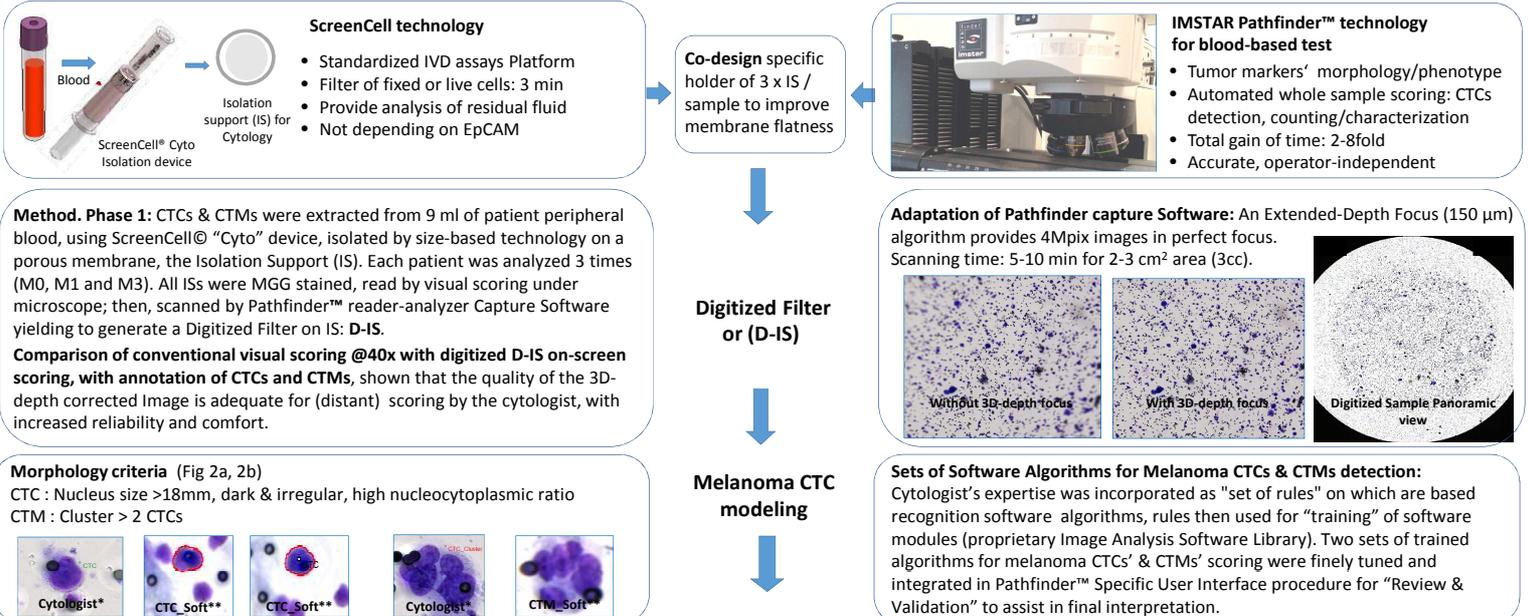


CTCs/CTMs Automated detection after size-based selection from blood of patients with melanoma

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Introduction: Circulating Tumor Cells (CTCs) and Clusters (CTM) in the blood play a critical role in cancer staging and treatment management. Counting of CTCs/CTMs during cancer evolution was shown to be helpful for early detection of cancer relapse, but is limited by the current methodology constraints. Methods based on CTCs recognition by immunological technics could give rise to false negative results because the expression level of markers may differ in CTCs as compared to tumor tissues. And methods based on Cyto-Pathologist observation of CTCs/CTMs are more accurate, but time consuming and observer-dependent, thus cannot be applied in clinical use. In this study, we analyzed 166 blood samples from a cohort of 131 patients with stage IV melanoma, from the onco-dermatology department in Saint-Louis Hospital, Paris.

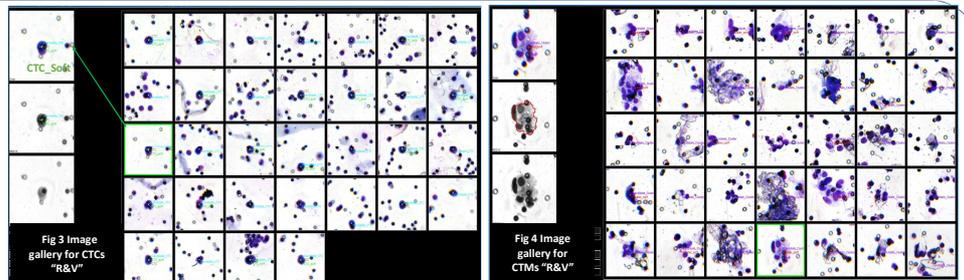


AUTOMATED DETECTION & VALIDATION

Method Phase 2: In parallel, all Digitized Filters are analyzed by Pathfinder™ CTC-CTM BF software module and the cytologist counts CTCs and CTMs by visual scoring, and set these labels on each of D-IS.

Cells automatically detected as suspicious are displayed in an Image gallery for fast review & validation on Pathfinder™ CTC – CTM "R&V screen", for final scoring and classification of CTCs as well as CTMs (Fig 3, 4).

All Images and Data are recorded in the Pathfinder software database.



RESULTS & DISCUSSION

CTCs: n= 166 digitized filters. Cytologist's on-screen CTCs counting on D-IS was compared to CTCs automated counting using the specific analysis/detection software (CTC_Soft).

The cytologist' on-screen counting yields to a total of 2382 CTCs, while automated counting yields to 2375 CTCs. For 32 D-ISs, cytologist' on-screen CTCs number is inferior, and for 24 D-ISs, the cytologist on-screen CTCs counting is superior to automated counting.

The 166 D-IS set were split in 2 groups: A = 85 IS with <8 CTCs and B = 85 IS with >8 CTCs. For group A, automated scoring is equal or superior to visual scoring in over 98% cases. For group B: Visual scoring is equal or superior to the automated one in 90% cases.

CTMs: n= 70 digitized filters. Cytologist's on-screen CTMs counting and automated counting using specific analysis/detection software yields to 418 CTMs and 410 CTCs_Soft, respectively.

Both methods are in concordance in terms of CTCs' and CTMs' counting, thus in Digitized filters' (D-IS) classification success rate.

Total time/sample: 5 - 6 min.

CONCLUSION

The Pathfinder™ CTC software module was developed and partly funded in the frame of a French consortium project: **ExpeVivo-CTC, for highly specific automated detection and counting of GMM stained melanoma CTCs/CTMs on IS Cyto® device.** The accuracy and robustness validation of CTCs & CTMs scoring on Digitized – Filter (IS) was performed on stage IV melanoma patients from Saint-Louis Paris Hospital Onco-Dermatology Department.

The essential benefits of automated CTCs/CTMs detection are:

- High CTCs & CTMs counting and characterization accuracy – Sensitivity 96,6% - Specificity 100%.
- 2-fold gain of time reducing to 2 - 3 min the Expert time per D-IS (2 -3 cm² spread; 3ml blood).
- Operator independency - Facilitate Junior Cytotech' training in a shorter time

We demonstrated that the combination of IMSTAR Pathfinder™ technology for assisted accurate scoring of CTCs /CTMs, adapted to ScreenCell® Cyto devices simple-to-use, inexpensive technology, could substantially facilitate melanoma patient's treatment follow-up, in clinical trials and ultimately for clinical application.