Combining analysis of solid and liquid biopsy: insights into tumor heterogeneity

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INTRODUCTION

Liquid biopsies are a promising tool for molecular tumor profiling and monitoring (Siravegna *et al.*, 2017). One of their main advantages over solid biopsies is that they can detect intratumoral heterogeneity, which is unappreciated by single-site tissue biopsies. However, we are still at the beginning of their incorporation into routine oncology practice.

Aim of the project: *What is the clinical utility of combining solid and liquid biopsies in the molecular profiling of tumor patients?*

MATERIALS AND METHODS

We analysed 112 samples from patients with different cancer types, stage III or IV, using **OncoSTRAT&GO™** (OncoDNA):

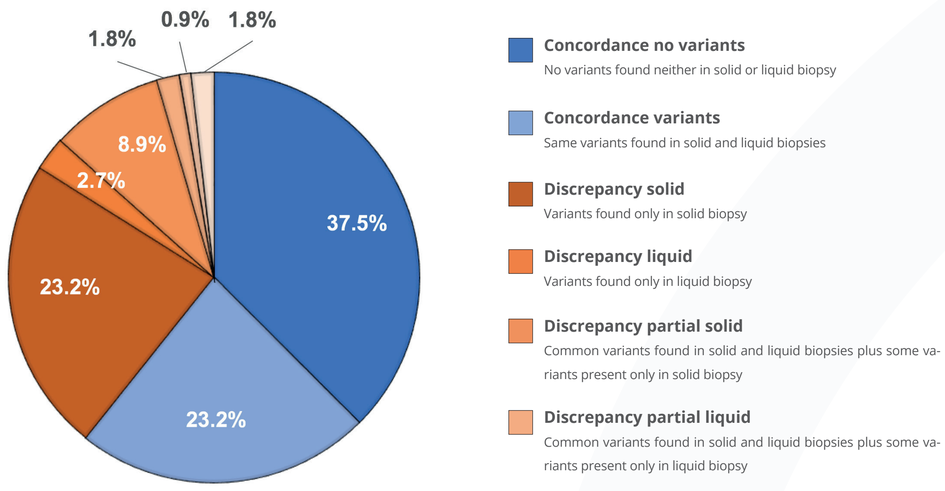
- **Solid biopsy (FFPE block)** 
  - Next-generation sequencing → more than 200 genes
  - (Immunohistochemistry)
- **Liquid biopsy (blood sample)** 
  - Next-generation sequencing of ctDNA → **27 genes**

RESULTS

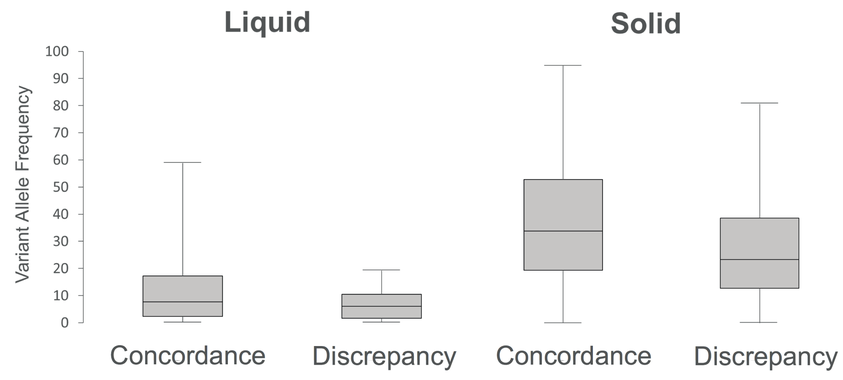
First, we wanted to study the concordance between solid and liquid biopsies in detecting actionable variants present in the tumors → **60.7% complete concordance** (68 out of 112 samples):

		CONCORDANCE
TUMOR TYPE	PATIENT NUMBER (%)	PATIENT NUMBER (%)
Breast Cancer	29 (25.9)	14 (48.3)
Lung Cancer	15 (13.4)	11 (73.3)
Colorectal Cancer	13 (11.6)	8 (61.5)
Gynecologic Cancer	12 (10.7)	5 (41.7)
Pancreatic Cancer	9 (8.0)	5 (55.6)
Others	34 (30.4)	25 (73.5)
TOTAL	**112**	**68 (60.7)**

The rest of the samples (39.3%) presented different discrepant patterns (in orange tonalities):



We then compared the concordant and discrepant variant allele frequencies, and they showed similar distributions with no significant statistical differences: mean values of 7.8/9.4% (P= 0.58, Mann-Whitney test) and 34.9/25.7% (P= 0.08, Mann-Whitney test) in liquid and solid biopsy, respectively:



CASE STUDY

Colorectal cancer patient

TP53 (L194R, 39.34%) → No related treatments available

TP53 (L194R, 33.78)
KRAS (G12D, 13.13%)
PIK3CA (E545A, 12.24%)

→ ***KRAS* (G12D)** : Metastatic patients should not be treated with cetuximab or panitumumab (FDA)

***PIK3CA* (E545A)** : PI3K/mTOR dual inhibitor might be useful (ASCO 2015)

CONCLUSIONS

The discrepancy found in the data cannot be explained by the sensibility of the analysis, fact that points to a key influence of the heterogeneity of the tumor, which is only captured by liquid biopsies. So, combining solid and liquid biopsies would give a full picture of the tumor.

Indeed, our results show the usefulness of the combination of both biopsies in clinical practice, as it provides additional information in 39.3% of the cases. This leads to a broader characterization of the tumor molecular profile and therefore to a better disease management.

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