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(RESEARCH ARTICLE)

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Verification of the Lactate Dehydrogenase dosage method using Abbott Architect ci8200 experience of the biochemistry laboratory, CHU Mohammed VI Oujda, Morocco

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Abstract

Introduction: This work describes the verification procedure to evaluate the analytical performance of lactate dehydrogenase (LDH) assay, a key enzyme in glycolysis. It catalyzes the reversible conversion of pyruvate to lactate, with simultaneous production of NADH from NAD^+. This evaluation forms part of a comprehensive process to validate the methods used in the central laboratory of the Mohammed VI University Hospital in Oujda, with the objective of assembling an accreditation file that meets the NF ISO 15189 standard requirements.

Objectives: The aim of this study was to validate the analytical method for lactate dehydrogenase determination by evaluating key criteria such as repeatability and reproducibility. This validation process sought to ensure that the method complies with the required standards and delivers reliable and accurate results for clinical diagnostics.

Results and Discussion: The verification of the LDH assay criteria demonstrated satisfactory repeatability across all three levels, with CV1=1.34%, CV2=0.71% and CV3=0.60% respectively. Similarly, intra-laboratory reproducibility was deemed satisfactory for all levels, with CV1 = 3.06%, CV2 = 2.50%, and CV3 = 1.77% for the respective levels.

The verification of an analytical method is a critical step in ensuring that the obtained results closely align with the reference values of the sample. A comparison of our findings with the CV standards set by the SFBC (a quality control system) and RICOS (an international quality control network) indicates that our results comply with, and remain below, the acceptable limits.

Conclusion: By implementing rigorous analytical performance verification, laboratories guarantee reliable clinical outcomes. This study enhances the existing knowledge base regarding the accuracy and reliability of serum LDH measurements.

Keywords: LDH; Verification; Repeatability; Reproducibility; Architect ci8200; Quality; Biochemistry laboratory; Mohammed VI University Hospital

1. Introduction

Lactate dehydrogenase (LDH) is a key enzyme in the anaerobic metabolic pathway. It facilitates the reversible conversion of lactate into pyruvate, coupled with the reduction of NAD+ to NADH, and the reverse reaction as well [1].

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The quantification of LDH holds significant clinical value, as serum concentrations of LDH isoezymes can indicate tissue-specific pathological conditions. Tissue damage may result from various diseases, including acute myocardial infarction, anemia, pulmonary embolism, hepatitis, and acute renal failure. LDH serves as a reliable marker for disease staging (S-classification), monitoring prognosis or treatment response, and assessing body fluids beyond blood. A reduction in LDH levels during treatment suggests an improved prognosis and/or an effective therapeutic response in conditions such as acute myocardial infarction or liver injury [2].

Abbott's Architect ci8200 analyzer represents a major advance in clinical chemistry, offering a high level of performance, precision and efficiency. Validation of analytical methods, essential for guaranteeing reliable results, it is based on standardized protocols and comparison with reference criteria established by organizations such as RICOS and the SFBC. This approach ensures accurate analyses and clinically relevant interpretations, for the benefit of patients and healthcare professionals alike.

In this work, we present the results of a protocol for verifying the analytical performance of LDH assay method using an Abbot kit on the Architect ci8200 automated system in the biochemistry laboratory of the Mohammed VI University Hospital of Oujda.

1.1. Principle of the assay method

Lactate dehydrogenase catalyzes the conversion of lactate to pyruvate with the mediation of NAD+ as a hydrogen acceptor. In an aerobic environment, it catalyzes the conversion of lactate into pyruvate, which enters gluconeogenesis. In anaerobic conditions, it participates in glycolysis, hydrolyzing glucose to lactate [3].

The method is based on the spectrophotometric measurement of the formation (or disappearance) of NADH, a coenzyme that absorbs light at 340 nm. The increase or decrease in absorbance is proportional to the enzymatic activity of the LDH present in the sample. This method uses The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) recommended forward reaction Lactate to pyruvate [4,5].

2. Materials and Methods

This prospective study was carried out in the biochemistry laboratory of Mohammed VI University Hospital over a 30 days period. The study was divided into two distinct phases.

