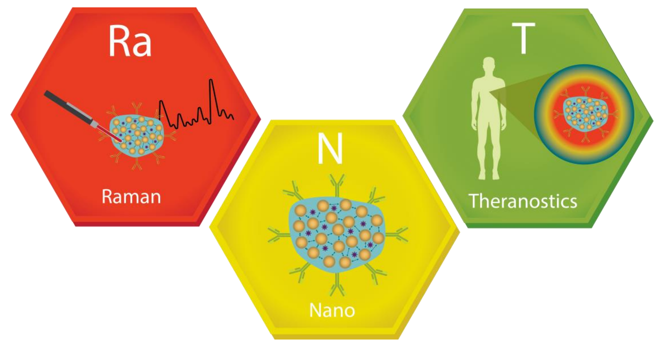
Non-invasive Determination of Depth in Turbid Media using Spatially Offset and Transmission Raman Spectroscopy

Science and Technology Facilities Council



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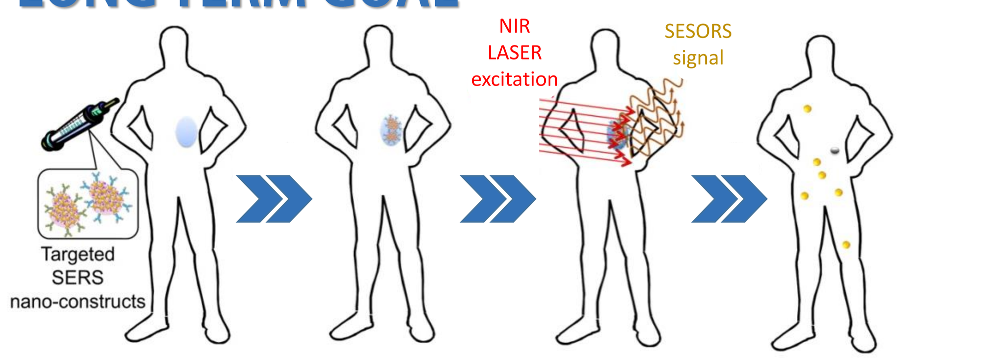
Aim

Depth prediction of a **buried object (e.g. lesion)** within a turbid medium using Raman Spectroscopy

LONG TERM GOAL



Target nano-construct injected into patient's body and accumulate in specific tumour site

Deep Raman set-up detect signal

Treatments (i.e. Hyperthermic therapy)

1. Localization target
2. Knowledge of depth from the surface

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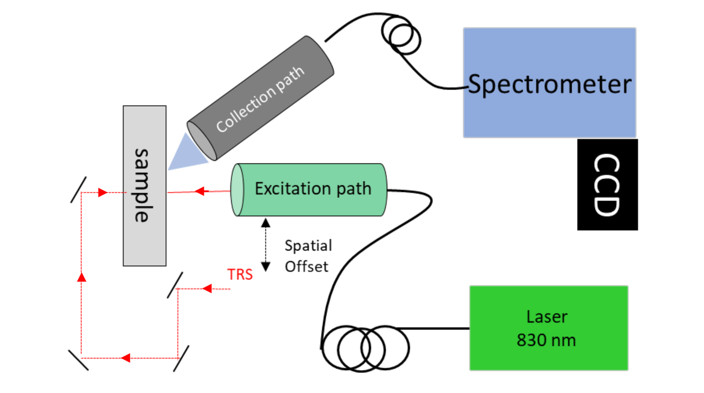
Increase effectiveness of treatment

