The application of reflectance confocal microscopy as a non-invasive imaging tool to improve the diagnostic process of vulvar premalignancies

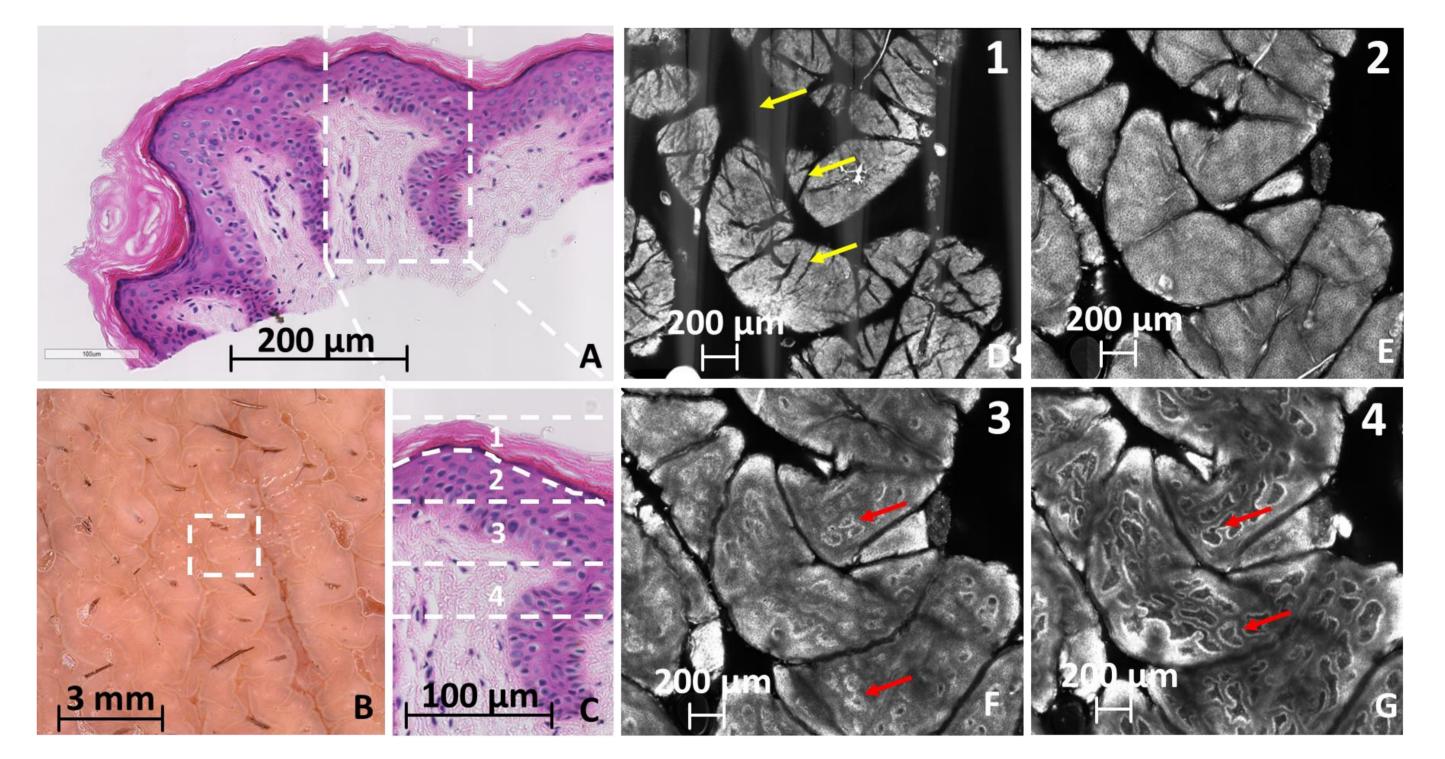
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INTRODUCTION

Incorrect or delayed diagnosis of vulvar high-grade squamous intraepithelial neoplasia (vHSIL) and lichen sclerosus (LS) can have detrimental consequences as both diseases can predispose to vulvar squamous cell carcinoma (VSCC). Recognition of disease margins for biopsy or therapy is challenging. Pathological examination is necessary for VSCC and vulvar HSIL diagnosis. There is a need for improved (non-invasive) tools to recognize vulvar disease. Reflectance confocal microscopy (RCM) is an imaging tool that provides a non-invasive and real-time visualization of the epidermis and superficial collagen layers at a cellular level.

