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

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INTRODUCTION

Multiple myeloma (MM) is the second most common hematological cancer, which 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. The relapse rate of this plasma cell neoplasm is of 85-90%. Assessment of measurable residual disease (MRD) has emerged as a sensitive prognostic tool to monitor MM response, and many studies show that MRD negativity after treatment is associated with improved progression-free survival (PFS) and overall survival (OS). Here, we present a standardized panel for MRD detection in the XF-1600 and its comparison with two CE-IVD flow cytometers, providing compelling evidence that the XF-1600 flow cytometer is a reliable and accurate instrument for measuring MRD in MM.

MATERIALS AND METHODS

Bone marrow samples from 31 post-treatment MM patients were analyzed. 100 µL of marrow were stained with 10 µL CyFlow™ PE-CD27, PE-DyLight594-CD56, PerCP-Cy5.5-CD138, PE-Cy7-CD117, APC-CD19, AF700-CD81, APC-Cy7-CD38, and PO-CD45 (Sysmex) and incubated for 20 min at room temperature, followed by 10 min fixation with 1 mL CyLyse FX 1x. After a PBS-BSA 0.2% wash, samples were acquired on XF-1600 to obtain at least 1 million cells. Flow cytometry data acquired in parallel on XF-1600 (Sysmex) and DxFlex or Navios (Beckman Coulter) 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 displayed in **Figure 1**. The correlation between the percentage of abnormal plasma cells measured on the DxFLEX/Navios EX and the XF-1600 for each bone marrow sample was evaluated using Pearson's correlation coefficient, Bland-Altman analysis and linear correlation. Graphs and statistics were obtained in Prism v.9 software (GraphPad).

