Verification of the Sediplus® S 2000 NX Blood Sedimentation Monitor

Simple and hygienic determination of up to 40 sedimentation rates within one hour

Müller-Drebelhof C.[1], Dietrich S.[1], Will D.[1]

[1] SARSTEDT AG & Co. KG, Research & Development, Nümbrecht, Germany

Abstract

The erythrocyte sedimentation rate (ESR) is usually measured automatically in the clinical routine. The accuracy and precision of automated measurements must be verified by the manufacturer for the in vitro diagnostics market. In this study, the successor model for the determination of ESR, the Sediplus® S 2000 NX, was verified by comparative measurements in comparison to the current accepted market standard, the Sediplus® S 2000. The verification study was conducted according to the recommendations of CLSI H02-A05. Comparative measurements were performed on 64 blood samples with ESR values in a range of 2 - 84 mm/h Westergren. The mean values found [mm Westergren / 1 h] were almost identical (31.3 mm/h with Sediplus® S 2000 vs. 31.2 mm/h with Sediplus® S 2000 NX; p-value = 0.689). Subsequently, the precision (SD max. 1.6 mm/h with the Sediplus® S 2000 vs. SD max. 2.1 mm/h with the Sediplus® S 2000 NX) of the two devices was determined by multiple measurements. Again, we confirmed very good agreement. The high accuracy and the associated compliance with clinical acceptance criteria as well as the high precision of the Sediplus® S 2000 NX's ESR values confirm the conformity of the device for the in vitro diagnostics market.

Introduction

The determination of the erythrocyte sedimentation rate (ESR), was first described in 1921 by Dr R. Fahraeus and Dr A. Westergren (Fahraeus, 1921; Westergren, 1921).[1] It quickly became a common screening test for acute phase proteins and chronic diseases worldwide (Westergren, 1926). Its ease of determination makes this nonspecific disease indicator a widely used test for screening and surveillance in cases of unclear disease to even monitoring the success of treatment for certain diseases.

During blood sedimentation, erythrocytes sediment due to their higher density compared to blood plasma.[2] Due to the negatively charged erythrocyte surface (zeta potential), neighboring cells repel each other when they are below a certain distance and remain in suspension. In the case of inflammatory diseases, the increased content of acute phase proteins such as fibrinogen in the plasma presumably leads to a lowering of the zeta potential and thus to a faster sinking of the erythrocytes.[3]

To determine the ESR, blood anticoagulated with citrate solution is filled into a standardized column (sedimentation pipette) and after one hour the distance travelled by the descended erythrocytes is read off in mm. For decades, the S-Sedivette® has been a popular in vitro diagnostic tool in clinical laboratories. In addition to its function as a closed blood collection system, the S-Sedivette® also serves as a sample vessel for blood sedimentation. The S-Sedivette® differs significantly in geometry and preparation from the Westergren sedimentation pipette (Fig.2). This simplified handling and made it safer for the user. However, this led to the fact that the BSG scale is now not linear as with the Westergren sedimentation pipette, but has a non-linear scale that is increasingly compressed towards the bottom. In order to further simplify the BSG determination, the Sediplus® S 2000 was developed over time for the automated reading of the BSG.

The Sediplus® S 2000 NX, as verified here, complies with the latest directive for in vitro diagnostic medical devices (2017/746/EU) (Fig. 1). The requirements for electrical safety and electromagnetic compatibility were tested according to DIN EN 61010 and DIN EN 61326. The intuitive operation of the device via the touch display allows the measurement to be started quickly. The BSG values are then output via the display and optionally via the network interface (HL7). This allows the values to be transferred to the laboratory's own computer system (LIS). Up to 40 measurements can be carried out in parallel.

The measuring principle for determining the ESR is based on infrared (IR) transmission. The S-Sedivettes are inserted vertically into the openings intended for this purpose. A measuring table mounted on the device is moved linearly up and down during the measuring process. At the same time, each individual S-Sedivette® is illuminated by an infrared measuring beam during

the movement of the measuring table. This beam hits phototransistors integrated within the measuring table, which detect the boundary between supernatant (plasma) and sedimented erythrocytes by light intensity. The height of the border between supernatant and erythrocyte sediment is measured by counting the steps of the stepper motor inside the device. This sampling process takes place for each sample (S-Sedivette®) at user-defined times (0 h, ½ h and 1 h or 0 h, 1 h and 2 h). A software-supported conversion into Westergren values [mm/h] takes place on the basis of the determined height in millimetres and the specified time. The verification of the software-supported conversion was already carried out on the predecessor model Sediplus® S 2000.[4]

In this study, comparative measurements against the accepted market standard (gold standard), the Sediplus® S 2000, were therefore performed to verify the automated ESR determination with the Sediplus® S 2000 NX.