In the first phase, reproducibility was assessed by performing daily control measurements at three levels: low, medium, and high over 30 days to evaluate consistency. In the second phase, serum samples with evenly distributed lactate dehydrogenase levels across the measurement range were collected. These samples were categorized into three groups based on LDH concentrations: low, medium, and high. For each sample, 30 replicates were analyzed to determine repeatability.

The data processing was facilitated by the BYG middleware, which connects the Architect ci8200 platform to the iLab result validation software. The coefficient of variation (CV) values obtained were then compared to standards set by recognized professional organizations (FSCB and RICOS).

3. Results

3.1. Reproducibility results

In the reproducibility test, the same sample is analyzed under varying conditions to evaluate the influence of factors such as operators, time, reagent batches, and calibrations on the results. The variability of these results is quantified using the Coefficient of Variation (CV), which serves as a key indicator of consistency and reliability.

The Coefficient of Variation (CV) values for the low, medium, and high levels were determined as CV1 = 3.06%, CV2 = 2.50%, and CV3 = 1.77%, respectively. These findings are presented graphically in the Levey-Jennings charts (Fig. 1, Fig. 2, Fig. 3).

The analysis concludes that the CV values for reproducibility are acceptable, as they remain below the permissible limits. Additionally, the standards defined by FSBC (a quality control system) and RICOS (an international quality control network), including their respective expansion factors, were considered. A comparison of the obtained CV values with these standards (Table 1) confirms their compliance with the established thresholds.

Table 1 Reproducibility results of lactate dehydrogenase assay by level with comparison to FSBC and RICOS data (with expansion coefficient k = 1.211)

Level of IQC	Number of values	Mean (U/l)	Standard Deviation	Coefficient of Variation CV (%)	Reference CV: FSBC 1999 (%)	Reference CV: RICOS (%)
Low	30	115.07	3.325	3.06	6.00	4.30
Medium	30	213.77	5.335	2.50	6.00	4.30
High	30	430.33	7.608	1.77	5.0	4.30

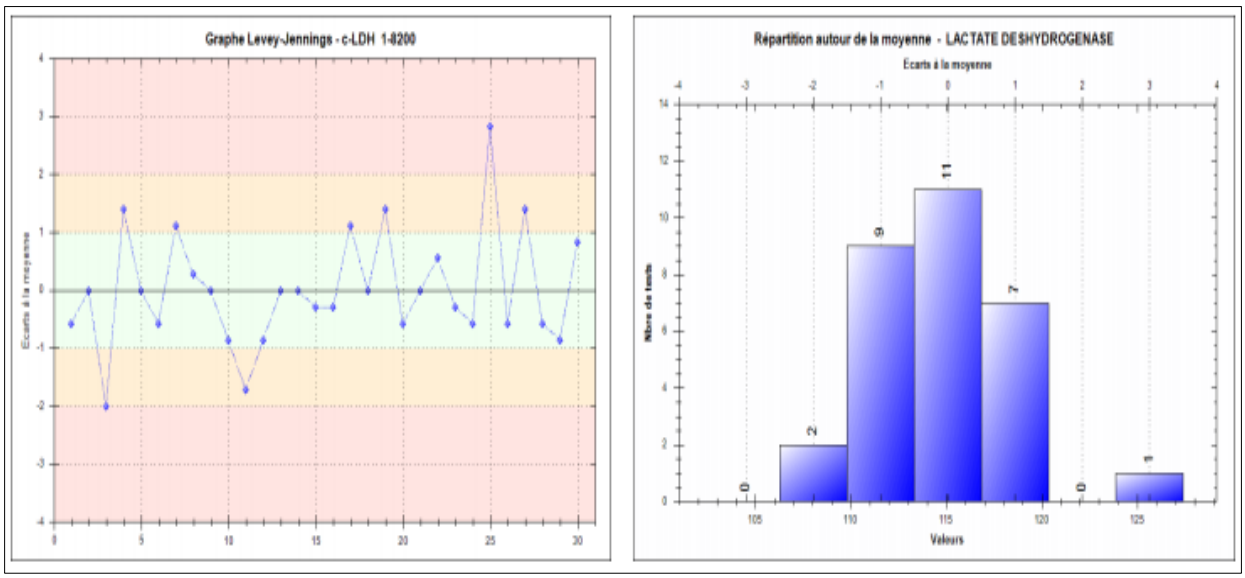

Figure 1 Low Level of Reproducibility: Levey Jennings graph and the distribution around the mean - LDH

