Comprehensive Cutaneous Volatile Organic Compound Profiling for Skin Cancer Detection by GC×GC-MS

Kleidisa Rrushka[1,2], Christian Dorado Cortez[3], Kenny Velia[3], Martinha Donghia[4], Elisa Cinotti[4], Yves Rozenholc[5], Jérôme Vial[2], Sarah Eliraki[1], Nathalie Gagey-Eilstein[1], Jean Luc Perrot[3], Nabil Moumane[1]

[1]Sensebiotek, 21 Grande Rue, 78240 Aigremont, [2]LSABM, ESPCI, 10 rue Vauquelin, 75005 Paris, [3]Dermatology, CHU Nord, Saint-Etienne, France, [4]Dermatology Unit, Department of Medical, Surgical and Neurological Sciences, University of Siena, 53100 Siena, Italy, [5]BioSTM, Faculté de Pharmacie, Université Paris Cité, 4 avenue de l'Observatoire, 75006 Paris

Human skin constitutes a dynamic biological interface that continuously emits a complex volatilome composed of hundreds of volatile organic compounds (VOCs). Growing evidence suggests that VOC patterns reflect tumor-associated metabolic activity, offering a promising non-invasive sensing layer for cancer detection.
Melanoma, in particular, is a leading cause of cancer-related mortality among young adults, highlighting a critical unmet need for accessible and scalable screening strategies. Early detection remains the most critical factor for improving outcomes. While dermatology is shifting toward quantitative and technology-driven diagnostics, current high-performance imaging tools remain costly and largely confined to specialized centers, limiting their applicability for routine population triage. Analytical volatilomics studies, including GC/MS-based tissue profiling, indicate that melanoma is associated with measurable alterations in VOC patterns. Canine melanoma discrimination reports provide additional anecdotal support for the existence of detectable cancer-related volatile signals.
To enable clinical translation, an analytical sensing platform is being applied within the ongoing prospective Scent-Skin-001 study, integrating standardized clinical sampling and high-resolution VOC profiling.

Methods: Scent-Skin-001 is a prospective, multicenter clinical study, designed to characterize the VOCs profiles associated with skin cancers. The study enrolled 90 patients with biopsy-confirmed melanoma, basal cell carcinoma, or squamous cell carcinoma, together with age and sex-matched healthy volunteers. Cutaneous VOCs were sampled non-invasively for one hour using SkinVOCs®, a passive sampling device developed by SenseBiotek. Samples were collected from multiple anatomical locations, including the lesion and contralateral healthy skin site. The collected VOCs were subsequently analyzed by a high-sensitivity thermal desorption-comprehensive two-dimensional gas chromatography coupled with time-of-flight mass spectrometer (TD-GCxGC/ToFMS).

Results: Analysis of VOC profiles is currently ongoing, with clinical molecular signature results expected in the near term. SkinVOCs® enables standardized VOC collection while minimizing background contamination and ensuring efficient compound trapping and release. In parallel, the TD-GCxGC/ToFMS analytical workflow generates high-resolution, information-rich chromatographic profiles, allowing robust discrimination of compounds within the complex skin volatilome and establishing a critical foundation for the identification of subtle cancer-specific molecular patterns.

Discussion/Conclusion: Within the ongoing Scent-Skin study, a robust methodological foundation for the characterization of VOC signatures associated with major cutaneous malignancies has been established. Beyond its analytical value, this approach supports a shift in non-invasive skin cancer screening from purely morphological assessment toward functional metabolic readouts. In addition, the standardized sampling and high-resolution analytical workflow presented here offer a transferable protocol for future volatolomic investigations, potentially extendable to other systemic diseases. Ultimately, this framework defines a translational pathway toward scalable point-of-care electronic-nose triage tools for at-risk populations in decentralized clinical settings.