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Visualizing Measurable Residual Disease in Research: Imaging for Characterization of Rare Abnormal Plasma Cells in MM Bone Marrow

Poster #133

Siobhán Cashman,[1] Woodrow E. Lomas III,[2] Aaron Middlebrook,[2] Scott Bornheimer[2]
[1]Waters Biosciences, Castletroy, Limerick, Ireland V94V500 , [2]Waters Biosciences, 155 N McCarthy Blvd, Milpitas, CA 95035

1 Need & Objective for Clinical Research

Accurate measurable residual disease (MRD) assessment in multiple myeloma (MM) relies on identifying rare abnormal cells within a background of normal bone marrow cells.

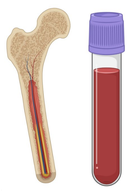
Conventional flow cytometry provides limited morphological information. BD CellView™ Imaging Technology combines flow cytometry with single-cell imaging to further characterize the single-cell origin of rare events.

Objective: To determine whether BD CellView™ Imaging Technology can provide orthogonal visual information to support characterization of rare events identified by MM-MRD gating and help distinguish true cellular events from artefacts or coincident events.

2 Workflow & Methods

Samples: Residual de-identified bone marrow aspirate samples from individuals with multiple myeloma analyzed by research-use MRD flow cytometry (2 representative cases). Analytical feasibility was examined separately using the whole-blood spike-in model described below.

Workflow

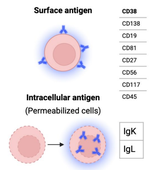


1. Bone Marrow Aspirate

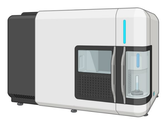
Samples



2. Sample is bulk Lysed



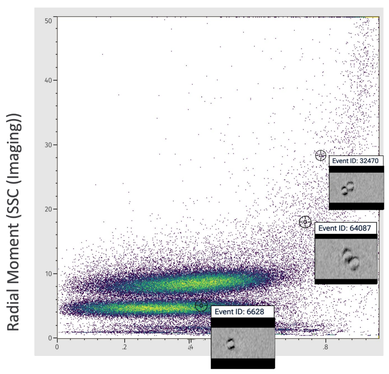
3. Sample is stained



4. Sample is analyzed using FACS Discover platform with CellView™ Imaging Technology

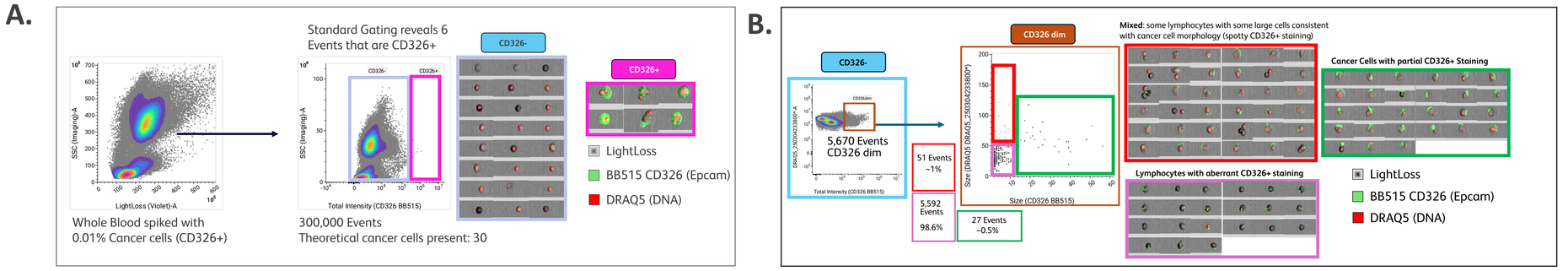
Spike-in model: CD326+ (EpCAM+) cells were spiked into normal whole blood at 0.01% (~30 cells expected in 300,000 events). Samples were stained for CD326 (BB515) with DRAQ5 nuclear counterstain and acquired on the BD FACSDiscover™ platform. Image analysis was used to help confirm candidate events as single cells expressing CD326+.

Image-Based Event Characterization



Morphometric parameters support discrimination of intact single cells from debris and coincident events

3a Results: BD CellView™ Image Technology May Support Visualization and Characterization of Single Tumor Cells in Spike-In Model System

