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Clinical Utility of the XF-1600 Flow Cytometer for MRD Assessment in Multiple Myeloma

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ABSTRACT

Abbreviations: MM: Multiple Myeloma; IMWG: International Multiple Myeloma Working Group; MDE: Myeloma Defining Events; PFS: Progression Free Survival; OS: Overall Survival; MFC: Multiparametric Flow Cytometry; NGS: Next Generation Sequencing; NGF: Next-Generation Flow Cytometry; CR: Complete Response

Introduction

Background

Multiple myeloma (MM) is a plasma cell neoplasm with an incidence of 1 – 1.8% of all cancers, and the second most common hematological cancer. Despite the significant improvements in treatment and management, this neoplasm poses a significant challenge to healthcare providers and patients alike, since 85 – 90% of patients eventually relapse. This disease arises from the uncontrolled growth and accumulation of abnormal plasma cells in the bone marrow, leading to the dissemination and accumulation of these cells in the blood, bones, kidney and other tissues and organs [1]. These abnormal plasma cells produce a monoclonal immunoglobulin, an antibody that is identical in structure and function. This monoclonal immunoglobulin can lead to a variety of symptoms, including hypercalcemia, renal injury and dysfunction, anemia, and bone pain and lesions, also known as CRAB symptoms [2]. According to the revised International Multiple Myeloma Working Group (IMWG) criteria, diagnosis of multiple myeloma requires the presence of more than 10% of clonal plasma cells in bone marrow and the presence of one or more myeloma defining events (MDE) which include CRAB features, >60% of clonal plasma cells, serum-free light chain ratio >100, and more than one focal lesion detected by MRI [3]. Additionally, patients are tested for the presence of M protein by serum protein electrophoresis (SPEP), serum immunofixation (SIFE), and the serum FLC assay. Molecular studies including fluorescence in situ hybridization (FISH) analysis and gene expression profiling (GEP) are made at diagnosis to identify multiple myeloma cytogenetic alterations and classify patients according to the Revised International Staging System for Multiple Myeloma [4,5].

Measurable residual disease (MRD) assessment has emerged as a powerful strategy that has revolutionized the management of multiple myeloma. MRD is a sensitive prognostic assessment in multiple myeloma monitoring to determine depth of response, supported by many studies demonstrating that MRD negativity after treatment is associated with a better progression free survival (PFS) and overall survival (OS) in multiple myeloma patients [6-9]. Moreover, MRD detection has been instrumental in evaluating the efficacy of novel therapeutic agents and in identifying patients who may benefit from early intervention or alternate treatment strategies. The ability to detect MRD at low levels has opened up new avenues for personalized medicine in multiple myeloma [10-13]. The detection of MRD in multiple myeloma requires highly sensitive and specific technologies. Traditional methods, such as light chain restriction analysis and immunohistochemistry, have been largely replaced by multiparametric flow cytometry (MFC) and next generation sequencing (NGS). MFC is a sophisticated technique that simultaneously analyzes multiple cellular markers allowing for the precise identification and quantification of abnormal plasma cells. The sensitivity of MFC has been further enhanced through the development of next-generation flow cytometry (NGF), which employs advanced microfluidics and data analysis algorithms to detect even smaller numbers of myeloma cells. NGF has the potential to transform MRD assessment, enabling the detection of residual disease at the earliest stages and guiding treatment decisions with greater precision. The IMWG MRD criteria indicates that MRD assessment should be performed when a patient achieves complete response (CR) after treatment reaching a minimum sensitivity of 1 abnormal plasma cell in 100,000 normal cells (10^{-5}), by next-generation sequencing or next-generation flow cytometry [14].

Flow Cytometry in Multiple Myeloma Management

Flow cytometry has emerged as a powerful tool in the diagnosis, classification, and disease monitoring in MM. This key technique allows for the precise identification and characterization of myeloma cells in bone marrow samples, providing valuable insights into disease progression and treatment efficacy. One of the most significant improvements in the response criteria in multiple myeloma is the introduction of MRD analysis in the bone marrow using flow cytometry. MRD detection has assumed primary importance in post-treatment monitoring studies. Numerous studies have consistently demonstrated a positive correlation between MRD negativity assessed by flow cytometry and superior patient outcomes. Specifically, individuals with undetectable MRD following treatment after diagnosis or relapse exhibit prolonged progression-free survival (PFS) and overall survival (OS), signifying a significantly reduced risk of relapse and death from MM. Multiple myeloma monitoring through MRD assessment by next-generation flow cytometry has been found to be a surrogate endpoint in patients receiving first-line treatment [8], therefore, MRD may be used as an endpoint to accelerate drug development.

