Assessment of light transmission aggregometry on the routine coagulation analyzer Siemens CS-2500 using CE-marked agonists from Hyphen Biomed

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INTRODUCTION

Light transmission aggregometry (LTA) is still considered as the **"gold standard"** for platelet function assessment but, as a completely manual technology, it is **labour intensive**. This challenge can be overcome by performing platelet aggregometry in an **automated method** on a routine **coagulation analyzer**.

AIM

To compare and correlate results obtained from a traditional **manual LTA solution** using platelet agonists provided from different manufacturers and realized in our Referent Center with a complete solution including the **CS-2500 (Siemens)** optimized automated system and CE-marked agonist **reagents from Hyphen Biomed**.

METHOD

- Platelet rich plasma from patients with **suspected platelet disorders**, **von Willebrand disease** or **antiplatelet therapy** have been assessed using a wide range of agonist concentrations : **ADP (0.5- 10 µM)**, **collagen (2 mg/µL)**, **ristocetin (0.625-1.2 mg/mL)** or **arachidonic acid (1 mM)**.
- The **APACT-4004 aggregometer** (Elitech, France) was used as the **reference instrument** with platelet agonists provided from different manufacturers.
- We evaluated the **CS-2500 analyzer** using dedicated software and **CE-marked agonists** from Hyphen Biomed.
- Results were expressed as **Maximal Platelet Aggregation** and correlation between the CS-2500 and the APACT-4004 was analyzed using the **Passing and Bablok** regression test and the **Bland-Altman** analysis .

RESULTS

- Between October and December 2017, platelet aggregometry studies were performed in **49 samples** (**35 samples** concerned patients with **suspected platelet disorders**, **6 samples** were **RIPA** and **8 samples** corresponded to **antiplatelet therapy tailoring**).
- Maximal aggregation response with ADP (0.5-10 µM), collagen (2 mg.mL^{-1}), ristocetin (1.2 mg.mL^{-1}) and arachidonic acid (1 mM) agonists showed **significant correlation between the two aggregometers** (p<0.01) (Figure 1).
- We observed a more **variable response using low doses of ADP** (≤ 5 µM).
- We also noted **discrepancies with low dose of ristocetin** (0.625 mg.mL^{-1}), showing excessive paradoxical agglutination with the CS-2500.
- **Bland and Altman plots** showed that 95% of the differences were located within acceptable range with most of the agonists, allowing to conclude that the two **compared devices could be considered as consistent** (Figure 2).
- Eight samples had **platelet count in PRP below 150x10^9 L^{-1}** (range from 34x10^9 L^{-1} to 142x10^9 L^{-1}). In most of these cases, platelet maximal aggregations were **consistent between the two systems** (Table I).
- One sample of PRP was tested 5 times with 5 µM ADP, showing 1.5% intra-serial imprecision (CV%) of maximal intensity of platelet aggregation assessed with the CS-2500 instrument compared to 6.6% with the APACT-4004.

Table I. Comparison of maximal platelet aggregations between the APACT-4004 and the CS-2500 systems in eight samples with low platelet count in PRP

Samples	PRP (G/L)	ADP 0,5 µM (%)		ADP 2,5 µM (%)		ADP 5 µM (%)		ADP 10 µM (%)		AA 1 mM (%)		Col 2 µg/mL (%)		Ris 0.6 mg/mL (%)		Ris 1.2 mg (%)	
1	96	33	39	92	72	89	73	NT	NT	87	78	95	82	NT	NT	NT	NT
2	44	11	21	25	41	NT	NT	43	49	39	33	24	27	1	8	47	53
3	34	NT*	NT	51	76	NT	NT	NT	NT	83	74	78	78	73	3	80	76
4	49	NT	NT	NT	NT	NT	NT	0	6	50	45	7	0	70	15	63	63
5	126	25	20	71	71	76	68	NT	NT	75	70	75	69	1	3	74	74
6	142	NT	NT	NT	NT	NT	NT	46	52	5	9	NT	NT	NT	NT	NT	NT
7	92	23	18	58	63	76	84	70	80	66	64	73	66	1	1	67	80
8	141	21	12	44	50	66	58	63	68	62	54	35	45	1	4	36	53

* Not tested
Values in red correspond to the CS-2500

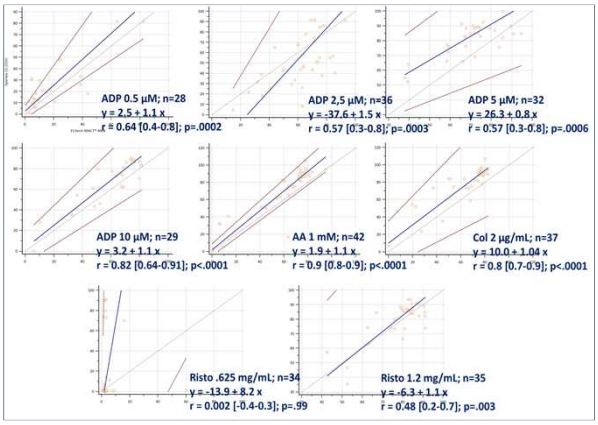

Figure 1. *Correlations between the APACT-4004 and the CS-2500 using the Passing and Bablok regression test (blue lines: fitted regression lines; dotted lines: regression line confidence bands).*

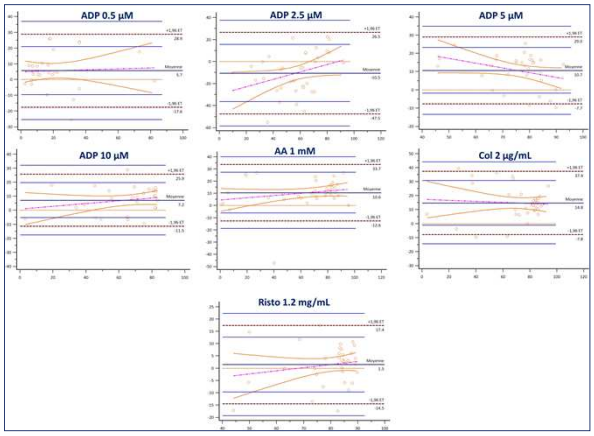

Figure 2. *Bland and Altman plots between the APACT-4004 and the CS-2500 systems.*

CONCLUSIONS

Comparison of platelet aggregometry on the manual APACT-4004 with the automated CS-2500 platform showed **good agreement** between the two platforms in a **clinical setting**. Implementation of LTA in this fully-automated routine coagulation analyzer system should make **platelet function testing more widely available** and could have the capacity for a **high sample throughput**.