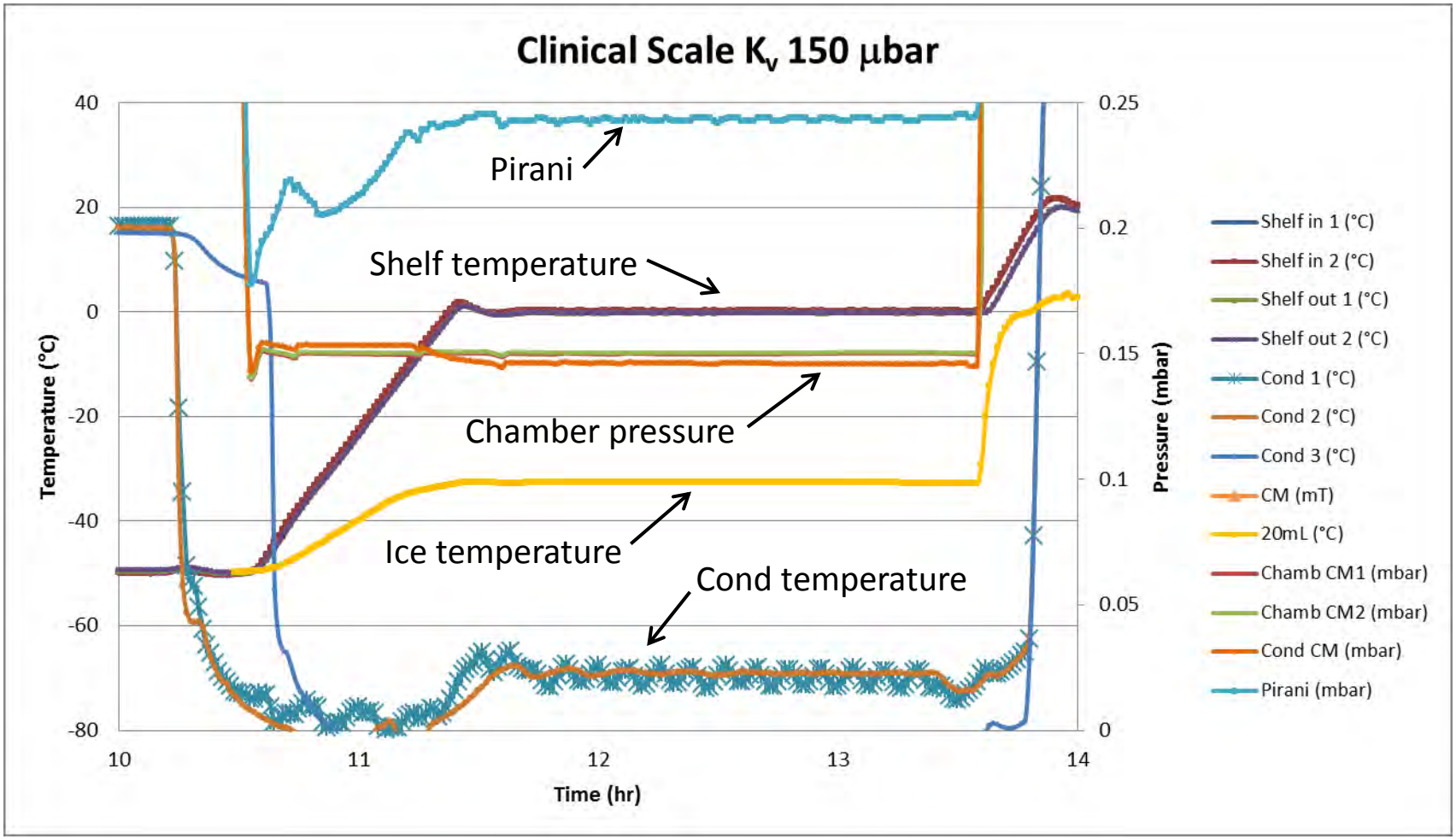
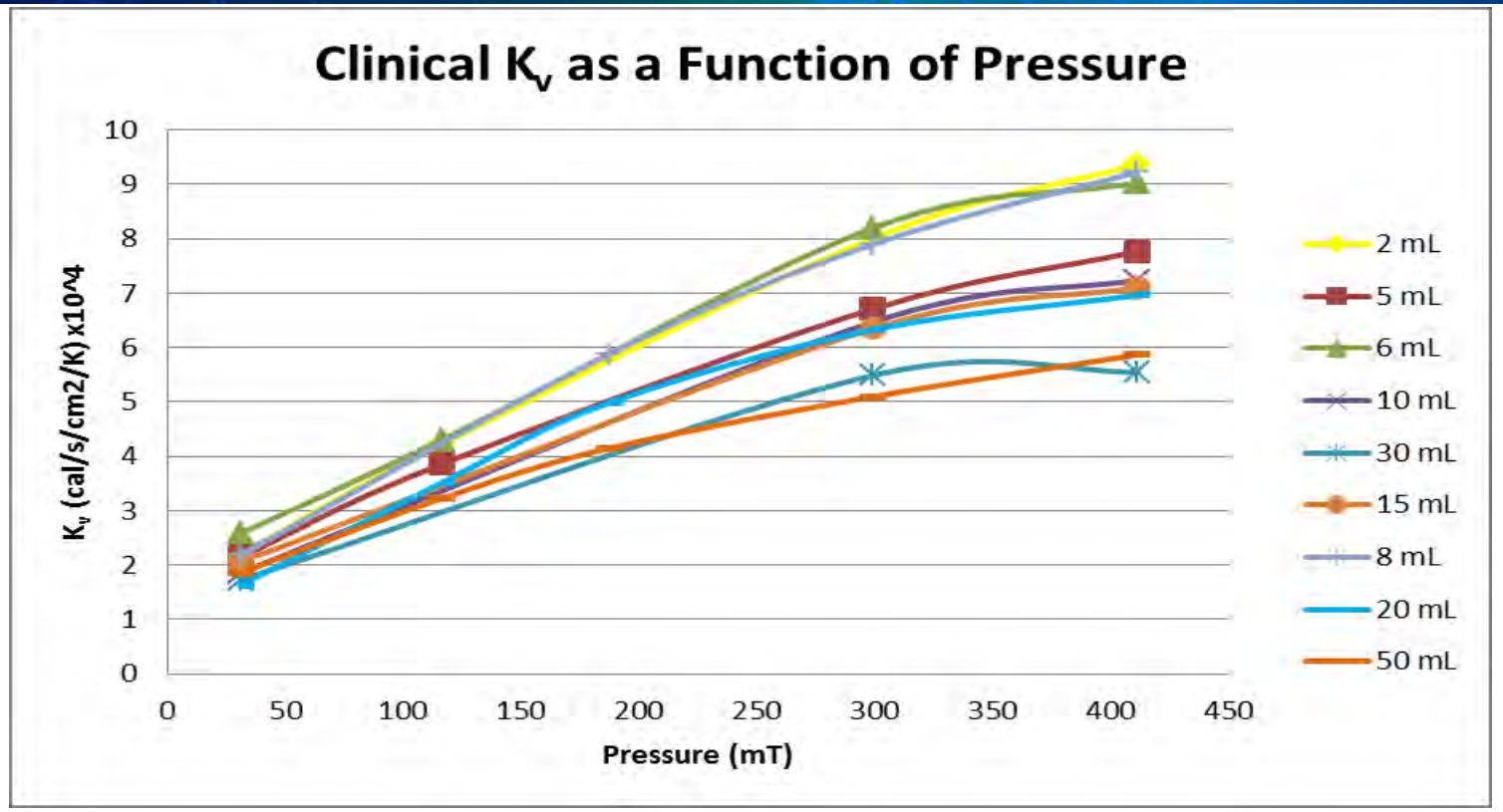
# $K_v$ Cycle Trace