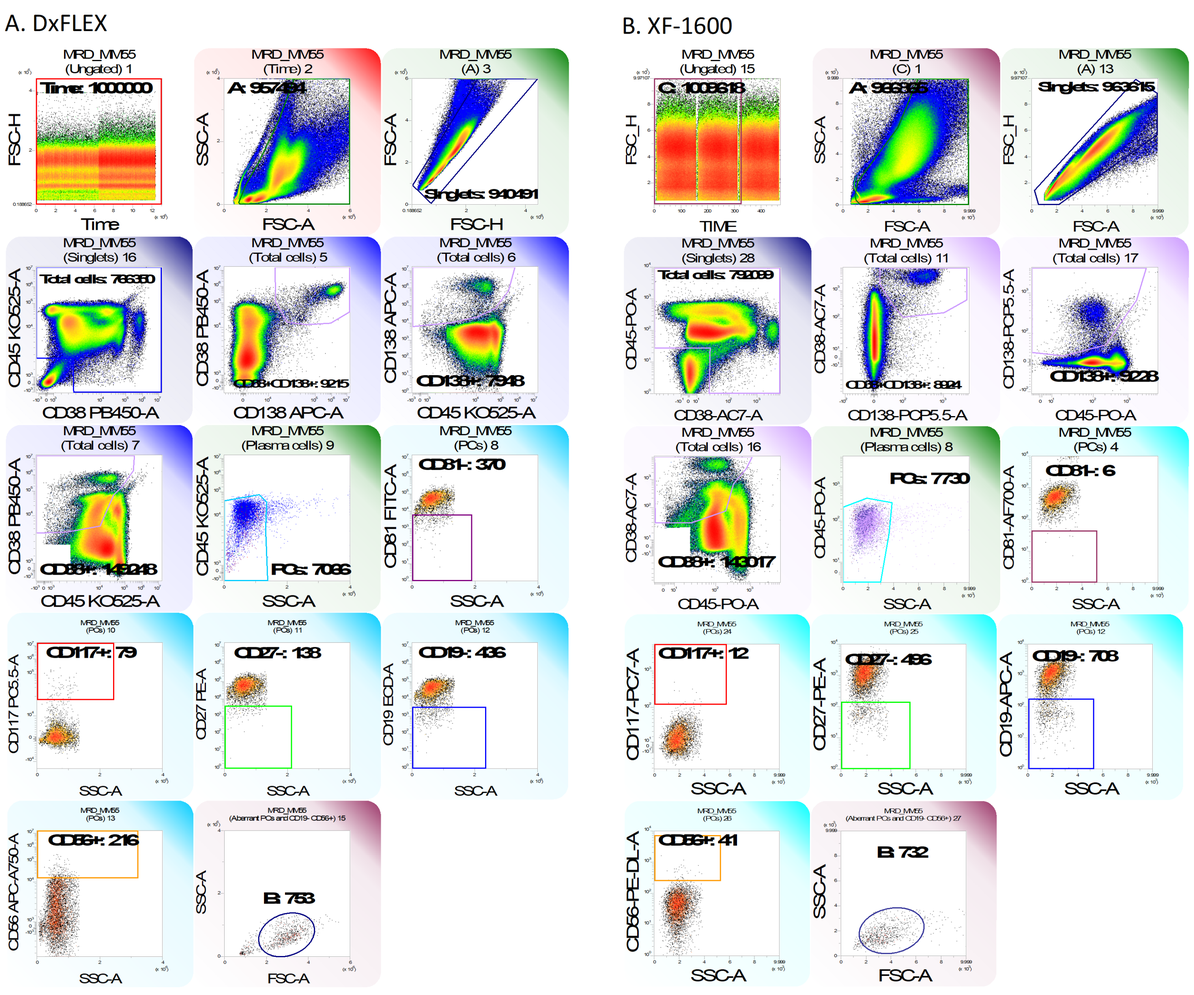

Figure 1. Representative analysis of measurable residual disease in a multiple myeloma patient. Comparison of DxFLEX and XF-1600 flow cytometers using VenturiOne® software.

RESULTS AND DISCUSSION

Bland-Altman analysis of n=31 MM patients showed that the mean difference between XF-1600 and DxFLEX/Navios measurements of MRD was of -0.1577 ("95% CI", 1.045 to 0.7295). The obtained Pearson correlation coefficient was 0.9987 ("95% CI", 0.9973 to 0.9994; p-value<0.0001; R^2 = 0.9974), indicating that the MRD measurements from the instruments were significantly correlated (**Figure 2**). In the samples with MRD measurements less than 0.1% (n=12), the mean difference between the XF-1600 and DxFLEX/Navios was 0.001433, ranging from -0.02874 to 0.03161. This slightly different concordance in MRD values is likely due to the increased contribution of small difference values to the MRD measurement percentages, which can interfere with precise agreement between instruments. The obtained Pearson correlation coefficient was 0.8991 ("95% CI", 0.6720 to 0.9717; p-value <0.0001; R^2 = 0.8085) (**Figure 3**).

