Making Platelet Aggregation Testing More accessible to everyone

Platelet function tests for assessment of antiplatelet drug therapy

Sep.2,2023

Sysmex Corporation
Customer Support JEA Region (Taiwan,Korea,Mongolia and Japan)

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Together for a better healthcare journey

Heard from Sysmex Taiwan

- Neurosurgery and Cardiovascular Surgery: Interested in Platelet Aggregation Testing
- View it as specialized: Requires special facilities, equipment, and technician's skills, etc

Hard to evaluate

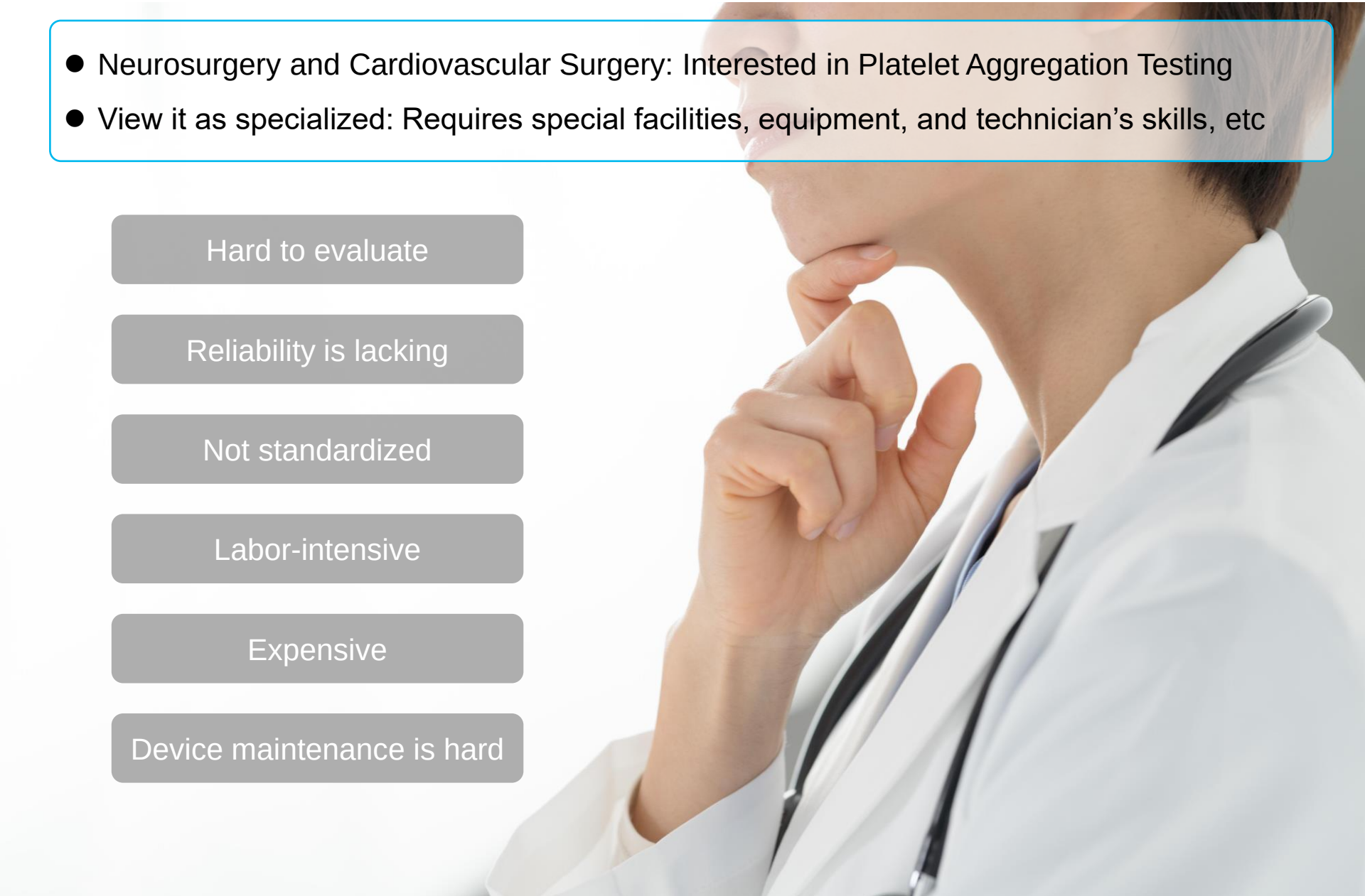
Reliability is lacking

Not standardized

Labor-intensive

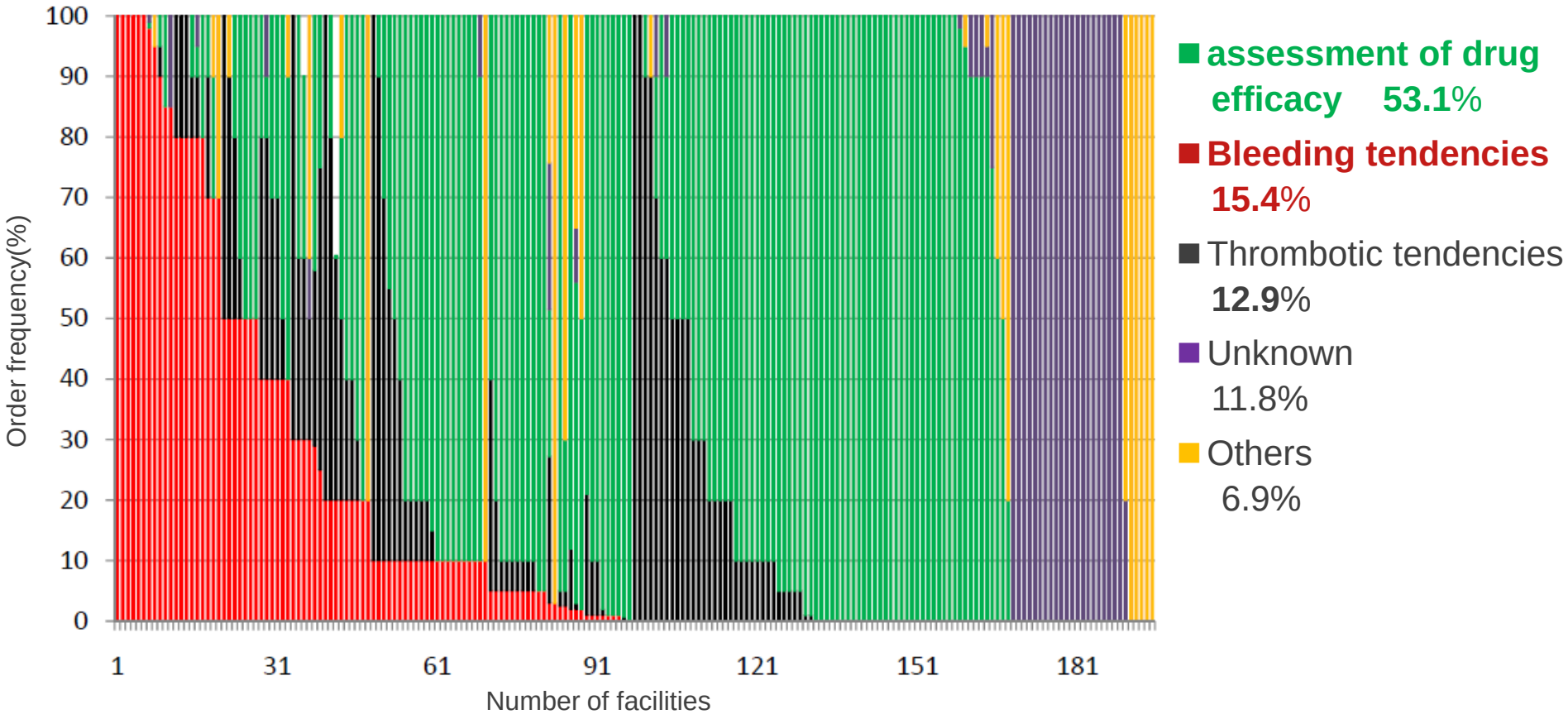
Expensive

Device maintenance is hard



Platelet aggregation testing Purpose : Japan

- Assessment of drug efficacy is the primary purpose