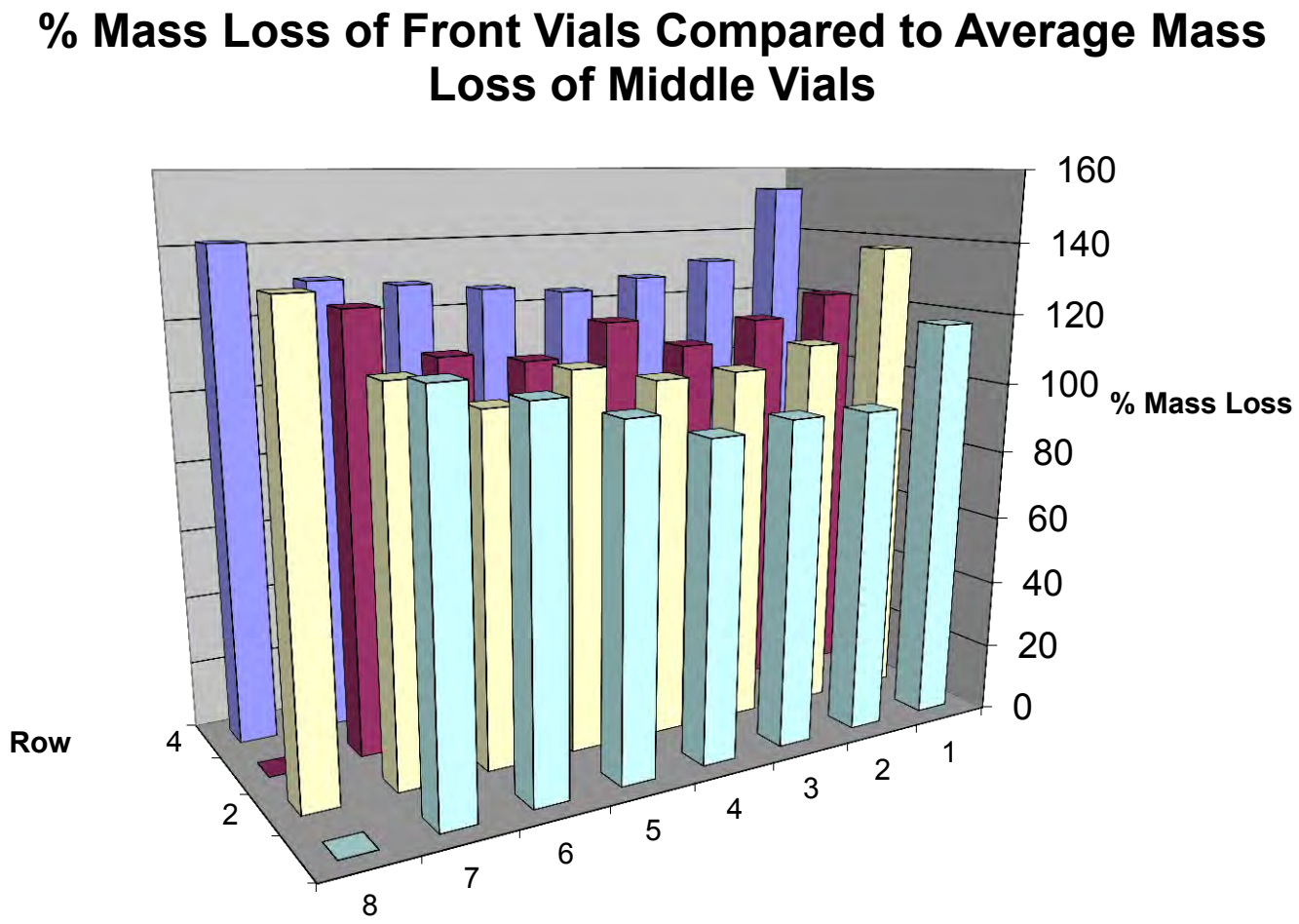
# Clinical $K_v$ Results




$$K_v\left(\frac{Cal}{s * cm^2 K}\right) = a + \frac{bP(Torr)}{1 + cP(Torr)}$$

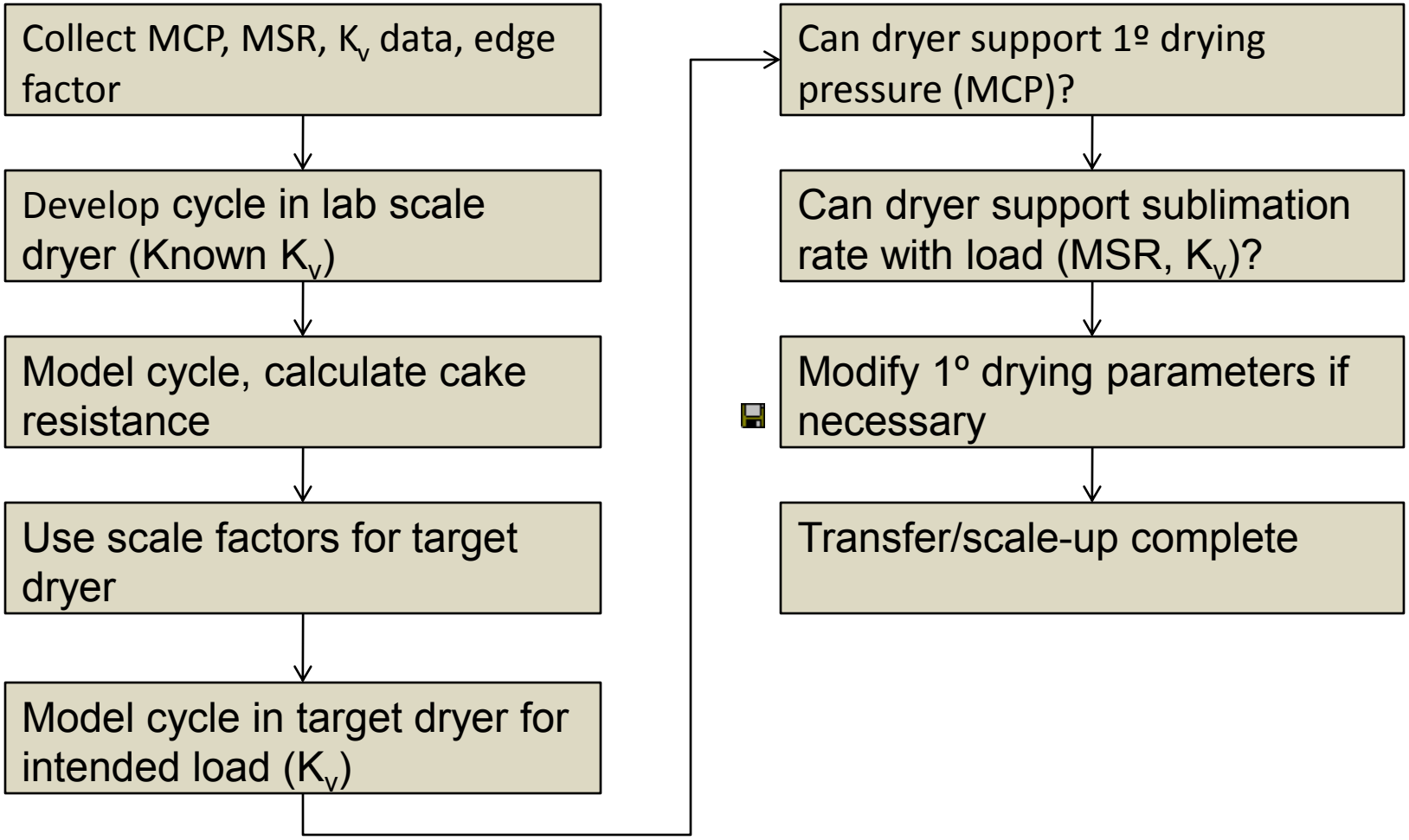
**Coefficients a, b and c are inputs in the model for $K_v$**

