Temporal concordance rates of pathogenic variants in liquid biopsies taken after solid tissue NGS profiling in a real-world pan-cancer cohort

Abstract #: 62

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INTRODUCTION

Pathogenic genomic alterations can be identified through either a biopsy of solid tissue or the detection of circulating tumor DNA from plasma. Little is known about the concordance rates of pathogenic variants between cell free DNA (cfDNA) and solid tissue biopsies, including how concordance varies over time, by cancer type, or in response to treatment. Here we examine the concordance of pathogenic variants identified in solid tissue biopsies to patient-matched cfDNA in one of the largest pan-cancer datasets.

METHODS

De-identified records of stage 4 patients with both a cfDNA (Tempus xF) and solid tissue (Tempus xT) assay were analyzed across 5 cancer types: breast, colorectal, non-small cell lung cancer (NSCLC), pancreatic, and prostate (Table 1).

Pathogenic SNVs and indels within overlapping probe regions of xF and xT meeting assay limits of detection were included for analysis. Only one cfDNA and solid biopsy were analyzed per patient, and records were binned for certain analyses (Figs. 2&3) based on time between sample collection. cfDNA was taken after the solid tissue biopsy in all cases except the first time bin (+/- 14 days).

Dataset overview

Cancer type	# of patients	Total pathogenic variants identified	# of patients w/ pathogenic variant identified in both xF and xT
Breast	890	2129	595
Colorectal	1153	4677	908
NSCLC	1382	3554	958
Pancreas	573	1580	397
Prostate	713	1181	303
PanCan	4711	13121	3161

Table 1. Overview of patient cohort and pathogenic variant numbers (the union from both assays), as well as the number of patients with variants identified via both solid and cfDNA assays (used in Figs. 2&3).

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SUMMARY

When analyzing patients with pathogenic variants identified in both assays,

- cfDNA identified 86% of solid tissue variants when samples were taken within two weeks of each other; this value decreased as time between assays increased
- Across all time points, 44% of patients had additional variants identified in cfDNA which were not found in solid tumor profiling alone
- Temporal cfDNA profiling can identify the emergence of new pathogenic variants

RESULTS

Solid-tissue and cfDNA NGS identifies both overlapping and unique sets of pathogenic variants across cancer types

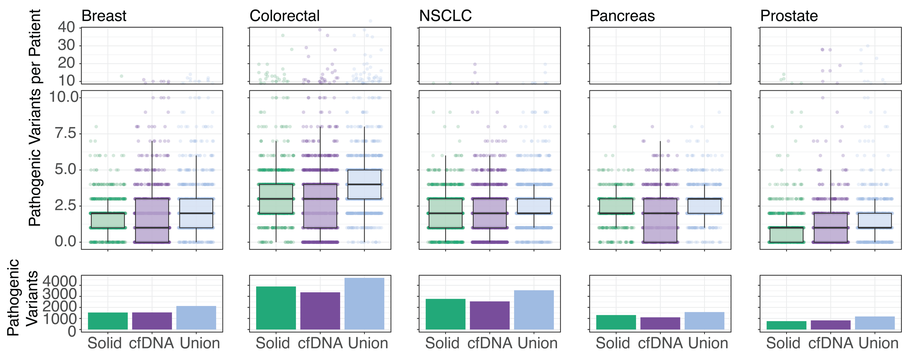

Figure 1. For each cancer type, boxplots (top) show the number of pathogenic variants identified per patient in solid-tissue (green) and cfDNA (purple) NGS, as well as the union of both (blue, which includes the set of all unique variants found by either assay at the patient level). Bar plots (bottom) show the absolute number of pathogenic variants found for each cancer type and each assay as well as the union, as described above.

Unique variants are captured and lost in a time and cancer-type dependent manner

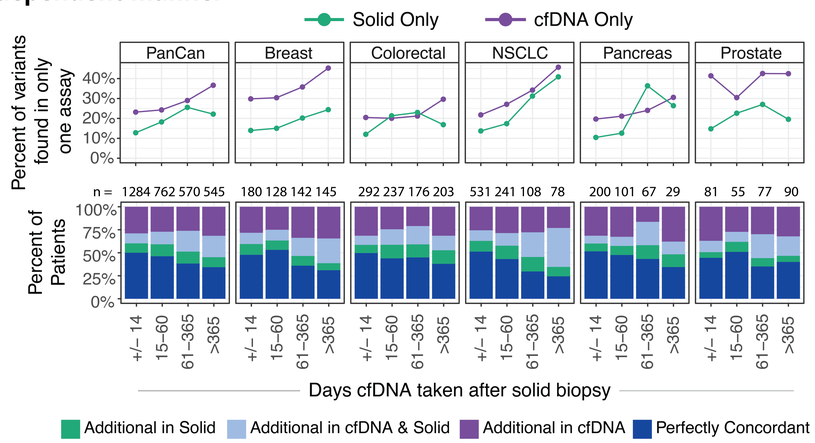

Figure 2. For the subset of patients with at least one pathogenic variant found in both solid and liquid assays, line plots (top) show the percentage of variants discovered per time bin that were found only in cfDNA (purple) or only in solid tissue (green). Stacked bar plots (bottom) show variant concordance information on a per patient level: all variants were perfectly concordant (dark blue), patient had concordant variants and additional variants were found only in cfDNA (purple) or solid (green), or both assays identified at least one unique variant (light blue).

Temporal analysis identifies the emergence of pathogenic variants in key resistance genes

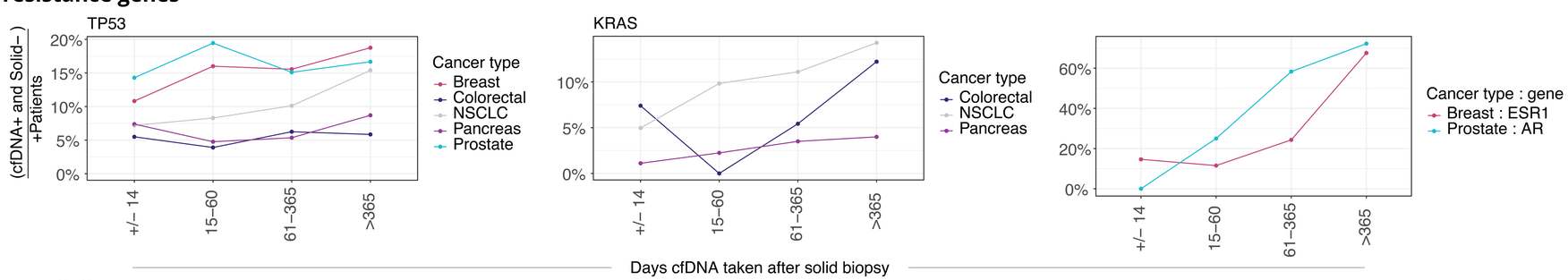

Figure 3. Considering only the subset of patients with at least one pathogenic variant found in both solid and liquid assays, individual line plots show the percentage of patients with a pathogenic gene variant (+patient) which was only identified through cfDNA profiling only (cfDNA+ and solid-). Only genes that have pathogenic variants in at least 10% of the cancer cohort are shown.