REGIONE DEL VENETO

ULSS8 BERICA

410

EVALUATION OF STA-NeoPTimal, THE NEW EXTRACTION THROMBOPLASTIN WITH ISI = 1.0

M. Carta[1] , F. Bonente[1] , M.T. Comberlato[1] , T. Pellizzari[1] , E. Marotto[1] , R. Tomasiello[1] , A. Tosetto[2] , D. Giavarina[1]

[1]U.O.C Laboratorio Analisi, AULSS 8 Berica, Vicenza

[2]U.O.S. Malattie Emorragiche e Trombotiche, AULSS 8 Berica, Vicenza

Introduction: Prothrombin time (PT) evaluates the extrinsic coagulation pathway. The measurement is based on activation of the coagulation cascade with thromboplastin (tissue factor + phospholipids). The thromboplastin reagents commercially available show different characteristics and can be from different origins.

Study scope: evaluation of 4 different STAGO thromboplastin reagents:

- TriniCLOT PT HTF, obtained from cultured human cells, with an ISI of 1.12,
- STA-NeoPTimal, extracted from rabbit brain, with ISI = 1.01,
- STA-Neoplastine CI+ (routinely used in our lab), extracted from rabbit brain, with ISI = 1.26,
- STA-Neoplastine R: recombinant source, with ISI = 0.97

Material and methods: All measurements were done on STA-R Max (STAGO).

As per LG CLSI-H47-A2, the mean normal prothrombin time (MNPT) was calculated on 50 samples from healthy donors for each thromboplastin. As also recommended in LG CLSI document EP09-A3, the comparison of thromboplastins was done through simultaneous testing on the instrument of the 4 thromboplastins on patients samples from different groups:

75 samples	individuals without any known coagulation defect
100 samples	patients on anti-vitamin K (VKA) therapy
10 samples	patients with congenital or acquired defect of the extrinsic pathway
32 samples	patients on direct oral anticoagulant therapy (DOACs)

25	INR < 2
27	2 < INR < 3
26	3 < INR < 4
22	INR > 4

4	FVII deficiency
1	FV deficiency
1	FX deficiency
1	Fibrinogen deficiency
3	Lupus anticoagulant

16	Rivaroxaban
7	Apixaban
9	Dabigatran

Results:

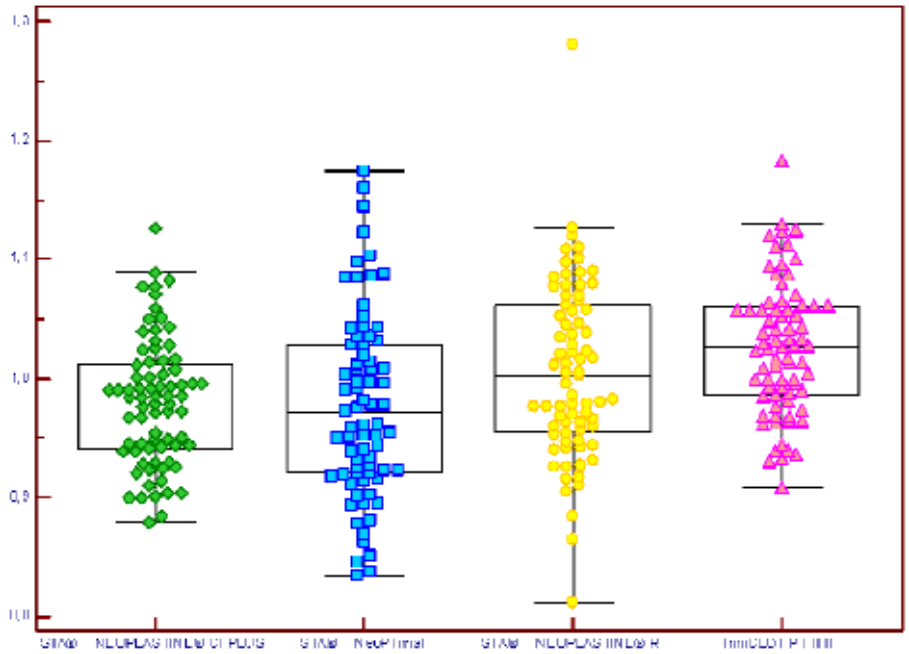
Calculation of MNPT to be able to report PT as a ratio:

	MNPT	Range	SD
STA-Neoplastine CI+	**12.7 seconds**	(12 - 13.8)	0.44
STA-NeoPTimal	**13.5 seconds**	(12.2 - 15)	0.65
STA-Neoplastine R	**13.8 seconds**	(12.8 - 15)	0.55
TriniCLOT PT HTF	**12.7 seconds**	(11.0 - 13.8)	0.44

Analysis of samples without any known coagulation defect:

Reference ranges

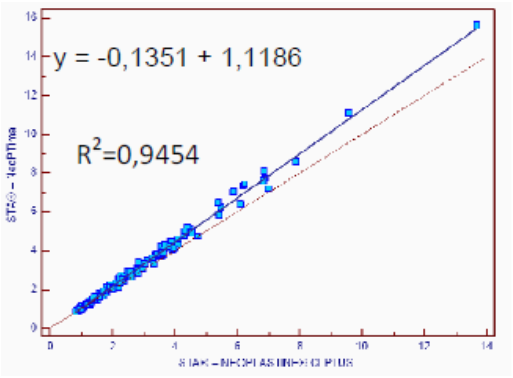
	sec	ratio
STA-Neoplastine CI+	11.47-14.21	0.88-1.08
STA-NeoPTimal	11.12-15.23	0.82-1.13
STA-Neoplastine R	11.87-15.86	0.86-1.15
TriniCLOT PT HTF	11.54-15.03	0.91-1.13

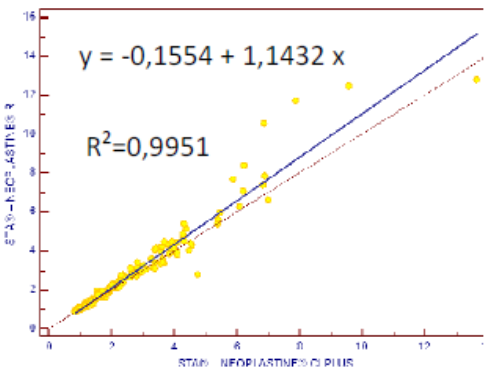


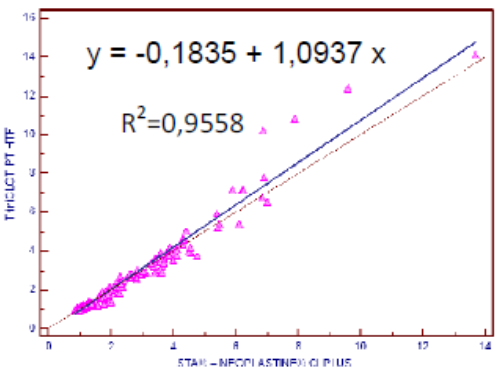
Comparison of the different thromboplastins: PT expressed in ratio

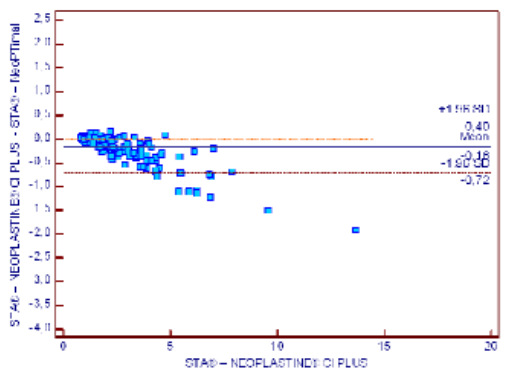
STA-NeoPTimal	**ISI = 1.01**
STA-Neoplastine CI+	**ISI = 1.26**
STA-Neopastine R	**ISI = 0.97**
TriniCLOT PT HTF	**ISI = 1.12**

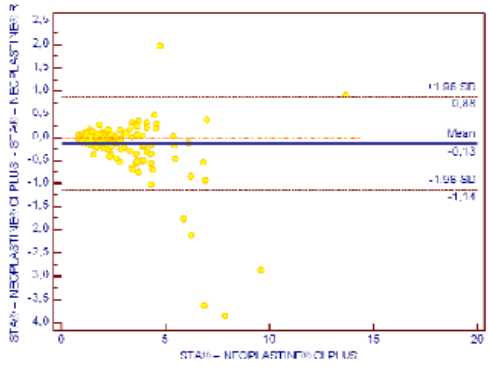
Results: Comparison of the different thromboplastins: PT expressed in INR