- Doctors in Taiwan and Japan seem to have the same testing goals



From the questionnaire of the Platelet Subcommittee of the Academic Standardization Committee of the JSTH

Japanese Intracranial Arterial Stents Guidelines vs Reality

頭蓋内動脈ステント（脳動脈瘤治療用 Flow Diverter）適正使用指針
第 3 版
2020 年 9 月
日本脳神経外科学会、日本脳卒中学会、日本脳神経血管内治療学会

術前管理

治療 10 日以上前を目安に複数の抗血小板薬の投与の開始が推奨されている。血小板凝集能を確認し、十分な抗血栓効果を確保していることを確認すべきとされている。術前の VerifyNow（Accumetrics, San Diego, California USA）を用いた P2Y12 reaction units(PRU)値（PRU<60 or >240）が周術期の血栓塞栓性および出血性合併症の発生と相関すると報告されており[58]、抗血小板薬開始後は VerifyNow などによるモニタリングを行うことが望ましい。一方で、血小板凝集能値と症候性有害事象との相関性はなく、高用量(>300mg)アスピリンの 6 ヶ月以上の投与は塞栓性および出血性合併症の減少に、クロピドグレルの 6 ヶ月以内の中断は塞栓性合併症の増加に関連するという報告がある[63]。その他、脳動脈瘤に対する一般的血管内治療、特にステント支援コイル塞栓術(stent assisted coil embolization、SAC)に準じた術前管理が必要である[63]。

