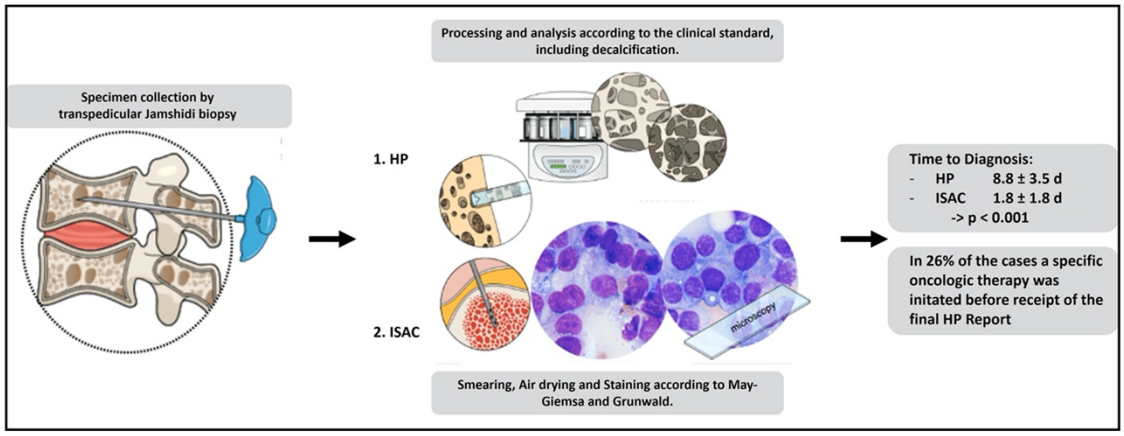
Introduction:
A metastatic spine disease (MSD) is in up to 20% of cases the initial sign of a cancer of unknown primary (CUP). If an MSD is suspected, it is crucial to confirm the diagnosis and identify the primary as quickly as possible. Histopathological (HP) examination is the diagnostic gold standard. However, HP can take up to 14 days due to the decalcification of bone samples. Intralesional spinal aspiration cytology (ISAC) has not been routinely performed in spine surgery, although it allows a shorter time to diagnosis (TTD) and the safe differentiation between hematologic and solid neoplasms. In 2020, complementary ISAC was introduced in our clinic as part of a multidisciplinary approach to shorten TTD in patients (pts) with MSD and CUP.
Methods:
As part of initial spinal surgical care, ISAC is performed by a transpedicular Jamshidi biopsy. This involves aspiration of 3-5 ml of spinal bone marrow in 2 ml of citrate using a syringe. The cytological samples are stained according to May-Grunwald and Giemsa and evaluated by a board certified hemato-oncologist. The HP specimens are also obtained and analyzed for final diagnosis confirmation according to the clinical standard. A retrospective statistical analysis comparing the TTD of ISAC and HP was performed using Student's t-test. Cohen's kappa was used to interpret the concordance of ISAC and HP.
Results:
To date, 50 pt (38% female) with a mean age of 48.9 ± 30.1 y were included. In five pts (10%) benign lesions were diagnosed. Hematologic- and solid neoplasia were diagnosed via HP in 11 pts (22%) and 33 pts (66%), respectively. ISAC was able to detect malignant lesions in relation to the reference pathology with a sensitivity of 0.97, a specificity of 0.80, and a diagnostic certainty of 0.9. In addition, the distinction between hematologic and solid malignant neoplasms concerning the reference pathology could be made with a concordance of 95% (Chone's kappa 0.90). The mean TTD using ISAC was 1.8 ± 1.8 d, whereas HP took 8.8 ± 3.5 d ($p < 0.001$). In addition, in 13 pts (26%), specific systemic oncologic therapy could be initiated before the final HP report was available, based on clinical parameters, staging, and ISAC.
Discussion:
Based on the currently presented data, it can be said that ISAC can be performed safely in the context of spine surgery, it has a high sensitivity (0.97) and specificity (0.80) as well as diagnostic certainty (0.9) in terms of identification of malignant lesions. In addition, it can distinguish between solid and hematologic malignant lesions with high concordance to the reference pathology (Cohen's kappa 0.90). TTD is significantly shortened by ISAC ($p < 0.001$) and specific oncologic therapy can be initiated in up to 26% of cases before receipt of the final HP report. For these reasons, ISAC complementary to HP should become the clinical standard to increase patient safety and shorten TTD and time to treatment.



Graphic 1: Graphical abstract*. This graphical abstract provides an overview of the sample collection procedure and sample processing for histopathology (HP) and intralesional spinal aspiration cytology (ISAC). It was shown that a significantly shorter time to diagnosis (TTD) could be achieved using complementary ISAC, compared to HP ($p < 0.001$). In addition, in 26% of the cases, specific oncologic therapy could be initiated before the final report of HP was received, based on information from ISAC in combination with clinical parameters and staging.*