FT-IR spectroscopy used for identification of cancer specific biomarkers in blood plasma

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ABSTRACT

Colorectal cancer is among the widespread benign types of digestive cancers. In this study the Fourier Transform InfraRed spectroscopy (FT-IR) method is used for the identification of specific features associated to the colorectal cancer from native and deproteinized blood plasma and from blood plasma proteins. The blood samples were collected from patients with confirmed colorectal cancer and from healthy voluntaries for comparison. Advanced FT-IR spectroscopy and ^{1}H NMR relaxometry and diffusometry are applyed. The FT-IR spectra can be divided into specific regions. A numeric deconvolution procedure can be applied in order to quantify the integral area of peaks of interest which finally can be associated with specific biomarkers of metabolites response in colorectal cancer. A statistical analysis in principal components can be applied in order to identify the most important FT-IR spectral parameters for the differentiation between samples belonging to patients with colorectal cancer and healthy volunteers, and for the evaluation of the degree of method sensibility and specificity.

INTRODUCTION

Colorectal cancer is the second most common cancer in the world [1] and has aggressive malignancy with a high tendency to deep invasion, lymph node metastases and distant metastases. Due to its frequently diagnosis only in the advanced stage, the incidence of colon cancer increases remarkably every year. Nowadays, patient management is based on tumor progression by determining tumor size, degree of spread to regional lymph nodes, the presence of distant metastases, and other comorbidity factors using laboratory and specific tumor markers and imaging methods [2, 3]. The study of blood-based samples, in particular blood plasma, by Fourier transform infrared spectroscopy (FT-IR) is not a new concept [4].

MATERIALS AND METHODS

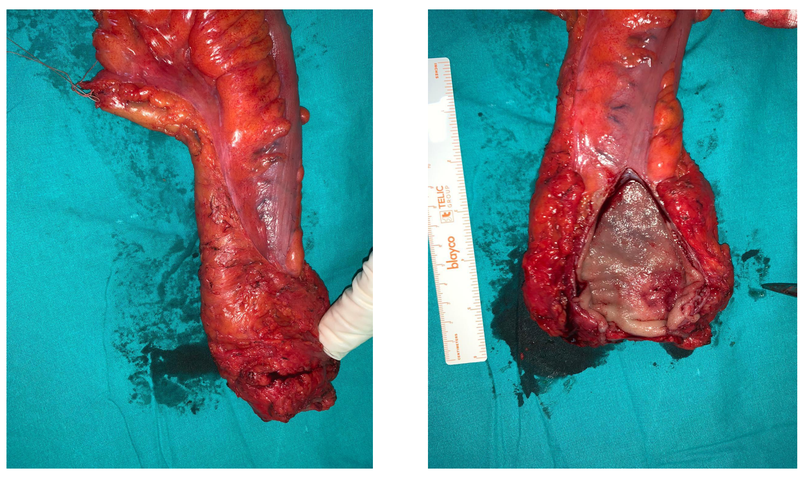

FIGURE 1. Rectal tumor (left) and section through the rectal tumor (right).

FIGURE 2. Centrifuge used first for the separation of blood plasma and then used for obtaining the deproteinized plama and proteins.

RESULTS

^{1}H NMR relaxometry: the T_2-distributions

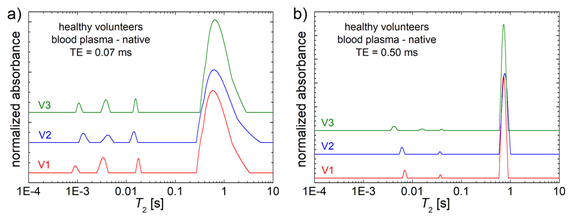

FIGURE 3. T_2 relaxation time distributions measured for blood plasma collected from healthy V1-V3 volunteers with an echo time of a) TE = 70 μs and b) TE = 500 μs.

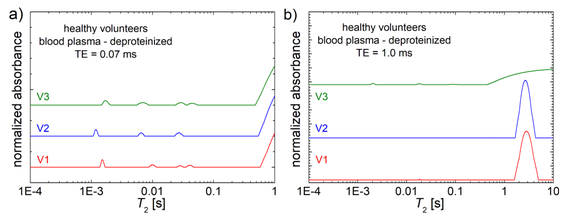

FIGURE 4. T_2 relaxation time distributions measured for deproteinized blood plasma collected from healthy V1-V3 volunteers with an echo time of a) TE = 70 μs si b) TE = 500 μs.

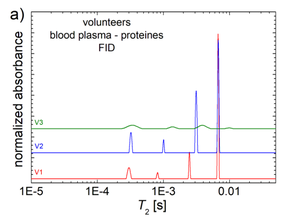

FIGURE 5. T_2 -distributions measured for proteines from blood plasma collected from healthy V1-V3.

