Automated Quantification of Mitotic Figures in Patients with Melanoma

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Introduction

Mitotic rate is an important factor for melanoma prognosis

Higher mitotic rate correlates with reduced survival

Provides tailored predictions of prognosis for patients

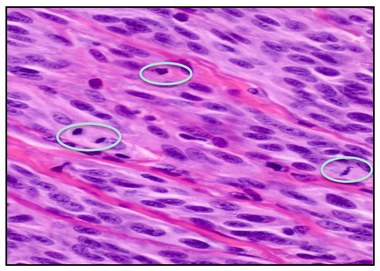

Fig 1: H&E sections showing melanoma cells and mitotic figures highlighted with blue circle

The mitotic rate **(proliferation index)**, is traditionally performed by **manually counting mitotic figures** (see Fig. 1) on hematoxylin-eosin (H&E) stained slides. It serves as an essential component of a pathology report.

However, the key issues with this method are…

- Manual counting is **too time-consuming**
- Inter and intraobserver **variation**
- **Few** mitotic figures in **large sample area**

Goal

This project's aim is to use computational pathology software to produce ***fast***, ***reproducible***, and ***less error-prone*** index computations for tumor regions.

Standard Method	• Count mitotic figures using a **standard light microscope**
Using the Algorithm	• Perform an **overall measurement** of the entire lesion using the **algorithm** • Determine an average per mm^2
Standard Method in Hotspot Only	• Experienced Dermatopathologists will manually identified **hotspot area.** • Mitotic figures will be counted in **1mm^2 sections** within the hotspot
Digital Method in Hotspot	• Will use **HALO from Indica Labs** to count mitotic figures in a 1mm^2 hotspot area after looking at a **heatmap of mitotic figures**

We will compare the findings of all these four measurements against clinic-histologic data

Methods and Results

Manual Counting

Prepare 50 hematoxylin and eosin stained slides from formalin-fixed, paraffin embedded tissue blocks. → Identify the hotspot region using a standard optical microscope → Calculate mitotic figures in 1mm^2 sections within the hotspot

Automated Count

Use algorithm to count the entire tumor surface area for mitotic figures → Find the hotspot region using heatmaps in the software → Count mitotic figures in 1mm^2 sections within hotspot

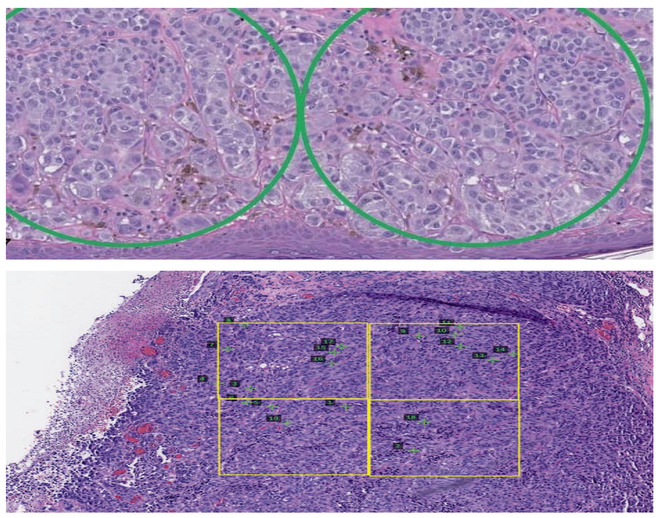

Fig 2: Annotation with 4 squares of 500x 500 µm (A) and 5 circles of 500 x 500 µm (B) on a 1080p monitor (original magnification x20). Illustration of annotation with 4 squares in extended tumor regions. Squares can be arranged in different ways (C and D) (original magnification x4)

Conclusion

Most goals envisioned in the beginning of this project are expected to be **achieved** with automated quantification **nearly matching** manual count

This study will provide data to determine the feasibility of digital counting of mitotic figures in melanoma and it will compare the results with standard, manual counting.

Future Work

1. Improve algorithm to detect mitoses
2. Use a combination of Ki67 (marker for cell proliferation) and MART1 (marker for melanocytes) and perform manual count of dual-stained cells.
3. Automate Ki67/MART1 detection using both QuPath, an open source digital pathology software and HALO by Indica labs.
4. Correlate mitotic count with melanoma prognosis and patient survival.
5. Correlate Ki67 indices (number of Ki67+/MART1+ divided by Ki67-/MART1+) with melanoma prognosis and patient survival.

References

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