVUS-guided, 700 angiography-guided) at 20 centers
- "Sustained 5-year clinical benefits resulted from both within 1 year and from 1 to 5 years' post-implantation."<sup>1</sup>



1. Hong S-J, et al. "Effect of Intravascular Ultrasound-guided Drug-Eluting Stent Implantation: Five-Year Follow-Up of the IVUS-XPL Randomized Trial, *JACC: Cardiovascular Interventions* (2019), doi: https://doi.org/10.1016/j.jcin.2019.09.033



# CTO Study

Clinical impact of Intravascular Ultrasound Guided Chronic Total Occlusion Intervention with Zotarolimus Eluting Versus Biolimus Eluting Stent Implantation Randomized Study Sponsored by: Yonsei University

### Methods and Results



#### Prospective, Multi Center, Randomized Trial



Study at a glance and flow chart. CTO indicates chronic total occlusion; IVUS, intravascular ultrasound; N-BES, Nobori biolimus-eluting stent; and R-ZES Resolute zotarolimus-eluting stent.

- Major adverse cardiac event rates were significantly lower in the IVUS-guided group than in the angiographyguided group (2.6% versus 7.1%; p=0.035; hazard ratio, 0.35; 95% confidence interval, 0.13-0.97).
- Occurrence of the composite of cardiac death or myocardial infarction was significantly lower in the IVUSguided group (0%) than in the angiography-guided group (2.0%; p=0.045).

Kim BK, Shin DH, Hong MK, et al. "Clinical Impact of Intravascular Ultrasound-Guided Chronic Total Occlusion Intervention With Zotarolimus-Eluting Versus Biolimus-Eluting Stent Implantation: Randomized Study" Circ Cardiovasc Interv. 2015 Jul;8(7):e002592.

#### Comparison of the Clinical Outcomes Between the IVUS-Guided Group and the Angiography-Guided Group



	IVUS-Guided Group (n=201)	Angiography-Guided Group (n=201)	P Value	Hazard Ratio (95% CI)
Composite Events				
MACE	5 (2.6)	14 (7.1)	0.035	0.35 (0.13–0.97)
Cardiac death or MI	0 (0.0)	4 (2.0)	0.045	*
Other components				
Death				
All	2 (1.0)	3 (1.5)	0.66	0.67 (0.11–3.99)
Cardiac	0 (0.0)	2 (1.0)	0.16	*
MI	0 (0.0%)	2 (1.0)	0.16	*
Stent thrombosis	0 (0.0)	3 (1.5)	0.11	*
Early	0	3		
Late	0	0		
Definite	0	2		
Probable	0	1		
Target-vessel revascularization	5 (2.6)	10 (5.2)	0.19	0.48 (0.17-1.42)
Repeat revascularization	5	9		
Bypass surgery	0	1		
Target-lesion revascularization	5 (2.6)	8 (4.1)	0.40	0.62 (0.20-1.89)
Non-target-vessel revascularization	3 (1.5)	2 (1.0)	0.66	1.50 (0.25-8.96)

Comparison of Clinical Outcomes Between the IVUS-Guided Group and the Angiography-Guided Group

Data are presented as n (% of the cumulative events), n (%), or mean±SD, P values are from the log-rank test, Cl indicates confidence interval;

IVUS, intravascular ultrasound; MACE, major adverse cardiac events; and MI, myocardial infarction

\*Not calculable because of nonoccurrence of the events in 1 group.

Kim BK, Shin DH, Hong MK, et al. "Clinical Impact of Intravascular Ultrasound-Guided Chronic Total Occlusion Intervention With Zotarolimus-Eluting Versus Biolimus-Eluting Stent Implantation: Randomized Study" Circ Cardiovasc Interv. 2015 Jul;8(7):e002592.

#### Angiography Guided Group vs. IVUS Guided Group





Cumulative event rate analysis using the Kaplan–Meier method; intravascular ultrasound–guided vs angiography-guided group. Occurrence of major adverse cardiac event (MACE; A); composite of cardiac death or myocardial infarction (MI; B); and target vessel revascularization (C). P values are from the log-rank test.

Kim BK, Shin DH, Hong MK, et al. "Clinical Impact of Intravascular Ultrasound-Guided Chronic Total Occlusion Intervention With Zotarolimus-Eluting Versus Biolimus-Eluting Stent Implantation: Randomized Study" Circ Cardiovasc Interv. 2015 Jul;8(7):e002592.