Healthy vulvar skin

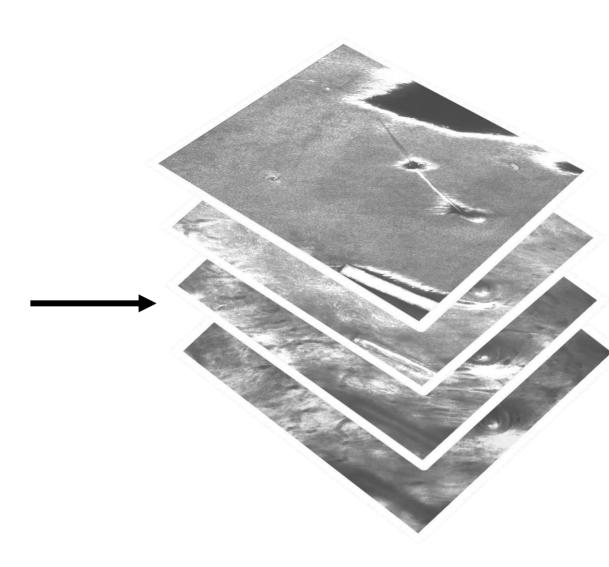


OBJECTIVE

- To explore technical feasibility of RCM on the vulva.
- To describe morphological RCM characteristics of vHSIL and LS.

METHODS

- Prospective, cross-sectional, observational clinical trial
 - 10 healthy volunteers
 - 5 patients with vulvar HSIL
 - 10 patients with lichen sclerosus
- RCM recordings (Vivascope 1500 and 3000)
- Vulvar biopsies