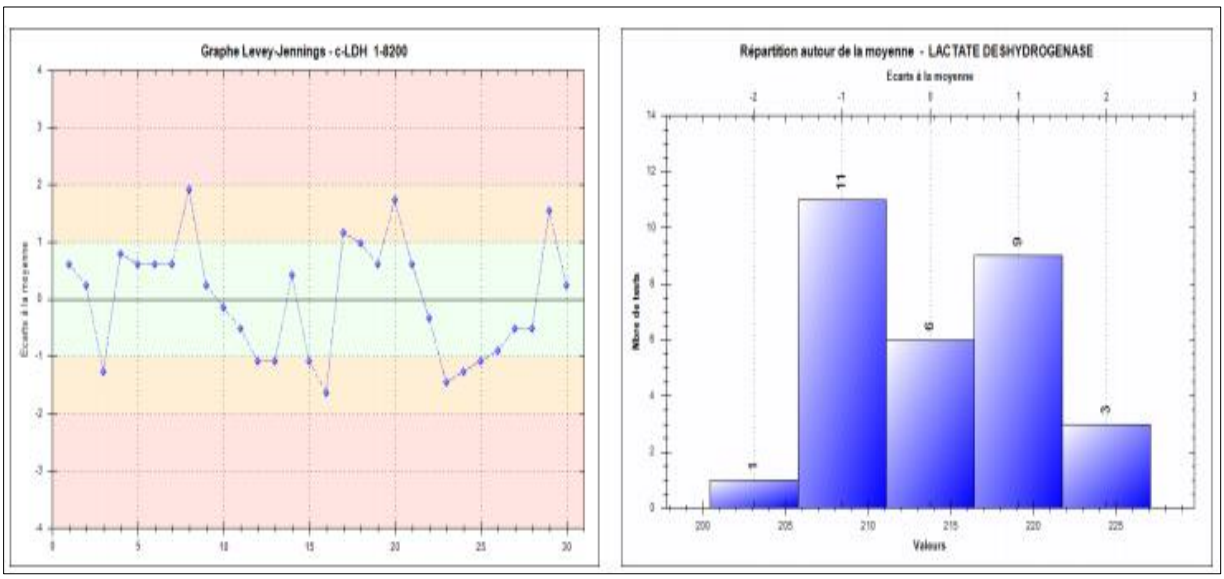

Figure 2 Medium Level of Reproducibility: Levey Jennings graph and the distribution around the mean – LDH

