CELL-FREE DNA DETECTED BY "LIQUID BIOPSY" AS A POTENTIAL PROGNOSTIC BIOMARKER IN PATIENTS WITH DIFFERENT SUBTYPES OF BREAST CANCER

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ABSTRACT

Conventional biomarkers used to define breast cancer (BC) subtypes are not always capable of predicting prognosis. Thus, the search for new biomarkers that can be easily detected by liquid biopsy is ongoing. Recent studies have shown that cell-free DNA (CF-DNA) could be a promising diagnostic marker in different tumor types. However, its prognostic value in BC has yet to be confirmed. This retrospective study evaluated the prognostic role of CF-DNA quantity and integrity of *HER2*, *MYC*, *BCAS1* and *PI3KCA*, frequently altered in BC. 79 serum samples were collected before surgery from women at first diagnosis of BC with surgery in Forlì Hospital (Italy) from 2002 to 2010. Twenty-one relapsed patients and 58 non relapsed patients were matched by subtype and

age. Blood samples were also collected from 10 healthy donors. All samples were analyzed by Real Time PCR for CF-DNA quantity and integrity of all oncogenes. A part *MYC*, significantly higher median values for the quantity (ng) of CF-DNA were found in BC patients than in healthy controls who showed higher apoptotic index and lower integrity than tumors (Table 1). A difference towards statistical significance was observed for *HER2* short CF-DNA (*p-value:* 0.078) and the AUC value was 0.6305. *HER2* short CF-DNA showed an odds ratio of 1.39 for recurrence of disease with a p-value of 0.056 (95%CI 0.991-1.973). Our study suggests that CF- DNA detected as liquid biopsy has enormous potential but widespread clinical application waits for rigorous prospective studies that will need robust assays to demonstrate clinical validity and utility.

Table 1. CF-DNA quantity (ng) in relation to the status (cancer / control)

Gene	Overall (n=89)	Cancer (n=79)	Control (n=10)	p-value[#]
	Median (iqr range)	**Median (iqr range)**	**Median (iqr range)**	
HER2 LONG	0.031 (0.012-0.121)	0.034 (0.011-0.137)	0.023 (0.015-0.033)	0.439
HER2 SHORT	0.202 (0.077-0.496)	0.238 (0.093-0.509)	0.067 (0.049-0.111)	**0.016**
BCAS1 LONG	0.241 (0.093-0.820)	0.266 (0.131-0.941)	0.039 (0.031-0.460)	**0.021**
BCAS1 SHORT	1.195 (0.476-2.069)	1.259 (0.536-2.133)	0.085 (0.050-0.916)	**0.001**
MYC LONG	0.421 (0.190-1.192)	0.421 (0.146-1.205)	0.426 (0.299-0.533)	0.658
MYC SHORT	1.124 (0.557-2.001)	1.145 (0.557-2.255)	0.771 (0.457-1.335)	0.193
PI3KCA LONG	0.089 (0.036-0.347)	0.108 (0.036-0.373)	0.056 (0.044-0.092)	0.398
PI3KCA SHORT	1.165 (0.231-3.434)	1.619 (0.296-4.332)	0.174 (0.140-0.390)	**0.001**

[#] Two-sample Wilcoxon rank-sum (Mann-Whitney) test