Confocal Microscopy for Special Sites and Special Uses

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KEYWORDS

- Reflectance confocal microscopy
 Special sites
 Mucosa
 Nail
 Tumor
 Infection
 Parasites
- Microcirculation

KEY POINTS

- The in vivo hand-held reflectance confocal microscopy camera allows one to explore skin appendages and oral, genital, and ocular mucosa.
- In vivo and ex vivo confocal microscopy is not only valuable to identify skin cancers but also for the diagnosis of skin infections and inflammatory diseases.
- In vivo reflectance confocal microscopy can be used to guide presurgical mapping of skin tumors.
- Confocal microscopy can provide videos that are particularly useful to study the cutaneous microcirculation.

Video content accompanies this article at http://www.derm.theclinics.com.

INTRODUCTION

In vivo reflectance confocal microscopy (RCM) was initially developed in dermatology for the evaluation of skin neoplasms. Recently, a hand-held (HH) camera (VivaScope 3000, Caliber, Rochester, NY; distributed in Europe by Mavig GmbH, Munich, Germany) has been developed expanding the applications of RCM. HH-RCM has three main advantages compared with the traditional wide probe (TWP) VivaScope 1500: (1) it is handy because it uses an optical fiber wiring the optical source to the detector, (2) it does not need fixation on the skin through a metal ring, and (3) it has a smaller tip (5 mm in diameter in the first version of the HH device, 1.5 cm in the second version of the HH device, and 2 cm in the TWP), enabling access to body sites with curved surfaces inaccessible to the TWP.¹

All these advantages have enabled the use of RCM for the study of the whole body skin, of the mucosa, and of the skin appendages. The HH-RCM has increased the use of RCM in clinical practice because of faster image acquisition (1–3 minutes per lesion vs 10–20 minutes).¹ Moreover, it has allowed the use of RCM for a rapid diagnosis of cutaneous inflammatory and infectious diseases and of epithelial cancers that do not require the architectural information provided by the mosaic image reconstruction of the TWP.^{2,3}

HH-RCM can be compared with modern dermoscopy, which started with the evaluation of tumors and now has been demonstrated to be a useful noninvasive diagnostic tool for a wide range of skin diseases.

A new field of confocal microscopy has also been opened by the development of an ex vivo device dedicated to the skin (VivaScope 2500,

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Caliber; distributed in Europe by Mavig GmbH). This new device has been conceived for the evaluation of cutaneous tumor margins in real-time, directly on freshly excised tissue in a perioperative setting. However, further applications are possible, such as the diagnosis of infectious diseases.

SPECIAL SITES

Mucosa, nails, and hairs can be examined by RCM. All these body sites are sensitive areas where noninvasive imaging techniques are of high interest to spare biopsies and excisions. RCM has a limit in the laser penetration depth and for this reason acral skin has not been initially investigated. However, in our experience RCM could also be useful in this area.

Genital and Oral Mucosa

Mucosa is particularly suitable for RCM because of its thin or absent cornified layer, which allows a deeper penetration of the laser and a resolution in the upper layers higher than in the skin. Thus, RCM permits a better-detailed visualization of the cellular morphology.¹

RCM is a promising tool for the differential diagnosis of pigmented lesions in the genital and oral mucosa^{4–6} and in particular to differentiate early melanoma from the more frequent melanosis.^{4,5} Melanoses correspond to the benign hyperpigmentation of basal keratinocytes and are characterized under RCM by the presence of chorion papillae rimmed by hyperreflective

monomorphous cells corresponding to hyperpigmented basal keratinocytes^{4–6} (**Fig. 1**). Mucosal melanoma is characterized by four major features: (1) high density of basal hyperreflective dendritic cells, (2) presence of pagetoid bright large cells in the epithelium (mainly roundish or fusiform with plump body), (3) loss of normal architecture of chorion papillae, and (4) sheet-like proliferation of atypical cells in the chorion.^{4,5}

RCM is also helpful for the differential diagnosis between in situ squamous cell carcinoma (SCC) and Zoon plasma cell balanitis, a benign idiopathic inflammatory disease.⁷ RCM criteria for mucosal SCC are similar to those used in the skin: atypical honeycomb pattern and disarranged epidermal pattern. Moreover RCM can be used to monitor laser photodynamic treatment of in situ SCC of the glans over time in a total noninvasive modality.⁸

Ocular Mucosa

Our group first applied the RCM devices dedicated to dermatology to the study of the ocular mucosa.⁹ HH-RCM can explore the whole cornea and conjunctiva surface, including the ciliary margin, the lacrimal punctum, the internal and external canthi, and both surfaces of the eyelids comprising the meibomian glands.¹ These regions have not previously been explored by RCM, because of the limited mobility of devices available for ophthalmology (Confoscan 4 slit-scanning confocal microscope, Nidek, Gamagori, Japan; and Heidelberg Retina Tomograph in association



Fig. 1. Clinical (*A*) and in vivo RCM (*B*) aspect of a gingival melanosis. RCM shows roundish chorion papillae rimmed by hyperreflective cells (*B*, red arrows) at the epithelium-chorion junction. Some melanophages are visible inside the papillae (*B*, yellow arrows). Scale bar: 100 μm.

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