STSM REPORT

STSM Application number: COST-STSM-BM1205-21003

STSM Grantee: dr Marilena Giglio

STSM title: OCT for skin cancer detection

Home Institution: Dipartimento Interateneo di Fisica "M. Merlin", Università degli studi di Bari-Politecnico di Bari, Italy

Host Institution: Academic Medical Center (AMC) - University of Amsterdam, The Netherlands

STSM period: 11-08-2014 to 17-08-2014

STSM purpose: taking part to meetings on Optical Coherence Tomography (OCT); make OCT measurements; writing a co-authored paper based on OCT measurements performed during both the STSM and the training of the master thesis.

Description of the work carried out during the STSM:

During the training of my master I studied the biomedical application of Optical Coherence Tomography (OCT) in Oncology. OCT is a non-invasive, non-contact imaging technique based on Low Coherence Interferometry, thus performing in-vivo optical biopsy. Several research groups correlated the OCT attenuation coefficient (μ_t) to pathology in various epithelial oncological scenarios. This method gives reliable results for tissues thicker than 100-200 μm. However, the suspected lesion typical of early stage cancer is usually developed into a thinner layer. Our objective was thus to test an innovative method, based on the study of the parameters of the speckle distribution in a thin superficial region of OCT images, to indirectly measure the μ_t in such thin tissues and check tissues abnormalities. The physical origin of the speckle pattern is the scattering of coherent light by a rough surface or a diffusive medium, such as a biological tissue. For OCT, the speckle pattern depends on the local distribution of scattering structures within a sample and could therefore act as an optical biomarker as well.

The objective of the STSM was to carry on the master project by both taking part to OCT meetings, in order to compare the state-of-the-art with the technology used during the training, and using the know-how and advanced instruments available at AMC to make new OCT measurements and investigate the working conditions of the innovative OCT speckle approach tested during the training. Finally, a co-authored paper showing the main results of our research was written.

The aim of "OCT for skin cancer detection" is to find a correlation between the parameters of the speckle distribution from a thin region of interest (ROI) and the attenuation coefficient evaluated by a thick ROI within the same OCT B-scan. For the first objective, we studied the attenuation coefficient in a thick region of interest (ROI) within OCT images (namely, B-scan) of increasing concentrations of Intralipid®, as a phantom of both healthy and tumorous human tissues. Second, we studied the parameters of the speckle distribution by means of the mean and the variance in a thin ROI within the same images and investigated on the shape of the speckle distribution. Afterwards, we correlated the speckle parameters to the attenuation coefficient. Final, we

assessed the effect of digital oversampling on the speckle parameters using our OCT system, in order to study the working conditions of the OCT speckle approach.

OCT images were acquired with a commercially available 50 kHz swept source OCT system (Santec Inner Vision 2000) with an optical depth (z-axis) resolution of 10 µm in air and lateral (x/y-axis) resolution of 37 µm, operating at a central wavelength of 1300 with a 120 nm bandwidth. The digital sampling resolution of B-scans was set at 400 a-lines per 15 mm in order to match the optical lateral resolution of the Santec.
All the samples have been diluted with milliQ [D_2O]. Starting from the phantom with 20 vol.% concentration, we prepared a set of 13 samples until 0.05 vol.% concentration.
Each prepared sample was injected into a 2ml plastic cuvette (square Sarstedt, 10 mm) which was placed at 0.75 mm from zero delay. The scanning interface of the OCT system was placed under ~10 degrees angle to avoid specular reflection from the air-cuvette interface.
For the measurement of the attenuation coefficient we selected a $ROI_{\mu_{oct}}$ in the B-scans thick enough, i. e. 605 µm. The width was set at 2mm, which is a standard in histology. For the measurement of the speckle statistics we chose a $ROI_{speckle}$ as thin as possible, 21µm deep. Since the number of pixels in the $ROI_{speckle}$ needs to be high enough to apply the statistical analysis, we set the scan range in lateral direction to 7mm.

Description of the main results obtained:

In a first analysis we measure the attenuation coefficient as a function of the volume concentration of samples. The results are plotted in the graph of figure 1. The red squares represent the results obtained in the condition of Intralipid just injected in the cuvette, while the blue rhombi correspond to the case of Intralipid injected 10 minutes before the measurements. It can be observed that there are no differences between these two sets of measurements, since the values are always within the error bars and the curve trend is the same. As a control, attenuation values measured by Kalkman et al. with a different OCT system [1] are plotted in Green.