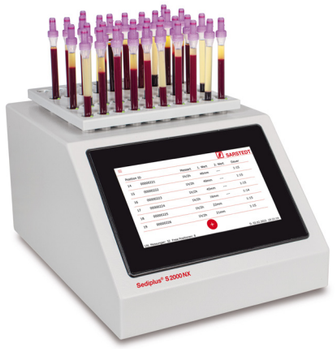

Fig. 1: Sediplus® S 2000 NX; optimized measuring instrument for the determination of blood sedimentation in S-Sedivettes; with touch display; allows parallel determination of up to 40 samples within one hour

Fig. 2: S-Sedivette®; the only validated closed blood collection system for the Sediplus® S 2000 NX

Material & Methods

- Sediplus® S 2000 NX (follow-up model)
- accepted market standard (gold standard) Sediplus® S 2000
- Comparative BSG measurements on both devices (part 1)
- Multiple measurements to determine the precision in the series (part 2)

The verification of the Sediplus® S 2000 NX was carried out in accordance with CLSI H02-A05.[5] For this purpose, 64 samples with ESR values over the entire measuring range were measured comparatively on both ESR devices. The different ESR values of blood from healthy donors were obtained by adding gelatine into the citrate solution.[6] Immediately before starting the measurements, the samples were thoroughly mixed again by inverting them five times.

To determine the precision, 10 repeat measurements of a sample from each of the four quartiles of the entire measuring range were carried out. For this purpose, 10 identical samples were measured in parallel on both devices.

Verification of the Sediplus® S 2000 NX Blood Sedimentation Monitor

White Paper

Results

Part 1: Comparative BSG measurements on the two Sediplus® devices, the accepted market standard S 2000 and the new S 2000 NX to be verified.

The data obtained (Tab. 1) were first tested for significant differences using paired T-tests.

Tab. 1: Measured ESR [mm Westergren] after 1 h, on the two Sediplus® devices

Sample	measuring position	S 2000 mm Westergren / 1 h	S 2000 NX mm Westergren / 1 h
1	1	4	6
2	2	14	13
3	3	71	73
4	4	22	17
5	5	29	26
6	6	57	50
7	7	73	71
8	8	5	5
9	9	14	13
10	10	44	46
11	11	71	67
12	12	69	67
13	13	71	69
14	14	16	17
15	15	23	22
16	16	56	50
17	17	84	84
18	18	81	81
19	19	79	81
20	20	7	7
21	21	17	18
22	22	39	42
23	23	69	69
24	24	4	5
25	25	11	13
26	26	61	65
27	27	32	30
28	28	5	6
29	29	16	17
30	30	49	47
31	31	71	71
32	32	5	6
33	33	8	8
34	34	33	32
35	35	65	65
36	36	2	5
37	37	4	7
38	38	16	16
39	39	46	44
40	1	6	2
41	2	9	9
42	3	18	18
43	4	30	35
44	5	59	52
45	6	2	2
46	7	6	7
47	8	9	9
48	9	16	17
49	10	44	41
50	11	4	4
51	12	11	11
52	13	17	17
53	14	23	23
54	15	50	47
55	16	5	6
56	17	12	13
57	18	23	23
58	19	33	33
59	20	61	63
60	21	4	6
61	22	12	13
62	23	21	21
63	24	29	30
64	25	57	63
	mean	**31,3**	**31,2**
	number n	64	
	p-value	0,689	

The mean values over all samples are almost identical for the two devices with 31.3 mm/h vs. 31.2 mm/h and do not differ significantly (p = 0.689).

For further comparison, a regression analysis according to Passing-Bablok was carried out (Fig.3).

