

measurements provided a product image resolution of $\sim 5\text{--}8\ \mu\text{m}$ over a $\sim 1\text{--}2\text{-mm}$ depth and a $\sim 3\text{--}4\text{-mm}$ height in a vial during product formulation freeze-drying. The OCT 2D image slices were used to construct 3D images which were combined with TC-based product temperature measurements during freeze-drying to determine the product collapse temperature, T_c , in a container of practical significance, a vial.

Instrument Description

The OCT-FDM system consisted of an optical microscopy system combined with a single-vial freeze-dryer as shown in the Fig. 4 schematic. The experiments focused on developing and demonstrating a product collapse temperature measurement system that enabled determination of T_c in a container of practical importance under drying conditions typically encountered during standard pharmaceutical product lyophilization. The new approach was designed to overcome the limitations of LT-FDM described above. The single-vial freeze-dryer included a temperature-controlled product shelf, a liquid nitrogen-cooled cold-finger-based condenser for cryo-pumping water vapor, a mechanical pump for removing the noncondensable gases, a Pirani gauge and capacitance manometer for monitoring the product drying chamber pressure, and a vacuum isolation valve and a window to enable optical interrogation of the product drying within the vial. A top-view photograph of the single vial dryer loaded with a vial and the imaging coordinate system is shown in Fig. 5. Optical interrogation was performed through the window port on the left side of the product chamber. Vacuum pump out was accomplished through the right side of the chamber.

A time domain OCT (TDOCT) imaging system was used to interrogate the pharmaceutical product contained in the vial during freeze-drying. Figure 6 shows a schematic of the TDOCT setup. The OCT system was driven by a fiber-coupled $1275 \pm 50\text{-nm}$ superluminescent diode whose output was split into two optical paths using a 90/10% fused fiber optic splitter. The 10% output from the splitter was used to illuminate the reference arm optics through an acousto-optic modulator (AOM)

Fig. 4 Schematic diagram of the OCT-FDM imaging system including the single-vial freeze-dryer and the optical microscopy system. OCT-FDM optical coherence tomography freeze-drying microscopy