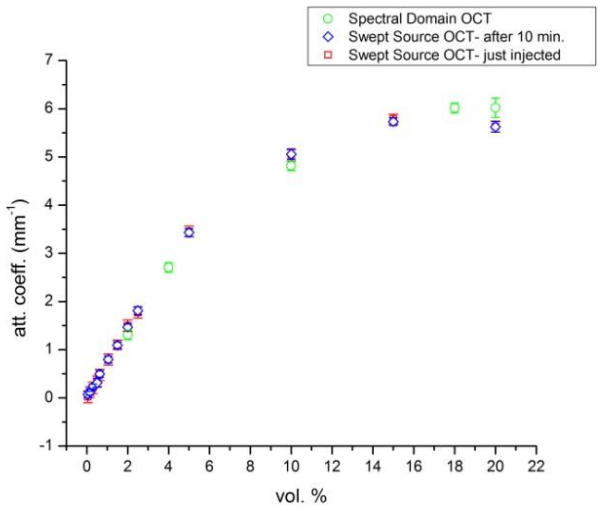

Figure 1: Attenuation coefficient as a function of the volume % concentration of the Intralipid phantoms, measured with our SS-OCT system (blue rhombi and red squares) and, by Kalkman et al. [1], with a SD-OCT system (green circles).

The average mean and average variance are plotted, respectively, in figures 2A and 2B, as a function of the volume % concentration, both in the condition of Intralipid just injected in the cuvette (red squares) and 10 minutes after the injection (blue circles). It can be observed that both the mean and the variance show a linear trend with the volume concentration at low concentration values, while the trends become nonlinear at higher concentration values.

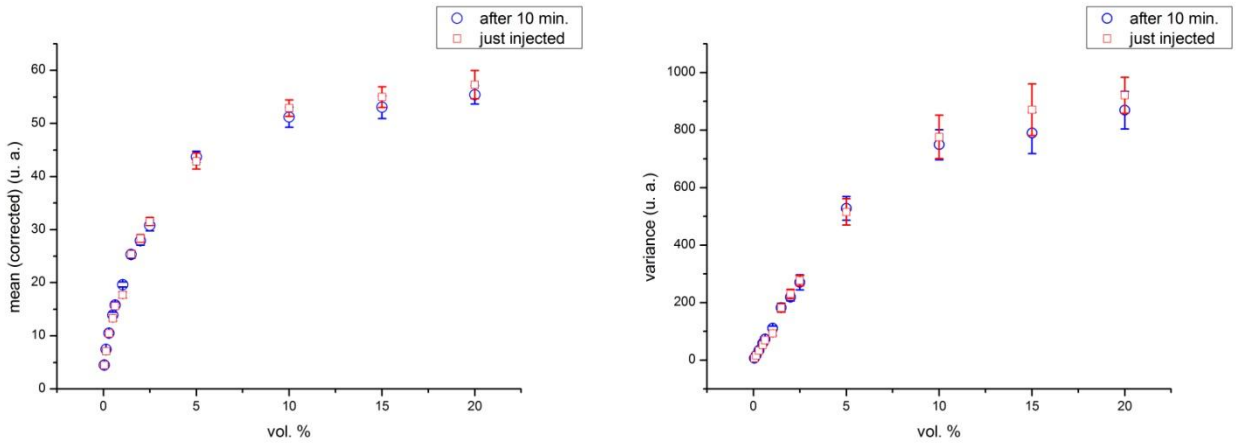

Figure 2: A) Corrected average mean and B) average variance of the speckle distribution as a function of the volume concentration, in the case of Intralipid just injected (red squares) and injected since 10 minutes (blue circles)

By plotting the variance values as a function of the squared mean values we found that the two speckle parameters are strongly linearly correlated. The slope of the linear fitting curve matches the theoretical value $\frac{4-\pi}{\pi}$ typical of the Rayleigh distribution, thus experimentally proving that speckle is Rayleigh distributed.

The similar trend of both the attenuation coefficient and the mean and variance with the concentration suggests the existence of a direct correlation between the μ_t and the statistical parameters of speckle, even though their different origins. In figures 3A and 3B we plot the evaluated and corrected mean and variance against the measured attenuation coefficient, in the two cases of Intralipid just injected (red squares) and injected since 10 minutes (blue circles). It can be observed that both the mean and the variance of the speckle distribution show a strong correlation with the measured attenuation coefficient. In particular, the relation between the mean and the attenuation coefficient is square root-like, with a coefficient of determination R^2 equal to 0.994. The variance is linearly correlated with the attenuation coefficient, with a coefficient of determination R^2 included between 0.982 and 0.991.

