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Title: Subtyping agreement between small cyto-histological samples and surgical specimens in NSCLC patients

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Body: Background: NSCLC subtyping is crucial to select patients for chemotherapy or target therapy and provides prognostic information. In most patients, therapeutic decisions are based on small cyto-histological samples. Aim: To evaluate subtyping agreement between small samples and surgical specimens in surgically treated NSCLC patients. Methods: Subtyping obtained in small samples and surgical specimens was compared in NSCLC patients submitted to tumour resection between 1999 and 2012. Results: 213 patients were included. Diagnosis was obtained in cytological specimens in 58.6% and small biopsies in 41.4%. 160 (75.1%) cases had absolute agreement in subtyping, 35 (16.4%) were classified as NSCLC not otherwise specified (NOS) and in 18 (8.5%) subtyping was inadequate. The accuracy of NSCLC subtyping was statistically inferior in cytological specimens (66.4%) compared to small biopsies (88.1%; p<0.001) and inferior in poorly differentiated tumours (63.6%) compare to well differentiated (92.3%; p<0.001). In the two periods analysed (1999-2007 vs. 2008-2012), there was a significant decrease in the NSCLC, NOS (18.8% vs. 14.3%) and in the inadequate subtyping (10.9% vs. 6.3%). Conclusion: Lung cancer subtyping in small cyto-histological samples was very accurate. In recent years, there was an improvement in adequate subtyping probably due to the increase use of immunohistochemistry and reduction of cytological samples.