# Edge Effect: Extra Heat Added by radiation

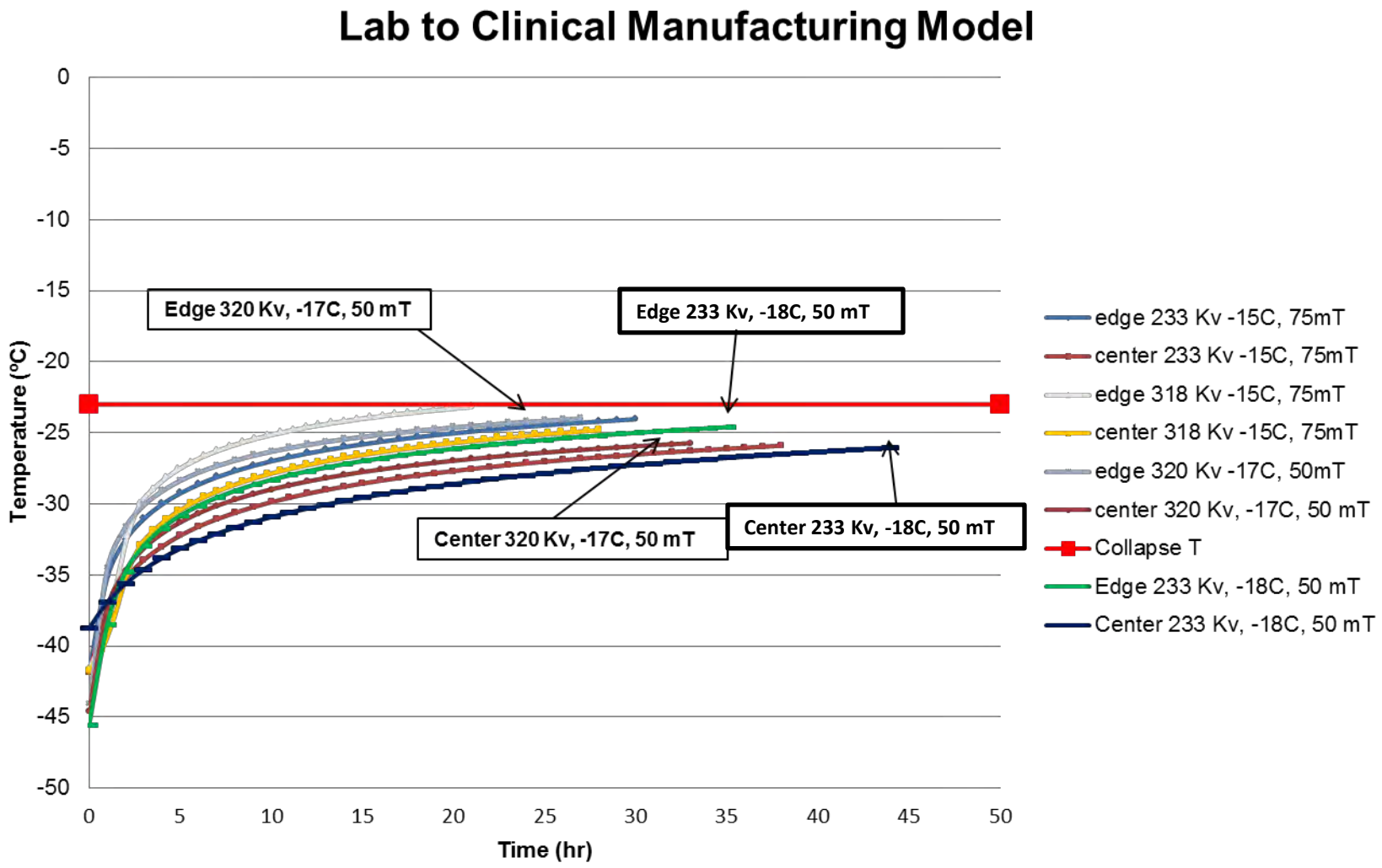



$K_v$(edge)=Factor*$K_v$(center)- input in lyo model