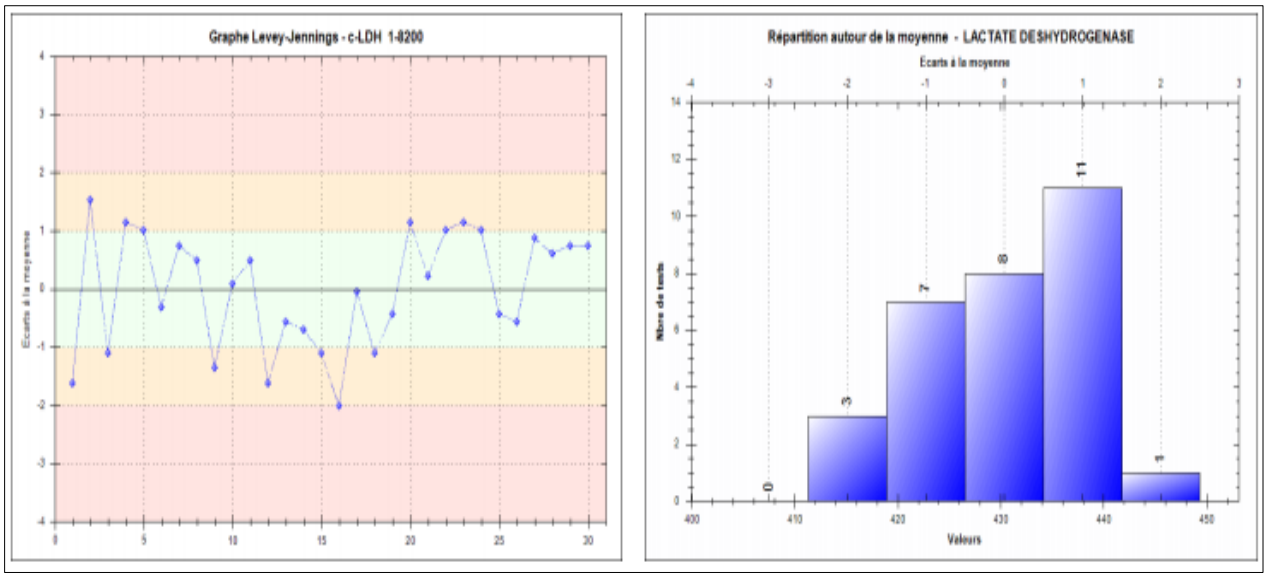

Figure 3 High Level of Reproducibility: Levey Jennings graph and the distribution around the mean – LDH

3.2. Repeatability results

The repeatability test evaluates the performance and functionality of the system by analyzing the same sample under optimal conditions. The variability of results is measured using the Coefficient of Variation (CV).

For the low, medium, and high levels, the CV values were as follows: CV1 = 1.34%, CV2 = 0.71%, and CV3 = 0.60%. These results are displayed on the Levey-Jennings graphs (Fig. 4, Fig. 5, Fig. 6).

The conclusion for each level indicates that the CV values for repeatability are acceptable, as they remain below the tolerated threshold. As with the reproducibility results, the FSBC and RICOS limits, along with their expansion factors, are referenced. A comparison of the CV values with these limits (Table 2) confirms that the results meet the required standards.

Table 2 Repeatability results of lactate dehydrogenase assay by level with comparison to FSBC and RICOS data (with expansion coefficient k = 1.211)

Level of IQC	Number of values	Mean (U/l)	Standard Deviation	Coefficient of Variation CV (%)	Reference CV: FSBC 1999 (%)	Reference CV: RICOS (%)
Low	30	117.13	1.570	1.34	4.50	3.23
Medium	30	212.70	1.512	0.71	4.50	3.23
High	30	432.63	2.606	0.60	3.75	3.23

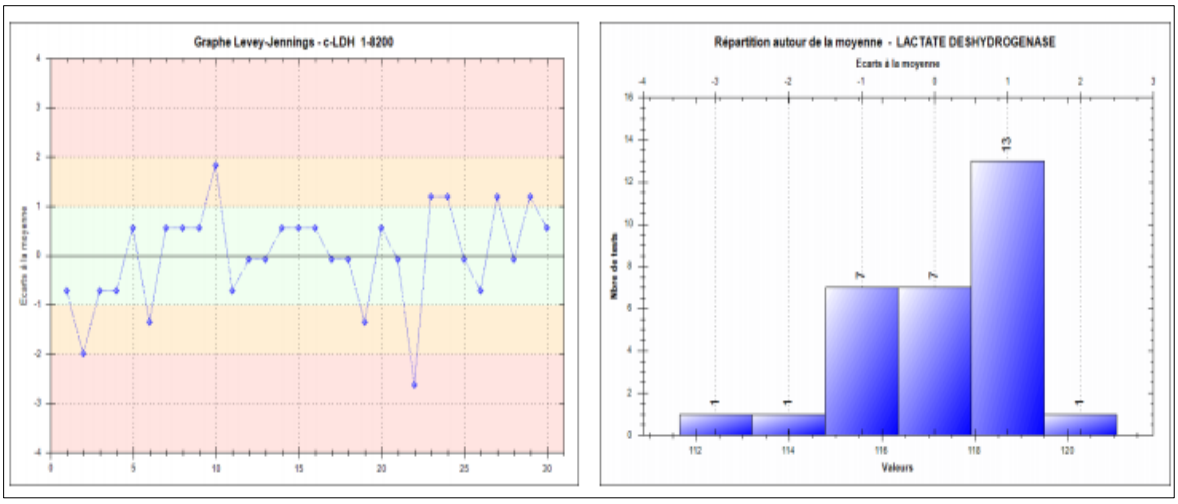

Figure 4 Low Level of Repeatability: Levey Jennings graph and the distribution around the mean – LDH

