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Analysis of paraffin-embedded slides of esophageal carcinoma after different treatments using QuPath

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Introduction :

The microscopic tumor extension during or after radiochemotherapy and its correlation with the tumor microenvironment are presently unknown. This information is, however, crucial in the era of image-guided high-precision photon or particle therapy. Therefore, we analyzed immunohistochemically stained paraffin-embedded tumor resection specimen from esophageal carcinoma patients, having undergone neoadjuvant radiochemotherapy followed by resection (NRCT+R) or resection (R) alone. Both, the overall distribution as well as the co-localization of markers with hypoxic tumor subvolumes were assessed.

Patient characteristics and treatment regimen :

This project comprised of four patient cohorts [n=20; five NRCT+R and five R from each, squamous cell carcinoma (SCC) and adenocarcinoma (AC)]. The NRCT+R treated patients received an irradiation dose of 40 Gy in 2 Gy/day fractions over four weeks. The chemotherapy regime combined two different drugs, SCC patients received Cisplatin and 5-Fluorouracil (5-FU), while AC patients were treated with Carboplatin and Paclitaxel. All ten NRCT+R patients underwent surgery between five to seven weeks after the end of NRCT.

Materials and Methods

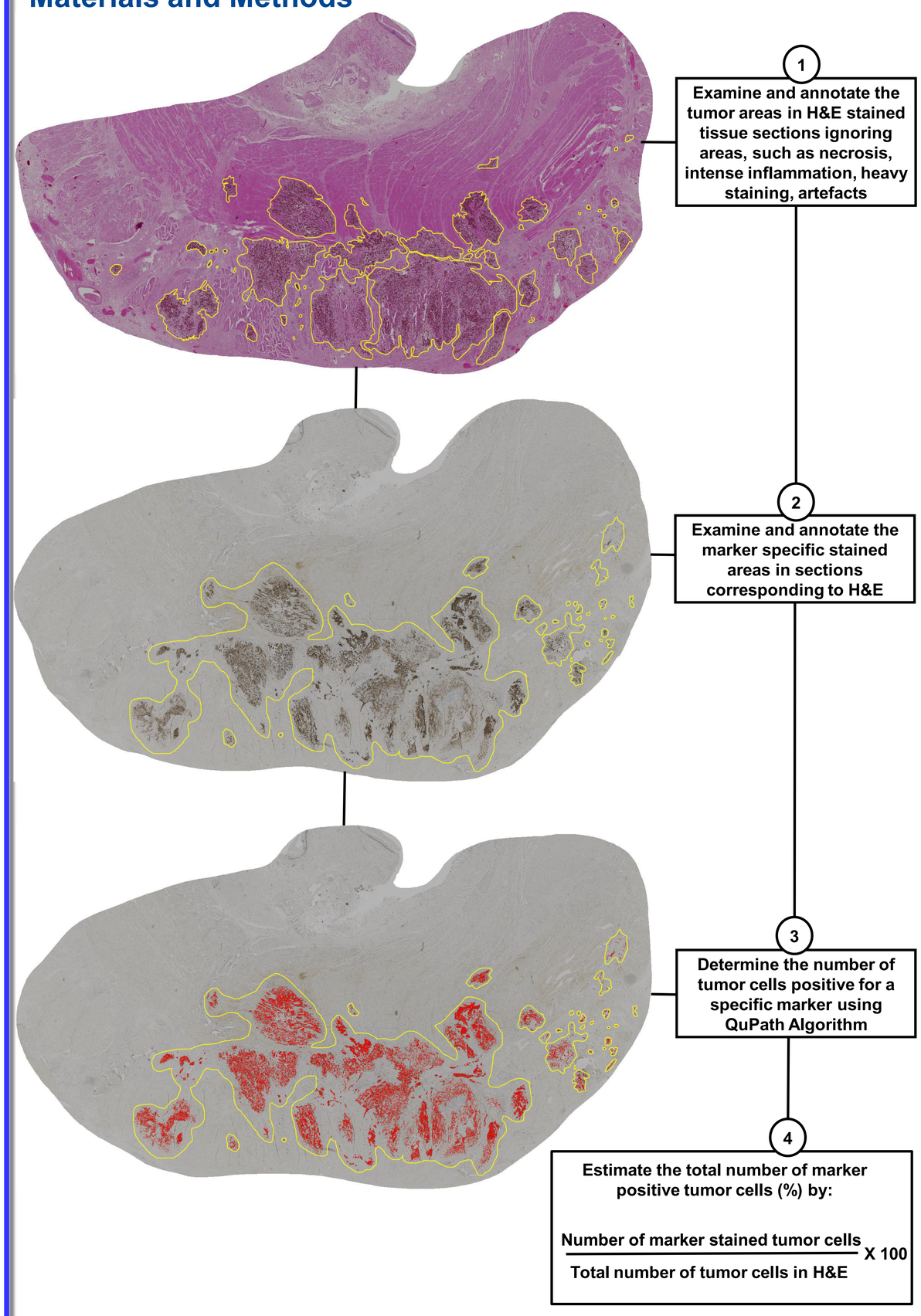

Fig. 1. Workflow for assessment of the percentage of tumor cells positive for a specific marker.

