AI-Assisted Detection of Sentinel Lymph Node Metastasis in Penile Squamous Cell Carcinoma: Reducing Immunostaining Dependence

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Introduction

Dynamic sentinel lymph node biopsy (DSLNB) is the standard for staging inguinal lymph node involvement in cN0 penile carcinoma (PSCC) cases. Evaluation of SLNB follows RCPath guidelines (1), incorporating Immunohistochemical (IHC) staining in all H&E-negative cases to exclude micro-metastatic deposits. This introduces additional costs and delays in the diagnosis and management of patients. A.I. algorithms have been developed for identification of lymph nodes metastasis mainly in breast and colon cancer, with consistent and reliable results (2,3). The present study aims to investigate the applicability of a commercially available A.I. algorithm (4), initially trained and validated for adenocarcinomas, in detecting Squamous Cell Carcinoma (SCC) metastasis in PSCC DSLNBs.

Materials and Methods

A total of 138 H&E-stained DSLNB slides from 107 cases were consecutively selected from the available clinical samples and subsequently scanned with a Hamamatsu S60 at 40x of magnification. The cohort was analyzed using the Visiopharm APP 10159 A.I. algorithm that was trained and validated in breast and colon cancer lymph node metastases (2,4).

The PSCC DSLNB status was determined using initial H&E slides from standard clinical diagnoses, the ground truth was defined by positivity in two pancytokeratin IHC markers supplemented: MNF116 and AE1/AE3. (Fig 1. A,B)

The algorithm classified results into four categories: Positive, Very Suspicious, Suspicious, and Negative. For this study, we defined "positive" as the first three categories. (Fig 2, A to F)

Accuracy, sensitivity, and specificity were calculated against the established ground truth.

Results

Out of the 138 slides, 50 (36%) were labelled as positive by morphology and pancytokeratin immunostaining.

The algorithm flagged 69 (50%) slides as “Positive” for metastatic involvement. All cases classified as “Negative” by the algorithm (63 cases) were true negatives. Six cases classified as "Suspicious" or "Very Suspicious" by the algorithm (6/25 cases) were true positive (5 micro-metastases and 1 with extensive tumour necrosis).

Overall, the algorithm reported 50 true positives, 63 true negatives, 25 false positives, and no false negatives. The model showed an accuracy of 0.82, sensitivity of 1.00, and specificity of 0.72, with a negative predictive value of 100%.

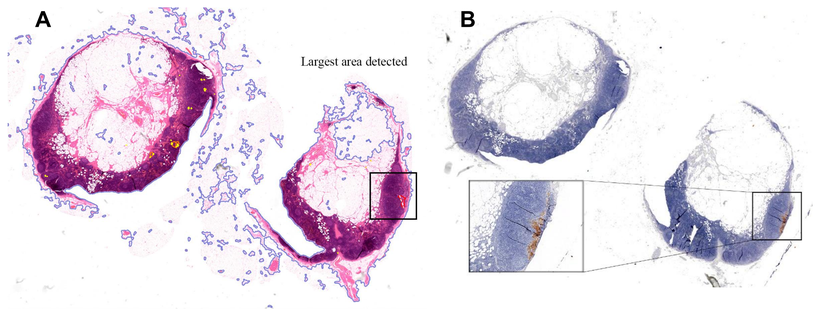

Figure 1. A. H&E, and B. AE1/AE3 Immunohistochemistry: Note how the A.I. algorithm marks the suspected area circling it in red on H&E. The metastasis was detected in the clinical setting by the pancytokeratin immunostaining (inset).