Role of Flow Cytometry in Multiple Myeloma Monitoring and Prognosis

By periodically assessing the bone marrow for MRD presence, physicians can effectively monitor the response to therapy and identify early signs of disease recurrence. The assessment of the MRD status by the application of standardized flow cytometry panels specifically designed for MRD analysis in multiple myeloma plays a pivotal role in patient monitoring and relapse prediction. The MRD-negative responses after induction therapy have strong implications in patient PFS and OS. Moreover, attainment of a negative MRD by flow cytometry after a relapse, also benefits patients by experiencing better outcomes. This also holds immense importance in clinical trials evaluating novel MM therapies, accelerating the development of novel therapies and the advancement of MM care [7-9,11,12].

Revolutionizing Clinical Flow Cytometry: An In-Depth Overview of the XF-1600™ Flow Cytometer

The XF-1600™ flow cytometer stands as a testament to innovation in clinical laboratory analysis, offering a robust, high-performance platform for reliable and efficient data collection. Developed by Sysmex, a global leader in healthcare solutions, the XF-1600 seamlessly integrates advanced optical technology with a proven fluidics design, ensuring exceptional sensitivity and precision.

Core Components and Operating Principles: The XF-1600 core comprises a multi-laser optical layout, comprising three lasers: blue, red, and violet. A sophisticated fluidics system ensures the precise and consistent delivery of cells to the interrogation point. This system, based on Sysmex's proven XN-Series hematology analyzers, boasts exceptional stability and reliability, even at high sample acquisition rates. This unwavering performance is crucial for accurate data analysis and reliable results.

Enhanced Sensitivity and Multiplexing Capabilities: The XF-1600's multi-laser configuration enables up to 10-color detection, plus forward scatter (FSC) and side scatter (SSC) signals, allowing for the simultaneous analysis of multiple cellular markers. This multiplexing capability provides a comprehensive view of cell populations, facilitating the identification and quantification of various cell types and their subtypes. The enhanced sensitivity of the XF-1600 enables the detection of even the smallest and most rare cell populations, making it ideal for applications such as measurable residual disease analysis in hematological malignancies. This capability is crucial for monitoring treatment efficacy and predicting disease progression.

User-Friendly Interface and Automated Workflows: The XF-1600 employs a user-friendly graphical interface that simplifies the operation and interpretation of data. The intuitive design allows even novice users to quickly learn and navigate the system, minimizing the learning curve and optimizing workflow efficiency.

Sample Preparation and Washing Integration: Together with the sample preparation system PS-10 and Rotolavit II-S, the XF-1600 offers an intelligent automation solution that helps laboratories simplify their processes and increase workflow efficiency with confi-

dence in their results. The complete system adds automation where it matters. Especially for busy clinical flow cytometry laboratories, this can offer an added level of standardization, reduction of human handling errors and ensure a traceability of samples, reagents, and processing steps through the entire process.

CE-IVD Certification for Quality Assurance: The XF-1600 carries the CE-IVD mark, indicating its compliance with the European Union's regulatory requirements for in vitro diagnostic (IVD) devices. This certification ensures the instrument's performance meets the highest standards of accuracy, reliability, and reproducibility, providing clinicians with confidence in their data-driven decision-making.

Applications and Impact in MRD Assessment: The XF-1600 flow cytometer stands as a transformative force in clinical laboratory analysis, providing researchers and clinicians with a robust, high-performance platform for advanced cell analysis. Its enhanced sensitivity, multiplexing capabilities, and user-friendly interface have revolutionized the field of flow cytometry, paving the way for more accurate diagnoses, personalized treatment approaches, and improved patient outcomes. As the field of medicine continues to evolve, the XF-1600 is poised to play an even more pivotal role in shaping the future of clinical diagnostics and patient care. Here we show evidence of the clinical utility of the XF-1600 as a valuable tool for MRD assessment in multiple myeloma patients.

Aim of the Study

We present a standardized and a reproducible panel for MRD detection in XF-1600 and compare the MRD assessment in n = 31 bone marrow specimens from multiple myeloma patients in XF-1600™ versus DxFlex and Navios EX Flow Cytometers (Beckman Coulter). MRD results obtained in XF-1600 strongly correlate with those ones obtained in DxFlex and Navios EX Flow Cytometers, providing compelling evidence that the XF-1600 flow cytometer is a reliable and accurate instrument for measuring MRD in MM.

Methods

Flow Cytometers

Three CE-IVD Flow Cytometers were used in this study: The XF-1600™, the Navios EX and the DxFlex™. All instruments were equipped with three lasers (blue, red, and violet) enabling up to 10-color and 13-color detection, respectively, plus forward scatter (FSC) and side scatter (SSC) signals.

