Introduction
Lung cancer remains the most common cause of cancer death worldwide. Approximately 70% of patients with non-small cell lung cancer (NSCLC) come to clinical attention at an advanced stage for the first time. These patients have no surgical options, and the only pathologic diagnostic material guiding systemic therapy should be small biopsy or cytological specimens.

Many investigators have reported cytological material obtained with minimally invasive procedures was adequate not only for accurate histological subtyping but also for molecular profiling. Cytology specimens provide high quality DNA for the evaluation of clinically relevant mutations. In our lab, we have increasingly used cytology specimens for molecular testing when cytology material was the only specimen source available.

The purpose of our study is to explore the establishment of content assessment system for tumor cells and the comparison of detection methods for target gene in liquid-based cytology samples from non-small cell lung cancer (NSCLC).

Methods
Tumor cell content was assessed by the number of tumor cells in HE smear and the pellet size of residual liquid-based cytology samples from 102 NSCLC. The consistency of targeted genes mutation status of paired samples was evaluated by amplification refractory mutation system (ARMS PCR), and the tumor cell content evaluation system for residual liquid-based cytology samples was established. 207 residual liquid-based cytology samples were collected and assessed by tumor cell content evaluation system, the mutation status of EGFR gene was detected by ARMS PCR and Super-ARMS PCR respectively, and then these two methods were compared by sensitivity and accuracy.

Results
Mutations of EGFR/ALK/ROS1 gene in 102 paired cytology samples detected by ARMS PCR were completely consistent and the total positive rate was 52.9% (54/102). The DNA quality from remaining liquid-based cytology group was good, and the number of tumor cells or the diameter of pellets is the key factor affecting DNA concentration. The results of HE smear group were unaffected despite its poor quality of DNA. EGFR mutation rates detected by ARMS PCR and super-ARMS PCR were 40.1% (83/207) and 44.9% (93/207) respectively. The total coincidence rate of the two methods was 95.2%, with the 100% positive coincidence rate and 91.9% negative coincidence rate. 12 samples with inconsistent EGFR mutation results were verified by digital PCR and second-generation sequencing methods. The results showed that 3 samples could not be verified, 7 samples were consistent with super-ARMS PCR results, and 2 samples were inconsistent.

Conclusions
Combination of the number of tumor cells and the size of sediment can be effectively used to evaluate tumor cell content before targeted gene detection. Both ARMS PCR and super-ARMS PCR can be used to detect targeted genes in liquid-based cytology samples, while for cytological samples with less tumor cells, sensitive detection method can be selected to reduce the probability of false negative.

Bibliography