

Circulating Tumor Cells: Challenges in Detection and Isolation

I. Papisotiriou, M. Chatziioannou, K. Pessiou, I. Retsas, G. Dafouli, C. Theodosiou, A. Kyriazopoulou, M. Toloudi, I. Vlachou, E. Kourtidou, E. Georgiou, D. Ntanovasilis, A. Pantopikou, E. Paparizou and P. Apostolou

Research Genetic Cancer Centre Ltd. (R.G.C.C. Ltd). Industrial Area of Florina GR53100, Florina, Greece

Introduction: Circulating Tumor Cells (CTCs) are cells that have detached from the primary tumor and flow into the blood or lymphatic circulation creating a secondary tumor. Their population is widely used as a predictive marker for cancer progression. Despite their importance, these cells are rare in cell population, thus their detection and isolation is under consideration of the scientific community. The present study aimed to evaluate an alternative fluidic-based method for CTCs identification in breast, colon, prostate, pancreatic and melanoma cancer.

Materials & Methods: Peripheral blood was collected from thirty (30) cancer and thirty (30) non-cancer donors. Samples were stained with different antibodies depending on the cancer type. The samples were run on a BD Accuri C6 cytometer and 50.000 events were recorded.

Results: Among the samples that were tested, 31 were positive for CTCs while 29 were not. The sensitivity, which means the true positive data, was **86.6 %**, and the specificity, which represents the true negative data was **83.3 %**. Regarding the positive predicted value (PPV) it is **83.9%** while the negative predictive value (NPV) is **86.2%**.

Condition	Positive	Negative	
Outcome			
Positive	TP=26	FP=5	PPV=83.9%
Negative	FN=4	TN=25	NPV=86.2%
	Sensitivity	Specificity	
	86.6%	83.3%	

Table 1: Raw Data and Analysis

Conclusion: Up to now, the most platforms exploit the physical properties and/or gene expression profiling of CTCs. Some others target the molecules on CTCs' surfaces. However, the loss of CTCs is the main drawback of the above methods. The alternative fluidic-based method that presented in this study, tried to overcome most of the limitations. This new methodology is based on detection of CTCs by using many biomarkers for each cancer type.

Moreover, no enrichment step was performed, thus reducing the possibility of cells loss. Furthermore, the results included not only the most common types of cancer but also and other, equally important. The comparison with non-cancer individuals revealed that this platform has higher sensitivity and specificity compared with well-established methods.

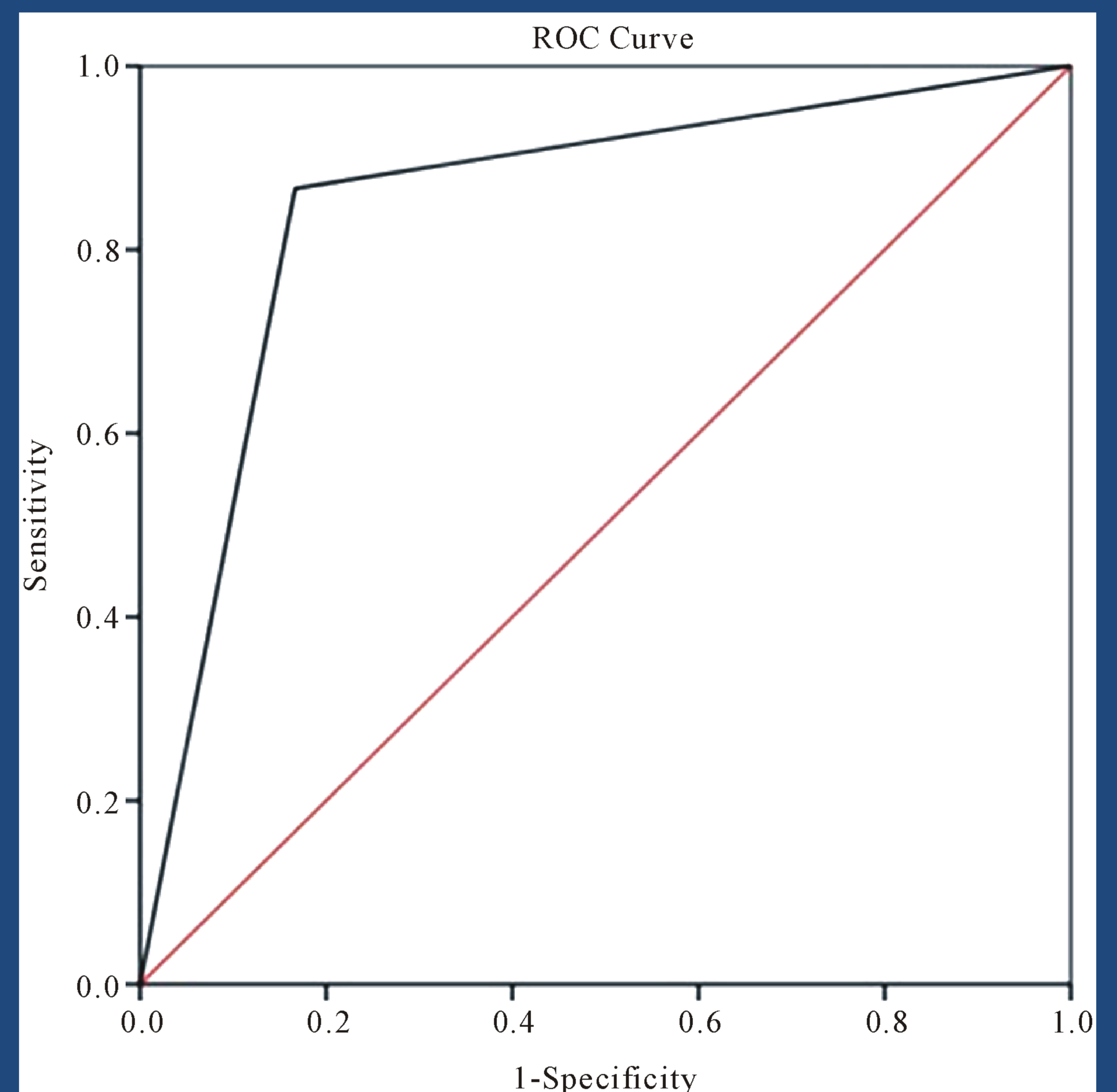


Figure 1: Roc Curve Analysis test. The results show a specificity (true negative rate) of 86.6% (71.3% - 91.6%) and sensitivity (true positive rate) 83.3% (72.7% - 94.4%) when analyzing all cancer types ($p < 0.05$).

Selected References:

- Papisotiriou, I., et al. (2015) Detection of Circulating Tumor Cells in Patients with Breast, Prostate, Pancreatic, Colon and Melanoma Cancer: A Blinded Comparative Study Using Healthy Donors. *Journal of Cancer Therapy*, 6, 543-553. <http://dx.doi.org/10.4236/jct.2015.67059>
- Williams, S.C. (2013) Circulating Tumor Cells. *Proceedings of the National Academy of Sciences of the USA*, 110, 4861. <http://dx.doi.org/10.1073/pnas.1304186110>
- Cristofanilli, M. (2009) The Biological Information Obtainable from Circulating Tumor Cells. *The Breast*, 18, S38-S40. [http://dx.doi.org/10.1016/s0960-9776\(09\)70270-x](http://dx.doi.org/10.1016/s0960-9776(09)70270-x)