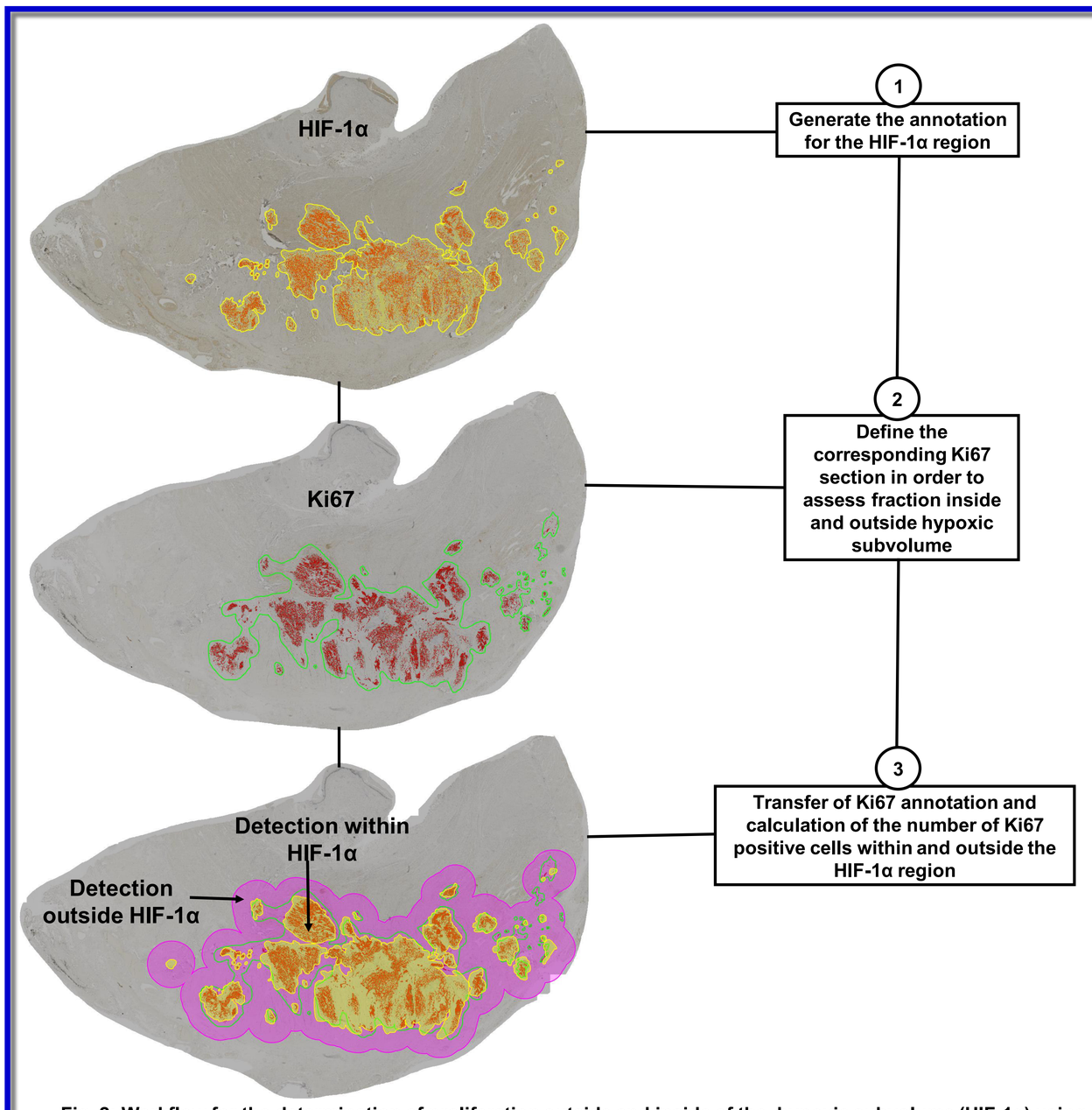

Fig. 2: Workflow for the determination of proliferation outside and inside of the hypoxic subvolume (HIF-1α) using the QuPath Distance to annotation command.

Results

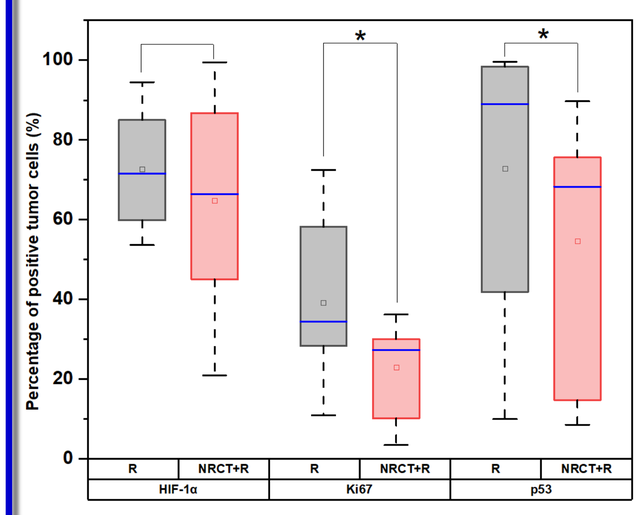

Fig. 3: Squamous cell carcinoma cells positive for one of the assessed markers
* p<0.05 ** p<0.01 *** p<0.001: Mann-Whitney test

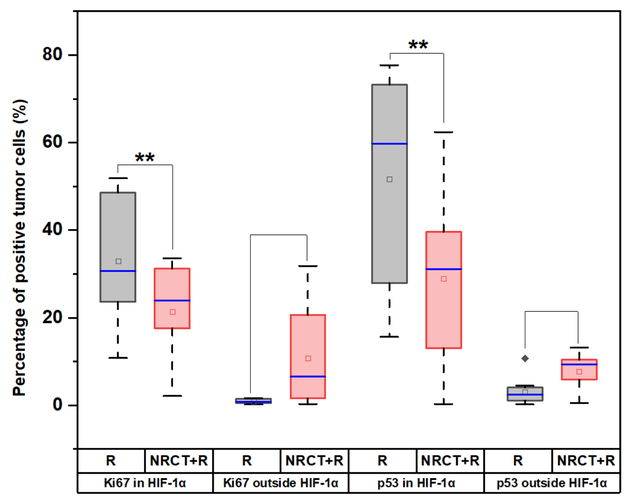

Fig. 4: Adenocarcinoma cells positive for a marker depending on hypoxia (HIF-1α)
* p<0.05 ** p<0.01 *** p<0.001: Mann-Whitney test

- In tumor resection of patients with SCC, the Ki67 and p53 tumor positive cells overall were statistically significantly lower in the NRCT+R than in the R cohort (Ki67: p=0.021, p53: p=0.044; Fig.3).
- Conversely, Ki67 or p53 tumor positive cells within hypoxic regions were statistically significantly lower in patients with AC having received NRCT+R compared to R (Ki67: p=0.005; p53: p=0.003; Fig.4).

Conclusion and Outlook:

In this cohort of esophageal carcinoma resection specimen, a quantification workflow to assess the microscopic tumor extension after different treatments [NRCT+R or R alone] was established. Changes in the tumor microenvironment induced by NRCT were detected in both SCC and AC. A larger study is planned to validate these preliminary results.

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