Experimental settings



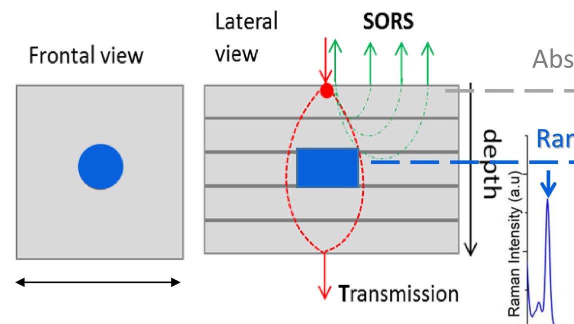
Exc. wavelength: 830 nm; Power 200 mW

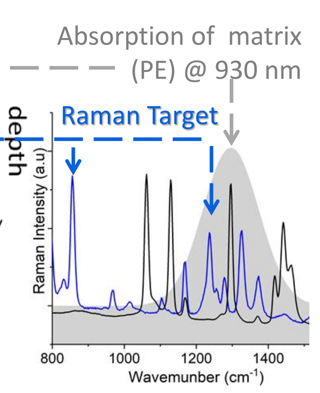
Spot size: SORS ~500 µm; TRS s ~ 1.5 mm

Materials - Layer system

Target = Paracetamol (APAP)

Diffusive matrix = Polyethylene (PE)





Lateral size (x,y) 50 mm

Thickness 3 mm (each layer)

Conclusions

☺ Non-invasive prediction of depth for a single buried object within a turbid medium

☺ Combined used of SORS and TRS improved the prediction

☺ More robust to variation of thickness and amount of target

Model	Error of calibration RMSEC (%)	Error of prediction RMSEP (%)
1: SORS + TRS	3.4	4.3
2: TRS	4.9	6.2
3: SORS	5.6	6.7

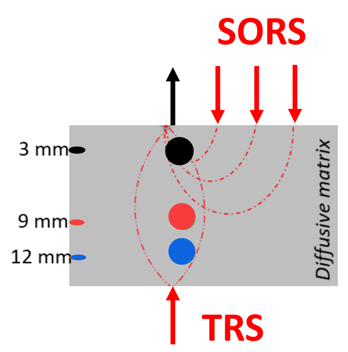
Principle

Spatially Offset (**SO**) and Transmission (**T**) Raman Spectroscopy (**RS**) have different penetration depth inside turbid media and different Raman bands are attenuated differently[1]

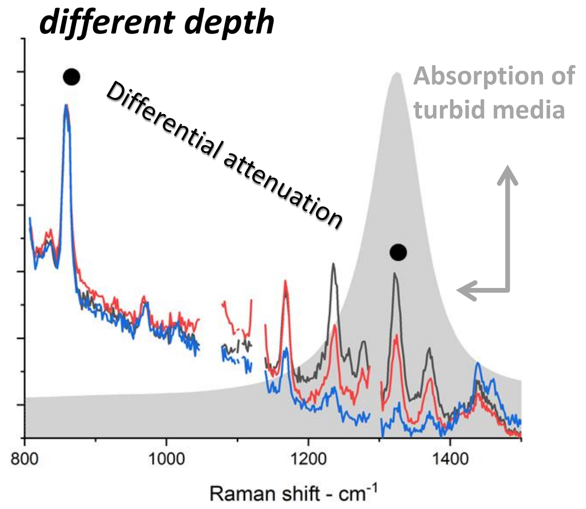
... due to multiple scattering and absorption event

Raman photons generated at a smaller depth → undergo smaller relative intensity distortion

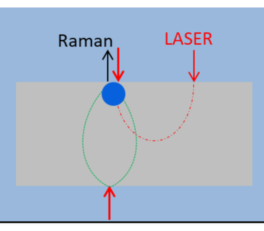
Raman photons generated at a larger depth → undergo a larger relative intensity distortion



TRS spectra of the inclusion at different depth



Calibration[2]



STEP 1: Alignment of the inclusion on the optical axis (z-axis) by moving sample

STEP 2:

i. Place equivalent target at the surface (d=0)

