Heat transfer due to radiation, which is affected by the material emissivity, is an important heat transfer mode during lyophilization [11]. In laboratory dryers, the chamber may be fitted with a Plexiglas door which has higher emissivity than stainless steel. Due to emissivity differences, the vials close to the door (front edge vials) dry at a higher rate than the vials placed in the center of the array. These vials also dry faster than the vials on either side (left or right) of the array and back of the array. This phenomenon is known as the edge effect [39]. The percentage of edge vials in a commercial lyophilizer is less than a laboratory-scale lyophilizer. Moreover, presence of a stainless steel door reduces the atypical heat transfer as observed on a laboratory-scale lyophilizer.

The contribution of radiation to the overall heat transfer model has been studied in detail [11]. It has been shown that radiation is an important source of heat transfer under vacuum conditions for a vial in direct contact with the shelf. As expected, the closer to the wall or door, the higher the contribution of radiative heat transfer, which is also represented in the form of weight loss in Fig. 1. It was reported that the contribution of radiation to the overall heat transfer is about of 49% for a vial directly in contact with the shelf at a pressure of 100 mTorr and a shelf temperature of +25 °C. Similar radiation contribution was found at a shelf temperature of −20 °C at the same pressure condition [11].

An uncontrolled vial manufacturing process can lead to differences in the area of actual contact between vial and shelf (i.e., the term K_c) and the gap between the shelf and the bottom of the vial (l_v) for vials manufactured either in the same batch or within batches. Variation in the term "l_v" can lead to differences in the heat transfer through K_g and variation in the vial surface area can affect all modes of heat transfer [35]. Therefore, it is critical to have a good estimate of the differences in the K_v between vials within a batch and also between different batches of vials.

It is important to understand the impact of K_v on product temperature and product quality. It is well documented that a higher K_v results in a higher product temperature profile and in turn a higher rate of sublimation. A higher product temperature may result in an already aggressive primary drying step to become much more aggressive and potentially resulting in cake collapse or even melt, although actual melting is rare. Collapse may result in stability issues for protein formulations. In addition, an increase in the product temperature and subsequent increase in sublimation rate may result in the inability to control pressure due to limitations imposed by dryer capability.

The measurement of K_v can be accomplished through a series of sublimation runs using water at different chamber pressure set points (refer to Fig. 1). Water is filled into the vial to a fill volume of 50% of the vial capacity and subjected to sublimation for a target time at which approximately 25% of water is lost due to sublimation. Thermocouples are placed in selected vials across the shelf to allow measurement of product temperature, and the weight loss (refer to Fig. 1a) is calculated for all vials by weighing each vial before and after the run. As heat transfer is a function of chamber pressure, it is important to measure K_v at several pressure set points close to the actual sublimation conditions. The K_v values measured for each set point are fitted using nonlinear regression analysis, resulting in a model for K_v