Noninvasive 3D Characterization of Layered Samples using Terahertz Pulsed Imaging and Infrared Optical Coherence Tomography

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***Abstract*—Terahertz pulsed imaging (TPI) and Optical Coherence Tomography (OCT) are two powerful techniques allowing high quality three-dimensional images from within scattering media to be obtained noninvasively. In this paper, we report experimental results of using TPI and OCT for characterizing layered samples including pharmaceutical coatings. We found that infrared OCT provides better axial resolutions whilst TPI is less prone to scattering problems thus is well suited for characterizing pharmaceutical tablet coatings.**

I. INTRODUCTION

Terahertz pulsed imaging (TPI) is a powerful technique for noninvasively characterizing the internal structures of a sample. In particular, THz radiation can penetrate most pharmaceutical excipients, and this makes TPI an increasingly popular tool for assessing information from various pharmaceutical solid dosage forms. These include coating thickness measurement, coating interface evaluation and tablet dissolution prediction[1-4]. Optical Coherence Tomography (OCT) is also a noninvasive and cross-sectional imaging technique, which permits, for example, micrometer-resolution three-dimensional images to be obtained from within the retina[5-6]. However, most commercially available OCT systems are optimized for medical applications, and its applicability to pharmaceutical samples has yet to be demonstrated. In this paper, we present a study of using both TPI and OCT techniques for nondestructive analysis of pharmaceutical tablets.

II. EXPERIMENT

All THz measurements were performed using TPIimaga2000 (TeraView Ltd, Cambridge, UK), which is capable of recording a complete terahertz waveform in 20 ms, within the spectral range of 2 cm^{-1} to 120 cm^{-1}. The TPI system has been purposely developed for the fully automated scan of typical pharmaceutical solid dosage forms[1]. In particular, a six-axis robot system was employed to handle the tablets. This ensures that the tablet is always at the terahertz focus position with its surface always perpendicular to the terahertz probe during a TPI measurement, even for tablets with curved surfaces.

All optical measurements were carried out using a benchtop OCT system, with an operating spectral range between 10000 cm^{-1} to 29000 cm^{-1}. As shown in Fig.1, the light from a 50W halogen lamp is imaged onto the entrance pupil of the interferometer using a biconvex lens. Light is then split into reference and sample beams by a beam-splitter. Both the "object image" and the "reference image" of the entrance pupil were formed at the entrance slit of a spectrometer. The phase-shifting method[7] is employed to increase the detection sensitivity by using a PZT actuator. One distinct feature of our OCT system is the combination of a broadband CCD-based spectrometer with a white light source, which has extremely short coherence length. This configuration provides good signal-to-noise ratio and excellent axial resolution.

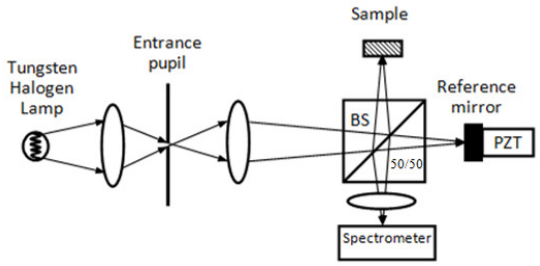

Fig.1. Spectral/Fourier domain OCT experimental set-up

III. RESULTS AND DISCUSSIONS

Two types of samples were used in this work: one is a pellet with flat surfaces and the other is a pharmaceutical placebo tablet with a single coating layer and curved surfaces. Fig.2 (a) and (b) show the terahertz waveform and cross-section image, respectively, of a polyethylene/lactose sample (a small lactose pellet sandwiched in a larger polyethylene pellet). The polyethylene/lactose interface at 1 mm below the surface can be seen clearly, demonstrating the excellent penetration capability of the TPI technique. Fig.2 (c) and (d) show OCT results of a multi-layered sample. The sample used has three layers: a top cling film layer (A), a polymer layer (B), a glue layer (C) and a plastic substrate (D). As shown in Fig.2 (c) and (d), the cling film and the polymer layer can be easily resolved. The achieved axial resolution is 0.7 μm, one of the best ever reported. Note that at a depth of 60 μm there is an additional OCT feature corresponding to glue/plastic interface. This OCT feature is very weak, possibly owing to the small refractive index difference between the glue layer and the plastic substrate. The optical scattering in the non-uniform glue layer will certainly decrease the signal further.