Challenges in Most Facilities:

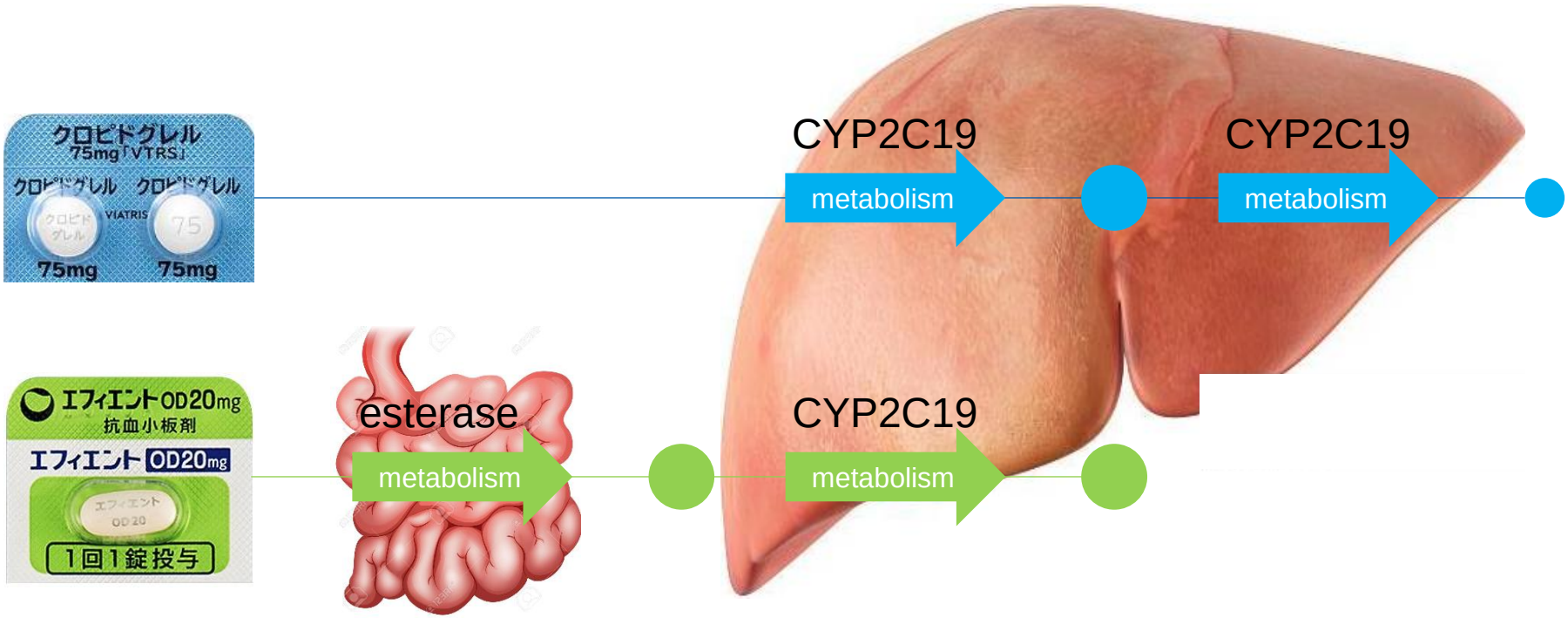
High Cost per Measurement, Limited to Single Measurement

From Werfen HP

FD Appropriate Use Guidelines FIN3

Not all medications work for everyone

- About 20% of Japanese have a CYP2C19 mutation (reduced effect of clopidogrel)
- Some patients show resistance to other antiplatelet drugs



