Urine circulating tumor DNA analysis in bladder cancer using a targeted NGS panel

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Background:
Precision medicine has revolutionized cancer care, significantly improving patient prognosis. This approach relies on molecular testing to identify specific tumor mutations, enabling targeted therapies. While tissue biopsy remains the gold standard for molecular characterization, it has limitations such as invasiveness and potential complications. Liquid biopsy, a minimally invasive alternative, offers real-time tumor evolution monitoring. Although blood-based liquid biopsies are common, urine is emerging as a promising source due to its non-invasive collection and abundant availability.

Objective:
This study aimed to evaluate the feasibility of using the Myriapod NGS Cancer Panel DNA, a diagnostic NGS panel validated for both tissue and plasma, to detect clinically relevant genetic alterations in urine liquid biopsy samples from bladder cancer patients.

Methods:
Urine and tissue samples were collected from 32 bladder cancer patients on the day of surgery. DNA was extracted from both urine (utDNA) and tissue (tDNA) samples, followed by targeted NGS using the Myriapod NGS Cancer Panel DNA. Concordance between urine and tissue results was assessed, along with sensitivity, specificity, positive predictive value, negative predictive value, and allele frequencies.

Results:
The most altered genes were EGFR (40.6%), FGFR3 (40.6%), KIT (34.4%), BRAF (28.1%), KRAS (25%), and NRAS (25%). Comparative analysis showed an overall concordance rate of 56.3% (18/32 patients), with identical alterations detected in both utDNA and tDNA in all 18 patients. Liquid biopsy identified more alterations in some patients, indicating its potential for providing a broader view of the tumor mutational landscape. The median DNA concentration in urine was significantly lower than in tissue (1.28 ng/µL vs. 13.17 ng/µL, $p=1.33e^{-05}$), and the median fragmentation index was higher in urine samples (0.53 vs. 0.22, $p=1.87e^{-08}$).

Conclusion:
Our findings demonstrate the feasibility of employing the IVD Myriapod NGS Cancer Panel DNA to detect clinically relevant genetic alterations in urine liquid biopsies from bladder cancer patients. Urine liquid biopsy presents a non-invasive method for real-time tumor monitoring and potentially captures a more comprehensive view of the tumor mutational profile. Future studies are needed to optimize DNA extraction techniques and further evaluate the clinical utility of urine-based liquid biopsy in the management of bladder cancer.

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