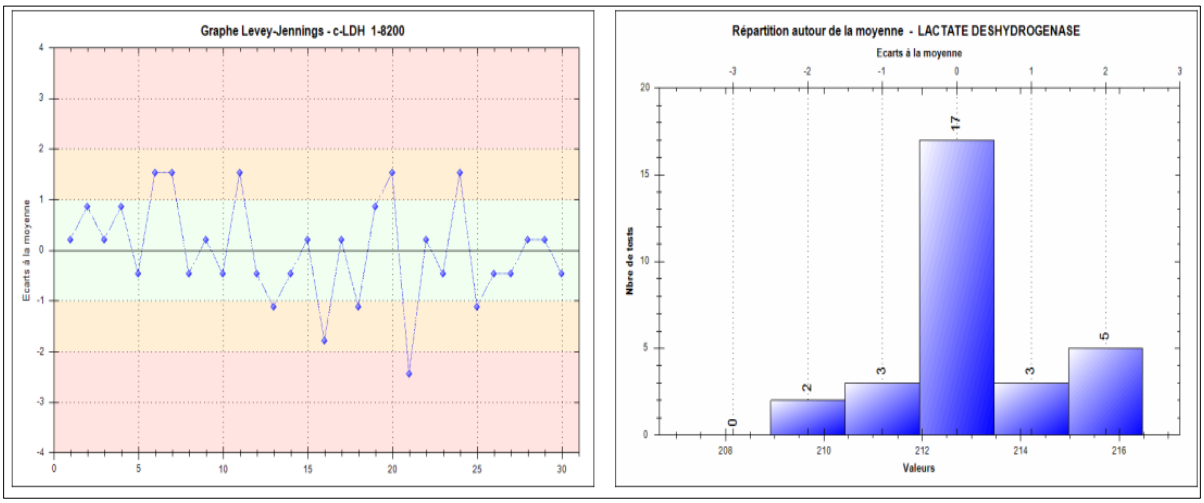

Figure 5 Medium Level of Repeatability: Levey Jennings graph and the distribution around the mean – LDH

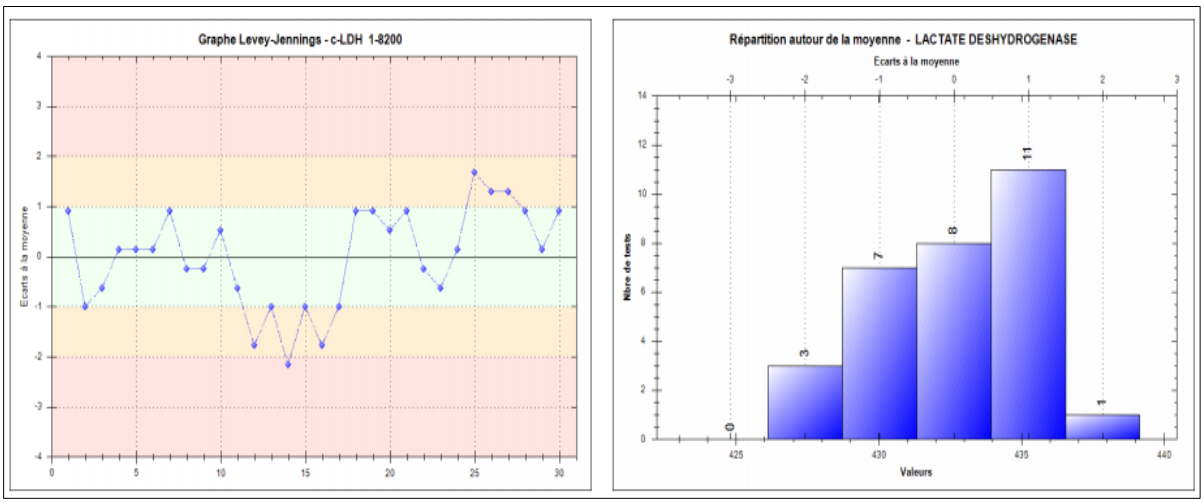

Figure 6 High Level of Repeatability: Levey Jennings graph and the distribution around the mean – LDH