Reagents

Daily QC beads were used to perform quality control and monitoring XF-1600 instrument performance over time. The CyFlow™ CompSet (Sysmex) beads were used for optimal gain setup on XF-1600 Flow Cytometer. Phosphate Buffered Saline (PBS) with 0.2% bovine serum albumin (BSA) was used for sample wash and final dilution. CyLyse™ FX Lysing solution was used to lyse and fix peripheral blood and bone marrow samples. CyFlow™ CD8 and CD19 monoclonal antibodies labelled with FITC, PE, PE-DyLight 594™ (PE-DL), PerCP-Cy5.5 (PCP5.5), PE-Cy7 (PC7), APC, Alexa Fluor 700 (AF700), APC-Cy7 (AC7), Pacific Blue™ (PB), Pacific Orange™ (PO), were used for optimal gain setup and single control preparation. CyFlow™ PE-CD27, PE-DL-CD56, PCP5.5-CD138, PC7-CD117, APC-CD19, AF700-CD81, AC7-CD38, and PO-CD45 were used for MRD assessment in multiple myeloma samples.

XF-1600™ Instrument Setup

The CyFlow™ CompSet (Sysmex) beads were used for optimal gain setup on XF-1600 Flow Cytometer by preparing single control tubes with 1 drop of Blank CompSet and 1 drop of Positive CompSet beads incubated for 20 minutes in the dark with CyFlow™ CD8 and CD19 monoclonal antibodies labelled with FITC, PE, PE-DyLight 594™ (PE-DL), PerCP-Cy5.5 (PCP5.5), PE-Cy7 (PC7), APC, Alexa Fluor 700 (AF700), APC-Cy7 (AC7), Pacific Blue™ (PB), Pacific Orange™ (PO) in ten flow cytometry tubes. PBS 0.2% BSA was used for washing and prepare the final sample dilution. Each single tube was acquired on the XF-1600 Flow Cytometer with the corresponding detector channel set up with gains ranging from 500 to 1000. After acquisition, the stain index (SI) was calculated for each gain. The optimal gain was the one showing the highest SI, with a negative population mean fluorescence intensity less than 50.

XF-1600™ Protocol Setup for MRD Detection in MM

8-Color Single Control Preparation: To prepare single controls for each fluorochrome, we followed the manufacturer's instructions. Briefly, we incubated the CyFlow™ CD8 and CD19 monoclonal antibodies labelled with PE, PE-DL, PCP5.5, PC7, APC, AF700, AC7, and PO with 50µl peripheral blood from a healthy donor for 20 minutes at room temperature. After incubation, 2 ml of CyLyse™ FX Lysing solution were added and samples were incubated for 10 minutes. Samples were then washed and diluted with PBS 0.2% BSA and acquired on XF-1600 using the gain instrument setup previously calculated.

Color Compensation Matrix Calculation: Compensation was calculated by using the XF-1600 compensation wizard and the data obtained with the single control acquisition for PE, PE-DL, PCP5.5, PC7, APC, AF700, AC7, and PO.

Validation Process for the Protocol for MRD Detection in MM in the XF-1600™ Flow Cytometer

The XF-1600™ flow cytometer has undergone a rigorous validation process to ensure its accuracy, precision, and reliability for the intended use of measuring the simultaneous expression of eight antigens: PE-CD27, PE-DL-CD56, PCP5.5-CD138, PC7-CD117, APC-CD19, AF700-CD81, AC7-CD38, and PO-CD45. This validation process was carried out by qualified personnel specifically trained for this purpose.

Key Components of the Validation Process: The validation process for the XF-1600™ flow cytometer included the following key components:

1. Establishing Specific Intended Use: The specific intended use of the XF- 1600 flow cytometer for measuring the simultaneous expression of eight antigens was clearly defined.
2. Developing Validation Protocol: A comprehensive validation protocol was developed that outlined the specific tests and procedures to be performed.
3. Acquiring Standardized Reference Materials: Standardized reference materials were obtained for each of the eight antigens to serve as the gold standard for comparison.
4. Performing Accuracy Tests: Accuracy tests were conducted to assess the ability of the XF-1600 flow cytometer to measure the expression of each antigen with the correct value.
5. Precision Tests: Precision tests were performed to determine the reproducibility of the XF-1600 flow cytometer's measurements. These tests involved analyzing multiple samples of known antigen expression levels.
6. Linearity Tests: Linearity tests were conducted to evaluate the range over which the XF-1600 flow cytometer provides accurate and precise measurements.
7. Dynamic Range Tests: Dynamic range tests were performed to assess the maximum range of antigen expression that the XF-1600 flow cytometer can accurately measure.
8. Data Analysis and Reporting: All validation data was carefully analyzed and documented in a comprehensive report.

Results of the Validation Process: The validation process demonstrated that the XF-1600 flow cytometer meets the specified requirements for accuracy, precision, linearity, and dynamic range for the intended use of measuring the simultaneous expression of eight antigens: PE-CD27, PE-DL-CD56, PCP5.5-CD138, PC7-CD117, APC-CD19, AF700-CD81, AC7-CD38, and PO-CD45. The XF-1600 flow cytometer can be confidently used for this purpose in clinical and research settings.

