ESR 1: Mid-IR Methodologies for Clinical Tissue Imaging

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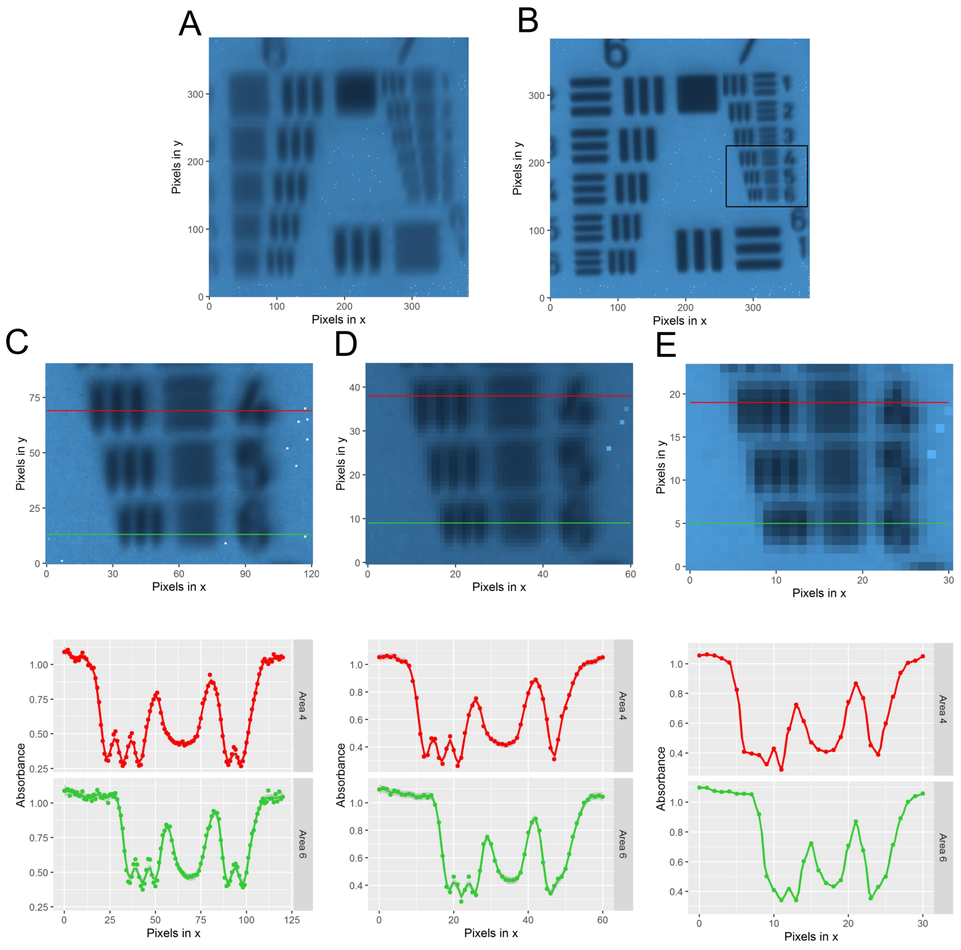
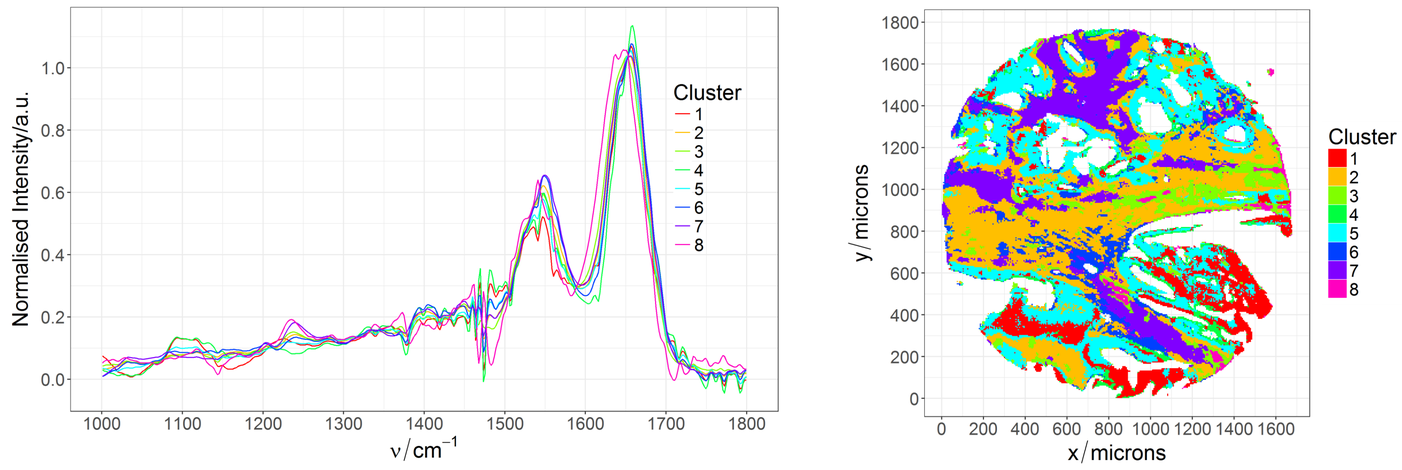
Outline: Overall goal of the project is to evaluate new schemes developed in the network for their use in a clinical environment. Mid-IR technologies in general are researched quit extensively for their clinical usability. We are contributing to this by adding improved tools to enable faster and more precise data collection. Therefore a benchmark for mid-IR microscopy set ups will be developed showcasing their capabilities for clinical diagnostics based on the ability to differentiate between healthy and cancerous areas in biopsies of the oesophagus. The benchmark will also contain technical figures of merit as spatial/spectral resolution. In this scope it is planned to find a definition for a 'chemical image resolution' or chemico-spatial resolution. We will compare state of the art FTIR imaging with the novel approaches developed by the ITN partners.

