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Prospects for Biomedical Diagnostics by Surface Enhanced Raman

Key Words

- Medical
- Diagnostics
- Raman
- Surface enhanced
- Biomarker
- Osteo-arthritis

Introduction

Disease diagnostics by 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 early stage.

Whilst chemical analysis may improve the reliability of some diagnosis, it is the potential to deliver significantly earlier diagnosis allowing treatment before disease impact becomes irreversible. Early treatment has a much better prognosis for the patient as well as offering significant cost savings to health providers by avoiding the potential for both in-patient care and reducing the long term cost of providing years and in some cases decades of symptom relieving drugs with the omnipresent danger of unforeseen side effects.

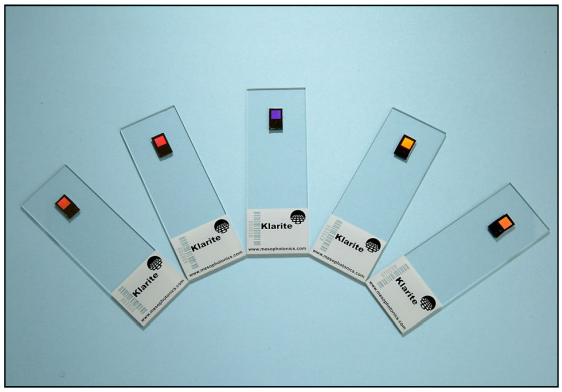
Whilst many test have been developed for disease diagnosis, many of them involve complex chemistry which can be both costly and lead delays of days or weeks in delivering test results to the patient. Thus modern test techniques need to be both highly sensitive to provide an earlier stage diagnosis but fast and ideally instant in delivering that diagnosis.

Surface enhanced Raman spectroscopy offers the ability to deliver both an extremely sensitive test and requires little to no sample preparation producing results in seconds which are ideal for the point of care environment. The technique delivers a unique trace of the molecular finger print of a sample in only a few seconds. This finger print can be used to identify one or more chemical compounds that are known indicators of a disease or 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 - Specific biomarker identification

Knee and other joints are lubricated by a special group of compounds, known as Glycosaminoglycans (GAGs) present in the joint cartilage which have elastic like 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.



Klarite test slides used for biomarker trace analysis

Prof Mike Morris from University of Michigan has reported [2] 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 subject synovial fluids.

Early stage detection of osteoarthritis is particularly important in improved patient care as drug diffusion into cartilage is very poor meaning treatment is only possible if detected at a very early stage. Treatment of later stage diagnosis is difficult with most attention given to long term prescription of pain killers to treat only the symptoms.

This is a classic case of identifying a biochemical marker, in this case hyaluronic acid, which has been previously associated with a disease and confirming that it can be identified and quantitatively measured in real bodily fluids. Importantly detection of both elevated levels and background levels has been confirmed providing an early indication that a reliable clinical test may be possible.

2- Bacterial vs Viral Eye infection differentiation via correlation diagnostics

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.

Prospects for Biomedical Diagnostics by Surface Enhanced Raman Spectroscopy

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 samples. Dr Nick Stone at Gloucester Royal infirmary has proposed using surface enhanced Raman spectroscopy to detect the differences in chemical make up of tears and therefore provide a simple and instant test to differentiate different infection types

The technique relies on building up a data base of 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 multi-day 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 Stones group have already demonstrated that this type of technique has the at least the same reliability as a traditional pathology test when using un-enhanced 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 surface enhanced Raman substrates and should provide eye disease differentiation almost instantly.

The strength of this technique is that is 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 chemical make up of bodily fluids which can give very early indications of disease. Raman spectroscopy has been available as a technique for almost 100 years but has been unable to detect trace levels of chemicals without some form of enhancement. Klarite surface enhanced Raman substrates from Mesophotonics reliably increase the intensity of the Raman finger print by over 1,000,000

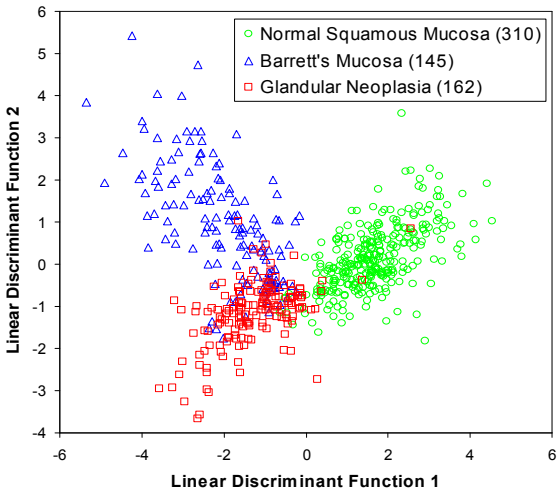


Illustration of the separation of dieases samples by Raman Spectrsocpy courtsy of Dr Nick Stone, Cranfield Post-graduate Medical School in Gloucestershire, Gloucester-shire Royal Hospital, UK

fold making it sensitive enough to see very small changes in trace level chemicals associated with the early onset of disease. As these measurements can be taken in aqueous bodily fluids, with measurement times of seconds to minutes, it opens the possibility to point of care real time diagnosis and treatment.

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 Discusion 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.

mesophotonics

Tel: +44 23 8076 3752
Email: sales@mesophotonics.com
Web: www.mesophotonics.com