#### Conclusion



The Chronic Total Occlusion Intervention with drug-eluting Stents (CTO-IVUS) study is the first randomized trial to demonstrate that IVUS-guided CTO intervention was associated with lower 12-month MACE rates after DES implantation when compared with conventional angiography-guided CTO intervention.

Kim BK, Shin DH, Hong MK, et al. "Clinical Impact of Intravascular Ultrasound-Guided Chronic Total Occlusion Intervention With Zotarolimus-Eluting Versus Biolimus-Eluting Stent Implantation: Randomized Study" Circ Cardiovasc Interv. 2015 Jul;8(7):e002592.



# Mintz Review Article

# Intravascular ultrasound and outcomes after drug-eluting stent implantation

### Mintz review article



There have been 9 published randomized trials and 30 published registry studies comparing IVUS-guided DES implantation with conventional angiographic guidance.

- These trials and registries have been evaluated and summarized in 11 meta-analyses
- In each meta-analysis, IVUS guidance was associated with a reduction in major adverse cardiac events as well as secondary hard endpoints of death (primarily cardiovascular mortality), myocardial infarction, and stent thrombosis, especially in randomized trial meta-analyses.

Mintz GS. Intravascular ultrasound and outcomes after drug-eluting stent implantation. Coron Artery Dis. 2017 Jun; 28(4):346-352

#### Mintz review article



- IVUS guidance minimizes stent under expansion, with more stents and longer stents to minimize geographic miss and treat edge dissections
- IVUS guidance was a dominant and cost-effective strategy, especially in patients with comorbid conditions who were at a higher risk of cardiac events and especially when the benefits of IVUS continued beyond 1 year

Mintz GS. Intravascular ultrasound and outcomes after drug-eluting stent implantation. Coron Artery Dis. 2017 Jun; 28(4):346-352



# ULTIMATE

### **ULTIMATE Randomized Controlled Trial**



Intravascular ultrasound-guided versus angiography-guided implantation of drug-eluting stent in all-comers

- Randomized prospective trial, IVUS vs. angiography guided PCI across 8 sites in China.
- 1448 all-comer patients undergoing 2<sup>nd</sup> generation DES implantation

IVUS standardization with 3 defined criteria to achieve optimal PCI:



Zhang J et al. The ULTIMATE trial. Journal of the American College of Cardiology Sep 2018, 25553; DOI: 10.1016/j.jacc.2018.09.013





**Optimal vs. Suboptimal IVUS-guided PCI:** 

TVF at 12 months

#### Angiography-guided vs. IVUS-guided PCI: TVF at 12 months



Significantly improved outcome for all all-comers when IVUS is used, particularly when the IVUS-defined optimal PCI criteria were met.

(TVF = cardiac death, target vessel MI, and clinically driven TVR)

Zhang J et al. The ULTIMATE trial. Journal of the American College of Cardiology Sep 2018, 25553; DOI: 10.1016/j.jacc.2018.09.013



# Samsung Medical Center Registry

### Samsung Medical Center Registry



6,005 patients who had at least 1 complex lesion undergoing PCI with drug-eluting stents were enrolled in a prospective institutional registry. IVUS guidance was used on 1,674 enrolled patients. IVUS-guided PCI was associated with 43% lower risk of cardiac death during 64 months of median follow-up compared with angiography-guided PCI.<sup>1</sup>



#### Clinical outcomes

1. Choi KH, Song YB, Lee JM, et al. Impact of Intravascular Ultrasound-Guided Percutaneous Coronary Intervention on Long-Term Clinical Outcomes in Patients Undergoing Complex Procedures. JACC Cardiovasc Interv. 2019;12:607–20.