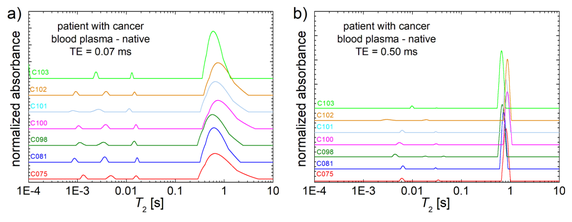

FIGURE 6. T_2 relaxation time distributions measured for blood plasma collected from patients with cancer with an echo time of a) TE = 70 μs and b) TE = 500 μs.

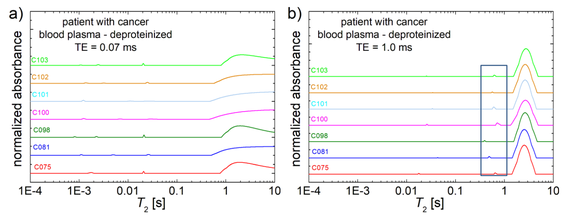

FIGURE 7. T_2 relaxation time distributions measured for deproteinized blood plasma collected from patients with cancer with an echo time of a) TE = 70 μs si b) TE = 500 μs.

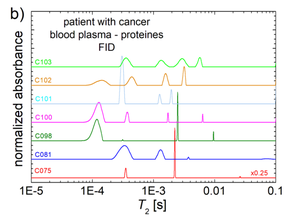

FIGURE 8. T_2 -distributions measured for proteins from blood plasma collected from patients with cancer.

^{1}H NMR diffusometry: the D-distributions

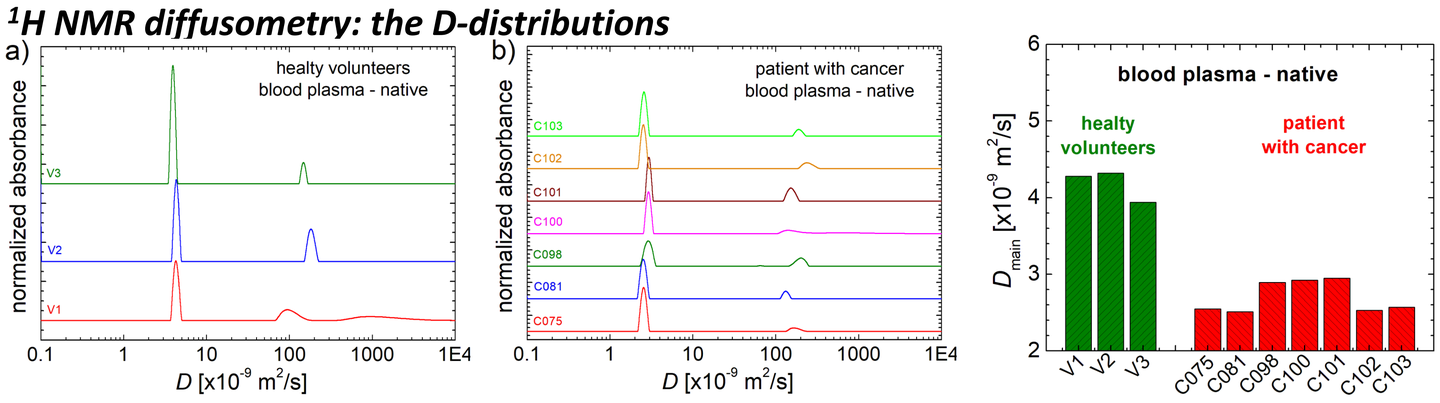

FIGURE 9. ^{1}H NMR self-diffusion coefficient *D*-distribution measured for a) healthy (V1-V3) voluntainers and b) patients with cancer.

FIGURE 10. The main value of the self-diffusion coefficient *D* measured for healthy voluntainers and patients with cancer.