From Viatris Pharmaceuticals' website

From Daiichi Sankyo' website

Two purposes for platelet aggregation testing

- Particularly, High need for medication efficacy evaluation

Screening for platelet dysfunction

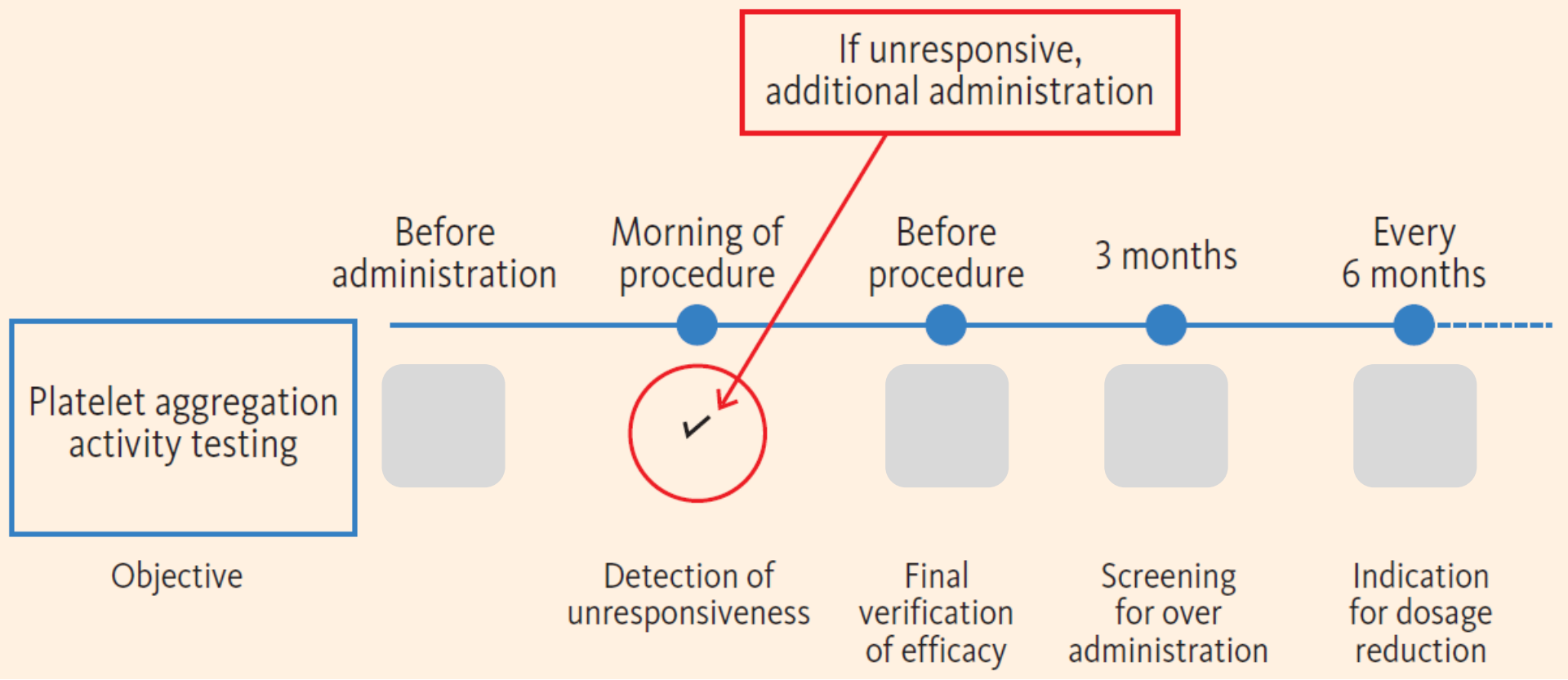
Hematology dept

Evaluation the efficacy of antiplatelet medication

Neurosurgery & Cardiovascular surgeon dept

Challenges & Ideals of Antiplatelet Therapy : Japan

- Challenges：Can't measure frequently
- Ideals　　：Conduct continuous monitoring measurements for various events



From Antithrombotic Treatment Management Using Platelet Aggregation Activity Assay

What do we expect from the testing?

- Ease of evaluation
- Reliability, Standardization
- Easy-to-handle test
- Low Cost
- Easy maintenance

Measurement name	Sample	Measurement method	Advantages	Disadvantages
Light Transmission Aggregometry	Platelet rich plasma	Platelet aggregation induced by an agonist such as ADP is evaluated using light transmittance	• Used as the gold standard • Low running cost • Various agonists and concentrations can be selected	• Labor intensive, requiring tasks such as centrifugal separation and dispensing • Time is required • Interpretation of results is not standardized
Cartridge method	Whole blood	A dedicated cartridge is used to evaluate platelet aggregation as a light transmittance	• Easy • Fast	• High running cost
Flow cytometry method	Whole blood	Quantifies VASP phosphorylation, P-selection expression, and other parameters by flow cytometry to evaluate platelet reactivity.	• Quantification is possible	• Requires special equipment that is expensive • Not in common use
ELISA method	Blood serum	Measures metabolites of anti platelet drugs such as 11-dehydro TXB2 in urine and TXB2 in blood serum.	• Quantification is possible	• Labor intensive • Requires time

From Antithrombotic Treatment Management Using Platelet Aggregation Activity Assay

Solving various challenges with Sysmex's device

- No troublesome technique
- No lengthy testing time
- Operation is simple
- Improvement in data reliability
- Easy maintenance
- Adhere to the ISTH guidelines on agonist concentrations