Assessment of Optical Setup

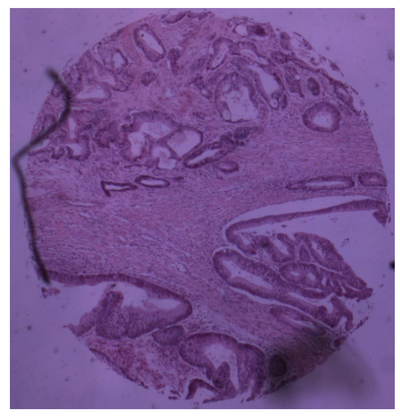


FTIR image of chrome on glass USAF 1951 target. Average intensity per pixel in the region 1400–1000 cm^{-1} (A) and 3900–3800 cm^{-1} (B); zoomed in area of the boxed region from B with its corresponding average intensity along the coloured lines (C); 2×2 (D) and 4×4 (E) binned image of B with its corresponding average intensity along the coloured lines. Published in Vibrational Spectroscopy from *Nallala et. al.* [1].

Imaging of Clinical Samples

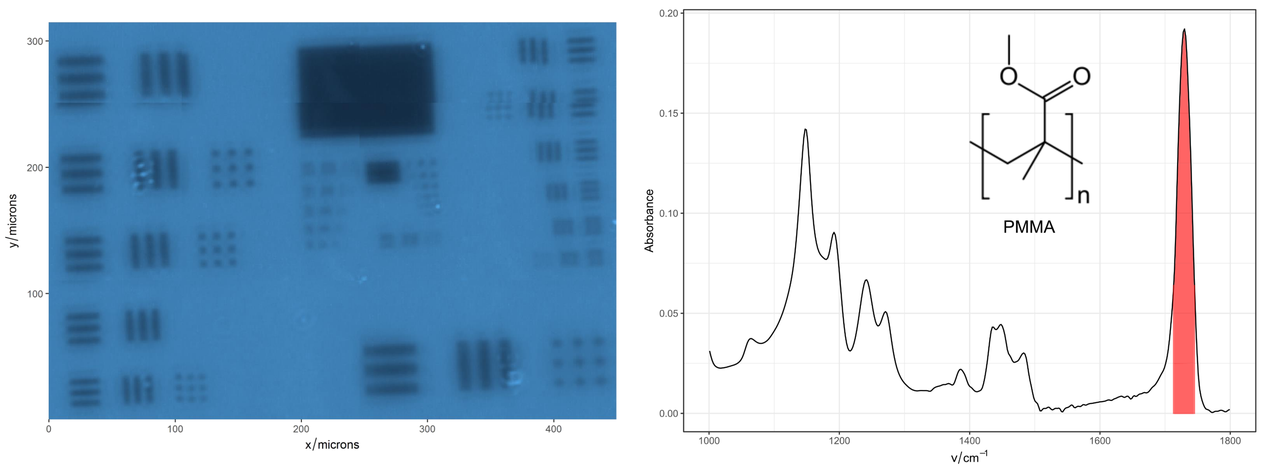


Using clinical samples for a benchmark implies that these samples need to be highly stable to use them over a longer period of time. Therefore, the tissue sections need to be embedded in paraffin to conserve them. Paraffin embedded samples however are more challenging to investigate, as paraffin has a spectral signature on it's own. Working with these samples therefor requires a method to eliminate those contributions. Displayed here is a core from a tissue micro array with biopsies containing areas with colon cancer, which are currently used for method development.



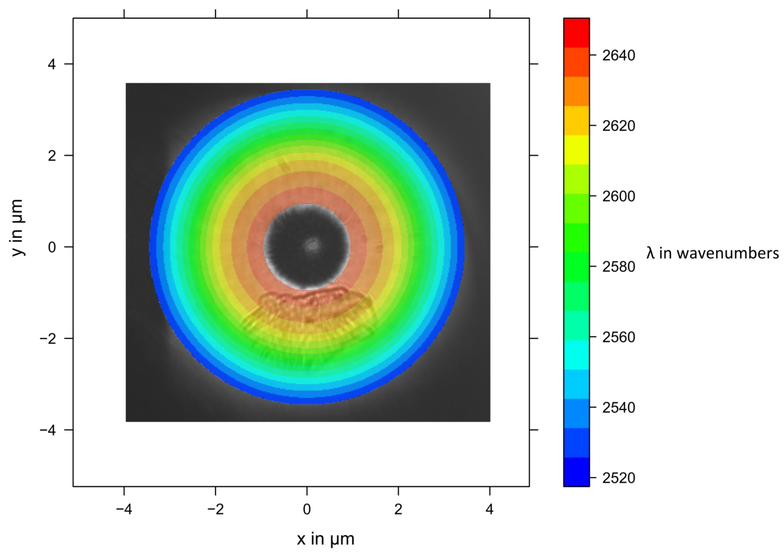
Planed secondments: There is a second and possibly longer stay at DTU scheduled as soon as their set ups fulfil the requirements worked out in the last stay. Until then I secured external funding to visit Rohit Bhargava's Laboratory at the Beckman Institute, Illinois (USA) in February 2017 to learn about quantum cascade laser based mid IR imaging.

Development of New Test Chart



