P34.05
Perioperative Driver Mutation Detection in Circulating Tumor DNA from Lung Cancer Patients across Multiple Timepoints

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Introduction: Liquid biopsy using circulating tumor DNA (ctDNA) has received tremendous attention during the past decade. It allows detection of clinical actionable mutations in a noninvasive way. Though previous studies showed mutations and its variation allele frequency (VAF) in ctDNA can be used to monitor molecular residual disease and surgical prognosis, the detectable mutations at different perioperative blood collection timepoints still need to be investigated. **Methods:** A total of 19 lung cancer patients were enrolled in this study, including 13 stage I patients, 3 stage IIA-IIIB and 3 stage IV patients. For each lung cancer patient, 20 mL blood samples were collected at three timepoints: one day before surgery, before surgical anesthesia, and during surgery, respectively. The paired tumor tissue samples were collected from patients and subjected to a 500-gene next generation sequencing panel for mutation assay. Driver mutations in each plasma sample were detected using our previously reported PEAC technique, which allows to detect a SNV mutation at 0.01% allele frequency. In addition, partial blood samples were validated by droplet digital PCR (ddPCR) for further confirmation. **Results:** All the 19 tissue samples had driver mutations detected, including EGFR 19del, L858R, and KRAS G13D, etc. Among plasma samples collected from the three timepoints, the mutation detection rate from blood collected during surgery had highest concordance with the tumor tissue, which showed an overall detection rate of 44.4% (8/18), 83.3% (5/6) in stage II-IV, 42.9% (3/7) in stage IB, and 0% (0/5) in stage IA, respectively. The detection rate from available pre-anesthesia blood samples was 31.3% (5/16), and that in pre-operative blood samples was 26.3% (5/19). In blood samples detected by both PEAC and ddPCR, PEAC detected 5 more positive cases, showing that PEAC has a higher detection sensitivity than ddPCR. Considering patients' tumor stages, driver mutations in blood samples from patients in stage IIA-IIIB were consistent with that in paired tumor samples at all three blood collection timepoints. In contrast, for stage I patients, the concordance rates varied widely at different timepoints, with a 25% (3/12) concordance in blood samples during surgery, and 9.1% (1/11) and 0% (0/13) in pre-anesthesia and preoperative blood samples, respectively. Finally, quantification of the number of mutant copies per milliliter of plasma using ddPCR showed that the mutant copies had an increasing trend in preoperative, pre-anesthesia and intraoperative blood samples. **Conclusion:** By collecting blood samples from 19 lung cancer patients, plasma ctDNA driver mutations were examined using the PEAC technique at three timepoints (one day before surgery, before surgical anesthesia, and during surgery). Comparing with results from paired surgical tumor tissue samples, we found that blood samples collected during surgery had the highest concordance rate, indicating intraoperation is a better blood sample collection time. In addition, the PEAC technique had a higher ctDNA detection rate than ddPCR, which strengthens the usability of PEAC in detecting ctDNA and monitoring perioperative prognosis in early stage and resectable lung cancer patients. **Keywords:** Liquid biopsy, perioperative prognosis, multiple timepoints

P34.06
The Clinical Utility of Liquid Biopsy by Digital Droplet PCR in Patients with Advanced NSCLC

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Introduction: *EGFR* mutations occur in 15% of Caucasian and up to 50% of Asian patients with advanced NSCLC. Tissue genomic profiling is the gold standard but the liquid biopsy is a good surrogate of the tissue for molecular diagnosis. The digital droplet PCR (ddPCR) is a rapid and low-cost liquid biopsy technique for genomic analyses. We aimed to evaluate the clinical utility of the ddPCR for genomic profiling of advanced NSCLC with *EGFR* mutations. **Methods:** The ddPCR technique was prospectively applied in a cohort of advanced *EGFR* mutant (*EGFR*mut) NSCLC patients either at baseline or at the time of at failure to tyrosine kinase inhibitor (TKI). Ten ml of blood sample were collected and centrally analyzed. Blood samples were centrally analyzed by ddPCR. Clinical and molecular data were also recorded. We assessed the liquid biopsy sensitivity at baseline for activating *EGFR* mutations (*EGFR*mut) and at progression for activating and T790M resistance *EGFR* mutations. **Results:** A total of 70 samples (15 collected at baseline and 55 at disease progression) were collected in 41 patients included (27 (66%) with *EGFR* exon 19 [Del19], 14 (34%) with *EGFR* exon 21 mutations [L858R], median age of 62 years, 27 (66%) were females, 27 (66%) never-smokers and 37 (90%) had adenocarcinoma). At the moment of sample collection, patients had a median number of 3 metastatic sites [range: 1-6]. At baseline, ddPCR detected 87% of cases (13/15) with an *EGFR*mut; 90% (9/10) and 80% (4/5) for Del19 and L858R, respectively. The 2 negative cases had single sites of progression in bone and pleura, respectively. At disease progression, *EGFRmut* by ddPCR was detected in 55% (30/55); 58% (22/38) for Del19, and 47% (8/17) for L858R. Of note, brain was the most common site of progression (42%). Among the cases with activating *EGFRmut* detected in blood at progression after first and second generation TKI, the *EGFR* T790M mutation was found in 35% (6/17) samples. The median number of metastatic sites was 4 [2-4] in T790M-positive vs. 2 [1-5] in T790M-negative. In patients with isolated central nervous system progression (iCNS), *EGFRmut* was detected in 33% (5/15), and 2 cases had *EGFR* T790M. In patients with isolated thoracic progression, 60% (9/15) had positive *EGFRmut*, among who one case had the *EGFR* T790M mutation. **Conclusion:** Liquid biopsy by digital PCR is a high sensitive tool for *EGFR* detection at diagnosis. At progression, liquid biopsy positivity for activating and resistance mutations was more likely observed in case of systemic progression and a high tumor burden. ddPCR could be used to provide a rapid molecular result to guide treatment selection in NSCLC. **Keywords:** EGFR, digital PCR, NSCLC

P34.07
Quantification of BIM mRNA In Circulating Tumor Cells Of Osimertinib-treated Patients with EGFR Mutation-positive Lung Cancer

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Introduction: Osimertinib has a high response rate in untreated epidermal growth factor receptor (EGFR) mutation-positive non-small cell lung cancer (NSCLC) patients. However, currently there are no biomarkers to determine the efficacy of osimertinib. This study investigated whether BIM-γ mRNA expression in circulating tumor cells (CTCs) predicted a poor prognosis of osimertinib treatment in patients with EGFR mutation-positive NSCLC. **Methods:** Patient selection criteria included EGFR-tyrosine kinase inhibitor untreated NSCLC patients with advanced stage or postoperative recurrence with EGFR sensitive mutations (exon19 deletion or L858R mutation). Informed consent was obtained from the participants. The candidate biomarker