CS-2000i,2100i,2400,2500

CS-5100

CN-3000,6000

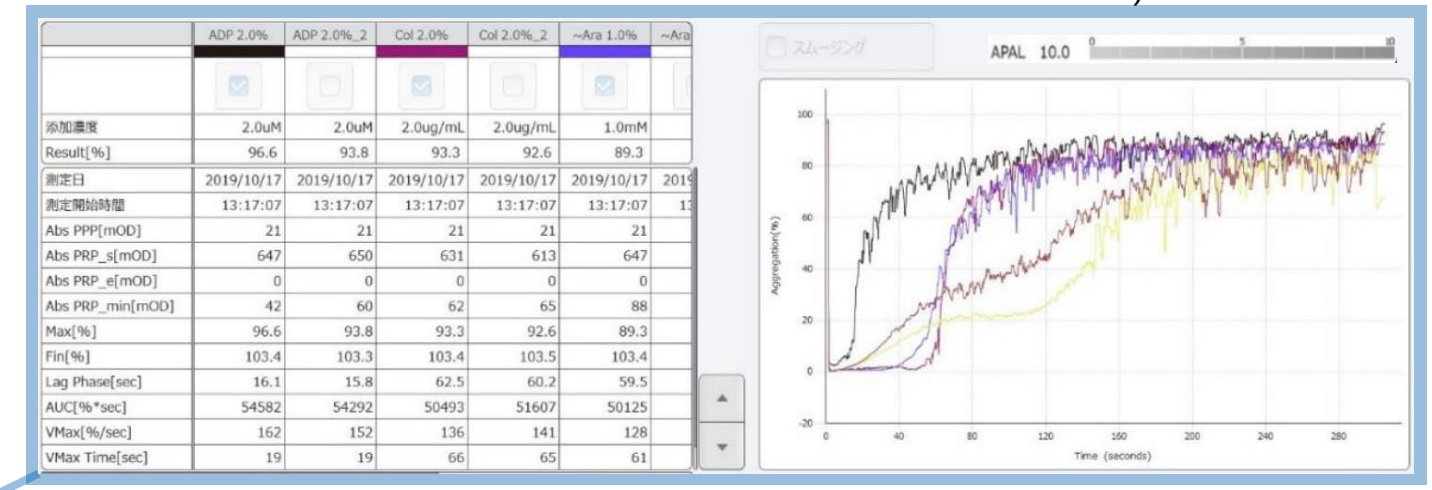
Clotting time, Synthetic substrate, Immunoturbidimetric, and…!

No special operation needed

- Mostly the same procedure as always, with automatic measurement
- Can obtain test results easily (Max%, waveform, new index: PAL)

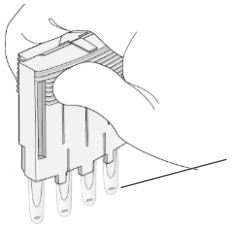
Ex) CN6000IPU screen

	ADP 2.0%	ADP 2.0%_2	Col 2.0%	Col 2.0%_2	~Ara 1.0%	~Ara
添加濃度	2.0uM	2.0uM	2.0ug/mL	2.0ug/mL	1.0mM	
Result[%]	96.6	93.8	93.3	92.6	89.3	
測定日	2019/10/17	2019/10/17	2019/10/17	2019/10/17	2019/10/17	201
測定開始時間	13:17:07	13:17:07	13:17:07	13:17:07	13:17:07	1
Abs PPP[mOD]	21	21	21	21	21	
Abs PRP_s[mOD]	647	650	631	613	647	
Abs PRP_e[mOD]	0	0	0	0	0	
Abs PRP_min[mOD]	42	60	62	65	88	
Max[%]	96.6	93.8	93.3	92.6	89.3	
Fin[%]	103.4	103.3	103.4	103.5	103.4	
Lag Phase[sec]	16.1	15.8	62.5	60.2	59.5	
AUC[%*sec]	54582	54292	50493	51607	50125	
VMax[%/sec]	162	152	136	141	128	
VMax Time[sec]	19	19	66	65	61	

