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Verification of analytical performance of Carcinoembryonic antigen assay on the Abbott Alinity ci®: Experience of the central laboratory of Mohammed VI University Hospital of Oujda

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Abstract

The aim of our study was the verification of the analytical performance of Carcinoembryonic antigen determination on the Abbott CI analyzer utilizing the immuno-chemiluminescence method. The verification process was conducted in the biochemistry laboratory of Mohammed VI University Hospital of Oujda. The working methodology adapted is based on the recommendations of the protocol of the French accreditation committee (COFRAC) accreditation technical guide (GTA) 04, by the evaluation of reproducibility and repeatability. The results obtained by this evaluation were overall satisfactory and have meet the recommended criteria set by supplier and the French society of clinical biology. This study shows that the biochemistry laboratory of Mohammed VI University Hospital of Oujda can deliver an accurate and precise results which can be used for clinical diagnosis and decision making.

Keywords: Carcinoembryonic Antigen; Tumor Marker; Analytical Performance; Repeatability; Reproducibility; Alinity CI Analyzer; Immuno-Chemiluminescence

1. Introduction

Carcinoembryonic antigen (CEA) is a non-specific serum biomarker that is elevated in various malignancies such as colorectal cancer, medullary thyroid cancer, breast cancer, mucinous ovarian cancer, etc. It was first detected in colon cancer cells by Freedman and Gold and eventually was found in various other epithelial cells in the stomach, tongue, esophagus, cervix, and prostate. It is a glycoprotein with a molecular weight of 200 kDa and is normally derived from embryonic endodermal epithelium in the fetus, controlled by fetal oncogenes. It usually disappears from serum after birth; however, small quantities of CEA may remain in colon tissue (1)

Amidst advancements in laboratory methodologies, the application of chemiluminescent technology in CEA assays has emerged as a promising avenue, offering heightened sensitivity and accuracy in detecting CEA levels.

Our study delves into the crucial process of method verification of the CEA assay using immune-chemiluminescence technology used by Abbott analyzer Alinity Ci. This method involves assessing the analytical performance, measuring them through standardized operational procedures, and then comparing them against criteria set by recognized societies (RICOS, FSCB). This comprehensive approach provides the laboratory with essential insights into its analytical methods, their capabilities, and limitations. Ensuring that these measures meet the standards for delivering reliable analytical outcomes and clinically meaningful interpretations.

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1.1. Interest of Carcinoembryonic antigen determination

The carcinoembryonic antigen (CEA) is a heterogenous glycoprotein composed of mannose, galactose, N-acetylglucosamine, fucose, and sialic acid that are usually produced for the duration of fetal development, but its production ends prior to birth. Its increase is mostly utilized as a tumor marker to monitor the treatment of colorectal carcinoma or other carcinomas, to recognize recurrences, and for the staging of tumors (2).

1.2. Principle of CEA assay method

This assay employs a two-step immunoassay to determine the presence of CEA in human serum and plasma, using Chemiluminescent Microparticle Immunoassay (CMIA) technology,

In the first step, sample and anti-CEA coated paramagnetic microparticles are combined. CEA present in the sample binds to the anti-CEA coated microparticles. After washing, anti-CEA acridinium-labeled conjugate is added in the second step. Pre-Trigger and Trigger Solutions are then added to the reaction mixture; the resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of CEA in the sample and the RLUs detected by the optical system.

2. Materials and methods

This study is a prospective investigation conducted within the biochemistry laboratory of Mohammed VI University Hospital, spanning a duration of 30 days. The working methodology adapted is based on the recommendations of the protocol of the French accreditation committee (COFRAC) accreditation technical guide GTA 04. It was structured around two distinct phases. The initial phase involved evaluating the reproducibility of results. This was achieved through daily testing of control samples at three concentration levels—low, medium, and high—over the course of 30 days. The primary aim was to assess the consistency and reliability of the assay. In the subsequent phase, a comprehensive collection of serum samples was amassed, ensuring an equitable distribution of CEA values across the full measurement spectrum. These collected samples were categorized into three groups representing low, medium, and high CEA levels. To gauge repeatability, each serum sample underwent 30 individual assay runs.