Using chrome and glass for a resolution test chart is a poor choice for working in the mid-IR as both materials are not transparent for those wavelength. Therefore imaging can only be performed in reflection mode unless very strong light sources are used. In order to overcome this limitation I am currently working to design an improved target. Displayed above is an FTIR image of a new resolution test chart with features written into PMMA (Poly-methyl- methacrylate) on CaF_2. The image was obtained as a hyperspectral image in transmission mode. Visualised here is the integrated intensity of the carbonyl vibration at 1713-1745 cm^{-1} (coloured red in the spectrum). The contrast in this case is PMMA vs air as the intensity drops in the areas where the pattern is written into the PMMA.

Super Continuum Imaging



The above image shows an pconverted super continuum image of a tissue section from a biopsy obtained from a patient with an adenocarcinoma in the oesophagus. The image was generated during my first stay at DTU in August 2016 together with Laurent Huot (ESR 6). Furthermore images using a Globar as light source have also been obtained together with Saher Junaid (ESR 9). From this data requirements for the clinical imaging have been worked out to improve the upconversion set-ups to get them ready for working with clinical samples.

[1]: J. Nallala, G. R. Lloyd, M. Hermes, N. Shepherd and N. Stone
Enhanced spectral histology in the colon using high-magnification benchtop FTIR imaging
Vibrational Spectroscopy, In Press, **2016**

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