Vulvar HSIL

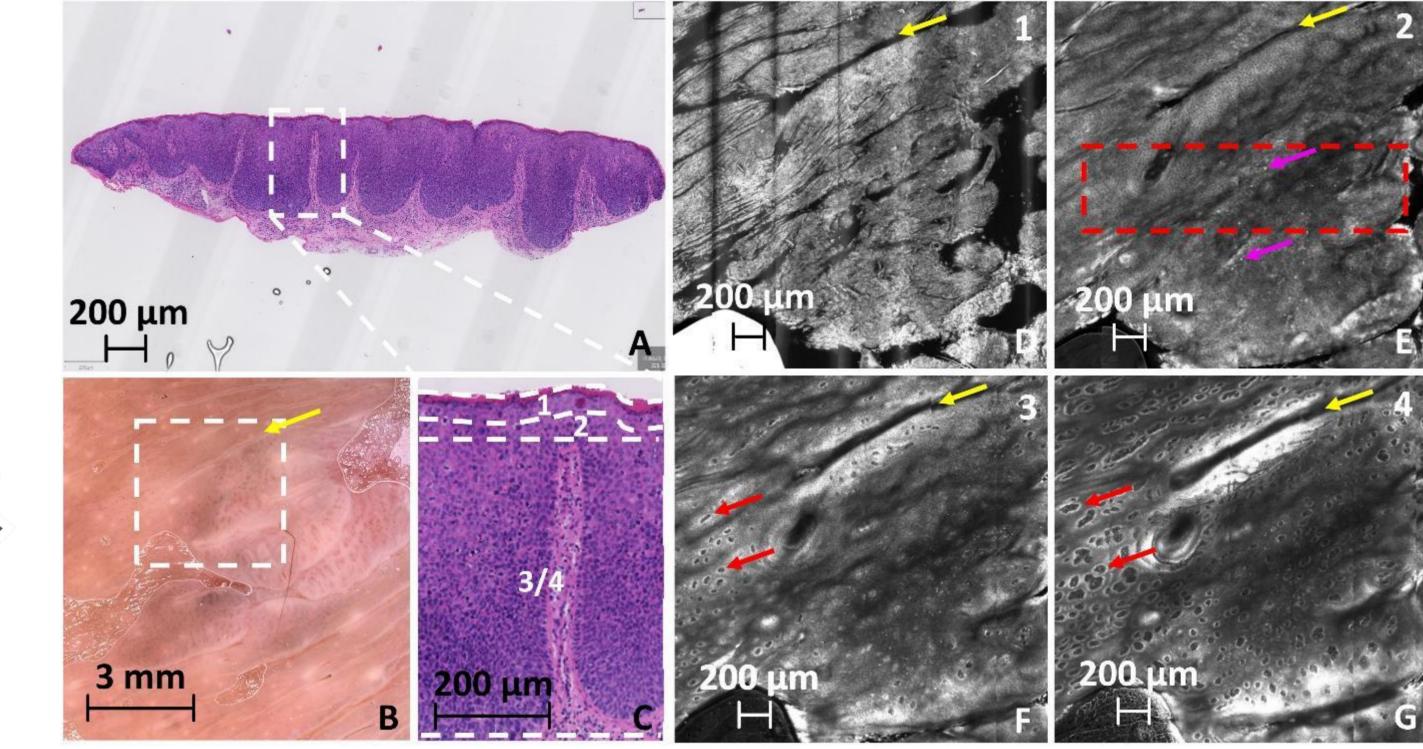




Figure 1: Principle of RCM imaging.

Lichen sclerosus

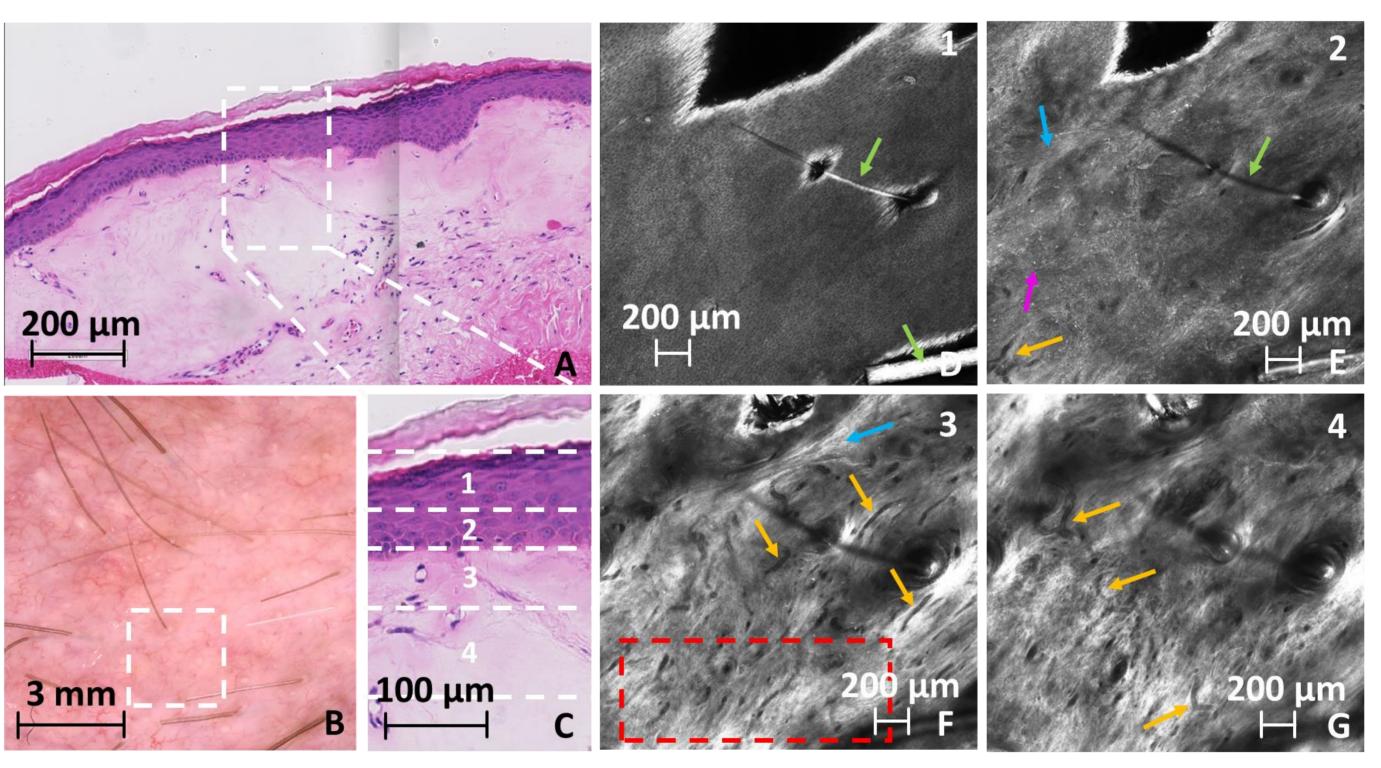


Figure 3: RCM images of representative healthy vulvar skin, vulvar HSIL and lichen sclerosus. A) HE staining of a 4mm biopsy. B) Macroscopic dermatoscopic image of corresponding biopsy with white insert of the closeup of the RCM images in D-G. C) Insert of HE staining represented in A. Dashed areas 1,2,3 and 4 represent skin layers stratum corneum, stratum granulosum, stratum spinosum and epidermal-dermal junction (EDJ), respectively, correlating to the layers shown 1-4 in the RCM images D-G.