FT-IR spectroscopy

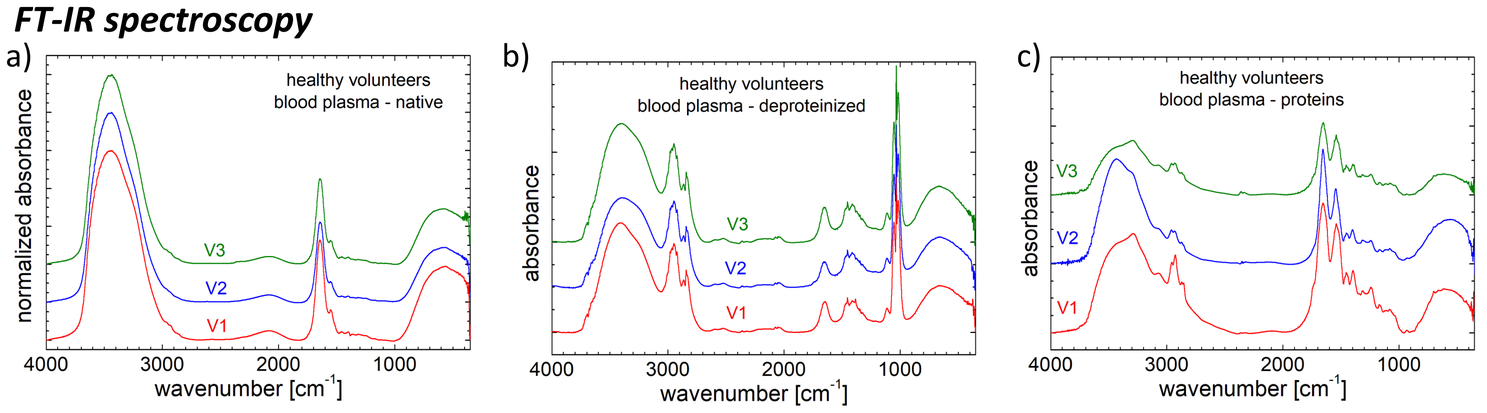

FIGURE 11. FT-IR spectra of a) blood plasmaș b) deproteinizated blood plasma and c) proteins from blood plasma measured for healthy volunteers.

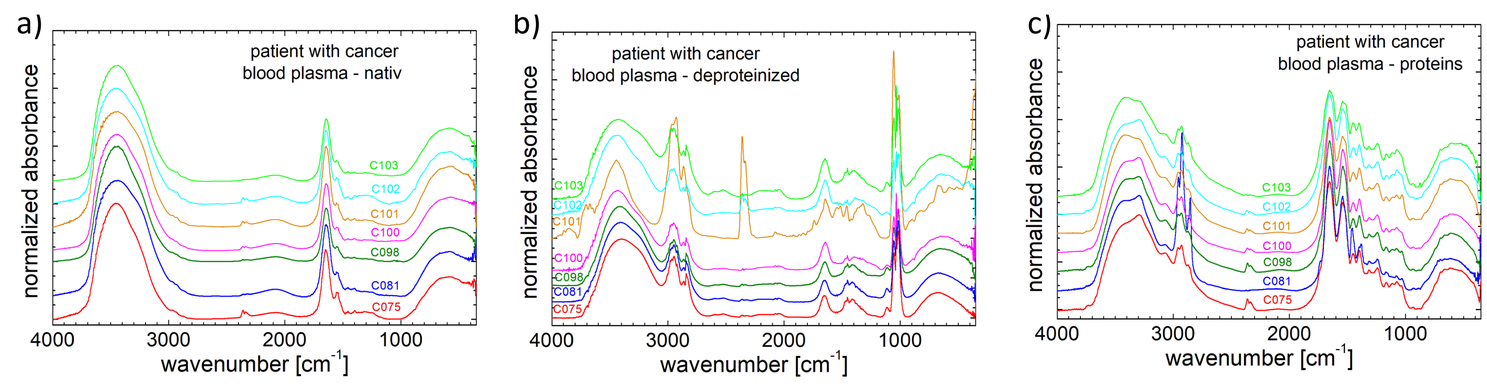

FIGURE 12. FT-IR spectra of a) blood plasmaș b) deproteinizated blood plasma and c) proteins from blood plasma measured for patient with cancer.

CONCLUSIONS

It was proposed to use ^{1}H NMR relaxometry and diffusometry correlated with advanced Lapalce transform analysis and FT-IR spectroscopy to characterize blood plasma (native plasma, deproteinized plasma and plasma proteins) in order to identify some parameters from specific spectroscopic features leading to the identification of colorectal cancer. The distributions of T_2 for native plasma, deproteinized plasma and plasma proteins for three healthy volunteers and 7 colorectal cancer patients were measured. It has been observed that in cancer patients the Laplace spectra (T_2 distributions) measured for deproteinized plasma using the CPMG pulse sequence with TE = 1 ms show a small peak located between 500 ms and 1000 ms. The distributions of self-diffusion coefficient, *D* for native plasma, deproteinized plasma and plasma proteins were measured for three healthy volunteers and 7 colorectal cancer patients. It was observed that in cancer patients the distributions of *D* measured for native plasma show a main peak whose maximum appears at a value of less than 3×10^{-9} m^2/s while the maximum value of the main peak in the distribution of D measured for healthy volunteers appear at a value greater than 3.9×10^{-9} m^2/s . FT-IR spectra were measured for native plasma, deproteinized plasma and plasma proteins for three healthy volunteers and 7 colorectal cancer patients. No visual features specific to cancer patients have yet been detected in the visual analysis.

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