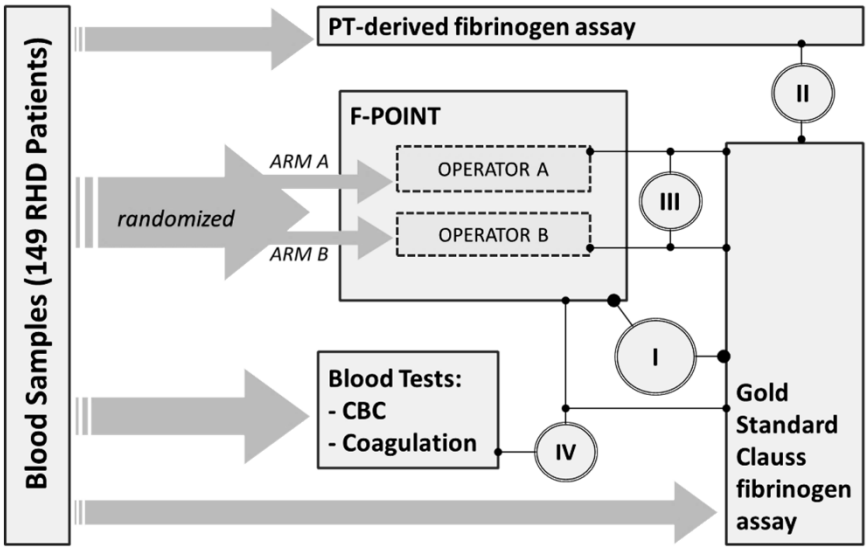
PREMARKET CLINICAL PERFORMANCE EVALUATION OF F-POINT FIBRINOGEN IVD ASSAY

SUMMARY & KEY FINDINGS

DUBLIN, 01NOV2019

TASKS

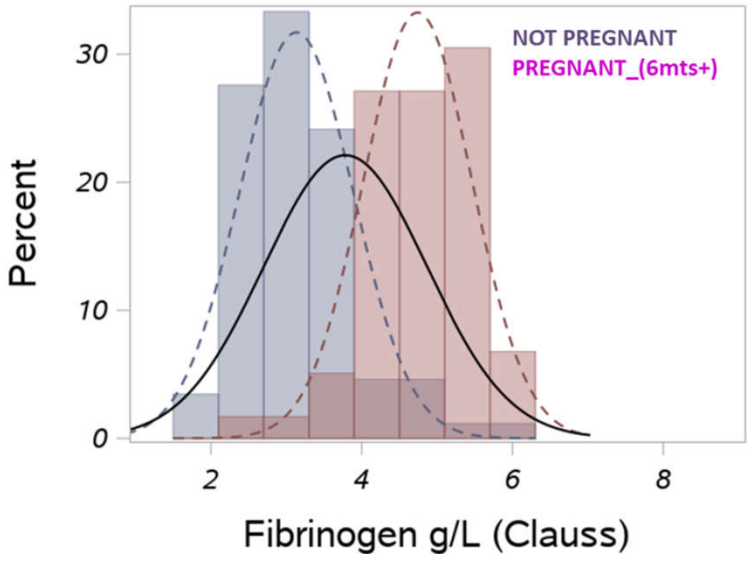
I. *What is the agreement between F-Point and the Gold Standard?*
II. *Does F-Point outperform a known alternative to the Gold Standard?*
III. *Is F-Point performance the same for various operators?*
IV. *Is F-Point fibrinogen test selective?*



THE ROTUNDA HOSPITAL DUBLIN

DEMOGRAPHIC NOTES

- 149 Rotunda patients were recruited, where 2 cohorts were selected, namely **"**NOT PREGNANT" (General Gynecology patients, n=88, 20-39 yo) and "PREGNANT_(6mts+)" (Pregnant patients, n=61, 24-39 yo).
- The choice of such cohorts enabled a wide range of fibrinogen concentration values (fibrinogen gets naturally increased at pregnancy)