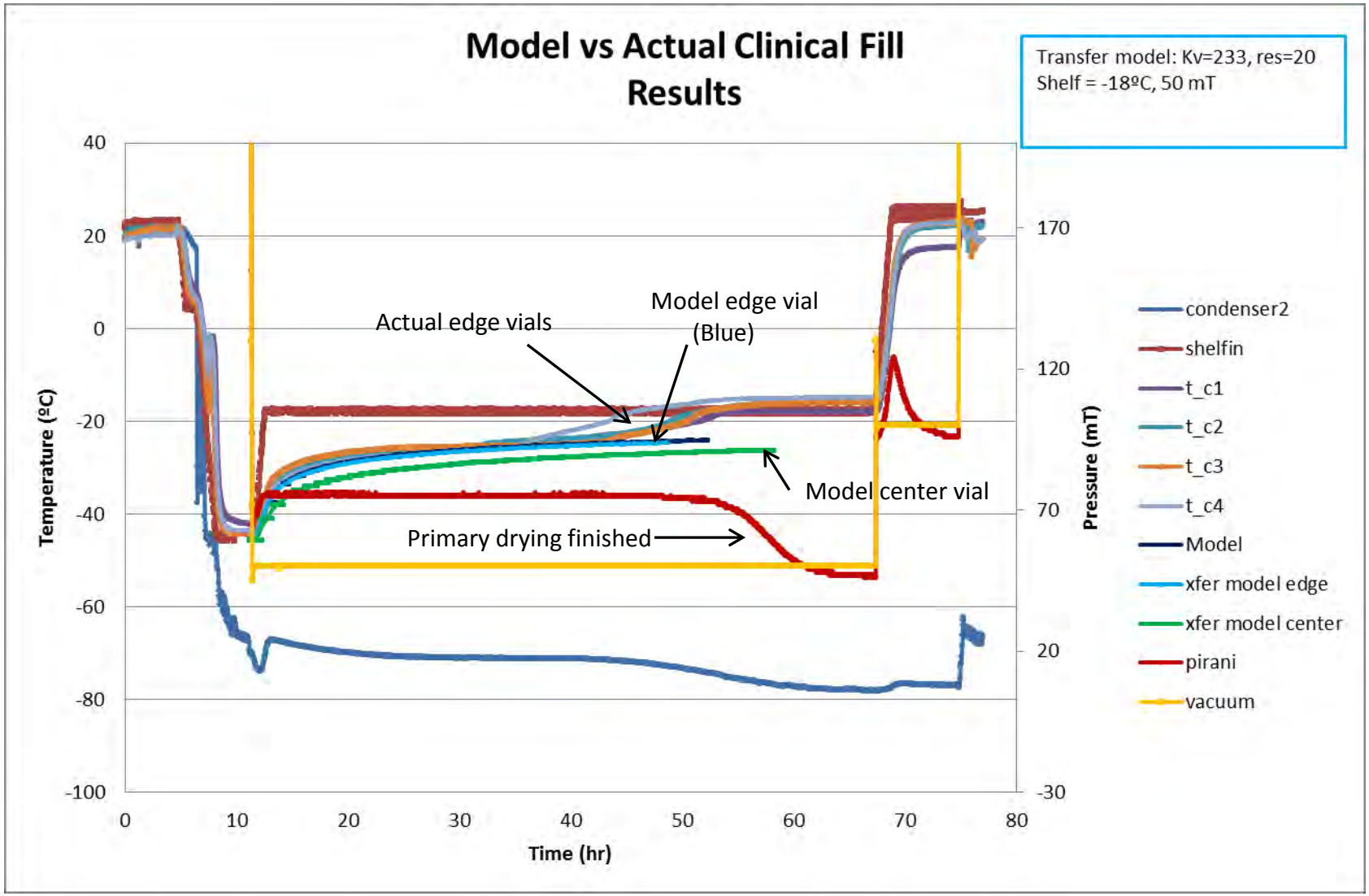
# Application of Characterization Data



# Scale up from Lab to Clinical Manufacturing



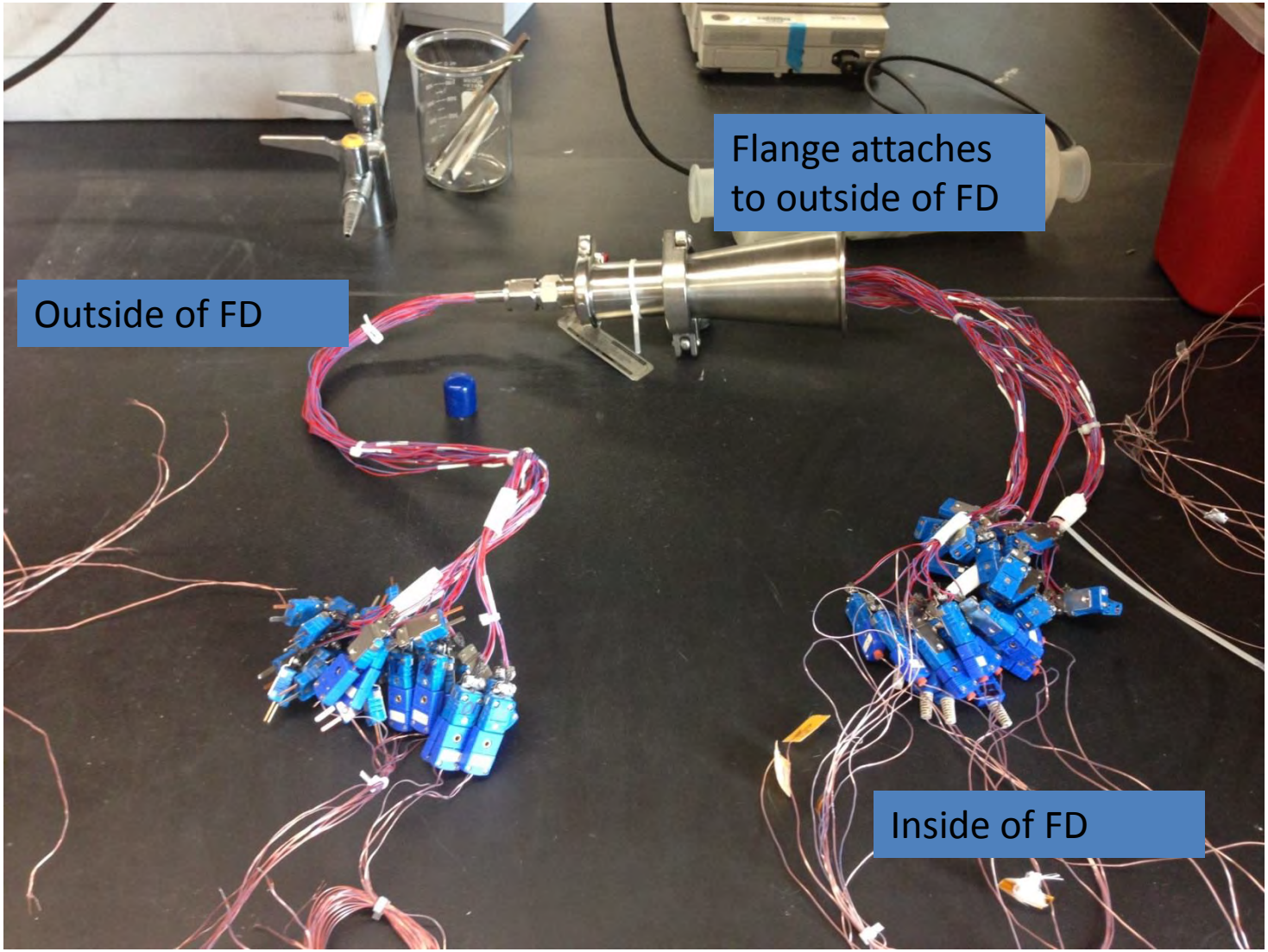
