Summary

Introduction: Current guidelines for treatment of lung cancer and lung metastases are based on morphology of the tumor and clinical stage of the disease. Correct determination of disease stage allows us to choose the optimal treatment therefore it is mandatory to determine the TNM classification as accurately as possible. State of lymphatic nodes together with the size of the primary tumor and the number of the metastases determine the adjuvant oncological therapy. According to guidelines, standard oncological treatment of pulmonary cancer, consist in radical removal of tumor tissue and in systematic nodal dissection, or more precisely in the specific lobar lymphadenectomy in indicated cases. The removed nodes are subjected to standard histopathological evaluation, which is able to reliably identify macrometastases, although micrometastases may not always be detected. There may be a situation, when lymph nodes are not found to be affected by cancer dissemination during the common histopathological evaluation, but may still contain micrometastases. Since carcinomas are tumors of epithelial origin, their essential proteins of intermediate cytoskeleton are the cytokeratins (CK). This fact can be used to detect micrometastases in regional lymph nodes. Since unaffected lymph nodes are formed by connective tissue and immune system cells where no cytokeratins are present, the verification of cytokeratins in removed lymph nodes is an indicator of the metastatic process in this tissue. There is a wide range of CK, but the most specific for diagnostic process in primary lung tumor or lung metastates of carcinoma is CK19. The possibilities of detection of CK19 offer evaluation of CK19 and also molecular-genetic method OSNA (One-Step Nucleic Acid Amplification) based on an assessment of mRNA CK19 by RT-LAMP method (Revers Transcription – Loop-Mediated Isothermal Amplification).

Aim: The aim of our study was to verify the possibilities of more sensitive detection of micrometastases in regional lymph nodes in patients with lung cancer or with pulmonary metastases of colorectal carcinoma due to IHC CK19 and OSNA method in comparison with HE staining and the assessment of the presence of micrometastases in nodes to follow-up these patients.

Material and methods: 100 surgically treated patients for primary non-small cell lung tumor or pulmonary metastases of colorectal carcinoma were enrolled to our study in the period since February 2013 to November 2017 in Surgical Department of Faculty Hospital in Pilsen. The whole cohort was surgically treated by posterolateral thoracotomy. Lobectomy was the smallest procedure in case of primary lung tumor. In lung metastases, the extent of procedure was

determined by the number, size and location of the metastases. Simultaneously, systematic nodal dissection was performed in all patients. All nodes were examined by three different methods: HE staining, immunohistochemically with CK19 antibody and by OSNA method. All obtained results were compared and statistically processed.

Results: From achieved results of an evaluation of 1429 of lymph nodes in 100 patients indicate that the most accurate diagnostic method of examination of lymphatic nodes is molecular OSNA method, where the rate of up-staging was 16% in comparison to the histologic method. Contrary to our expectation, the immunohistochemical method in comparison to the standard recommended histopathological methods of lymph nodes evaluation looks appears to be without contribution. Overall survival contrary to our expectation did not change significantly, although the follow-up is still short.

Conclusion: Our results show, that in comparison with standard histopathological method of examination of lymphatic nodes, the immunohistochemical method appears to be without any contribution because the results obtained due to this method were compared to the results of histopathological methods. The most accurate diagnostic method of evaluation of lymph nodes for the presence of metastatic process of epithelial lung tumors or lung metastases of the epithelial tumor (in our study the lung metastases of colorectal carcinoma) is the OSNA method. By introducing these methods into routine practice would lead to up-staging of disease in patients, whose clinical stage of disease was during the examination by standard histopathologic method underestimated, and these patients would receive adequate adjuvant oncologic therapy, which is fully indicated in case of the metastatic process in lymph nodes, or more precisely in a higher stage of the disease. The overall survival, contrary to our expectation, was not statistically changed, although according to our opinion, following closely monitoring of these patients is mandatory.