Subtyping of rare types of gastric carcinomas and organoids for diagnostics using MALDI imaging [ID 253]

Pia Hönscheid[1,2,3], Linna Sommer[1,2,3], Patrick Moller Jensen[3,4], Jan Lellmann[5], Christian Sperling[1,3], Daniel Stange[6,2,3], Daniela Aust[1,2,3], Herbert Thiele[5,7], Gustavo Baretton[1,2,3]

1: Institute of Pathology, Medical Faculty and University Hospital Carl Gustav Carus, Technical University Dresden, Dresden, Germany
2: National Center for Tumor Diseases Dresden, Germany
3: German Cancer Consortium, Dresden, Germany
4: Department of Applied Mathematics and Computer Science, Lyngby, Denmark
5: Institute of Mathematics and Image Computing, Universität zu Lübeck, Lübeck, Germany
6::Department of Visceral, Thoracic and Vascular Surgery, Medical Faculty and University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany
7: Fraunhofer Institute for Digital Medicine MEVIS, Lübeck, Germany

Gastric carcinomas are an extremely diverse group of tumors that can be divided into histologically different subtypes. Diagnostic methods and tumor markers are of great interest to improve early detection and identify new therapeutic targets. MALDI imaging detects protein and peptide masses projected onto geometric coordinates and aligned with the microscopic image to advance rapid proteomic diagnostics of cancer subtypes. The presented study shows that the histological morphology defining gastric cancer subtypes can be reproduced by the MALDI spectra and demonstrates the potential of data-based analysis of tumor tissue on a minimal amount of tissue. **Organoids** are histologically difficult to be traced back to the original tumor tissue. Based on their specific peptide fingerprints, they could be assigned to the corresponding patient sample and showed a higher degree of compatibility than other analogous samples. **30 FFPE gastric cancer tissue and 5 organoids** were analyzed. Each sample contained both tumor and normal tissue for classification and validation of the validation of the mass spectra. In this analysis, for example, **mass peaks 1441, 1775 and 2886 m/z** were associated with gastric tumor areas. The transferability and comparability from one sample to another was calculated by leave-one-out classification. Mass spectra of unknown tissue that matched the reference tumor spectra yielded positive predictive values of up **to 77 %. Overall**, the classification of organoids and donor tissues was **on average 54 %** successful and needs to be improved by sample size and training method.

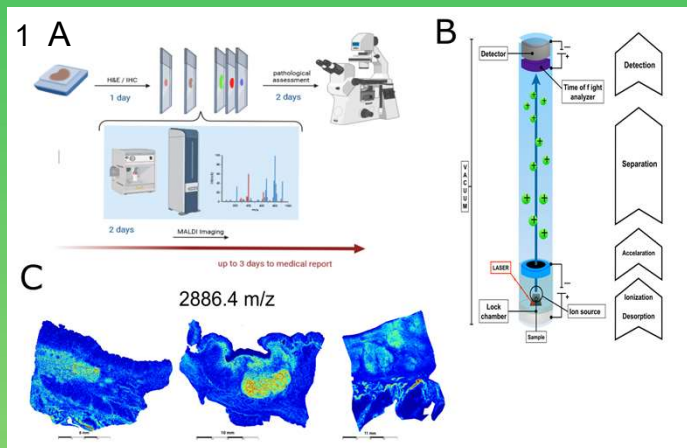


Fig. 1: (A) workflow (B) MALDI TOF principle (C) Tumor peak identification on stomach cancer