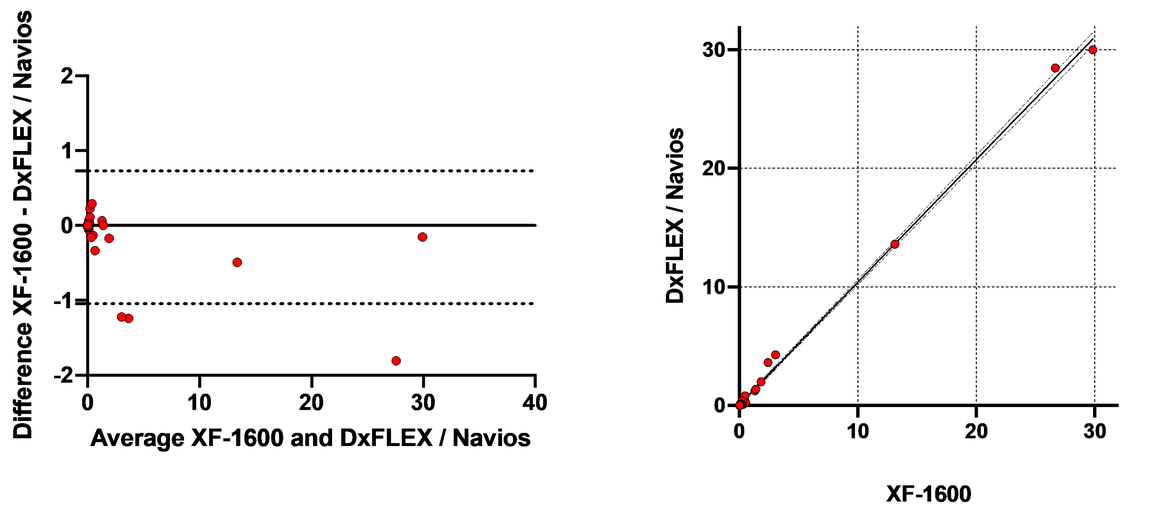

Figure 2. Comparison of DxFLEX/Navios and XF-1600 flow cytometers in MRD patients. MRD was analyzed in n = 31 MM patients. Bland-Altman analysis (left) showed that the mean difference between XF-1600 and DxFLEX/Navios results was -0.1577 with a 95% confidence interval of -1.045 to 0.7295. In the right plot, the linear regression equation y = 1.034x + 0.06752 accurately predicts the DxFLEX/Navios value from the XF-1600 value (R2 = 0.9974).

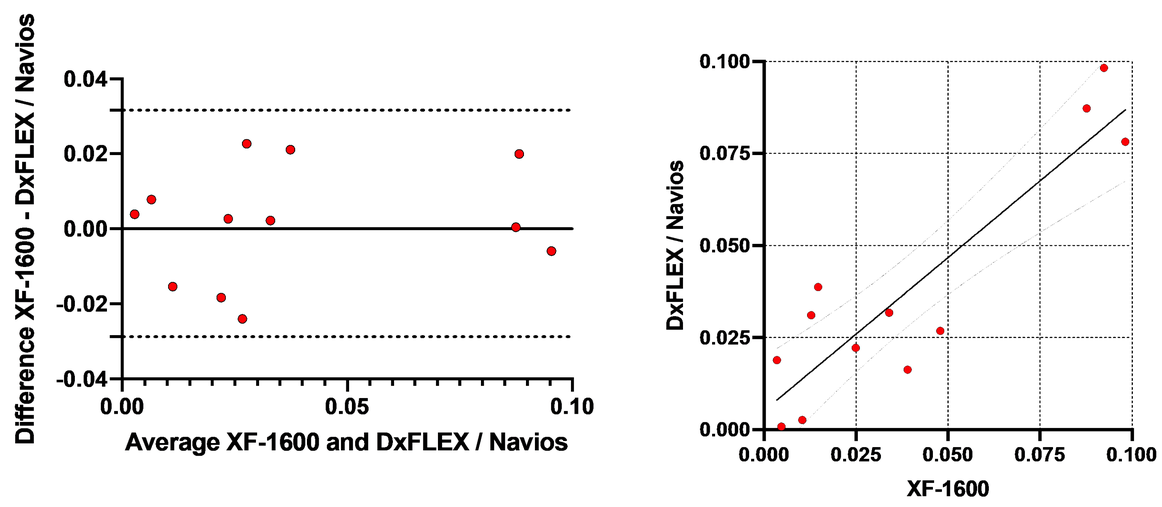

Figure 3. Comparison of DxFLEX/Navios and XF-1600 flow cytometers in patients with ≤0.1% MRD. MRD was analyzed in n = 12 MM patients. Bland-Altman analysis (left) showed that the mean difference between XF-1600 and DxFLEX/Navios results was 0.001433 with a 95% confidence interval of -0.02874 to 0.03161. In the right plot, the linear regression equation y = 0.8321x + 0.005144 predicts the value of DxFLEX/Navios from the value of XF-1600 (R2 = 0.8085).

CONCLUSIONS

The XF-1600 flow cytometer is a reliable and accurate instrument for measuring MRD in MM. By implementing strategies to minimize the impact of sample preparation and collection 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 small measurement discrepancies between the XF-1600 and DxFLEX/Navios instruments, particularly for MRD levels below 0.1%. During this delay, cell viability and antigen expression may change, resulting in subtle variations in MRD measurements. With continued research and technological advances, MRD will play an even more critical role in shaping the future of myeloma treatment.

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ESCCA European Society for Clinical Cell Analysis

sysmex

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