# Results of Clinical Cycle



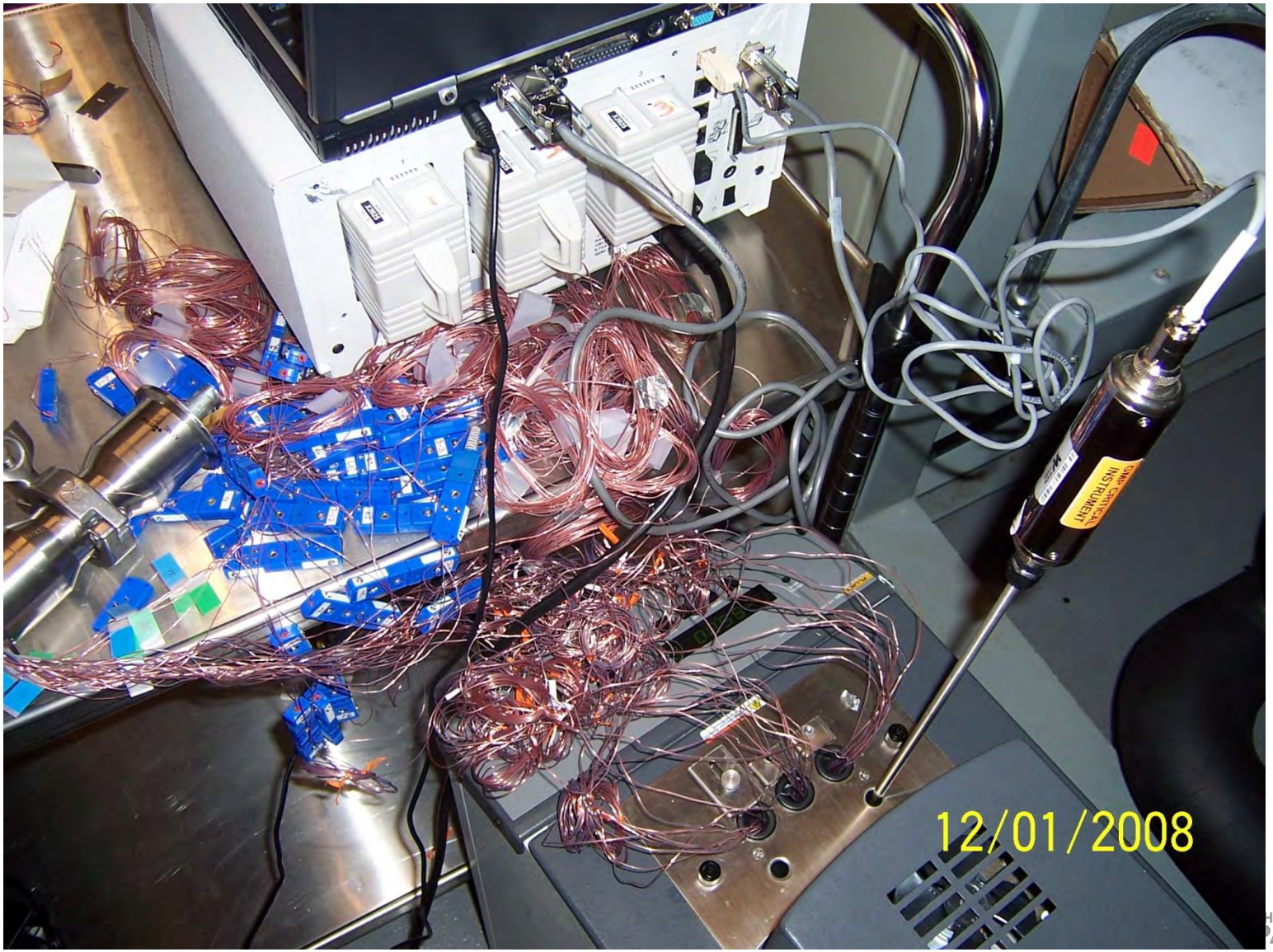
# Challenges Involved in Execution of Characterization Work