Representative Samples: To ensure that the XF-1600 flow cytometer can produce accurate results for a variety of samples, the samples used for validation were representative of the types of specimens that are used in clinical practice. This included bone marrow aspirates, peripheral blood smears, and bone marrow biopsies.

Comparison to the DxFLEX™ and Navios EX: The XF-1600 sample files were compared to the corresponding sample files obtained in DxFLEX™ and Navios EX (Beckman Coulter), two widely used flow cytometers in clinical settings, and by using the same analysis strategy in the VenturiOne® software. These comparisons demonstrated that the XF-1600 provides comparable results to the DxFLEX and Navios EX for the simultaneous measurement of eight antigens.

Development of the 8 Color Tube: The 8-color tube used in this validation study was developed by consensus among all clinical hematology diagnostic laboratories in hospitals affiliated with the Catalan Institute of Health (Catalonia, Spain). This collaborative effort ensured that the tube represents a standardized and clinically relevant panel for the assessment of multiple myeloma.

Overall Validation Results: The comprehensive validation process demonstrated that the XF-1600 is a reliable and accurate instrument for measuring the simultaneous expression of eight antigens: PE-CD27, PE-DL-CD56, PCP5.5-CD138, PC7-CD117, APC-CD19, AF700-CD81, AC7-CD38, and PO-CD45. This validation provides strong evidence for the clinical utility of the XF-1600 in the study and diagnosis of multiple myeloma.

MRD in MM assessment on DxFLEX™, Navios EX and XF-1600™ Flow Cytometers: Acquisition, Analysis and Comparative Study

To validate the performance of the XF-1600 flow cytometer for the simultaneous measurement of eight antigens in multiple myeloma (MM), a comparative study was conducted using 31 MRD MM samples obtained from the Hematology Laboratory of the Germans Trias i Pujol Universitary Hospital (Catalonia, Spain). Samples were processed in parallel in the DxFLEX or Navios from the Hematology Laboratory and in the XF-1600 from the Functional Cytomics Laboratory of the Germans Trias I Pujol Research Institute (Catalonia, Spain). The samples were processed by different operators within the first 24h of extraction and with a maximum delay of 5 hours between parallel analysis.

Sample Preparation:

- Step 1: Combine 100 µL of bone marrow specimen with 10 µL CyFlow™ PE- CD27, PE-DL-CD56, PCP5.5-CD138, PC7-CD117, APC-CD19, AF700-CD81, AC7-CD38, and PO in a flow cytometry tube. Vortex the tube gently to mix the contents thoroughly.
- Step 2: Incubate for 20 minutes at room temperature and light protected
- Step 3: Add 1 mL CyLyse FX 1x and vortex
- Step 4: Incubate for 10 minutes at room temperature and light protected to allow the CyLyse FX to effectively lyse the erythrocytes.
- Step 5: Wash with 1 mL PBS BSA 0.2% for 5 minutes at 500g to remove unbound monoclonal antibodies and debris. Discard the supernatant and resuspend the pellet in 1 mL of PBS BSA 0.2% for analysis.
- Step 6: Acquire the sample on the flow cytometer.

Sample Acquisition: Up to 10^6 total cells were acquired for each sample whenever possible. This was done to ensure that a sufficient number of cells were analyzed for a reliable assessment of antigen expression levels.

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Flow Cytometry Data Analysis: The flow cytometry data acquired on the three mentioned cytometers were analyzed using VenturiOne® software to determine the frequency of abnormal plasma cells based on the expression levels of the eight antigens: CD19, CD27, CD38, CD45, CD56, CD81, CD117, and CD138. The gating strategy is presented in (Figure 1).

