with prolonged usage, heat transfer via radiation can become significant due to the increasing emissivity of the filament; some periodic maintenance/replacement may be needed to ensure accuracy.

A capacitance manometer (CM, also called MKS Baratron) is commonly put in the drying chamber to measure and control the chamber pressure during lyophilization [18]. The CM device is made of a metal diaphragm placed between two fixed electrodes, with one side being evacuated to high vacuum to serve as a zero reference pressure, and the other side being exposed to the chamber pressure. Since a change in device output voltage is directly proportional to the applied pressure, the CM is able to measure the absolute pressure independent of the gas composition, which is different from the Pirani gauge [19]. In addition, CM can give a stable output within a very wide pressure range (0–760 Torr), and can withstand steam sterilization. Therefore, the CM is commonly used for chamber pressure measurement in the freeze-drying process.

The joint use of a Pirani gauge with a CM has been employed to determine the endpoint of primary drying for the entire batch. At the early stage of primary drying, essentially all of the gas in the drying chamber is water vapor, and thus the Pirani gauge gives about 60% higher result than CM reading because thermal conductivity of water vapor is about 60% higher than that of nitrogen [22]. At the late stage of primary drying, the gas composition in the drying chamber changes from mostly water vapor to mostly nitrogen, and thus the Pirani gauge will show a sharp drop in pressure and finally merge with CM readout as shown in Fig. 1. This sharp transition and the small pressure differential (ΔP) between Pirani and CM is an indication of the completion of primary drying. Once the primary drying endpoint has been reached, ΔP will be close to zero and remains constant. The $\Delta P = 0$ criteria could be used as a reliable detection of endpoint of primary drying, and this ΔP between Pirani and CM can be used as a control tool if a feedback loop is programmed to allow the automatic progression to the next drying step.

The drying process can also be monitored by taking vials out of chamber at different stages of primary drying using a "sample thief." A systematic study was performed for both 5% sucrose and mannitol systems, and residual water was measured either by gravimetric or Karl Fischer method [20]. Figure 3 shows the Pirani and CM pressure trends and percent residual water profile during primary drying for 5% sucrose (a typical amorphous system). At the onset, midpoint, and offset points of pressure drop in the Pirani gauge, the residual water content is about 25, 9, and 5%, respectively. When the sample vial is warmed to ambient temperature, the midpoint vial cake (taken out at about 48 h) showed collapse behavior, suggesting that residual moisture present is high enough to depress T_g to be below 25 °C. However, the offset point gives acceptable cake structure due to sufficiently low moisture. For the 5% mannitol system, the onset, midpoint, and offset points of pressure drop from the Pirani gauge give about 9, 5, and 4% residual water, respectively. Also, all three points give good cake structure for this crystalline system [20].

It is often helpful to define the endpoint of primary drying based on the Pirani transition alone. After primary drying is complete, most "unfrozen" water has been removed. However, the product still contains a relatively high level of residual water