The CEA determination was conducted utilizing a dedicated reagent kit on the immunology module of Abbott Alinity CI analyzer. Subsequent data processing was carried out via the BYG middleware, serving as an intermediary software bridging the gap between the Alinity platform and the iLab result validation software. The coefficient of variation (CV) values yielded by this study were subsequently juxtaposed against the standards stipulated by established learned societies, namely the Federation of Clinical Chemistry and Laboratory Medicine (FSCB) and the Reference Institute for Bioanalytics (RICOS).

3. Results

3.1. Intermediate fidelity results

The outcomes of the intermediate fidelity examination yielded satisfactory results for all levels low, medium, and high levels, yielding coefficients of variation (CV1, CV2 and CV3) of 7.57%, 4.36% and 4.85% respectively (Table 1).

These findings have been graphically presented using Levey-Jennings plots (Fig. 1, Fig. 2, and Fig. 3) to further illustrate the obtained results.

Table 1 Reproducibility results of blood assay by level with comparison to FSBC

Level of IQC	Numbers of value	Mean (ng/ml)	Standard deviation	Coefficient of variation CV (%)	Reference CV: FSBC 1999
Low	30	2.11	0.160	7.57%	15.0%
Medium	30	17.13	0.747	4.36%	8.0%
High	30	46.53	2.258	4.85	8.0%

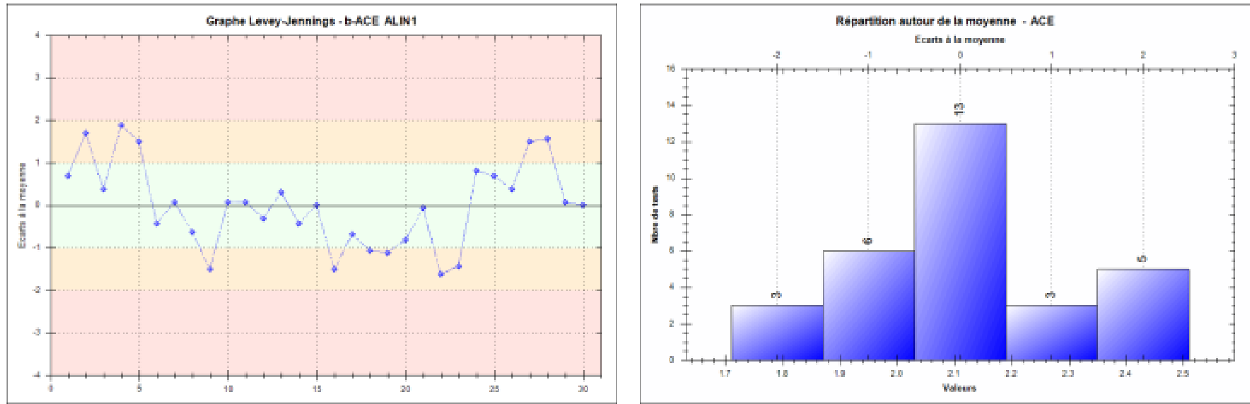

Figure 1 Low Level of reproducibility: Levey Jennings graph and the distribution around the mean

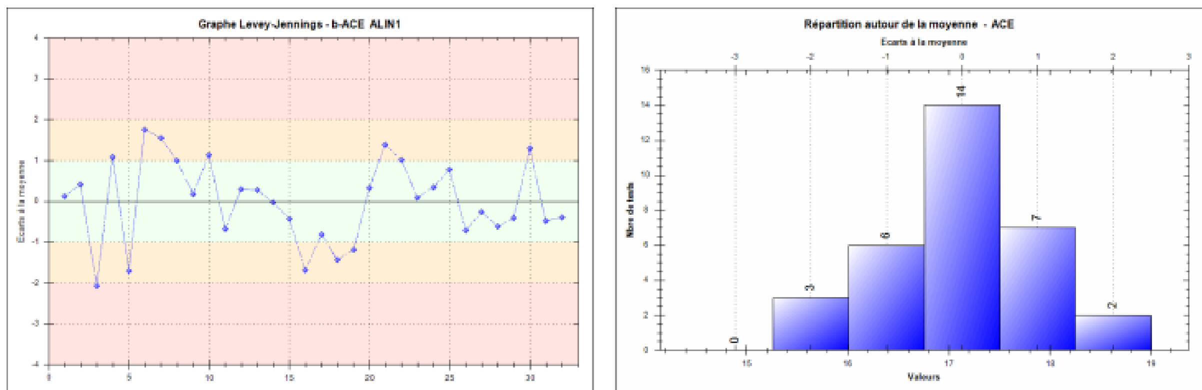

Figure 2 Medium Level of reproducibility: Levey Jennings graph and the distribution around the mean