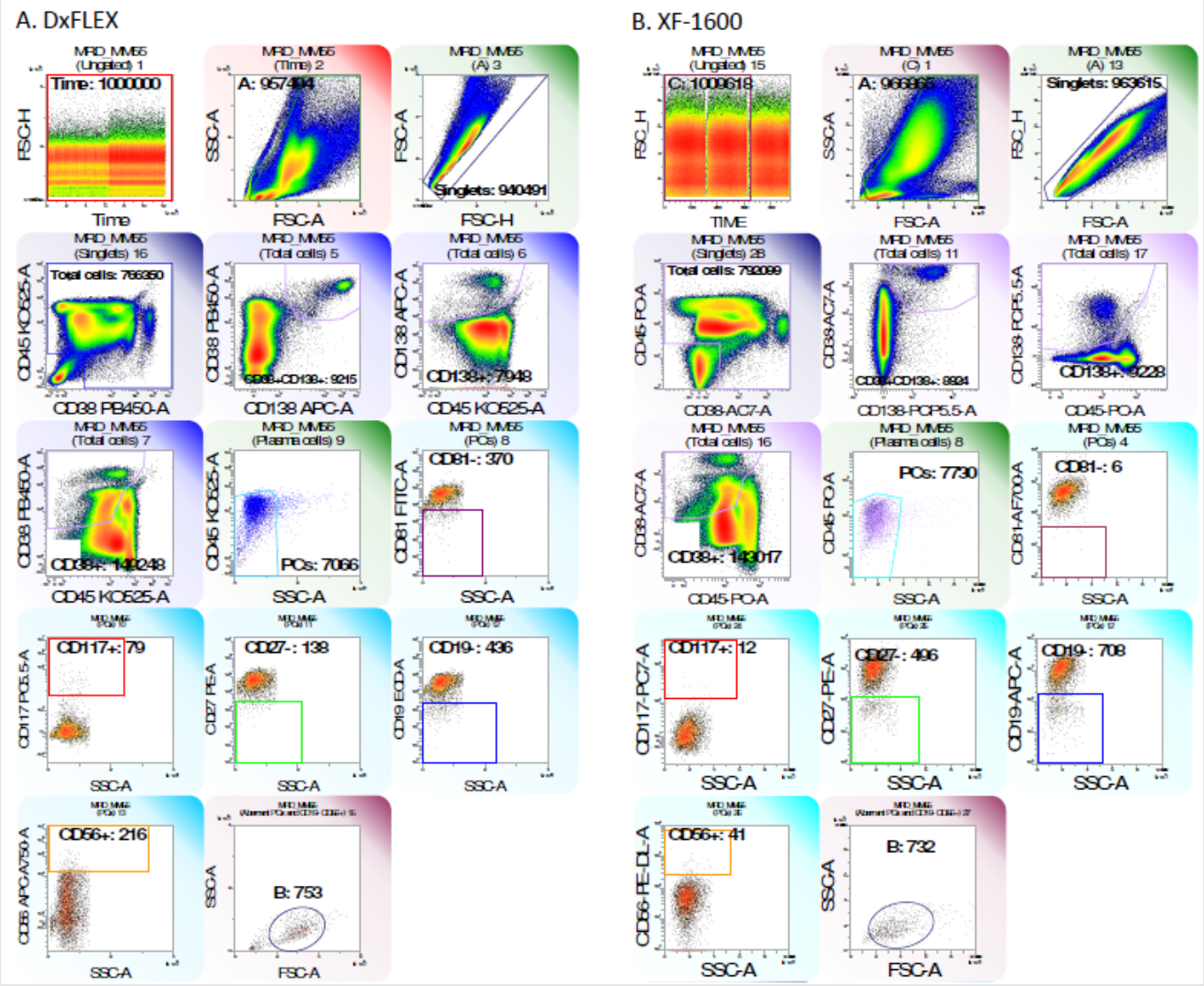

Figure 1: Representative analysis of MRD MM using the VenturiOne® software.

Validation and Comparative Analysis: The correlation between % of abnormal plasma cells measured on the Beckman DxFLEX/Navios EX and the XF-1600 for each bone marrow sample was assessed using Pearson's correlation coefficient, Bland-Altman analysis and linear correlation. Pearson's coefficient provides a measure of the strength and direction of the linear relationship between two variables. The Bland-Altman analysis provides the agreement between the two sets of measurements and identifies any systematic bias or offset. Graphs and statistics were obtained in Prism v.9 software (GraphPad).

Results

Validation Study

The validation study demonstrated that the XF-1600 provides highly correlated results to the DxFLEX/Navios EX in MM samples. The Pearson's correlation coefficient was statistically significant and ranged from 0.9973 to 0.9994 (n = 31). This indicates that the XF-1600 can reliably measure the expression of these antigens in MRD MM samples. The validation study provides strong evidence that the XF-1600 is a reliable and accurate instrument for the assessment of the MRD in MM using an 8-color panel. This validation provides valuable information for clinicians and researchers who are using flow cytometry to assess the MRD status of MM patients.

