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# Study of paraffin-embedded colon cancer tissue using terahertz spectroscopy

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## HIGHLIGHTS

- Colon cancer detection by THz-TDS.
- Paraffin-embedded samples.
- Sample cancer affected tissue zones, low transmittance.
- High absorption coefficient and refractive index for affected tissue.
- Dehydration of bio-tissues lead *t* low contrast.

## ARTICLE INFO

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## ABSTRACT

In this work, samples of non-neoplastic and adenocarcinoma-affected human colon tissue samples were analyzed using multipoint transmission time-domain THz spectroscopy (THz-TDS) to sort out the contrast-contributing factors other than water, the main contrast mechanism factor in *in-vivo* or in freshly excised bio-tissue. Solving the electromagnetic inverse problem through THz-TDS and, analyzing the transmittance spectra that yielded the frequency-dependent absorption coefficient $\alpha$ and refractive index $n$ of non-neoplastic and neoplastic tissues, we show that it is possible to distinguish between non-neoplastic and neoplastic regions in paraffin-embedded dehydrated. Results and discussion are presented.



## Introduction

Colon cancers is among the most commonly diagnosed cancers and mortality cause (1.23 million, 9.7%) worldwide according to estimates [1]. Early clinical diagnosis is crucial for in time patients' treatment. Colon cancer is neither rare anywhere in the world, nor mainly confined to high-resource countries.

Terahertz time domain spectroscopy (THz-TDS) has had a breakthrough in the middle of 80's, and followed by a THz imaging with THz-TDS. Presently, several THz-TDS systems are commercially available, some of them being directly derived from laboratory setups while others are compact and integrated with more sophisticated man–machine interfaces. The main advantage of a THz-TDS resides on the determination of the broadband response of a sample at once in combination with the actual high stability of the mode-locked lasers, which leads to a very good signal-to-noise ratio (SNR). Moreover, the SNR is reinforced by the time-windowing approach that eliminates a large part of the noise, and the coherent

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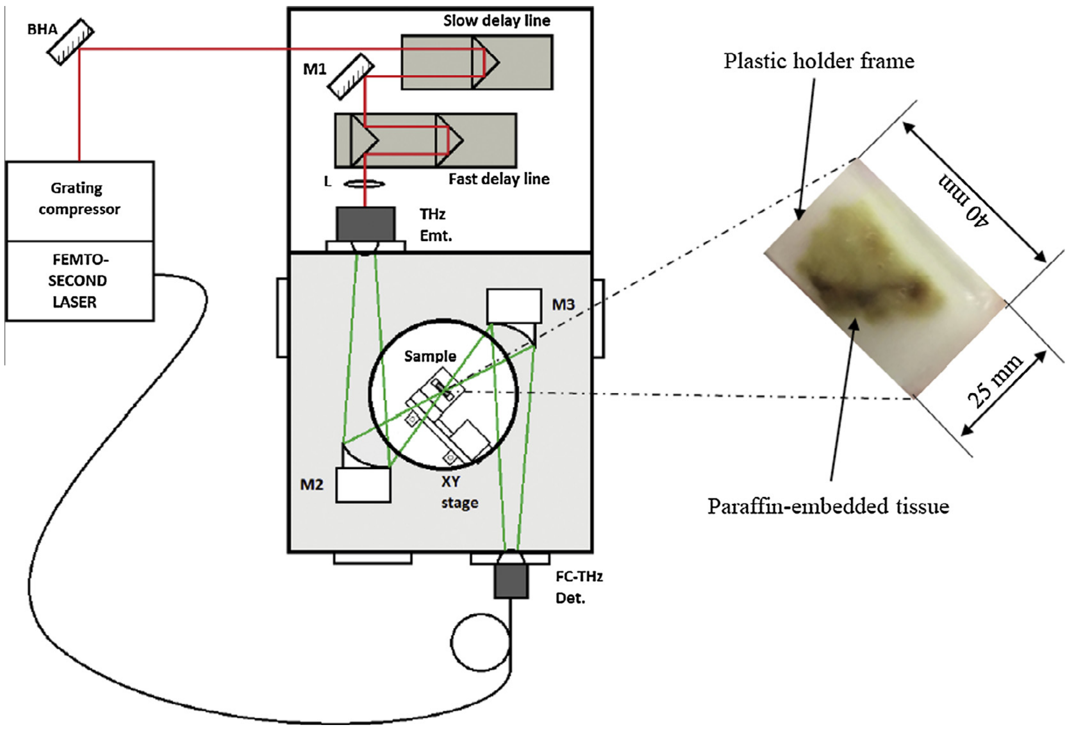


