Morphology-dependent compositional differences in breast microcalcifications revealed by Raman spectroscopy

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Microcalcifications (MCs) are heterogeneous calcium-containing deposits observed in both benign and malignant breast lesions, and the biological significance of their presence remains incompletely understood. While mammography enables their detection and provides information on spatial distribution, it offers limited insight into the chemical nature of the deposits themselves. A more detailed characterization of MC mineral composition may therefore contribute to a better understanding of their formation and potential association with malignancy [1].

In this context, Raman spectroscopy (RS), a non-destructive, label-free technique that provides molecular-level information on MC mineral composition, including crystallinity and carbonate substitution, with high spatial resolution [2]. This study investigated whether breast MCs morphology correlates with differences in Raman spectral signatures, particularly carbonate–phosphate and whitlockite–hydroxyapatite ratios.

Eighteen patients affected by suspicious breast microcalcifications on screening mammography, undergoing a core biopsy and treated at the Breast Unit of ICS Maugeri (Pavia, Italy) from 2017 to 2024, were included. All patients provided written informed consent, and the study was approved by the Institutional Ethics Committee (Protocol 2281/2018 EC) in accordance with the Declaration of Helsinki. 3 patients reported ductal carcinoma *in-situ* (DCIS), 5 patients reported invasive ductal carcinoma (IDC) and 10 subjects with reported benign lesions. Following mammographic identification of suspicious lesions, tissue biopsies were obtained, processed as formalin-fixed, paraffin-embedded sections, and analyzed at RS, and scanning electron microscopy (SEM).

Five MC morphologies were identified by SEM, and classified as dense homogeneous, punctate, fragmented, spongy, and annular [3]. Raman analysis revealed that punctate morphologies exhibited a significantly higher whitlockite-to-hydroxyapatite ratio, while fragmented, spongy, and annular morphologies showed higher carbonate-to-phosphate ratios, with statistically significant differences between groups.

These findings suggest that MC morphology reflects underlying compositional differences detectable by RS, supporting its potential as a complementary tool for improved breast cancer characterization [2].

Keywords
Microcalcifications (MCs), Raman spectroscopy (RS)

References

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