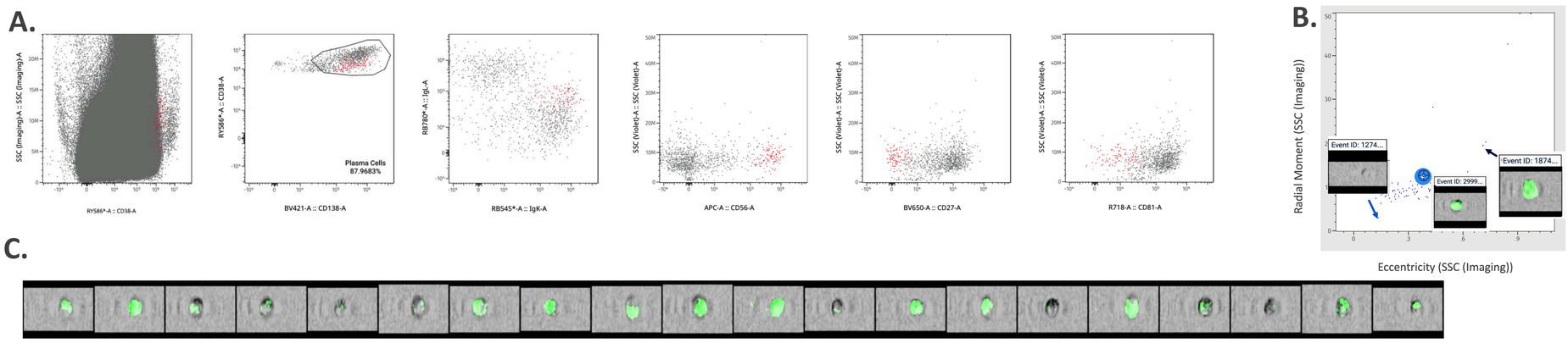


Rare-cell spike-in model system. A. CD326+ (EpCAM+) cells were spiked into whole blood with a theoretical concentration of 0.01%. 300,000 events were acquired and analyzed for presence of CD326+ cells (30 cells were anticipated). Gating of CD326+ bright events identified 6 events, confirmed as cells by imaging (CD326+ green, DRAQ5 nuclear staining red). Events from the CD326- gate were also confirmed by imaging as cells lacking CD326. **B.** The negative population was further analyzed for CD326dim events, resulting in 5,670 dim events. Image gating comparing size of nuclear (DRAQ5) and CD326 signals identified 27 candidate cancer cell events. The 27 in B and 6 in A results in 33 total, consistent with the theoretical spike-in value of 30.

3b Results: BD CellView™ Image Technology May Support Visualization and Characterization of Single Abnormal Plasma Cells in Bone Marrow Samples

MRD Sample 1

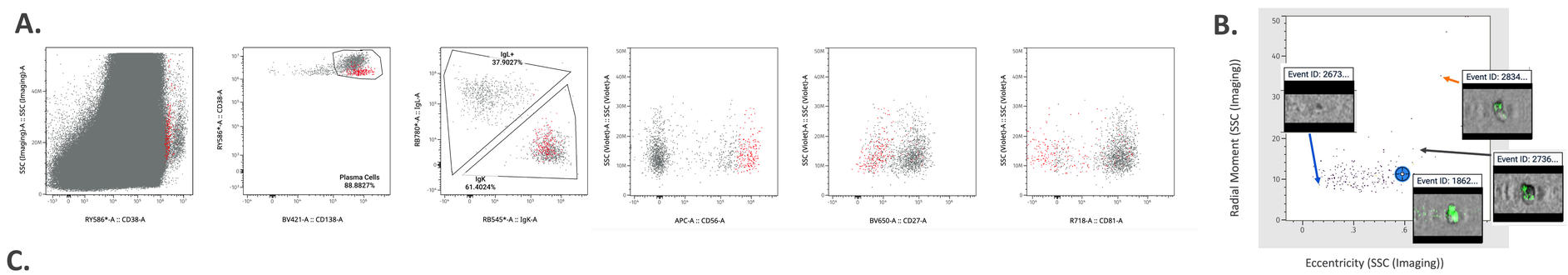
BD CellView™ images MRD 1



MRD Sample 1. Phenotypic and image-based findings that may support confirmation of MRD in a multiple myeloma sample. **(A)** representative flow cytometry plots show the abnormal plasma population (in red) identified as MRD-phenotype and its defining immunophenotype. The complete MRD gating hierarchy is not displayed; candidate events were identified through iterative multi-dimensional gating using the full complement of parameters within the panel. **(B)** eccentricity and radial moment derived from CellView images were used to assess event morphology. The blue arrow indicates a debris-associated event, while the blue crosshairs and black arrow identify representative single plasma cells. The black arrow highlights a particularly large plasma cell located within the region that could conventionally be interpreted as containing doublets. Combining assessment of eccentricity and radial moment and the corresponding cell image is consistent with this event representing a single plasma cell, allowing genuine large cells to be retained rather than incorrectly excluded by conventional doublet gating. **(C)** 20 representative images of the MRD-phenotype population are shown, confirming that the phenotypically identified events correspond to intact single plasma cells. From a total acquisition of 4 million events, 79 candidate MRD-phenotype events were identified. Following image review 1 debris associated event was excluded, leaving 78 image-confirmed single MRD-phenotype events.

MRD Sample 2

BD CellView™ images MRD 2



MRD Sample 2. Phenotypic and image-based findings that may support confirmation of MRD in a multiple myeloma sample. (A) representative flow cytometry plots showing the abnormal plasma cell population (in red) identified as MRD-phenotype: CD38+, CD45dim, CD138+, Igκ+, CD56+, CD27-, CD81-, CD19- and CD117-. The complete MRD hierarchy is not shown; candidate events were identified through iterative multi-dimensional gating using the full complement of parameters within the panel. **(B)** eccentricity and radial moment derived from BD CellView™ images were used to assess event morphology. The blue arrow shows a debris event, the orange arrow identifies a doublet, and the blue crosshairs and black arrow indicate representative single plasma cells. Evaluation of both imaging parameters supported the distinction between coincident events and genuine enlarged plasma cells (allowing large cells that might overlap a conventional doublet exclusion region to be retained). **(C)** 20 representative images of the identified MRD-phenotype population are shown. From a total acquisition of 5 million events, 189 candidate MRD-phenotype events were identified. Following image review 1 doublet and 1 debris associated event were excluded, leaving 187 image-confirmed single MRD-phenotype events.

4 Conclusions

- BD CellView™ Imaging Technology may support identification that rare abnormal plasma cells identified by MM-MRD flow cytometry represent single cells.
- Pairing flow cytometry with single-cell imaging may support visual identification of MRD in multiple myeloma.

BD CellView™ Imaging Technology supports characterization of rare events in clinical research and may help distinguish coincident events and doublets through morphological assessment..

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