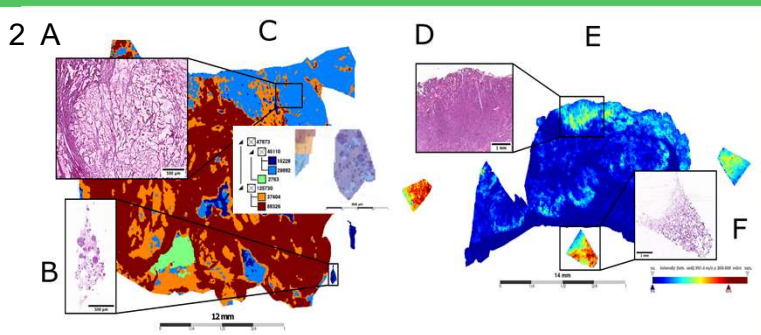
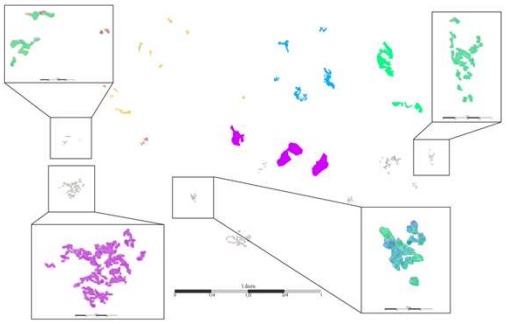
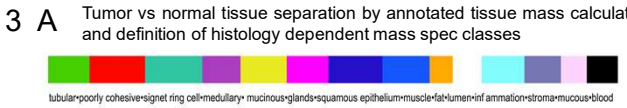
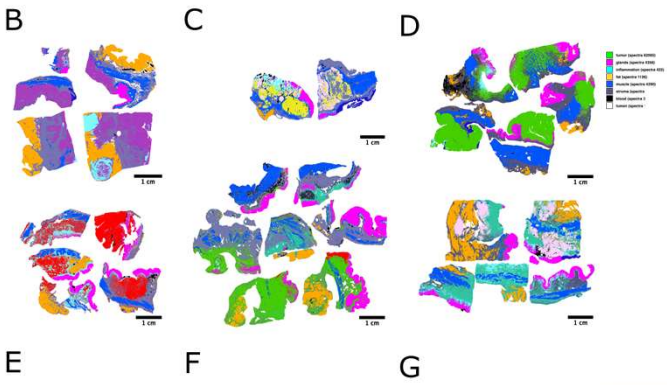


Fig. 2: (A) whole section (B) organoid with segmentation and tree (C) Tumor tissue (D+E) Tumor tissue and corresponding organoid intensity map of 901.6 m/z (F)

Right: Organoid classification of 4 different stomach cancer types and corresponding primary tumors (color map)







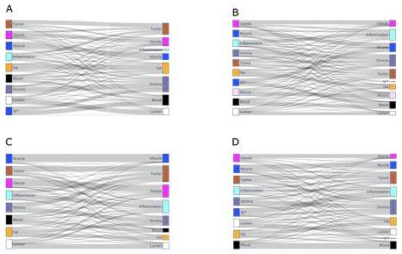


Fig. 3: (A) color map of training ROI (B) medullary (C) mucinous (D) tubular (E) poorly cohesive (F) mixed (G) signet ring cell

Left: Leave one out classification (LOC) to reveal similarities and differences between tumor classes and normal tissue types

A collection of 30 (39 total) formalin-fixed paraffin-embedded gastric cancer samples has been provided by the Institute of Pathology Dresden, Germany. Specimens were collected based on gastric cancer type, molecular stratification and specimen quality. All samples were pathologically assessed and label annotations were double-checked by pathologists for this study. Tumor grading was performed according to the standard WHO and Lauren classification. Tumor subtypes classified by WHO were medullary (n=5), signet ring cell (n=5), poorly cohesive (n=5), mucinous (n=5), tubular (n=5), mixed type (n=4). Tumor subtypes classified by Lauren were diffuse (n=10), intestinal (n=8), intermediate (n=5). Each tumor type can be assigned a mass signature based on its mass occurrence . The selection of tumor (2886 m/z) and normal tissue (1045 m/z) representative peaks alone shows a histologically comprehensible picture of the intensity distribution of masses in tumor, muscle and gland (C). Calculated mass signatures of training cohort (training spectra per class n=20/100) can identify the tumor areas of an unknown tissue and classes of tissue compartments are used to label the entire samples (Fig. 3).. Using the leave one out classification (LOC) principle show the quality of tissue recognition by MALDI imaging and how the classes are related. Gastric cancer organoids show correlation between primary tumors of each tumor subtype by comparing their mass spec signature. Supervised and unsupervised clustering of tumor tissue and corresponding organoid show high analogy and same class affiliation (Fig. 2).

DKTK German Cancer Consortium

IMSIS 2024 Münster

dkfz. German Cancer Consortium Partner site Dresden