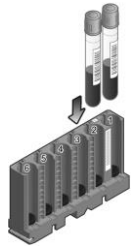


CS-2000i,2100i,2400,2500

Platelet aggregation reagent



Setting SB cuvette

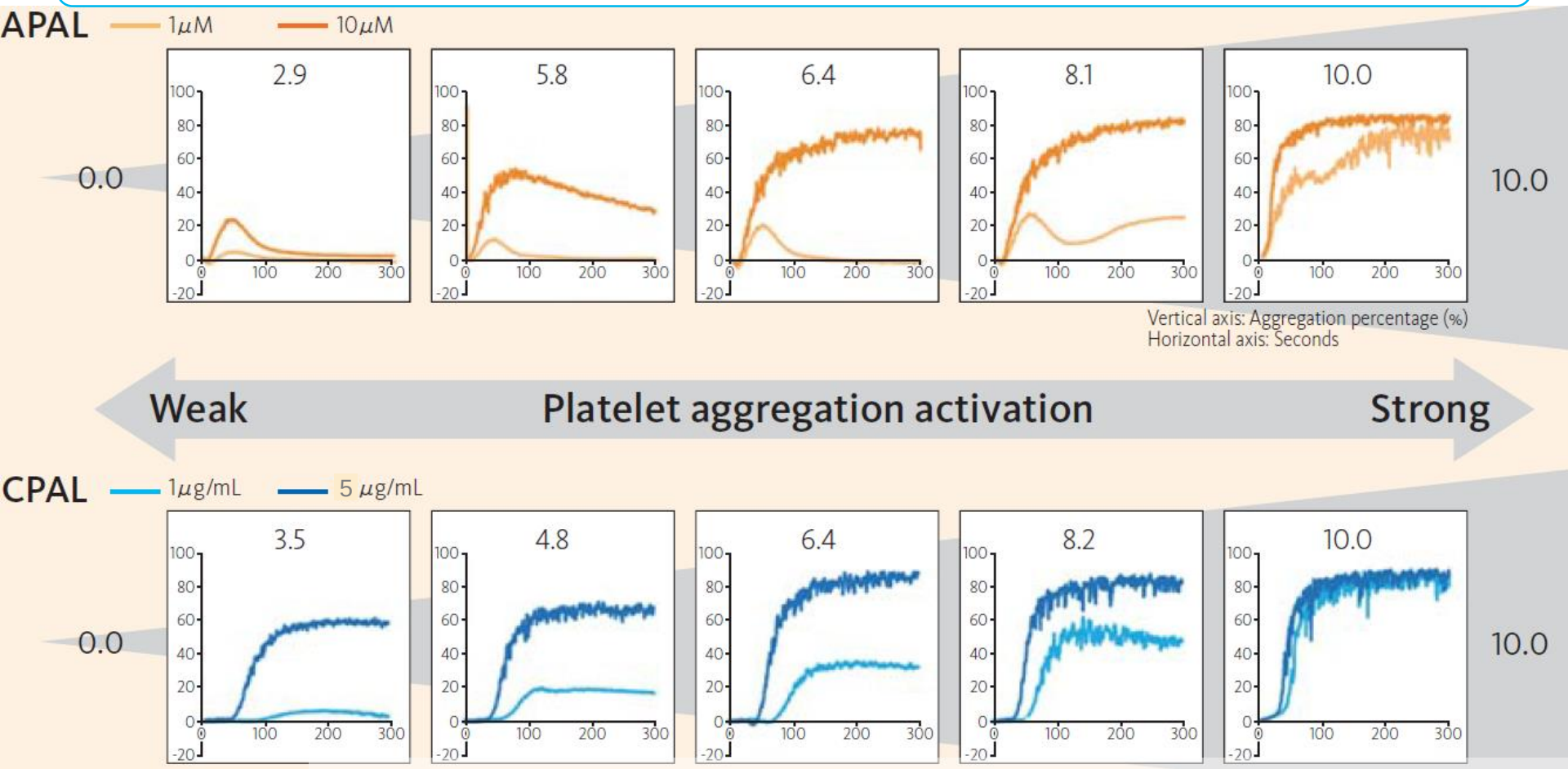


Setting PPP,PRP

new research parameter : PAL

- APAL : ADP-induced platelet aggregation level (ex.Clopidogrel administration)
- CPAL : Collagen-induced platelet aggregation level (ex. Aspirin administration)

100-point index ／ ref. 0.0-2.9 : Too effective, 3.0-6.9 : Moderate, 7.0-10.0 : Not effective



From Antithrombotic Treatment Management Using Platelet Aggregation Activity Assay