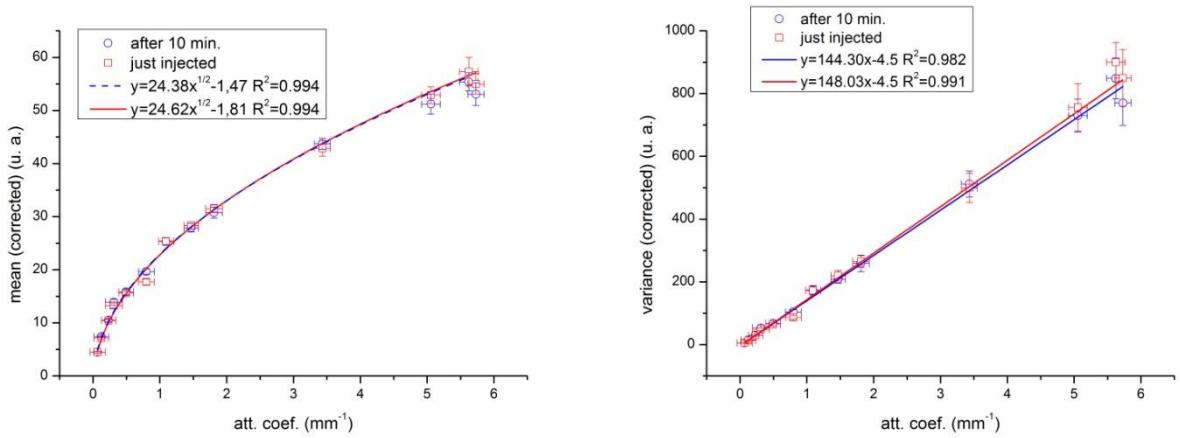

Figure 3: A) average mean and B) average variance vs measured attenuation coefficient and square root fitting curves in Intralipid, at different concentrations, just injected (red squares, red solid line) and injected since 10 minutes (blue circles, blue dashed line).

Finally, we have made some tests in order to investigate on the minimum required dimension of the $ROI_{speckle}$ and on the techniques that can be used to reduce this threshold. The results show that a digital sampling resolution of 1024 can fully compensate for the loss of statistics while reducing the $ROI_{speckle}$ width from 7 mm to 2.77 mm.

In conclusion, we found an that the parameters of the speckle distribution in a thin ROI are strongly correlated to the attenuation coefficient in a thick ROI within the same B-scan. In particular, by using our OCT system, a region of interest 21 µm deep and 2.77 mm large can be investigated to check variations in the refractive index, size, concentration or organization of scatterers within samples. OCT speckle approach can thus be used both to label samples and to distinguish between healthy (low concentration) and tumorous (high concentration) thin tissues. Our straightforward outlook is to apply the OCT speckle approach to human healthy and cancerous tissues.
Cost allowed us to exchange our knowledge and carry on our collaboration in an international project whose results have an important application in the oncological field and fulfill the aims of the BM1205 Action.

Mutual benefits for the Home and Host institutions: This STSM gave to the Home institution the opportunity of interfacing with technologies not available in its laboratories; on the other hand, Host institution had the possibility of carrying on an international collaboration obtaining extremely original scientific results for the use of OCT in skin cancer diagnosis.

Future collaboration with the Host institution (if applicable): We hope that the close collaboration between AMC and the department of Physics in Bari may continue in future STSM, by working together in the next steps of our international project.

Foreseen journal publications or conference presentations expected to result from the STSM (if applicable): Biomedical Optics Express, Journal of Biomedical Optics, Optics Letters.

References

[1] J Kalkman, AV Bykov, DJ Faber, and TG van Leeuwen. Multiple and dependent scattering effects in doppler optical coherence tomography. Optics Express, 18(4):3883–3892, 2010.

STSM outcome form

STSM application number	Home institution & country	Host institution & country	BM1205 WG	Objective of the collaboration	Results of the collaboration
COST-STSM-BM1205-21003	Dipartimento interateneo di Fisica "M.Merlin"- Università degli Studi di Bari - Politecnico di Bari - ITALY	Academic Medical Center - University of Amsterdam - THE NETHERLANDS	WG4	• OCT meetings • OCT measurements • Writing a paper about the main results	• State-of-the-art in OCT • Innovative approach (speckle distribution) to detect thin tissues anomalies • OCT for diagnosis of early stage skin cancer • Submitting a paper to: Biomedical Optics Express, Journal of Biomedical Optics, Optics Letters

Herewith I acknowledge that the described short term scientific mission was successfully carried out in the conditions here specified, according to the working plan.
Dr Marilena Giglio worked at her project "OCT for skin cancer detection" from 11th to 17th of August 2014 and fulfilled the objectives of her mission. I wish future collaborations within the BM1205 Cost Action.

Signature

Dr. D.M. de Bruin
Department of Biomedical Engineering &Physics
Department of Urology
email: d.m.debruin@amc.nl
tel: +31 (0) 2025665179