# Summary of IVUS Clinical Evidence

### Summary of IVUS clinical evidence



- **ADAPT-DES** largest study of IVUS guidance<sup>1</sup>, Change in PCI Strategy in 74% of cases
- Ahn Meta-Analysis 17 studies covering 26,503 patients<sup>2</sup>, IVUS guidance was associated with: Reduced MACE, MI, TLR
- Elgendy Meta-Analysis In the era of drug-eluting stents, IVUS-guided PCI is superior to angiography-guided PCI in reducing the risk of major adverse cardiac events
- SCAI Expert Consensus Statement "Definitely Beneficial ... to determine complete stent expansion and apposition and lack of edge dissections or other complications after implantation"<sup>3</sup>
- IVUS-XPL A Randomized Multicenter Clinical Trial of 1,400 patients (IVUS-XPL) reported IVUS guidance was associated with 52% Reduction in MACE at 1 year, 48% reduction from 1 to 5 years<sup>4</sup>
- CTO Study IVUS-guided CTO intervention was associated with lower 12-month MACE rates after DES implantation when compared with conventional angiography-guided CTO intervention<sup>5</sup>
- Mintz review article 9 published randomized trials and 30 published registry studies show IVUS guidance was a dominant and cost-effective strategy<sup>6</sup>
- ULTIMATE Angiography-guided PCI had 86% more TVF than IVUS-guided PCI in all-comers RCT<sup>7</sup>
- **Samsung Registry** IVUS-guided PCI was associated with 43% lower risk of cardiac death during 64 months of median follow-up compared with angiography-guided PCI.<sup>8</sup>
- 1. Witzenbichler B et al. Relationship Between Intravascular Ultrasound Guidance and Clinical Outcomes After Drug-Eluting Stents: The ADAPT-DES Study. Circulation 2014 Jan: 129,4;463-470.
- 2. Ahn JM, Kang SJ, Yoon SH, et al. "Meta-Analysis of Outcomes After Intravascular Ultrasound Guided Versus Angiography-Guided Drug-Eluting Stent Implantation in 26,503 Patients Enrolled in Three Randomized Trials and 14 Observational Studies" Am J Cardiol. 2014;113:1338-1347
- 3. Lotfi A, et al. Focused update of expert consensus statement: Use of invasive assessments of coronary physiology and structure: A position statement of the society of cardiac angiography and interventions. Catheter Cardiovasc Interv. 2018;92:336-347.
- 4. Hong S-J, et al. "Effect of Intravascular Ultrasound-guided Drug-Eluting Stent Implantation: Five-Year Follow-Up of the IVUS-XPL Randomized Trial, JACC: Cardiovascular Interventions (2019), doi: https://doi.org/10.1016/j.jcin.2019.09.033
- Kim BK, Shin DH, Hong MK, et al. "Clinical Impact of Intravascular Ultrasound-Guided Chronic Total Occlusion Intervention With Zotarolimus-Eluting Versus Biolimus-Eluting Stent Implantation: Randomized Study" Circ Cardiovasc Interv. 2015 Jul;8(7):e002592.

- 7. Zhang J et al. The ULTIMATE trial. Journal of the American College of Cardiology Sep 2018, 25553; DOI: 10.1016/j.jacc.2018.09.013
- Choi KH, Song YB, Lee JM, et al. Impact of Intravascular Ultrasound-Guided Percutaneous Coronary Intervention on Long-Term Clinical Outcomes in Patients Undergoing Complex Procedures. JACC Cardiovasc Interv. 2019;12:607–20.

<sup>6.</sup> Mintz GS. Intravascular ultrasound and outcomes after drug-eluting stent implantation. Coron Artery Dis. 2017 Jun; 28(4):346-352



# Economic impact of IVUS

Analysis of IVUS-guided PCI and angiography-guided PCI from an Italian healthcare payer perspective

### Economic impact of IVUS



Alberti study (Italian healthcare payer perspective)<sup>1</sup>

- Modeled incremental cost effectiveness based on based on DRG tariffs and outcomes data from the Ahn meta-analysis<sup>2</sup>
  - Most data points are in the south-east quadrant indicating better outcomes and lower costs with IVUS-guidance versus angiography alone.
  - Cost savings increased in patients with diabetes, renal insufficiency, or ACS and were associated with less MI and revascularization.

## **Conclusion:** "Negative ICERs imply that IVUS-guided PCI with DES is a dominant treatment option compared to angiography-guided PCI with DES."

- 1. Alberti. Understanding the economic impact of intravascular ultrasound. Eur J Health Econ (2016) 17:185–193
- Ahn JM, Kang SJ, Yoon SH, et al. "Meta-Analysis of Outcomes After Intravascular Ultrasound Guided Versus Angiography-Guided Drug-Eluting Stent Implantation in 26,503 Patients Enrolled in Three Randomized Trials and 14 Observational Studies" Am J Cardiol. 2014;113:1338-1347. Note: Analysis combines an Asian study with Italian healthcare payer costs.