Comparison between VerifyNow & our device

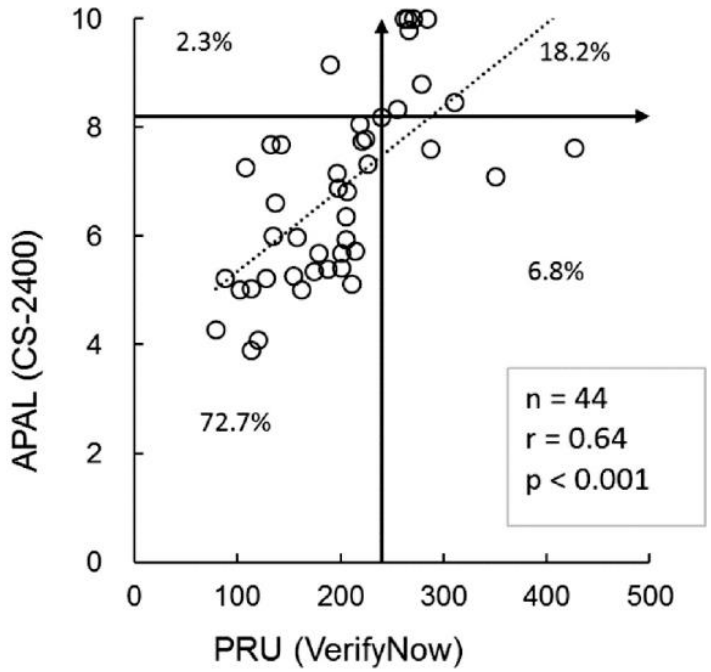
		
sample	Whole blood	Plasma(PPP,PRP)
method	Cartridge (Transmittance change)	LTA (Transmittance change)
result reporting time (after blood collection)	40min	1hour
Therapeutic evaluation ex) Clopidogrel	PRU, % inhibition	APAL
Therapeutic evaluation ex) Aspirin	ARU	CPAL
Reagent	P2Y12 Aspirin	ADP, Collagen, Epinephrine Arachidonic Acid Ristocetin
Cost (Japanese Yen) ex) 5 measurments	34,000 Yen	2,730 Yen

From Werfen HP

Comparison with VerifyNow P2Y12 Assay

- With the PRU cut-off value of 240 in VerifyNow, the APAL cut-off value is 8.2
- Using these cut-off values, the agreement rate for Max% is 90.9%

Control group: intracranial arterial stents & coils



Thresholds of PRU: 240
Thresholds of APAL: 8.2

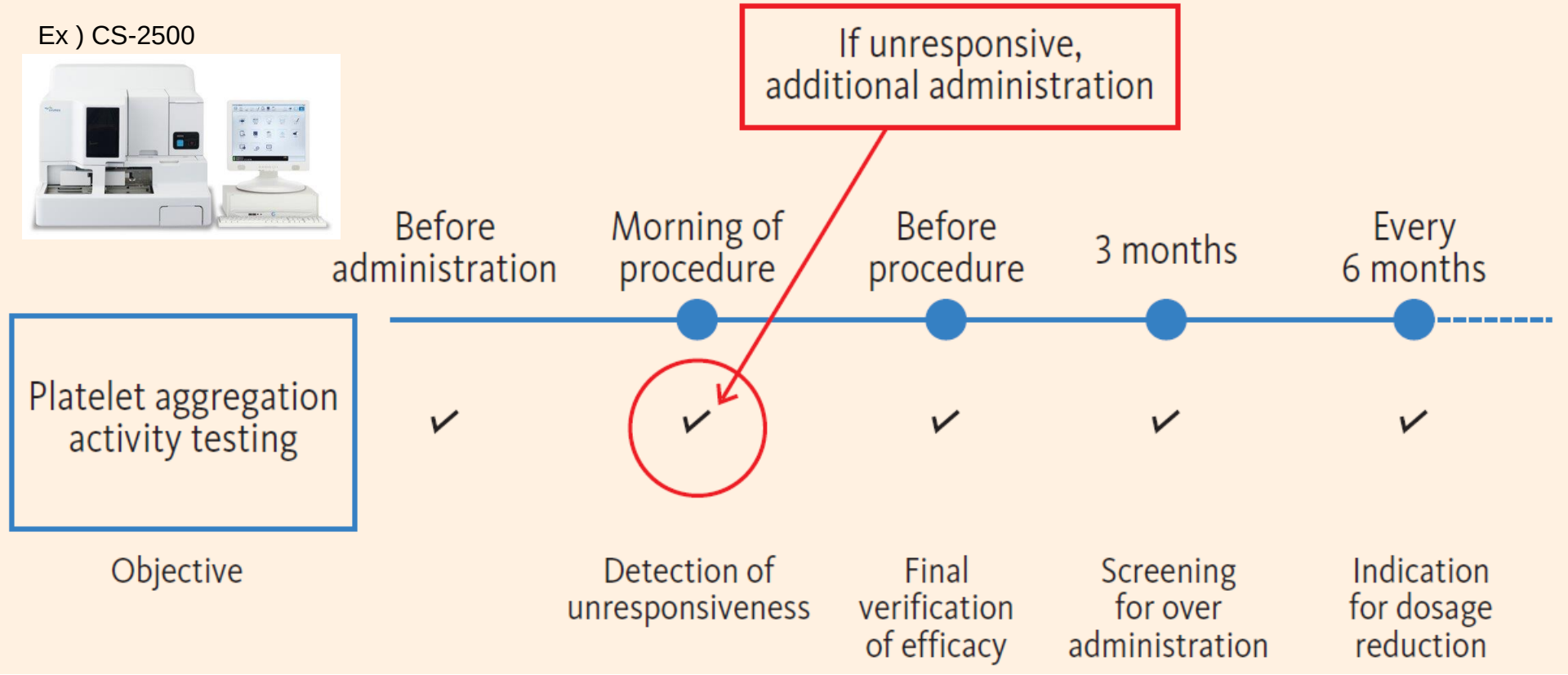
The thresholds at which ischemic complications in neuroendovascular treatment occur have been reported to be a PRU of 240 or % inhibition of 26% as calculated using VerifyNow. We therefore determined the thresholds using APAL, which were equivalent to a PRU of 8.2 and a % inhibition value of 8.1% by ROC curve analysis (**Figures 2&3**). Furthermore, the percent agreement values based on these thresholds were 90.9%, 77.3%, and 84.1% between PRU and APAL, % inhibition and APAL, and PRU and % inhibition, respectively (**Figure 2& Table 2**).