- → Hyperkeratosis
- - → Sclerotic vessel

RESULTS

Healthy vulvar skin

• Intact dermal-epidermal junction (DEJ) (100%) Vulvar HSIL

- Atypical honeycomb pattern (75%)
- Melanophage presence (62.5%)
- Lymphocyte infiltration in the dermis (71%) and epidermis (37.5%)

Lichen sclerosus

- Ectatic (63%) or hyalenised sclerotic (68%) vessels
- Dermal sclerosis (71%)
- Lymphocyte infiltration (79%)

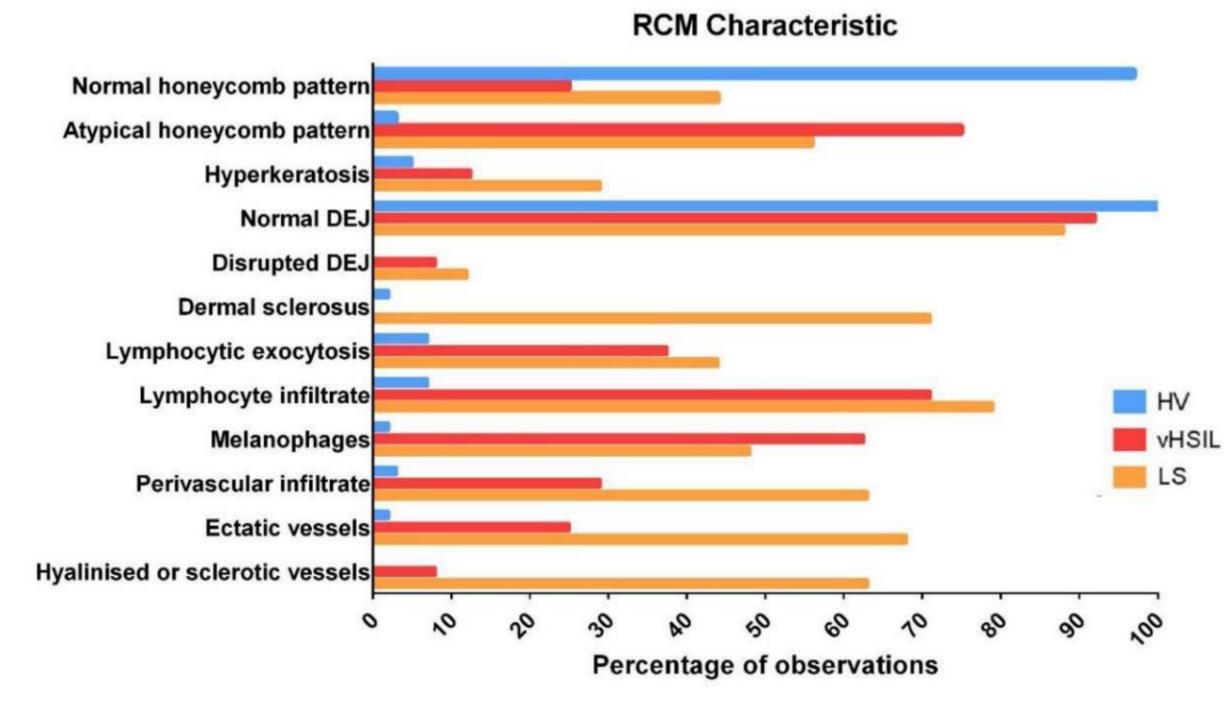


Figure 2: Percentage observed characteristics in RCM images, in HV, vulvar HSIL and LS.

CONCLUSIONS

Practical application of the RCM technique on the vulvar area is feasible and patient-friendly, also in premalignant disease. Morphological features may aid recognition of lichen sclerosus and vulvar HSIL from healthy vulvar skin, although a discriminative set of features per disease could not be identified. This would require expansion of groups and inclusion of additional vulvar diseases, including patients with VSCC.

DEJ Lymphocyte Melanophage Homogenized collagen Ectatic vessel Hair follicle

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