Comparative Study

In this study, the Bland-Altman analysis of n = 31 MM patients found that the average difference between the XF-1600 and DxFLEX/Navios EX MRD measurements was -0.1577. This means that, on average, the DxFLEX/Navios EX tended to measure MRD levels slightly higher than the XF-1600. However, the 95% confidence interval for this difference ranged from -1.045 to 0.7295, which means that the true difference between the two instruments could be anywhere between this range (Figure 2), indicating that the two instruments are generally in agreement, with only minor deviations. In addition, the Pearson correlation coefficient obtained was 0.9987 ("95% CI", 0.9973 to 0.9994; p-value of <0.0001), indicating that the MRD measurements from the two instruments were highly and significantly correlated. Therefore, the two instruments were in agreement, with only minor deviations. The linear regression equation provides further evidence for the close correlation between MRD measurements obtained on the XF-1600 and DxFLEX/Navios. The equation y = 1.034x + 0.06752 indicates that there is a strong linear relationship between the two sets of measurements. This means that for every percentage point increase in MRD measured on the XF-1600, there is a corresponding 1.034 increase in MRD measured on the DxFLEX/Navios. The R-squared value of 0.9974 confirms the strength of this correlation, indicating that approximately 99.74% of the variability in MRD measurements on the two instruments can be explained by the linear relationship (Figure 3). The linear regression equation and the Bland-Altman analysis provide compelling evidence that the XF-1600 and DxFLEX/Navios are highly comparable instruments for MRD assessment in MM. The ability to accurately predict DxFLEX/Navios results from XF-1600 measurements suggests that the XF-1600 can be used as a substitute for the DxFLEX/Navios in clinical settings, without compromising the accuracy or reliability of MRD assessments.

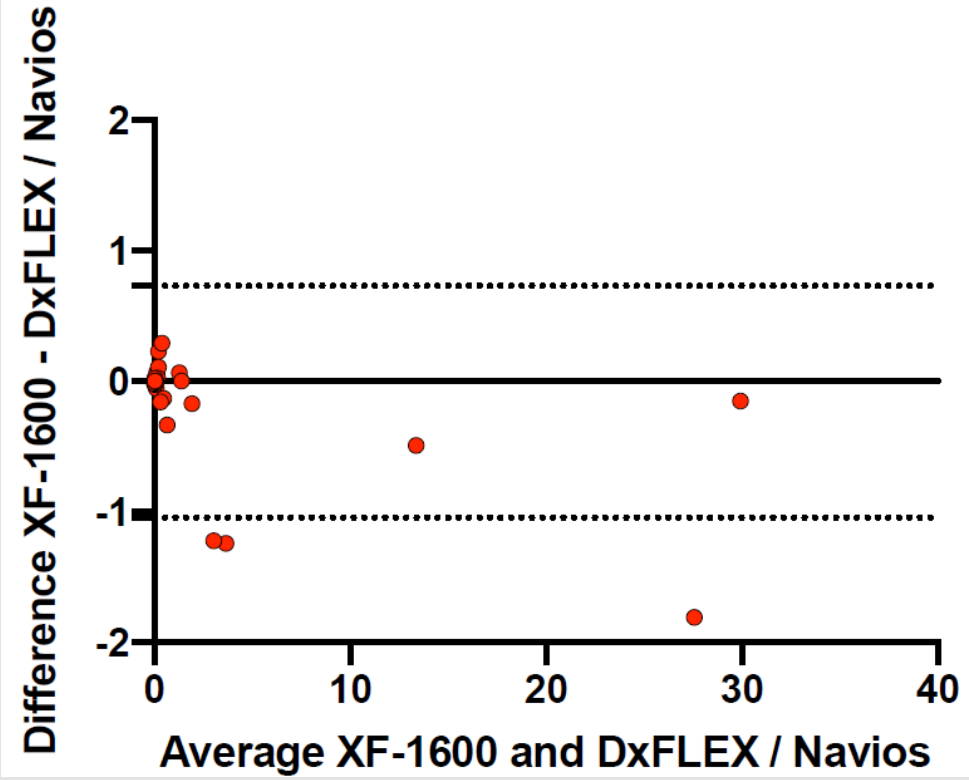

Figure 2: A Bland-Altman analysis (n = 31) found that the average difference between XF-1600 and DxFLEX/Navios results was -0.1577, with a 95% confidence interval of -1.045 to 0.7295, suggesting that there is no statistically significant difference between the measurements obtained on the two flow cytometers.

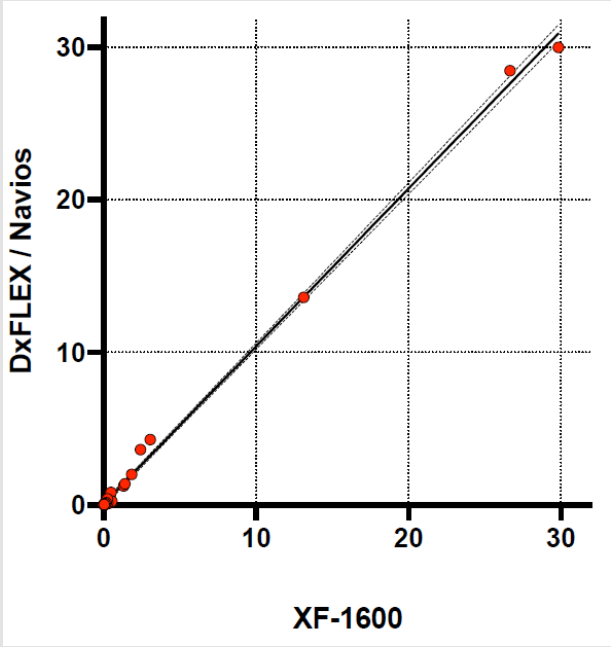

Figure 3: The linear regression equation y = 1.034x + 0.06752 supports this finding, as it accurately predicts the value of DxFLEX/Navios from the value of XF-1600 (R^2 = 0.9974) in a n = 31 patients. The results of this study demonstrate that the XF-1600 flow cytometer is a valuable tool for studying MM MRD in clinical diagnostic applications.