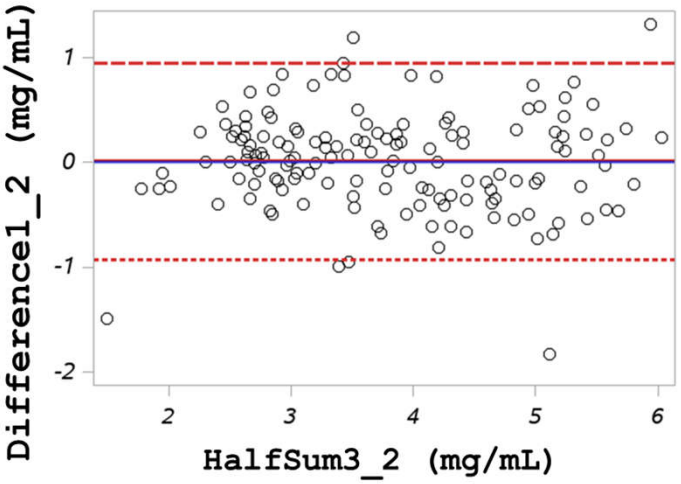


N = 149
FIBRINOGEN RANGE:
1.9 – 6.0 mg/mL

VARIABLES

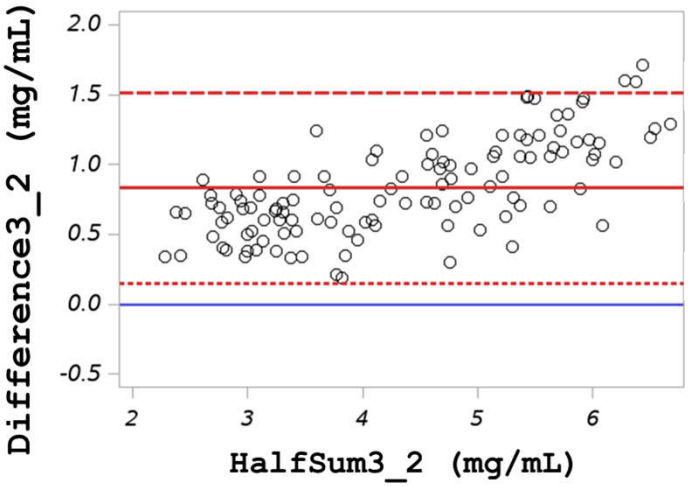
PARAMN	PARAMCD	PARAM	METHOD or FORMAT
LABORATORY FINDINGS			
1	FPOIN	F-Point Fibrinogen (mg/mL)	
2	CLFIB	von Clauss Fibrinogen (mg/mL)	
3	PTFIB	PT-derived Fibrinogen (mg/mL)	
4	APTT	APTT (sec)	
5	PT	PT (sec)	
6	HCT	Hematocrit (v/v)	
7	PLAT	Platelets (cells/nL)	
ARMS			
8	ARM	Operator randomly assigned	(BY_OPERATOR_A, BY_OPERATOR_B)
DERIVED			
9	HSUM1_2	HalfSum1_2 (mg/mL)	HSUM1_2 = ½*(FPOIN + CLFIB)
10	HSUM3_2	HalfSum3_2 (mg/mL)	HSUM3_2 = ½*(PTFIB + CLFIB)
11	DIFF1_2	Difference1_2 (mg/mL)	DIFF1_2 = FPOIN - CLFIB
12	DIFF3_2	Difference3_2 (mg/mL)	DIFF3_2 = PTFIB - CLFIB
13	RE1_2	Recovery1_2 (%)	RE1_2 = 100*(1 + DIFF1_2 / CLFIB)

F-POINT VS CLAUSS: BLAND-ALTMAN PLOT & ICC CALCULATION



INTRACLASS CORRELATION (FISHER): **ICC = 0.79**

PT-DERIVED VS CLAUSS: BLAND-ALTMAN PLOT & ICC CALCULATION



INTRACLASS CORRELATION (FISHER): **ICC = 0.44**

KEY OBSERVATIONS

Analysis Outcomes	F-POINT	PT-DERIVED
95% Detection range	±1 g/L	±0.7 g/L
Bias	NO (p>0.05)	YES (p<0.05)
Agreement (Koo, 2016)	GOOD	POOR

- F-Point can be used as a valid replacement to the Gold Stndard
- F-Point outperforms PT-Derived Assay

TASK III: OPERATOR EFFECT ON F-POINT PERFORMANCE

ARMS

- One of two operator (A/B) users of F-Point device was randomly assigned to each patient
- Operators:
  - A: new post training operator
  - B: more experienced operator
- The study was blind to operator