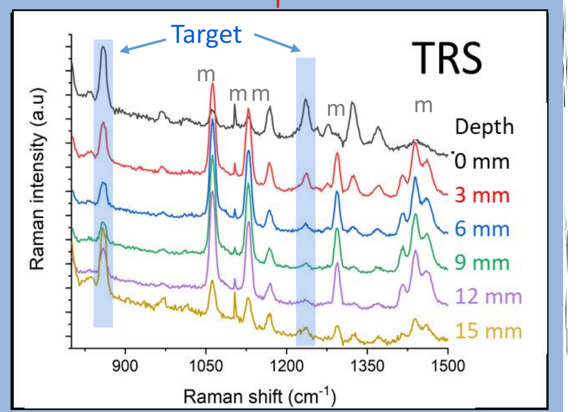
ii. Raman measurement of the layered system (SO = 0–12 mm and TRS)

iii. Repeat by changing the depth of the target along the z-axis in steps of 3 mm

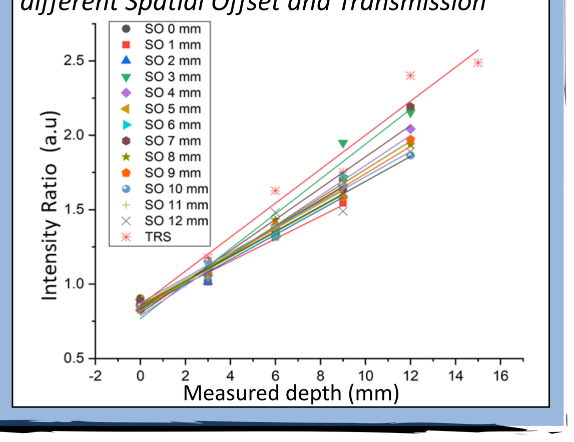
STEP 3: Creation of Calibration model

i. For each SO and TRS → evaluate Raman band intensities

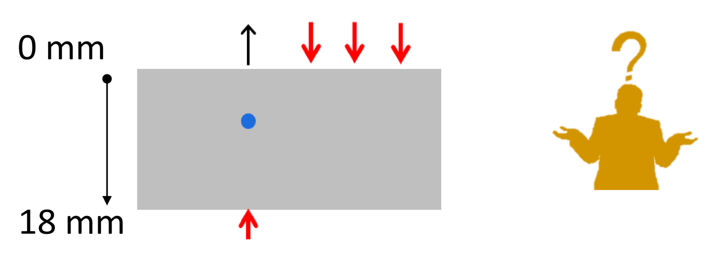
ii. Linear fit → intensity Ratio vs. depth



Model of intensities distortions vs. depth for different Spatial Offset and Transmission



