Surface Enhanced Spatially Offset Raman Spectroscopy for the Detection of Breast Cancer Using Turbid Optical Phantoms

Submitted by

Louise Margaret Joan Clark

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Abstract

Breast cancer is a prevalent disease within today's modern society, affecting 1 in 8 women and 1 in 870 men within a lifetime. With the introduction of mammographic breast screening in 1987 and marked improvements to targeted therapies, mortality rates declined, highlighting the need for early diagnosis and tailored treatment to halt disease progression in its foremost stages. Histology assessed biopsies, alongside initial two-view mammographic imaging, are paired as the current diagnostic "gold standard". The need to incorporate several techniques, applying an "all-angles" approach to diagnostics, provides an effective, streamlined diagnostic pathway, reducing patient wait times between testing and results – crucial in preventing disease progression.

Optical spectroscopic techniques for the characterisation of biomolecular compounds and structures present within tissue are fast becoming the biomedical analysis tools of choice, coming to the forefront of clinical applications. Raman spectroscopy is one such technique providing highly chemically specific results, in a non-ionising and non-invasive way. When used in conjunction with metal nanoparticle probes, the inherently weak Raman signals of the biomolecules surrounding the nanoparticle surface undergo extensive levels of enhancement – an eponymous technique, Surface Enhanced Raman Scattering (SERS).

This thesis is split into two principal areas of study. The first explores extrinsic SERS nanoparticles at depth within optical phantoms, "imaged" in a Transmission orientation, mimicking the composition of the breast within a cranio-caudal mammographic imaging position. The second concerns the micro-Raman quantification of gold nanoparticles, functionalised to a biocompatible level for the active targeting of hydroxyapatite – a calcium

apatite form which, when dominant within breast microcalcifications, act as a biomarker for malignancy.

Key aspects drawn from the results include a greater understanding of Raman reporter gold nanoparticles at depth, and how the absorption profile of the sample material affects the garnered intensity profile. The synthesis of a novel nanoparticle probe was also founded, with promising future applications in terms of targeting and theranostic capabilities. Furthermore, a protocol into the implementation of an automated mapping system within an open optical set-up is given, detailing the software, hardware and electrical installation requirements.

The advantages of Raman spectroscopy integration within current diagnostic practices are highlighted, with limitations such as nanoparticle biocompatibility issues, the inherent optical properties of biological tissues, and system conditions touched upon.