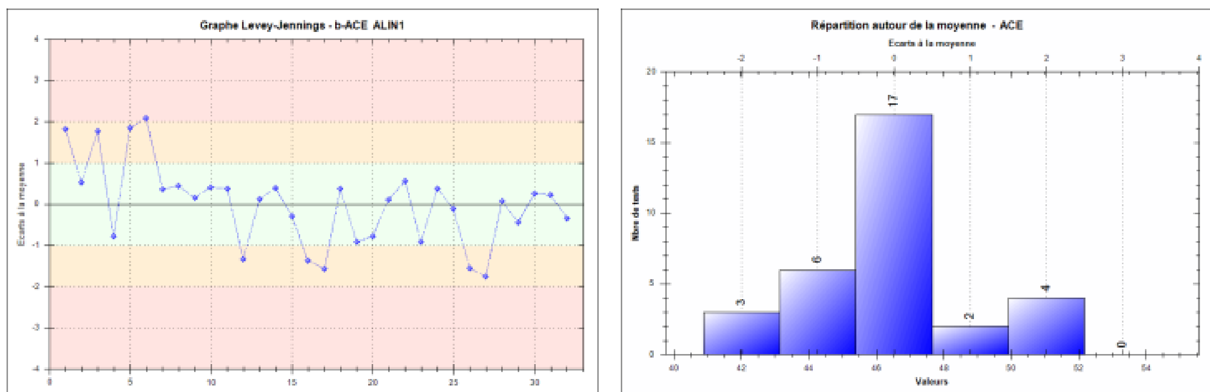

Figure 3 High Level of Reproducibility: Levey Jennings graph and the distribution around the mean

3.2. Repeatability results

The results obtained from this investigation exhibited commendable levels of repeatability for all levels low, medium, and high concentration ranges, as indicated by CV1 of 4.40%, CV2 of 2.20%, and CV3 of 1.81% respectively (Table 2).

These findings are visually expounded upon through Levey Jennings plots, illustrating the results in a more comprehensive manner (Fig. 4, Fig. 5, and Fig 6).

Table 2 Repeatability results of blood assay by level with comparison to FSBC and RICOS data

Level of IQC	Number of value	Mean (ng/ml)	Standard deviation	Coefficient of variation CV (%)	Reference CV: FSBC 1999
Low	30	2.09	0.092	4.40 %	11.25%
Medium	30	15.39	0.311	2.20%	6.0%
High	30	45.4	0.820	1.81 %	6.0%

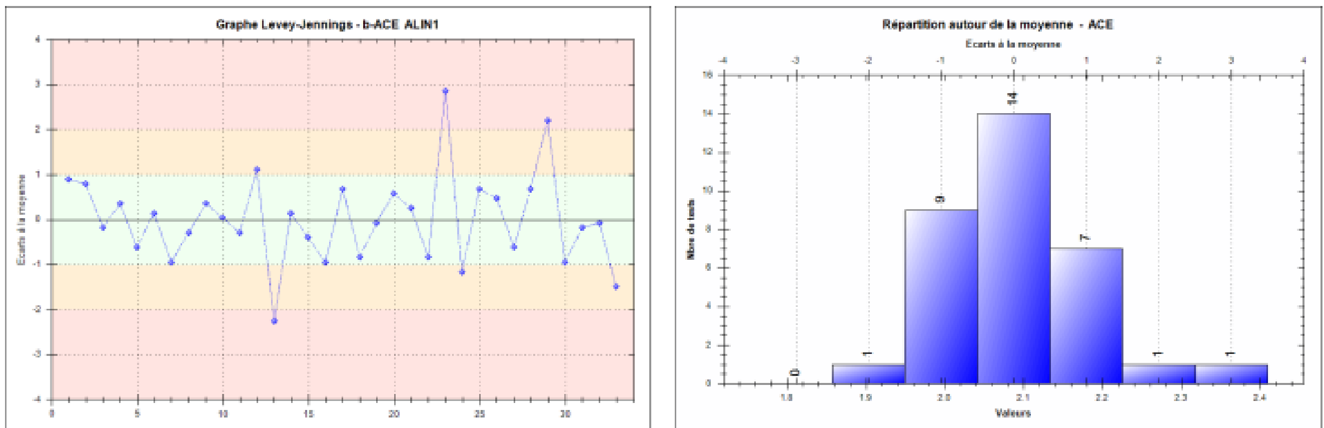

Figure 4 Low Level of Repeatability: Levey Jennings graph and the distribution around the mean