In the case of samples with MRD levels below 0.1% (n = 12), the average difference between the XF-1600 and DxFLEX/Navios EX MRD measurements was 0.001433, ranging from -0.02874 to 0.03161 (Figure 4). The Pearson correlation coefficient obtained was 0.8991 ("95% CI", 0.6720 to 0.9717; p-value <0.0001; R^2 = 0.8085). This slightly different concordance in MRD values is likely due to the increased contribution of small values of differences to the MRD measurement percentages, which can hinder the precise agreement among instruments.

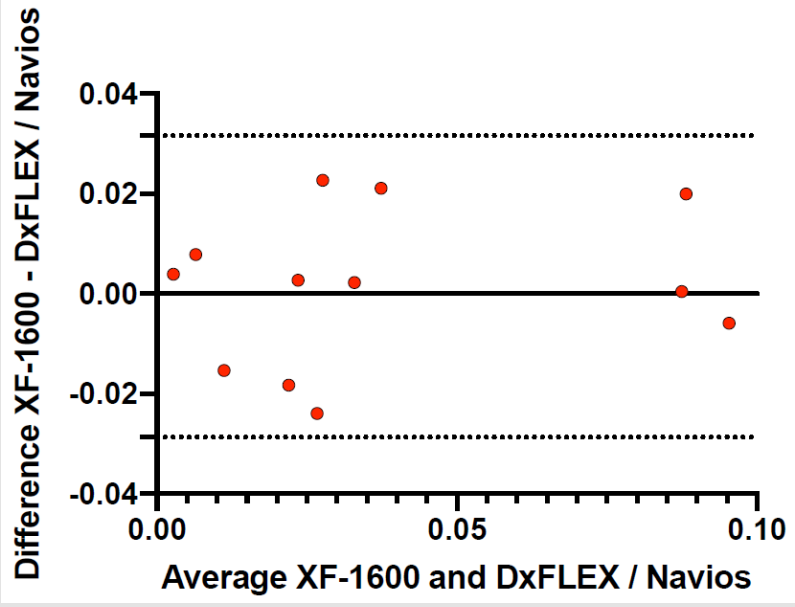

Figure 4: A Bland-Altman analysis of ≤0.1% MRD (n = 12) found that the average difference between XF-1600 and DxFLEX/Navios results was 0.001433, with a 95% confidence interval of -0.02874 to 0.03161, suggesting that there is no statistically significant difference between the measurements obtained on the two flow cytometers.

Despite this lower correlation, the linear regression equation y = 0.8321x + 0.005144 still provides a reasonable predictor of DxFLEX/Navios results from XF-1600 measurements (Figure 5). This indicates that the XF-1600 can still be used to assess MRD at lower levels, but clinicians should be aware that the accuracy of these measurements may be slightly less precise than at higher levels. However, the XF-1600's ability to provide an accurate estimate of MRD even at lower levels is still valuable for clinical practice, as it can help to identify and monitor MRD in patients who may be at risk of relapse. The findings of this study suggest that the XF-1600 can be used interchangeably with the DxFLEX/Navios for MRD assessment in MM. This means that clinicians can choose the instrument that is most convenient or accessible for their practice, without compromising the accuracy or reliability of their MRD measurements. The XF-1600 flow cytometer is a valuable tool for MRD assessment in MM. It is a reliable and accurate instrument that can provide highly correlated results with the DxFLEX/Navios. Furthermore, the XF-1600's ability to simultaneously measure eight antigens makes it a powerful tool for comprehensive MRD assessment, and its ease of use and flexibility make it well-suited for clinical practice.

