

# Biomarker Detection and Surface Enhanced Raman Spectroscopy

## INTRODUCTION

The identification of chemical changes in the body has become increasingly important in medical diagnostics over recent years. Rather than look at external symptoms to perform a qualitative diagnosis, analysing changes in body chemistry enables clinicians to perform more systematic quantitative diagnostics at a much earlier stage.

While chemical analysis may improve the reliability of some diagnosis, more important is the potential to deliver significantly earlier diagnosis, allowing treatment before disease impact becomes irreversible.

Whereas many tests have been developed for disease diagnosis, many of them involve complex chemistry which can be costly and can lead to delays of weeks in delivering test results to the patient. Ideally, test techniques should be not only highly sensitive, to provide an earlier stage diagnosis, but also instantaneous.

Surface enhanced Raman spectroscopy offers the ability to deliver an extremely sensitive test that requires little to no sample preparation, producing results in seconds. The technique delivers a unique trace of the molecular fingerprint of a sample in only a few seconds. This fingerprint can be used either to identify one or more chemical compounds that are known indicators of a disease or to show complex changes in the chemical balance of a sample that may be correlated with particular disease even if the indicator chemicals are unknown.

## EXAMPLES

### 1- EARLY STAGE OSTEOARTHRITIS DETECTION

The knee and other joints are lubricated by a special group of compounds, known as Glycosaminoglycans (GAGs), present in the joint cartilage, which have elastic properties and protect the joint against compression.

Damage to joint cartilage caused by osteoarthritis is known to cause GAGs to leach out of the cartilage into the synovial fluid surrounding the knee and into the blood. Detection of elevated levels of GAGs in the blood and synovial fluids therefore provides an early indication of the onset of osteoarthritis.

Prof Mike Morris from University of Michigan has reported <sup>(1)</sup> using Klarite surface enhanced Raman substrates from Mesophotonics to detect hyaluronic acid the most abundant GAG. Hyaluronic acid has been detected at both the background trace levels expected in healthy subjects and at the clinically relevant elevated levels associated with knee damage.

Critically, trace level detection of hyaluronic has been confirmed not just in simulated samples but also observed in real subjects' synovial fluids.

Early stage detection of osteoarthritis is particularly important in improved patient care as drug diffusion into cartilage is very poor, so that treatment is only possible if detected at a very early stage.

### 2- BACTERIAL VS VIRAL EYE INFECTION

Simple and rapid differentiation of the type of eye infection is extremely important for the clinician to assess the correct treatment. Incorrect treatment of eye infections can be associated to an increase risk of long term vision impairment. However the presented symptoms of bacterial and viral eye infections can be very similar and not easily differentiated. It is possible to take samples and grow cultures to determine the type of infection but this can lead to a critical delay of several days in patient treatment.



Klarite test slides used for biomarker trace analysis



Surface Enhanced Raman Spectroscopy

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However bacterial or viral infections are associated with very different changes in the chemical balance of eye fluids which can easily be accessed through tear fluid samples. Dr Nick Stone at Gloucester Royal Infirmary is collaborating with the University of Southampton and Mesophotonics to develop a diagnostic method for eye infections based on Surface enhanced Raman spectroscopy.

The technique relies on building up a data base of measurements from a significant number of healthy and infected individuals (~700 in total) who have had a diagnosis confirmed by an independent pathology laboratory using the traditional tests. Key components of changes in the chemical finger print recorded with surface enhanced Raman spectroscopy are then correlated to the traditional diagnosis and statistically processed so the finger print spectra can be grouped according to healthy, bacterial and viral or undetermined categories. This technique then has the power to classify a new sample with unknown infection into a bacterial or viral infection.

Dr Stone's group has already demonstrated that this type of technique has at least the same reliability as a traditional pathology test when using standard Raman to differentiate different cancers of the oesophagus from bulk histological samples [2].

Application to tear fluid samples requires enhancement of the Raman signal using Klarite substrates and should provide eye disease differentiation almost instantaneously.

The strength of this technique is that it does not require the underlying chemical changes or their precise cause to be known and can detect complex changes in the balance of many chemicals. The reliability comes from linking the observed change to that seen in a data bank of historical diagnosis. As such it can provide a very early indication of a diagnosis allow immediate treatment.

Such techniques may also be applied to streamline testing within a traditional pathology laboratory so that the most appropriate traditional tests can be applied with the highest priority to incoming samples.

### CONCLUSION

Surface enhanced Raman spectroscopy enables trace level detection of key chemical biomarkers and changes in the chemical make up of bodily fluids, which in turn can provide very early indications of disease. As these measurements can be taken in aqueous bodily fluids, with measurement times of seconds to minutes, it opens the possibility of real-time point of care diagnosis and treatment.

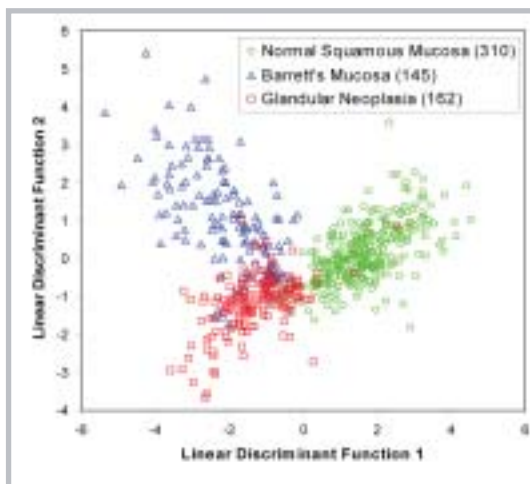


Illustration of the separation of diseased samples by Raman Spectroscopy, courtesy of Dr Nick Stone, Cranfield Postgraduate Medical School in Gloucestershire, Gloucestershire Royal Hospital, UK

### REFERENCES

- 1- G. S. Mandair, K.A. Dehring, B.J. Roessler, Michael D. Morris, "Detection of Osteoarthritis Biomarkers using Surface Enhanced Raman Spectroscopy in the Near-Infrared", RSC Faraday Discussion 132, London 2005.
- 2- C.Kendall, N. Stone, N.Shepherd, K. Geboes, B. Warren, R. Bennett, H. Barr. "Raman spectroscopy, a potential tool for the objective identification and classification of neoplasia in Barrett's oesophagus", Journal of Pathology 2003; 200: 602-609

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