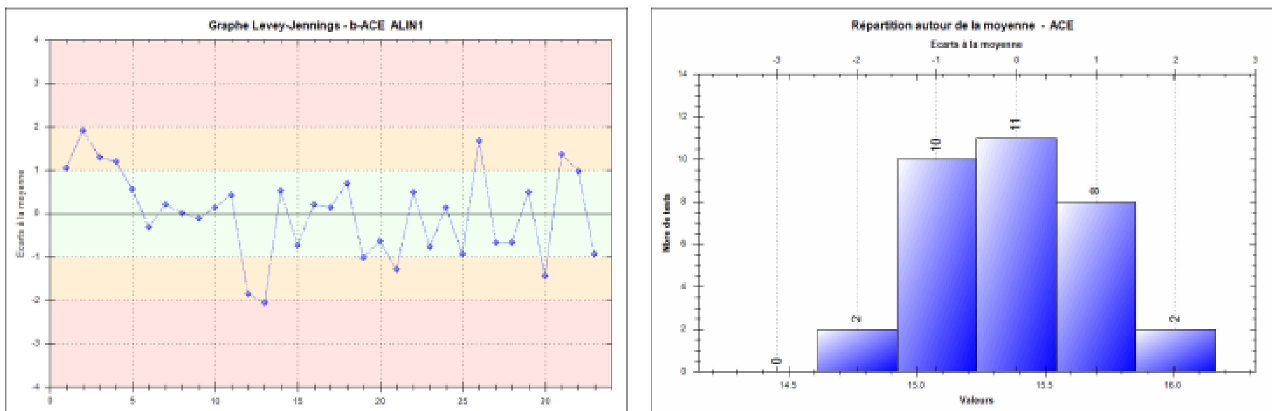

Figure 5 Medium Level of Repeatability: Levey Jennings graph and the distribution around the mean

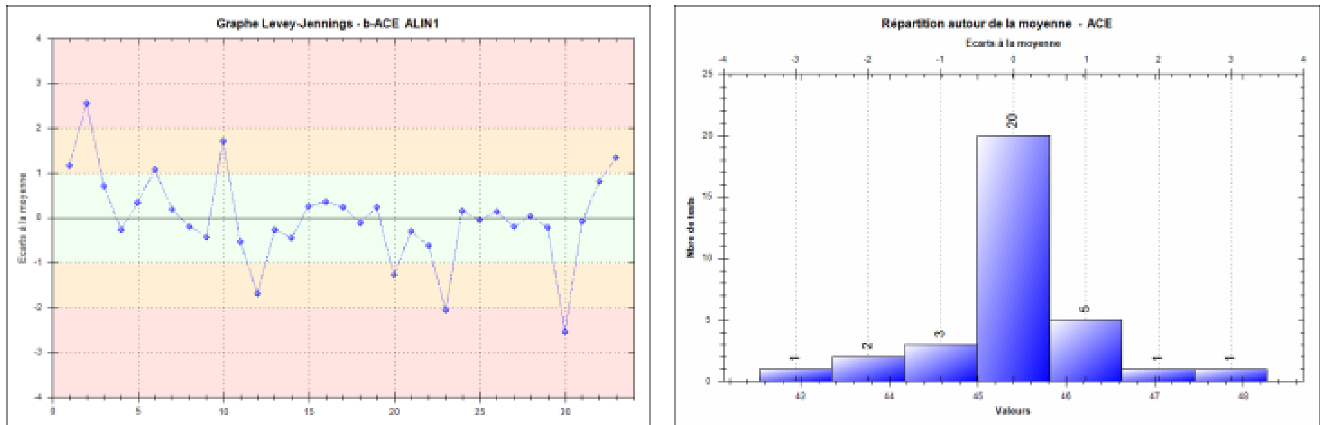

Figure 6 High Level of Repeatability: Levey Jennings graph and the distribution around the mean