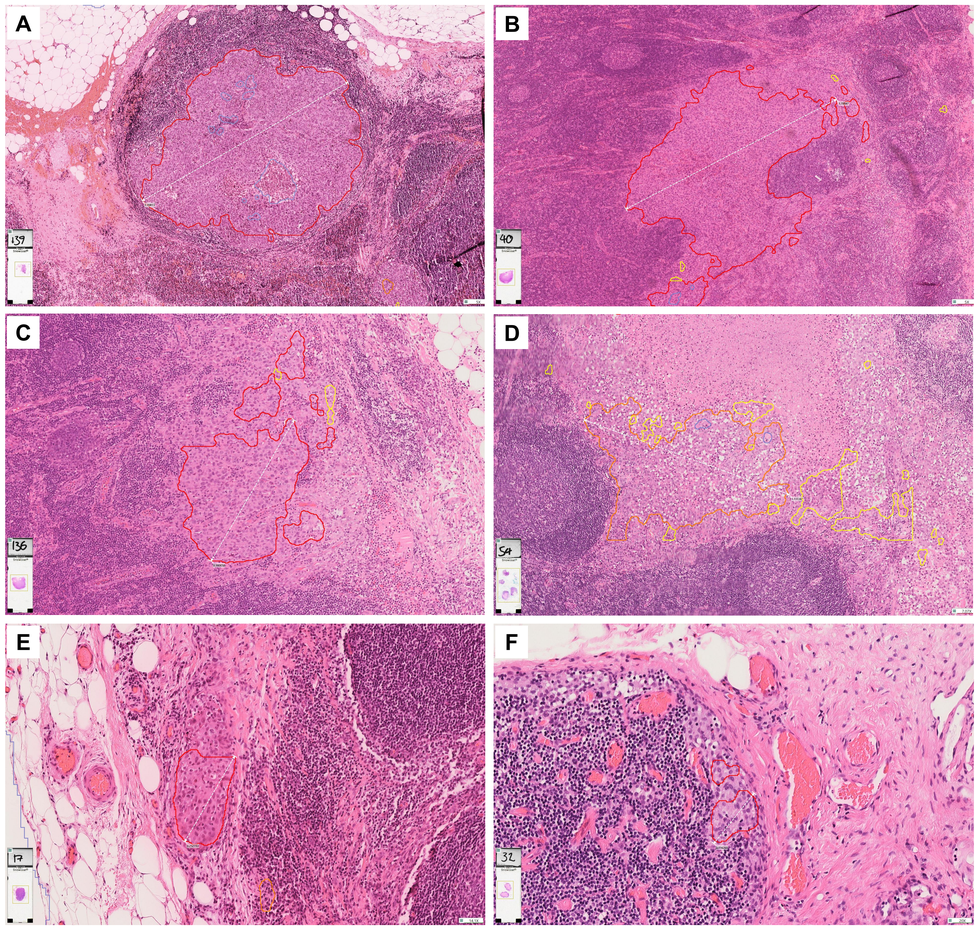

Figure 2. Dynamic sentinel lymph node biopsy samples stained with H&E, classified and marked by the A.I. algorithm. A and B. Cases labelled as “Positive”. **C and D**. “Very suspicious” labelled cases. **E.** small, 0.25 mm and **F.** small, 0.12 mm micro-metastatic cell aggregates were classified by the algorithm as “Suspicious”. The algorithm was tuned for high-sensitivity, avoiding loss of probable metastatic deposits, and requiring pathologist checking for the highlighted area.

Discussion

The introduction of sentinel lymph node biopsy (SLNB) has revolutionized surgical pathology, starting with its application in breast cancer and melanoma, and later expanding to other conditions such as PSCC. This expansion has led to increased costs and workforce demands. Moreover, SLNB histopathological procedures are time-intensive, slowing down case processing and delaying final reports. Our pilot study shows that an A.I. solution can effectively address these challenges, as evidenced in breast cancer cases. While initially trained on adenocarcinoma, our findings confirm that this A.I. solution can accurately adapt to squamous cell morphology, underscoring its versatility. However, the development of such systems necessitates pathologist oversight to ensure validation and clinical reliability.

To our knowledge, this is the first study evaluating A.I. for SLNB metastasis detection in PSCC. Given the rarity of PSCC, the broader impact of A.I. applications in this context may be limited to specialist referral centres. However, these findings hold potential for translation into other squamous cell malignancies, such as vulvar, cervical, and head and neck cancers, where they could streamline workflows by reducing unnecessary IHC requests. Considering PSCC as a case study, applying the current algorithm without any further parameter tunning would allow to avoid the use of IHC in 46% of the cases (63/138 true negative cases), saving time and monetary resources.

Finally, to ensure widespread adoption in the clinical setting; these algorithms must demonstrate consistent acceptable sensitivity. Further large-scale, multi-centre validation studies are necessary to confirm their suitability for routine clinical practice.

Summary and Conclusions

The A.I. algorithm, despite not being specifically trained on PSCC, showed promising results. It has the potential to reduce the systematic need for IHC staining by accurately identifying negative cases and flagging areas with potential metastasis for further assessment. True negative cases (46%) could be confidently classified as negative, thereby reducing diagnostic delays and costs. Further training and independent validation of the algorithm for PSCC are required to optimize its performance

References

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