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Machine learning & a novel patch sampling approach to generate biomarker cervicograms

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Aims

Demonstrate the utility of molecular lesion stratification using a non-invasive approach that preserves spatial architecture together with machine learning to identify clinically-relevant lesions

Background

Screening for cervical cancer precursors is by the detection of HPV DNA, due to its high sensitivity. However, mere presence of DNA doesn't correlate to HSIL and DNA screening has low specificity on its own, leading to a near tripling in colposcopy referrals. Thus, there is a clear requirement for a sensitive and specific HPV triage test.

Methods

We utilise a novel patch sampling approach to obtain the cervical surface cells together with spatial preservation. Patients attending colposcopy had a pre & post-acetic acid photo, interspersed by patch sampling. 17 patients with a high-grade smear and subsequent histology proven HSIL were recruited in one arm vs. 24 patients with LSIL. This patch was then probed with antibodies to MCM (HSIL) and E4 (LSIL). The signal for each antibody was analysed by a machine learning algorithm enabling the generation of a molecular heat-map of the cervical surface.

Results

Our approach safely samples the cells at the cervical surface. This in-situ approach facilitated the identification of entire MCM positive (HSIL) / E4 positive (LSIL) lesions. These patterns were correlated to the underlying histology with a HSIL sensitivity of 88%, PPV of 79% and an AUC of 84% ($p < 0.01$). Next, we successfully trained a machine learning algorithm to identify entire lesions which improved diagnostic objectiveness vs. cytology triage.

Conclusions

Our novel approach of in-situ cervical biomarkers is effective in identifying HSIL. Moreover, combining MCM with E4 enables objective discrimination of HSIL vs. LSIL. This coupled with machine learning provides a personalised molecular cervical surface map for HPV triage, reducing unnecessary