4. Discussion

Lactate dehydrogenase (LDH) is an enzyme ubiquitously present in nearly all body tissues. Elevated blood LDH levels can be observed in various pathological conditions, including liver disease, anemia, myocardial infarction, bone fractures, muscle trauma, cancers, and infections such as encephalitis, meningitis, and HIV. As a non-specific marker of tissue turnover, LDH levels can increase in many cancers, either through a general rise or by an elevation of specific isoenzymes. However, its non-specific nature limits its utility in identifying a particular type of cancer, making it a secondary tumor marker rather than a definitive diagnostic tool. The clinical utility of LDH is further limited by the lack of routine isoenzyme measurement in laboratories, resulting in incomplete diagnostic information. Consequently, alternative assays, such as creatine kinase (CK) for muscle damage, alanine aminotransferase (ALT) for liver conditions, or troponin for cardiac diseases, are often required to provide more specific diagnostic insights [6].

Moreover, LDH activity can be significantly affected by hemolysis of blood samples, as red blood cells (RBCs) contain their own LDH isoenzyme. Hemolysis can lead to artifactual increases in LDH levels, resulting in falsely elevated results. Additionally, any cellular necrosis can increase serum LDH concentrations, and its ubiquitous distribution across tissues imposes a significant limitation on its broader clinical application as a specific biomarker [7].

Mastering the methods used by biologists in the laboratory is an ongoing priority, as their verification and validation are both regulatory obligations (as outlined in the Moroccan Guide for Good Laboratory Practices) and normative requirements (ISO 15189:2012 standard) [8]. By setting predefined analytical objectives, this process ensures the production of accurate and reliable results.

The reproducibility of the lactate dehydrogenase assay was evaluated to ensure consistency under varying conditions. The study demonstrated robust reliability across three concentration levels: low, medium, and high. For each level, 30 measurements were analyzed, producing mean values of m_1 = 115.07 U/L, m_2 = 213.77 U/L, and m_3 = 430.33 U/L, with corresponding coefficients of variation (CV) of CV_1 = 3.06%, CV_2 = 2.50%, and CV_3 = 1.77%. These low CV values reflect the assay's ability to generate consistent results, even when external variables are introduced. This reproducibility is essential for medical diagnostics, where precision is critical for reliable clinical outcomes. Moreover, the compliance of these CV values with FSBC and RICOS standards, including their respective expansion factors, highlights the assay's adherence to recognized quality benchmarks, further validating its reliability for diagnostic applications.

The repeatability test focuses on evaluating the precision of the assay under controlled conditions. This assessment is crucial as it determines the method's ability to consistently produce reliable results when the same sample is analyzed multiple times. In our evaluation of repeatability across three levels: low, medium, and high 30 measurements were analyzed for each level. The results yielded exceptionally low coefficients of variation (CV): CV_1 = 1.34%, CV_2 = 0.71%, and CV_3 = 0.60%. These minimal CV values highlight the assay's high precision, demonstrating minimal variability and ensuring dependable performance.

The stability and reliability of assay results under controlled conditions are fundamental, particularly in clinical settings where small variations can have a significant impact on patient management and outcomes.

In our laboratory at the Mohammed VI University Hospital in Oujda, we have introduced a comprehensive quality policy that includes a strict method control protocol. This is essential to establish a credible route to accreditation for the analyses carried out. By positioning itself as a flagship institution in eastern Morocco, our laboratory not only ensures the care of referred and hospitalised patients, but also plays an important role in elucidating the overall health of the regional population through various scientific approaches [9,10].

5. Conclusion

Performance in terms of reproducibility and repeatability is remarkable, complying with FSBC and RICOS standards, including their respective expansion coefficients. These results clearly demonstrate the robustness and credibility of the serum lactate dehydrogenase assay. This research highlights the strict quality control procedures within medical laboratories, strengthening the crucial body of knowledge required for accurate serum Lactate dehydrogenase assays and, consequently, increasing the clinical value of this test.

Medical biology plays a crucial role in the healthcare system, transforming the approach to analytical techniques from one of simple random selection to a systematic approach governed by specific standards based on the principles of the method and its validation or control procedures. The central laboratory of the Mohammed VI University Hospital in

Oujda has shown a strong commitment to accreditation, considering method validation and verification to be crucial phases in this initiative.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflict of interest.

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