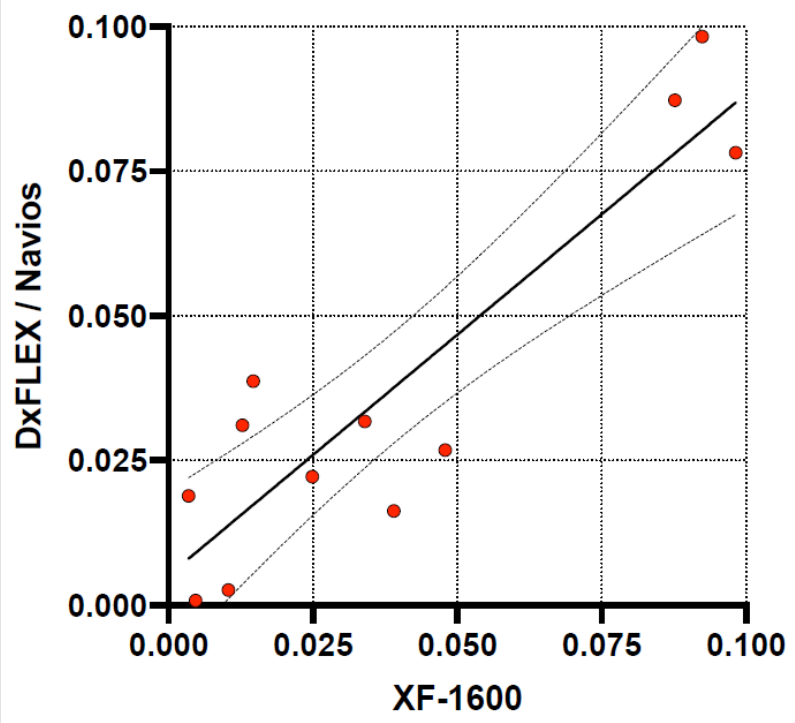

Figure 5: The linear regression equation y = 0.8321x + 0.005144 predicts the value of DxFLEX/Navios from the value of XF-1600 below ≤0.1% MRD (R^2 = 0.8085) in a n = 12 patients.

Conclusion

Clinical Utility of the XF-1600 Flow Cytometer for MRD Assessment in MM

The results of this study provide compelling evidence that the XF-1600 flow cytometer is a reliable and accurate instrument for measuring MRD in MM. The instrument's ability to simultaneously measure eight antigens, CD19, CD27, CD38, CD45, CD56, CD81, CD117, and CD138, is particularly valuable for comprehensive MRD assessment. The Pearson's correlation between the XF-1600 and DxFLEX/Navios EX was 0.8991 (95%CI, 0.6720 to 0.9717) and statistically significant (p<0.0001), indicating that the two instruments provide highly comparable results.

Impact of Sample Preparation and Acquisition Timing

The timing of sample preparation and acquisition can influence MRD measurements, particularly at low levels. That is why in this analysis all samples were analyzed within the first 24h of extraction. During the 24-hour delay, cell viability and antigen expression may potentially change, leading to subtle variations in the MRD readout. This is an inherent challenge in clinical MRD assessment, as patient samples may not be immediately available for analysis.

Strategies to Mitigate Potential Delay-Related Errors

To minimize the impact of sample preparation and acquisition timing on MRD measurements, several strategies can be employed:

1. Shortening the Delay Period: If possible, the delay between sample collection and analysis should be minimized. This can be achieved by optimizing laboratory workflow and ensuring that samples are promptly processed and analyzed.

2. Optimizing Sample Preservation: Implementing appropriate sample preservation techniques can help maintain cell viability and antigen expression during the delay period. For instance, using dimethyl sulfoxide (DMSO) to cryopreserve bone marrow samples can help preserve MRD information.

3. Utilizing Advanced Flow Cytometry Techniques: Employing advanced flow cytometry techniques, such as gating and compensation, can help compensate for potential variations in cell viability and antigen expression during the delay period.

4. Regular Calibration and Maintenance: Regular calibration and maintenance of the flow cytometer can ensure that it is functioning optimally and producing accurate results.

5. Data Reanalysis: In cases where minor discrepancies between the XF- 1600 and DxFLEX/Navios are observed, particularly for MRD levels below 0.05%, data reanalysis can be performed to assess the robustness of the results.

Overall, the XF-1600 flow cytometer is a valuable tool for MRD assessment in MM, even with the 24-hour delay. By implementing strategies to minimize the impact of sample preparation and acquisition timing, clinicians can use the XF- 1600 to accurately detect and monitor MRD in MM patients, contributing to improved disease management and treatment outcomes. The 24-hour delay between sample collection and analysis on the XF-1600 may have contributed to the minor measurement deviations between the XF-1600 and DxFLEX/Navios instruments, particularly for MRD levels below 0.1%. During this delay, cell viability and antigen expression may potentially change, leading to subtle variations in the MRD readout.

In summary, the field of MRD detection in multiple myeloma is rapidly evolving, with ongoing research focused on improving detection sensitivity, expanding the range of available techniques, and integrating MRD data into predictive models that can personalize treatment decisions. With continued research and technological advancements, MRD is poised to play an even more pivotal role in shaping the future of myeloma treatment, leading to a more durable and optimistic outlook for patients worldwide.

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