- Preparation
  - Planning should start ~6-9 months prior to execution
    - Generate protocols
    - Acquire equipment
  - Ensure cycle data collection
    - 1 minute intervals
    - Must be able to retrieve data (no manual data collection!)
  - Calibration of pressure gauges
    - Must be within calibration schedule
    - Must use the correct range (0-1000 mT, 0-1.333 mBar)
- Thermocouple data collection
  - TCs, Ellabs, Tempris
    - Must be calibrated
    - Collect data in 1 minute intervals
- Target a 25% mass loss for MCP
  - More than 35% creates error

# Challenges: Using a Feedthrough and TCs



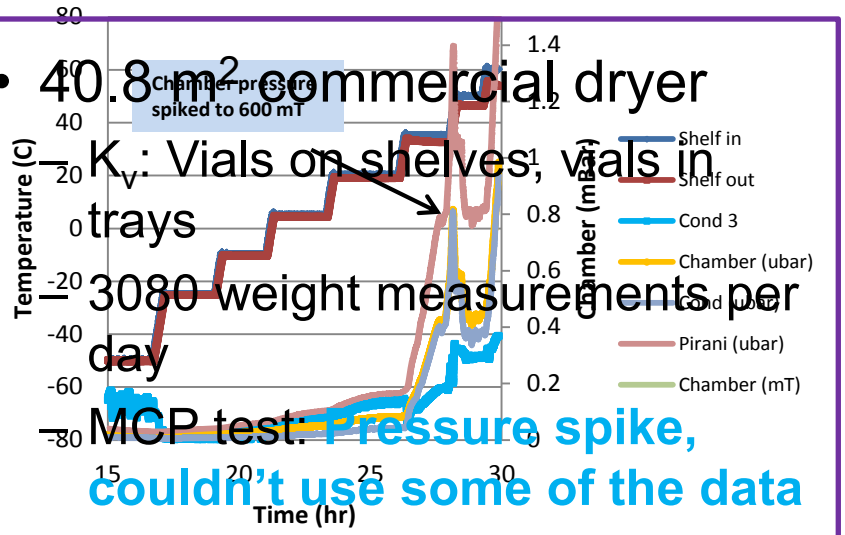
# Kaye Validator and Calibration: 3 Temperatures



# Examples of Challenges

- Fully loading a 42 $m^2$ dryer
  - Large trays were used
  - Some trays **developed leaks**
  - Required 24 hr to load

- 40.8 $m^2$ commercial dryer
  - $K_v$: Vials on shelves, vials in trays
  - 3080 weight measurements per day
  - MCP test: **Pressure spike, couldn't use some of the data**

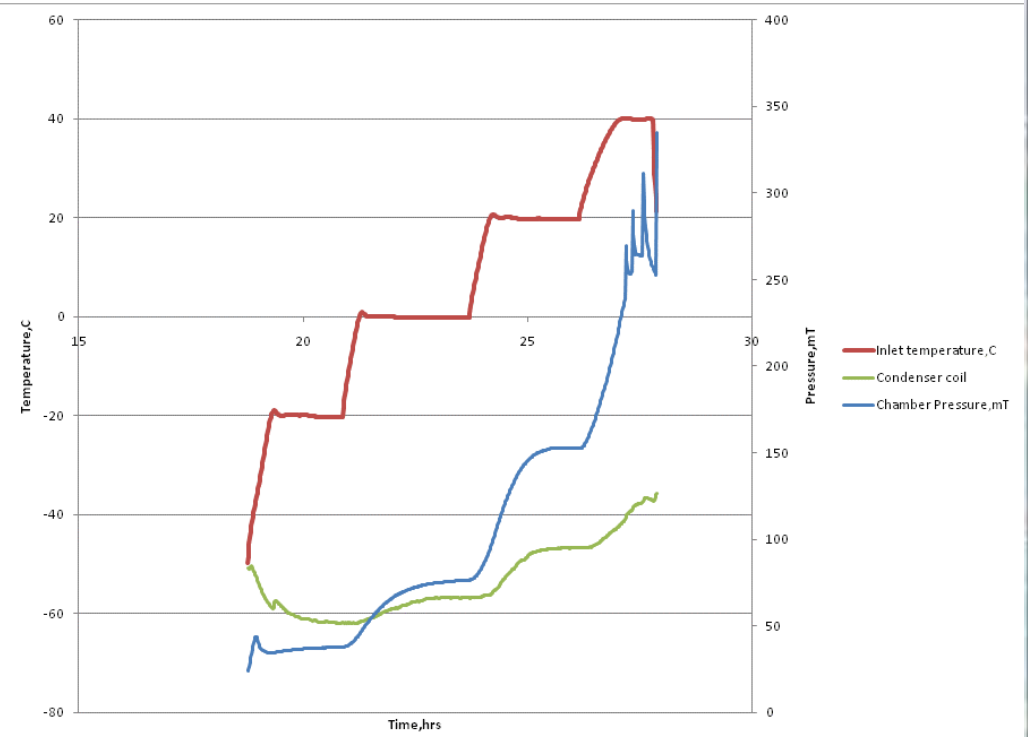



- 23 $m^2$ commercial dryer
  - **Ice breakage: salts in water**
  - Some trays **developed leaks**
  - One $K_v$ measurement had significant error

