SUMMARY

The actual dissertation is the result of Olena Koshyk's doctoral study at Charles University in Prague, Faculty of Medicine in Pilsen, from 2019 to 2023. The author focused the main part of her research on rare salivary gland tumors but also participated in studies related to sinonasal soft tissue tumors. The studies used a wide range of investigation methods including morphology, immunohistochemistry, and molecular genetic methods in order to provide new insights for accurate tumor diagnosis and to propose novel approaches and refinements in the classification of selected head and neck tumors.

The dissertation is divided into two parts. The first part represents four articles that present the latest data on rare salivary gland tumors.

The first paper concentrated on the new rare oncocytic variant of mucoepidermoid carcinoma with comprehensive morphological and immunohistochemical descriptions, and molecular alterations. Special attention was paid to the differential diagnosis with oncocytic tumors for accurate diagnosis.

The second study covered a clear cell subtype of myoepithelial carcinoma which showed *EWSR* gene rearrangements. Different fusions in *the PLAG1* gene were found in such tumors but fusion transcripts for *the EWSR* gene were not detected. The study also focusses on a comparison of the biology of myoepithelial tumors of the salivary gland and soft tissues and skin.

In the third article, rare *NR4A2* rearrangements in acinic cell carcinoma are discussed. We also investigated NR4A3 and NR4A2 immunostains as a cost-effective method for the accurate diagnosis of acinic cell carcinoma and surrogate markers of the gene rearrangements.

The next study is devoted to the newly reclassified neoplasm, sclerosing polycystic adenoma of the salivary gland. For the first time, diagnostic criteria for low-grade and high-grade dysplasia in the solid and cribriform epithelial proliferations in sclerosing polycystic adenoma were presented. We reported the molecular profile of these benign tumors with *PIK3CA*, *HRAS*, and *AKT1* mutations. In our work, we presented a unique case of a salivary gland apocrine intraductal carcinoma with transformation to salivary duct carcinoma, arising from sclerosing polycystic adenoma harboring a mutation in the *PI3K/Akt* pathway in all tumor components.

The second part represents two rare mesenchymal sinonasal malignant entities. First is the rare phenomenon of biphenotypic sinonasal sarcoma with *PAX3::MAML3* fusion with

transformation into high-grade rhabdomyosarcoma. The differential diagnosis and the mandatory use of molecular testing were discussed.

The last study covered a completely new aggressive polyphenotypic sarcoma with *EWSR::POU2AF3* fusion with sinonasal predilection. This type of sarcoma has only been described in two studies, where overall 11 cases of small round cell/spindle cell sarcoma with a novel *POU2AF3* rearrangement were presented. We analyzed 8 of our own cases and 11 cases from both previous studies. The subgroups with low and high-grade morphologies, were described for the first time, with comprehensive immunohistochemical and molecular characteristics, inlcuding the *EWSR1::POU2AF3* and *FUS::POU2AF3* fusion transcript, providing the evidence of a single entity with a wide morphological spectrum.