COHORTS / ARMS	A	B	TOT
NOT PREGNANT	40	48	88
PREGNANT_(6mts+)	25	36	61
TOT	65	84	149

QUALITY OF RANDOM ASSIGNMENT

ARM	N	VAR	MEAN	STD	MIN	MAX
BY_OPERATOR_A	65	HCT	0.38	0.04	0.29	0.44
		PLAT	254	65.5	129	407
		APTT	28.2	3.44	22.0	37.0
		PT	12.1	0.87	10.5	14.1
		CLFIB	3.93	1.08	2.24	6.03
BY_OPERATOR_B	84	HCT	0.37	0.04	0.24	0.47
		PLAT	236	53.0	136	352
		APTT	28.7	2.87	22.0	36.0
		PT	12.2	0.87	10.4	14.0
		CLFIB	3.67	1.08	1.90	5.91

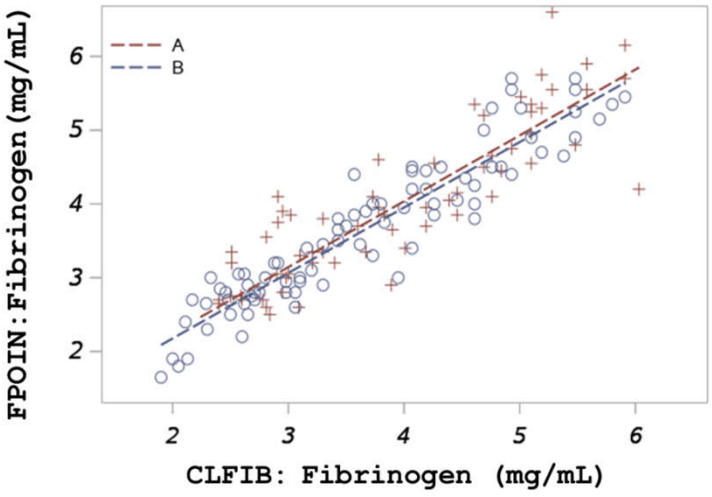
HOTELLING'S T2 TEST:
F = 1.8; p = 0.12

ASSIGNMENT IS FAIR AND ARMS ARE INDEPENDENT

CORRELATION ANALYSIS

BY_OPERATOR_A:
Pearson **PCC = 0.86** (0.79 – 0.92)
Intraclass **ICC = 0.73** (0.64 – 0.81)

BY_OPERATOR_B :
Pearson **PCC = 0.94** (0.90 – 0.96)
Intraclass **ICC = 0.85** (0.81 – 0.87)



KEY OBSERVATIONS

- Performance of the assay depends significantly on operator (both PCC and ICC aren't equal ($p \ll 0.05$ / $p \ll 0.05$)
- Experienced user demonstrated better performance

ADDITIONAL LAB TESTS

- F-Point is a whole blood assay in contrast to the conventional assays. Thus, the main question is if blood cells can affect the test result. F-Point assay may also be sensitive to variety of coagulation factors. 4 plasma/blood parameters were checked in such context.

CORRELATION MATRIX

		APTT	PLAT	HCT	PT
FPOIN	Pearson PCC	-0.38	-0.07	-0.33	0.04
	Prob>|r| under H0: Rho=0	<0.01	0.44	<0.01	0.62
CLFIB	Pearson PCC	-0.29	0.00	-0.35	0.05
	Prob>|r| under H0: Rho=0	<0.01	0.97	<0.01	0.53
RE1_2	Pearson PCC	-0.21	0.10	-0.05	-0.00
	Prob>|r| under H0: Rho=0	0.03	0.40	0.52	0.97

KEY OBSERVATIONS

- Both platelets and plasma proteins involved in PT cascade do not distort F-Point test
- Hematocrit level, HCT, can significantly distort the test as well as plasma proteins involved in APPT cascade. However, these effects were equally observed for the Gold Standard assay. Moreover, F-Point accuracy (evaluated by recovery value) doesn't correlate with HCT
- Moderate correlation of F-Point assay accuracy with APTT is the only concern here. This needs to be clarified and corrected if possible in future lab studies.

CONCLUSION

SUMMARY OF KEY OBSERVATIONS

- F-Point has no significant bias to the Gold Standard
- F-Point is in good agreement with the Gold Standard
- F-Point outperforms known alternative, PT-derived assay, by both bias and agreement

- F-Point accuracy depends on operator. Experienced operators demonstrate better performance. This mast be corrected at the next iteration of test development

- Whole blood F-Point assay is plasma assay equivalent: blood cells do not affect the test
- F-Point assay may be cross-sensitive to some plasma coagulation factors: future lab studies are needed