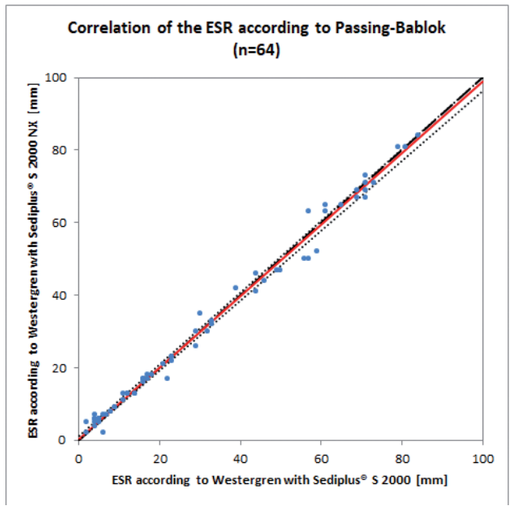

Fig. 3: Correlation according to Passing-Bablok, 1-h ESR values using Sediplus® S 2000 vs. Sediplus® S 2000 NX

The measured values of both devices are shown in Fig. 3. The maximum possible measuring range due to gelatine additives was well covered by the different samples. The dashed line represents the ideal straight line, the red line the Passing Bablok regression line, which here almost corresponds to the ideal (slope: 0.984; intercept: 0.377). The dotted lines represent the lower and upper 95 % confidence intervals. Since the slopes of the confidence interval limits enclose the value of 1 and for the intercept the value of 0, the measured values from both devices are assessed as not significantly different according to CLSI H02-A05.

The systems (Sediplus® S 2000 / Sediplus® S 2000 NX in combination with the S-Sedivette®) can technically measure ESR values up to 116 mm, but the range of values with the method carried out here to simulate artificially increased ESR (gelatin additives) is experimentally exhausted at 84 mm. Outside the measurement range tested here, equivalent data as described above were obtained with blood sedimentation up to 116 mm using Test-Sedivettes (Sedivettes filled with non-transparent plastic) (data not shown). The accuracy of the measured values obtained on the Sediplus® S 2000 NX was thus confirmed over the entire measuring range up to 116 mm.

Furthermore, a Bland-Altman diagram was used to visually check whether systematic differences exist between the measured values from the S 2000 and S 2000 NX (Fig.4).

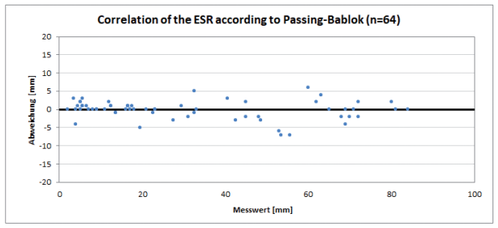

Fig. 4: The difference plot analysis according to Bland-Altman does not indicate any systematic measurement errors due to BSG measurement with the Sediplus® S 2000 NX.

The differences between the pairs of values are apparently evenly distributed upwards and downwards over the measuring range. There are no systematic differences between the readings of the two devices.

Part 2: Determining the precision in the series

Tab. 2: Multiple measurements of identically prepared donor blood samples on both Sediplus® devices

Sample	measuring position	S 2000 mm Westergren / 1 h	S 2000 NX mm Westergren / 1 h
1	1	11	9
1	2	11	9
1	3	6	11
1	4	8	9
1	5	11	9
1	6	9	9
1	7	11	11
1	8	9	11
1	9	9	9
1	10	9	9
mean		**9,4**	**9,6**
SD		1,6	1,0
min		6,0	9,0
max		11	11
2	11	14	17
2	12	17	17
2	13	16	17
2	14	14	17
2	15	17	17
2	16	16	16
2	17	16	16
2	18	16	17
2	19	16	17
2	20	16	17
mean		**15,8**	**16,8**
SD		1,0	0,4
min		14	16
max		17	17
3	21	46	49
3	22	47	50
3	23	47	52
3	24	49	54
3	25	46	50
3	26	46	52
3	27	46	54
3	28	50	56
3	29	49	52
3	30	49	52
mean		**47,5**	**52,1**
SD		1,6	2,1
min		46	49
max		50	56
4	31	73	73
4	32	75	73
4	33	73	73
4	34	73	73
4	35	73	73
4	36	73	73
4	37	73	73
4	38	73	73
4	39	73	75
4	40	73	73
mean		**73,2**	**73,2**
SD		0,6	0,6
min		73	73
max		75	75

The precision measurements were made at four different positions in the measuring range. The standard deviation (SD) was determined here as a measure of the precision in the series. Maximum SD deviations of 1.6 mm for the S 2000 and 2.1 mm for the S 2000 NX were measured.