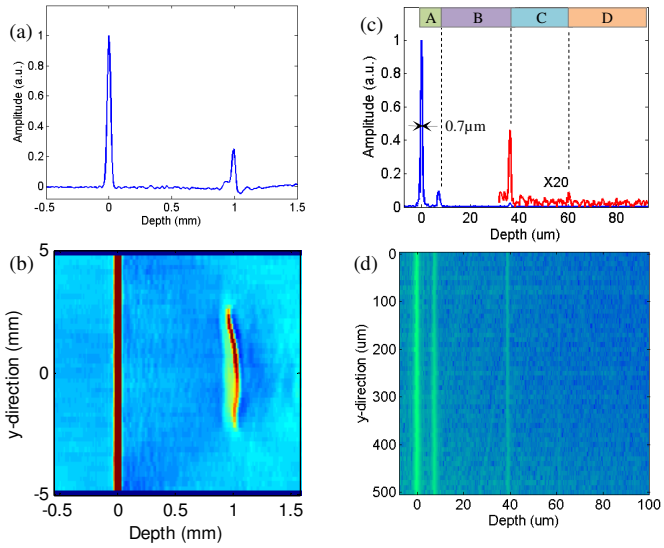

Fig.2 (a) Terahertz waveform, and (b) TPI cross-section map showing a buried structure at 1 mm below the sample surface; (c) FFT of coherent interference spectrum, and (d) OCT cross-section map showing layered features at 0, 7, 37 and 60 μm, respectively.

In order to demonstrate the capability of TPI and OCT for non-destructively characterising real-world samples, two coated tablets with different coating thicknesses were analyzed. Fig.3 (a) and (b) show the terahertz waveform and TPI cross-section map of the tablet with the thicker film coat. There is a clear tablet coating/core interface at about 80 μm beneath the coating surface. A mean coating thickness of 80 μm was subsequently determined for this tablet. For the tablet with the thinner film coating, the tablet coating/core interface was just visible in the TPI images (images are not shown here). However, the coating thickness was unable to be accurately determined because the coating thickness was below the 40 μm detection limit of the current TPI set-up [1-2].

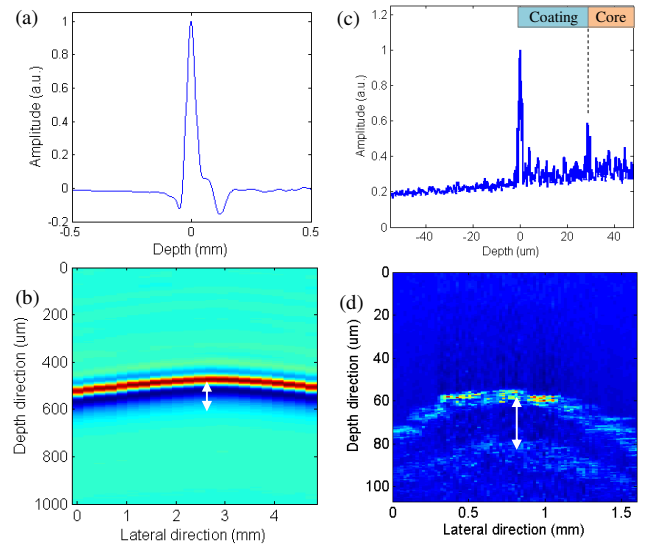

Fig.3 (a) Terahertz waveform, and (b) TPI cross-section map of a tablet with coating thickness of about 80 μm; (c) FFT of coherent interference spectrum, and (d) OCT cross-section map of a tablet with coating thickness of about 25 μm. The double-headed arrows indicate the thickness of the tablets.

Fig.3 (c) and (d) show the FFT of the coherent interference spectrum from the OCT set-up and the corresponding cross-section map of the tablet with the thinner film coat. There is a weak but clear OCT feature at about 25 μm below the tablet coating surface, which was confirmed as the tablet coating/core interface. Note that the surface reflection feature is broader than that of the layered sample in Fig.2 (d). This is mainly attributed to coating surface roughness[8]. The mean coating thickness was determined to be 25 μm. To the best of our knowledge, this is the first OCT cross-section image of a tablet ever reported. For the tablet with an 80 μm coating, however, the coating structure cannot be resolved using the current OCT system. More work is needed to improve the sensitivity of OCT in order to resolve thicker coating layers. Nevertheless, our results demonstrated that OCT has great potential to non-destructively characterise pharmaceutical tablets.

In conclusion, operating in shorter wavelength than TPI, OCT provides higher axial resolutions whilst TPI penetrates deeper into the sample and is less prone to scattering problems. With further improvements on the signal sensitivity, OCT demonstrated potential as a complementary analytical technique to TPI for characterizing pharmaceutical tablet coatings.

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