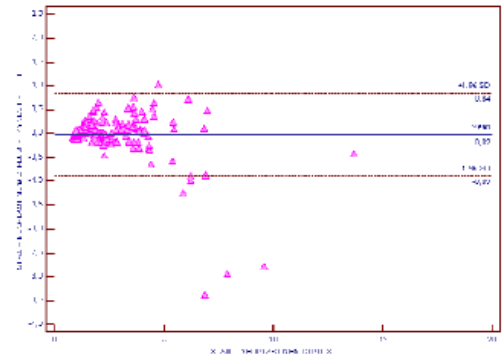


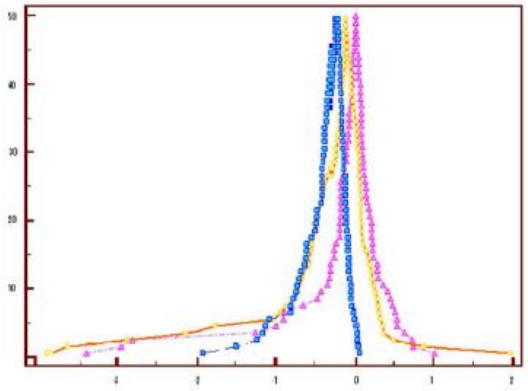












STA-NeoPTimal	**ISI = 1.01**
STA-Neoplastine CI+	**ISI = 1.26**
STA-Neoplastine R	**ISI = 0.97**
TriniCLOT PT HTF	**ISI = 1.12**

All thromboplastins correlate to STA-Neoplastine CI+, the reagent routinely used in our lab and as such considered as the reference.

The lowest bias on INR results was obtained with STA-NeoPTimal reagent (interval: -0.7 /+0.4).

The bias versus STA-Neoplastine CI+ increases as the INR increases for all the 3 tested thromboplastins, but this finding has limited clinical significance because the largest differences were obtained on samples with INR > 4.

Discussion and conclusion:

- PT is a fundamental test to screen for coagulation defects and to monitor oral anticoagulant therapies.
- Tissue factor (thromboplastin), the transmembrane protein activating the coagulation cascade through extrinsic pathway is of extreme importance for PT measurement. The thromboplastin used for PT test can be from extraction (animal or human origin) or chemically synthetized.
- The sensitivity to congenital of acquired factor deficiencies can vary a lot depending on the type of thromboplastin used and thus leading to very different PT results when expressed in seconds. This is why results are being expressed in ratio and, for patients under VKA, in INR through the use of the ISI, which is a characteristic of each thromboplastin and depends on the ability of the thromboplastin to react to the factor deficiency induced by the anticoagulant drug.
- The aim of our study was not to evaluate the sensitivities of thromboplastins to factor deficiency, but rather to evaluate globally if it was possible to use the STA-NeoPTimal thromboplastin as routine reagent in our lab, in comparison to 2 other thromboplastin, one recombinant with ISI=0.97 and another of human origin, with ISI = 1.12.
- STA-NeoPTimal is extracted from rabbit brain but as an ISI close to 1.
- The 3 evaluated thromboplastins correlate to the reference thromboplastin used in our lab, as evaluated on all the study samples (215) or analyzing groups separately (patients without coagulation defects, patients under VKA, patient with coagulation defects). In particular, STA-NeoPTimal as the lowest bias interval.
- From this analysis, we conclude that STA-NeoPTimal can be used in the lab and gives results comparable to those obtained with STA-Neoplastine CI +.

Adopting a thromboplastin reagent with an ISI close to 1 would solve an issue related to PT results expression: the INR results are optimal for patients under VKA, as the ISI standardizes the variability of sensitivity of thromboplastin reagents to coagulation factor defects induced by anticoagulant drugs, but is not appropriate for patients screened for other coagulation defects (liver disease, DIC…). In these patients, it is more appropriate to report PT in ratio.

Yet, from a practical standpoint, it is difficult for a laboratory to differentiate the PT result reporting depending on the PT testing request.

Therefore, adopting a thromboplastin reagent with ISI = 1 guarantees reporting a PT ratio equal to INR.