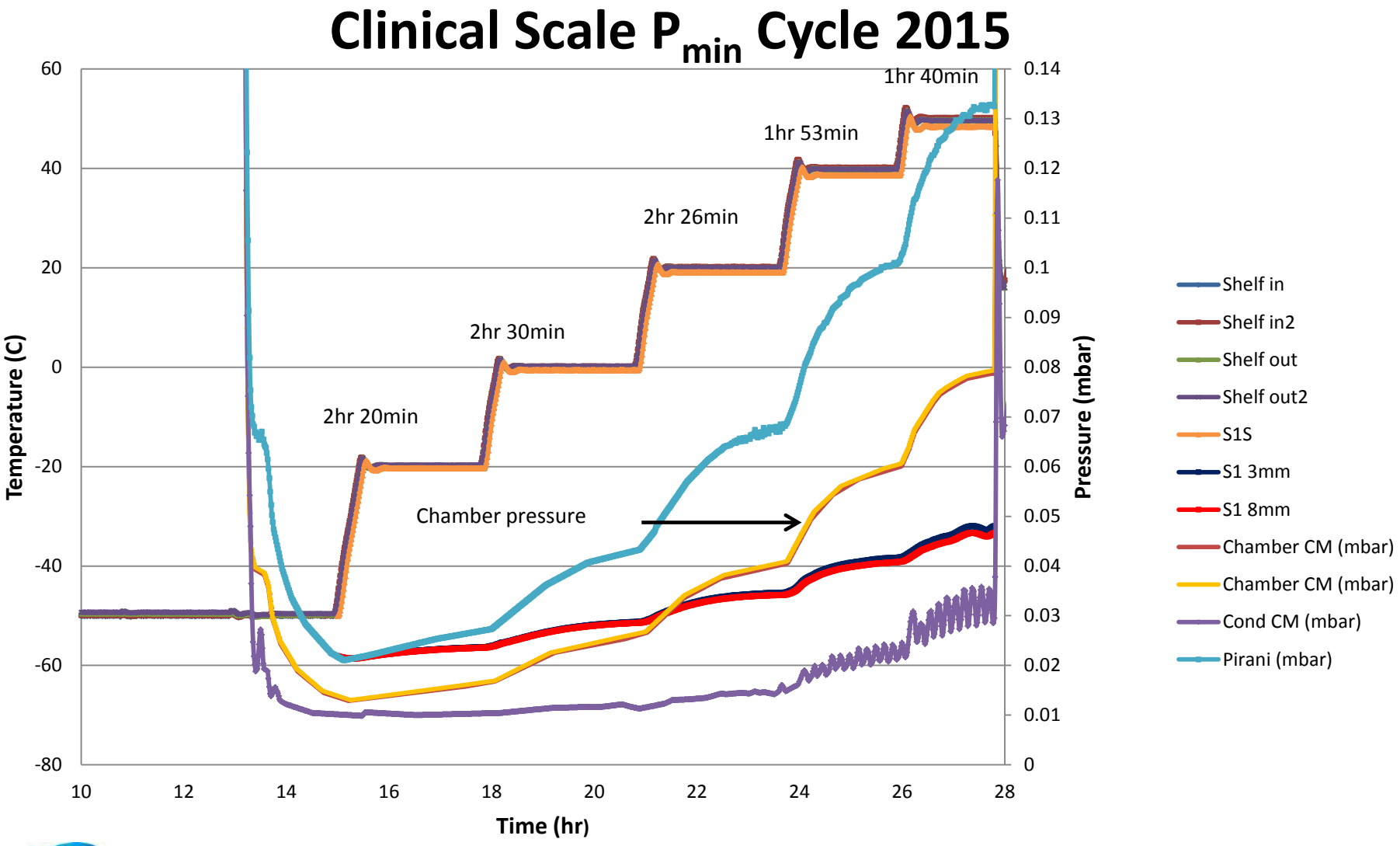
- Working in an aseptic processing area for 8 hr
- **Lost temperature data** from Ellabs®
- Using a TC feedthrough and Kaye validator

# Challenges: 23 $m^2$

- Leaking bags
- Ice breakage: Salts in $H_2O$
- Error with one $K_v$ measurement




# Clinical MCP: Thick Plastic Required Long Holds



# Conclusions

- Freeze dryer characterization:
  - Provides data for primary drying model
  - Allows prediction of product temperature profile
- Model:
  - Facilitates cycle design and transfer
  - Determine effects of shelf temperature and chamber pressure
- Challenges
  - Need to make investment
  - Technical and physical issues
  - Difficult at large scale
- Benefits:
  - More efficient and smooth scale-up and tech transfer
  - Save $ and time

# Acknowledgements

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