From Annals of Clinical & Laboratory Science, vol. 50, no. 4, 2020

Frequent measurements are possible with Sysmex device

- Conduct continuous monitoring measurements for various events
- Accurately understanding the patient's condition allows for appropriate treatment

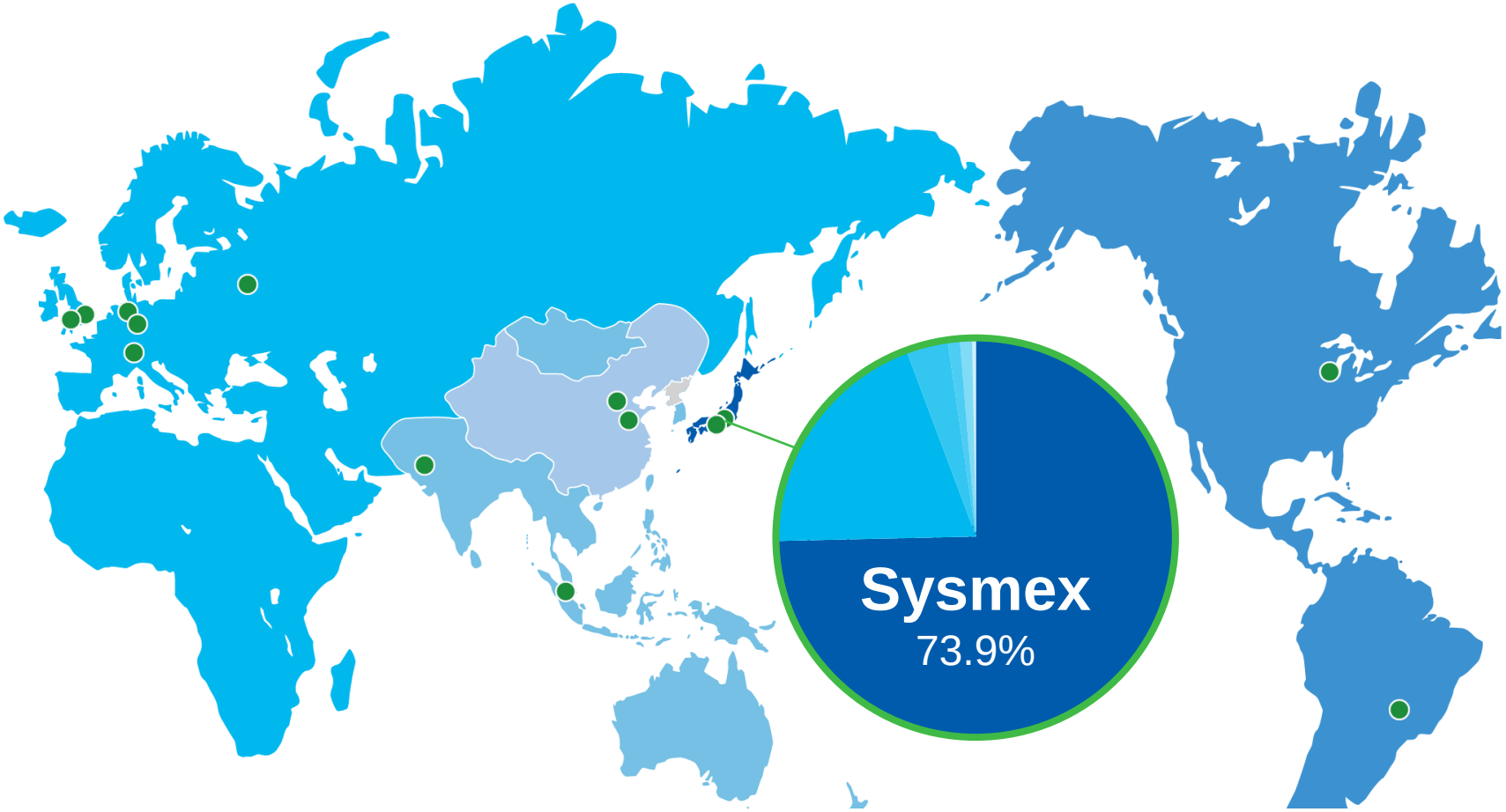
Ex) CS-2500



From Antithrombotic Treatment Management Using Platelet Aggregation Activity Assay

Sysmex's Vision

- Expand our market share and contribute to standardization!
- Bring happiness to patients through Sysmex’s products



Quoted from the 56th Japanese Clinical Laboratory Technician Survey Report

Together for a better
healthcare journey