Homologous Recombination Repair (HRR) mutation concordance between liquid biopsy (LB) and tumor tissue by NGS in a real-world prostate cancer (PC) database

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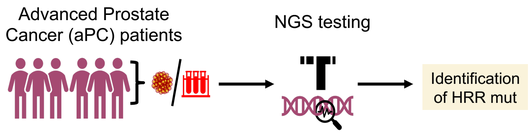
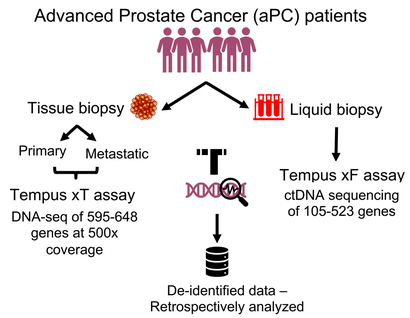
INTRODUCTION



In a large real-world (RW) database, we determined:

- **Concordance** between plasma ctDNA and primary tumor tissue (PT) and/or metastatic tissue (MT) for **BRCA1, BRCA2, and ATM** mut in PC patients who received both LB and tissue NGS any time during standard of care (SOC) management
- The **utility of LB** to detect **actionable mut** in these **HRR genes** and demonstrate the utility of combined LB and tissue testing

METHODS



- Paired analysis from primary tumor (PT), metastatic tumor (MT) and liquid biopsy (LB) of patients: 1) PT vs LB 2) MT vs LB.
- The results from the patient's earliest PT or MT and earliest LB were used for paired analyses.
- The prevalence of a pathogenic/likely pathogenic germline and/or somatic mut in BRCA1, BRCA2, or ATM was reported as N (%), 95% CI.
- The sensitivity of the LB to identify observed HRR mut in tissue was also reported as N (%), 95% CI.
- Concordance between pairs was evaluated by Cohen's kappa statistic with 95% CI.

SUMMARY

- Plasma ctDNA-based analysis of **BRCA1, BRCA2, and ATM mut** showed **greater concordance** between **liquid biopsy and metastatic tissue** than liquid biopsy and primary tumor tissue, in this large Real-World dataset, potentially influenced by greater proximity in time between the former paired samples.
- Liquid Biopsy is an effective initial tool for **HRR mut detection,** identifying 70% of HRR mutations found in metastatic tissue biopsies
- When liquid biopsy results are negative, further exploration with tissue-based testing may identify additional HRR mut to guide clinical decisions

RESULTS

Characteristic	Matched PT - LB, N = 1074[1]	Matched MT - LB, N = 451[1]
Age at Diagnosis	66 (60, 72)	64 (58, 72)
Unknown	3	12
Race		
White	434 (69%)	197 (70%)
Black or African American	147 (23%)	54 (19%)
Other	27 (4.3%)	20 (7.1%)
Asian	24 (3.8%)	12 (4.2%)
Unknown	442	168
Ethnicity		
Hispanic or Latino	80 (19%)	40 (25%)
Unknown	648	291
Match Type		
tumor/normal match	975 (91%)	403 (89%)
tumor only	99 (9.2%)	48 (11%)
HRR+, tissue (PT or MT)	94 (8.8%)	46 (10%)
HRR+, liquid (LB)	67 (6.2%)	47 (10%)

1 Median (IQR), n (%)

Table 1: Demographic/Clinical characteristics of the patient cohort

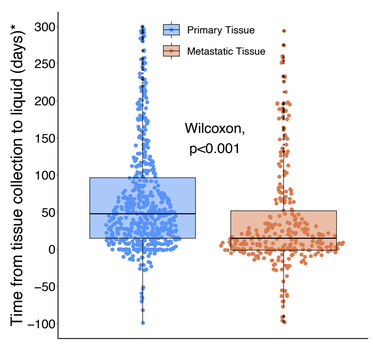
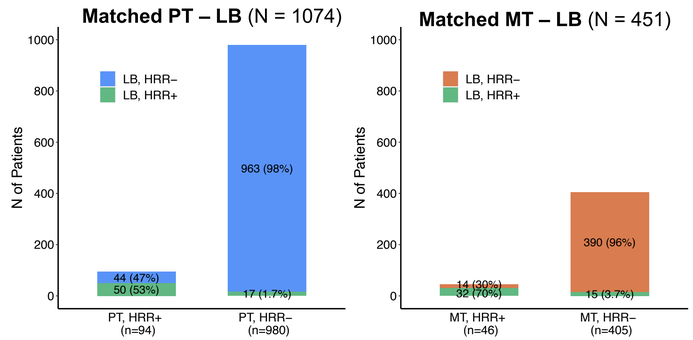


Figure 1 – Time from tissue collection to liquid was significantly shorter in MT vs LB analyses compared to PT vs LB analyses (median 21 vs 174 days, respectively)



Characteristic	PT vs LB[1], N = 1074	MT vs LB[1], N = 451
Sensitivity	53% (43%-64%)	70% (54%-82%)
Specificity	98% (97%-99%)	96% (94%-98%)
+ve Predictive Value	75% (63%-84%)	68% (53%-81%)
-ve Predictive Value	96% (94%-97%)	97% (94%-98%)
Cohen's Kappa	0.59 (0.50 – 0.68)	0.65 (0.54 – 0.77)

1statistic (95% C.I)

Figure and Table 2 – Agreement of HRR detection between tissue and liquid
Sensitivity: N LB, HRR+/N PT (or MT), HRR+, *Specificity*: N LB, HRR-/N PT (or MT), HRR-, *Positive predictive value*: N PT (or MT), HRR+/N LB, HRR+, *Negative predictive value*: N PT (or MT), HRR-/N LB, HRR-

Key Results

- HRR+ was identified in 8.8% of primary tissue (95% CI (7.2%-11%) and 10% of metastatic tissue (95% 7.6%-13%). **Table 1**
- HRR+ was identified in 6.2% (95% CI 4.9%-7.9%) and 10% (7.8%-14%) of liquid samples (PT vs MT analyses, respectively). **Table 1**
- Liquid biopsy demonstrated higher concordance of HRR+ detection with metastatic tissue compared to primary tissue (Cohen's kappa 0.65 vs 0.59, respectively, **Table 2**), potentially influenced by reduced time between tissue and liquid collection (**Figure 1**) and increased tumor burden in metastatic patients.

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