Discussion

In this study, the new Sediplus® S 2000 NX blood sedimentation measurement device should be verified for the in vitro diagnostics market in accordance with the Directive on In Vitro Diagnostic Medical Devices (2017/746/EU). For this purpose, the requirements of electrical safety and electromagnetic compatibility according to DIN EN 61010 and DIN EN 61326 were tested. The suitability of the measuring function was confirmed in accordance with CLSI H02-A05.

To verify the measuring function, comparative ESR determinations were carried out with the predecessor model Sediplus® S 2000. The comparative ESR measurements of 64 blood samples showed a very high correlation between the two devices. In the paired T-test, no significant differences (mean ESR: 31.3 mm/h vs. 31.2 mm/h) were observed between the two devices (p-value = 0.689) (Tab. 1).

Consistent with this, the correlation analysis carried out according to Passing-Bablok also showed no significant difference in the measured values. The 95 % confidence intervals enclose the value of 1 for the slope and 0 for the intercept.(Fig. 3). Furthermore, the measured values of both devices were visually examined for systematic abnormalities using a Bland Altman difference plot. Again, no systematic deviation between the two devices could be observed (Fig. 4).

The measuring range tested here was limited by the gelatine additive method (max. 84 mm/h). However, tests with Test-Sedivettes also showed equivalent results up to ESR values of 116 mm/h.

The accuracy of the measured values obtained on the Sediplus® S 2000 NX was thus confirmed over the entire measuring range up to 116 mm.

In the second step, the “precision in the series” was determined on both devices. The ESR was determined in parallel on 20 identical samples. The ESR measurements were taken at four different positions with the widest possible distribution over the entire measuring range. Both devices showed comparably good precision with a maximum standard deviation of absolutely 2.1 mm/h Westergren for the S 2000 NX. This is a maximum of 0.5 mm/h Westergren above the maximum imprecision (SD) of the S 2000. In addition to the mechanical-physical imprecision, the small variances in blood sample preparation also contribute to the maximum imprecision. The minimal mean value differences in the determination of the imprecision can also be explained, among other things, by test delays and thus already incipient blood sedimentation until the start of the measurements. However, these minimal differences are not clinically relevant.

Conclusion

The data of the study conducted here show a very high correlation of the measured ESR values determined with the new Sediplus® S 2000 NX compared to the accepted market standard, the Sediplus® S 2000. In addition to the high accuracy of the measured values of both devices, comparably good “precisions in series” were determined on both devices. This means that the Sediplus® S 2000 NX blood sedimentation meter is equivalent to the Sediplus® S 2000 blood sedimentation meter (accepted market standard) in terms of accuracy and precision and thus confirms conformity for blood sedimentation measurements for the in vitro diagnostics market.

Verification of the Sediplus® S 2000 NX Blood Sedimentation Monitor

White Paper

SARSTEDT

The Sediplus® S 2000 NX is thus verified in accordance with the latest directive for in vitro diagnostic medical devices (2017/746/EU).

Disclosure

This work was funded by Sarstedt AG & Co. KG. The authors are employees of Sarstedt AG & Co. KG.

References

[1] J. M. Jou et al. ICSH review of the measurement of erythrocyte sedimentation rate, Int. Jnl. Lab. Hem. 2011, 33, 125-132

[2] Lothar Thomas, Labor und Diagnose, Online–Ausgabe, 10. Auflage 2020

[3] J. Fest et al: Erythrocyte sedimentation rate as an independent prognostic marker for mortality: a prospective population-based cohort study, Journal of Internal Medicine, 2019, 285; 341-348

[4] Comparative Study SARSTEDT Blood Sedimentation Systems https://www.sarstedt.com/fileadmin/user_upload/Mediacenter/Studien/Blood_Sedimentation_Systems/20_376_0000_200_BSG_Studie_1120.pdf

[5] CLSI H02-A5, Procedures for Erythrocyte Sedimentation Rate Test; Approved Standard – Fifth Edition, May 2011, 28

[6] R. Sümpelmann, R. Zander, Gelatine schützt Erythrozyten in vitro und in vivo vor mechanischer Belastung, Anästhesiol Intensivmed Notfallmed Schmerzther, 2001:36

For further information please send us an e-mail to marketing@sarstedt.com or visit us at www.sarstedt.com.

SARSTEDT AG & Co. KG

Sarstedtstraße 1
D-51588 Nümbrecht
Germany

www.sarstedt.com
info@sarstedt.com