4. Discussion

The result of clinical studies to date indicate that CEA, although originally thought to be specific for digestive tract cancers, may also be elevated in other malignancies and in some nonmalignant disorders. CEA testing can have significant value in the monitoring of patients with diagnosed malignancies in whom changing concentrations of CEA are observed. A persistent elevation in circulating CEA following treatment is strongly indicative of occult metastatic and/or residual disease. A persistently rising CEA value may be associated with progressive malignant disease and a poor therapeutic response. A declining CEA value is generally indicative of a favorable prognosis and a good response to treatment. Patients who have low pretherapy CEA levels may later show elevations in the CEA level as an indication of progressive disease. Clinical relevance of the CEA assay has been shown in the follow-up management of patients with colorectal, gastric, breast, lung, prostatic, pancreatic, and ovarian carcinoma. Follow-up studies of patients with colorectal, breast, and lung carcinoma suggest that the preoperative CEA level has prognostic significance. Thus, an accurate and precise results must be delivered to practitioners.

The verification/validation of methods within a medical laboratory is a crucial process that ensures precise and reliable measurements. It serves as both a regulatory requirement outlined in The Moroccan Guide for the good performance of Medical Laboratory Analysis (GBEA) and a normative standard according to ISO 15189:2022(3, 4). The CEA assay, utilizing the immunochemiluminescent method, is presently a validated method, thus necessitating verification rather than validation. In this study, we conducted a verification of the analytical performance of the Carcinoembryonic assay on the Abbott Alinity CI analyzer by using the COFRAC guide SH-GTA-04(5).

Repeatability and intermediate fidelity are statistical methods utilized in process control to measure precision and variability within our automated systems. The intermediate fidelity test, also known as intra-laboratory reproducibility, involves examining a single sample under various conditions by altering at least one factor: such as the operator, timing, reagent kits, or calibrations. This process helps establish acceptance criteria in line with prior data, considering biological variations. This is especially valuable in decision support Systems (6, 7).

The results of intermediate fidelity evaluation suggests that the CEA assay, employing the immune-chemiluminescent method, has shown consistency and agreement in measurements across different conditions. Which suggest that the technique is robust and reliable, and it can be trusted for clinical diagnosis.

As for, the repeatability test, it involves analyzing a single sample under precise conditions, including the same operator, reagent kits, instrument, and calibration, all completed within the shortest feasible timeframe(8). This process aims to characterize the optimal performance of the system (instrument/reagent) for the specific analyte, ensuring the verification of its proper functioning under these controlled conditions. For a given analyzer, this calculation must be performed for each analyte/matrix to be measured and at several concentration levels. The levels are chosen according to the medical decision areas (7, 9).

The results of the repeatability evaluation have demonstrated that the immune-chemiluminescent CEA assay utilized in our laboratory exhibits high precision. This is substantiated by consistently low coefficients of variation for repeatability, showcasing minimal variability in repeated measurements conducted under identical conditions. This results not only emphasizes the reliability this method but also underscores the stability and robustness.

The Coefficients of variation and Standard deviations obtained from the analysis of repeatability and the intermediate fidelity were highly acceptable. Fulfilling both the supplier's stipulated requirements and the criteria outlined in the SFBC Valtec protocol and RICOS. These findings affirm that the immuno-chemiluminescent method used by the biochemistry laboratory of Mohammed VI University hospital CEA determination on the Abbott Alinity CI analyzer for is not only consistent but also stable in replicating precise measurements across different concentration levels. The alignment of these results with SFBC and RICOS standards substantiates the method's robustness and reliability, signifying its suitability for accurate and dependable measurements in critical clinical diagnostics.

5. Conclusion

Our study showed satisfactory results, meeting the criteria set by the SFBC protocol. The Alinity ci demonstrated reliable analytical performance for the precise determination of CEA, a valuable marker for the diagnosis and monitoring of cancer diseases. Reliable results from CEA analyses are essential for the management and follow-up of cancer patients, particularly those with digestive diseases. Compliance with the ISO 15189 method verification standard ensures accurate and reliable laboratory results, and reinforces its credibility. The verification process, which forms the basis of accreditation, enhances the quality of patient care and strengthens trust between patients and healthcare providers.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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