Results



Target at an unknown depth

↓

Measure with different offset & TRS

↓

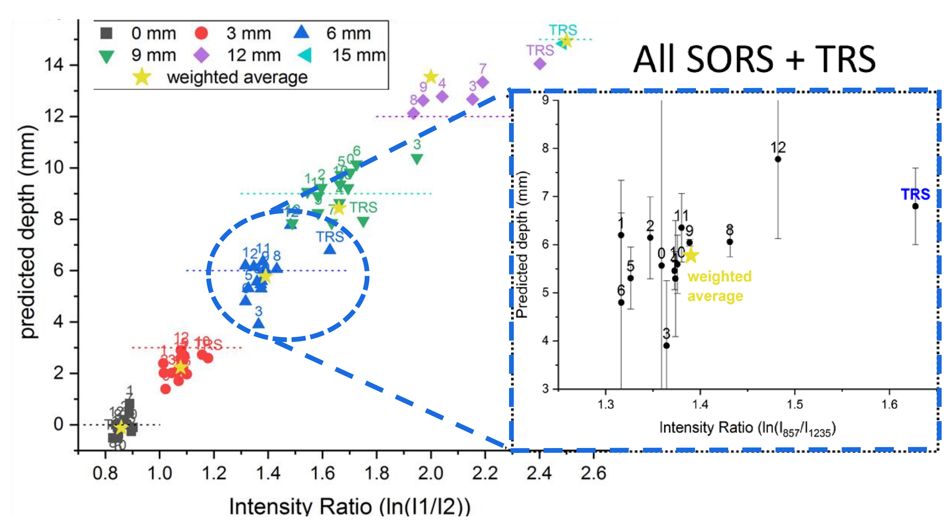
Evaluate the intensity distortion

↓

Use the calibration model to predict depth for each SO & TRS

↓

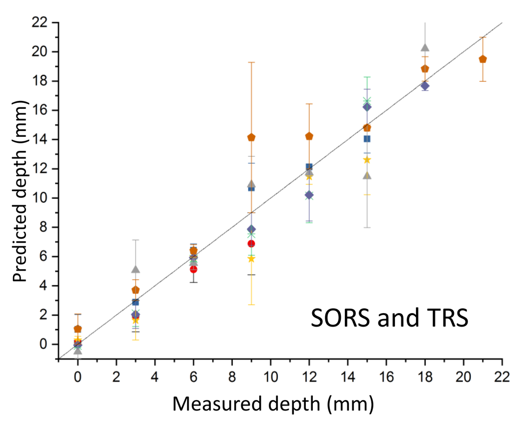
The depth of the target is extrapolated from a weighted average of all of the depth models



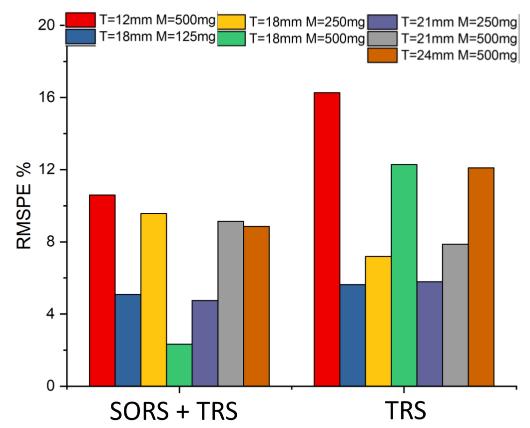
Error of Prediction

Does the prediction vary with:

- Thickness of diffusive matrix ?
- Amount of target ?



Amount of target	Matrix thickness (PE) 12 mm	18 mm	21 mm	24 mm
125 mg		●		
250 mg		●	●	
500 mg	●	●	●	●



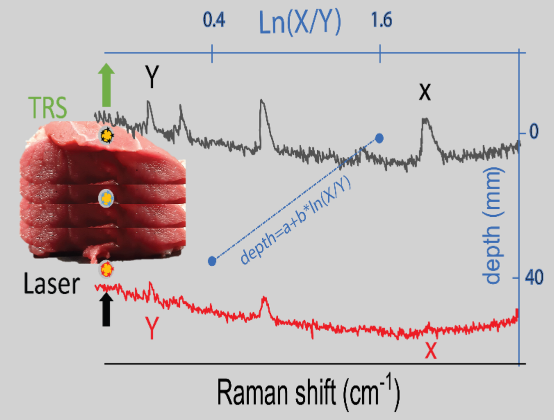
Next step

☹ Remove the need for internal calibration

→ Develop calibration model based on external measurements only

(fully non-invasive and *in vivo* applicable)

→ Validate on *ex vivo* tissue[3] (real case scenario)



References

[1] B. Gardner, N. Stone, P. Matousek, *Anal. Chem.* **2017**, *89*, 9730

[2] Mosca, S.; Dey, P.; Tabish, T. A.; Palombo, F.; Stone, N.; Matousek, Anal. Chem. **2019**, 91, 8994

[3] Mosca, S.; Dey, P.; Tabish, T. A.; Palombo, F.; Stone, N.; Matousek, P. J. Biophotonics, **2019**, 1–7

Acknowledgments

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