**Fig. 1.** Schematic experimental set-up used in the THz-TDS system.

time gated detection technique giving an efficient elimination of background noise that commonly leads to a very high signal to noise ratio.

The versatility of the THz-TDS set-ups based on quasi-optical elements offers a large variety of configurations. THz-TDS spectrometer measures simultaneously both the amplitude and phase of the THz pulse transmitted or, reflected by the sample, the determination of optical parameters of the sample such as refractive index ($n$) and absorption ($\alpha$) on a broad frequency range is possible without using the Kramers–Kronig analysis. The thickness as well as scattering or diffraction parameters of the sample material under study can also be extracted [2].

The terahertz waves having very low photon energy, i.e., energy levels of few meV (<1 $\mu$W) [3], which is well below the ionization energies of atoms and molecules, does not pose any ionization hazard for biological tissues.

Because of these characteristic properties combined with the fact that the characteristic energy of biological medium because of molecular motions such as rotational and vibrational ones, lies in the THz frequency band (that allows THz waves to directly detect spectral signatures of molecules), has spurred a worldwide interest in the exploitation of this frequency band and related techniques (spectroscopy and imaging) for biomedical application in the last two decades with more and more terahertz spectra being reported in spectroscopic studies of cancer particularly.

Water is essential in biological systems and, it plays a key role as the solvent in molecular reactions. It shows characteristic absorption features mainly the infrared (IR) and THz bands, owing to the fact that its resonance is related to symmetric stretch, bending, libration and rotation which are modified by hydrogen bonding in the liquid state [4]. THz waves are very sensitive to water content and strongly attenuated by water in which biological molecules reside. The presence of cancer often causes increased blood supply to affected tissues and a local increase in tissue water content may be observed: this fact acts as a natural contrast mechanism for terahertz spectroscopy and imaging of cancer. Furthermore the structural changes that occur in affected tissues have also been shown to contribute to terahertz spectroscopy and image contrast.

Presently diagnostic techniques such as X-ray imaging and magnetic resonance imaging (MRI), and biopsy are one of nowadays ones in use. Histo-pathologists use microscopic imaging methods of biopsied tissue parts to provide structural and functional information. Whereas X-ray imaging and MRI provide images of living tissues at the macroscopic level, but at much lower resolution and specificity [5]. Techniques of highly-resolved imaging for *in vivo* diagnostic screening that would provide the best information for the early detection of disease are not yet available. THz techniques are thus expected to bring a more comprehensive screening and diagnosis of human disease, particularly in the case of cancer, namely as a non-invasive detection tool, ideally also in early phases of tumor development.

THz transmission spectroscopy has previously been used to obtain the THz optical characteristics of skin tissue [6,7]. THz pulsed spectroscopy has also been used to successfully characterize DNA and proteins, allowing intermolecular interactions to be probed [8]. The THz-TDS combined with THz imaging can be used for macroscopic visualization of tumor margins in fresh tissues according to first published results on cancer tissue imaging using THz pulsed radiation [9–12], and later confirmed by studies on various cancer types and organs.

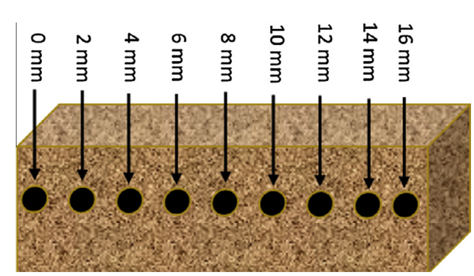


**Fig. 2.** Sketch of a sample with indicated measured points.