BD Sterilization Services

Mathematical Modeling - Support of Change Control

CIRMS
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Mathematical Modeling

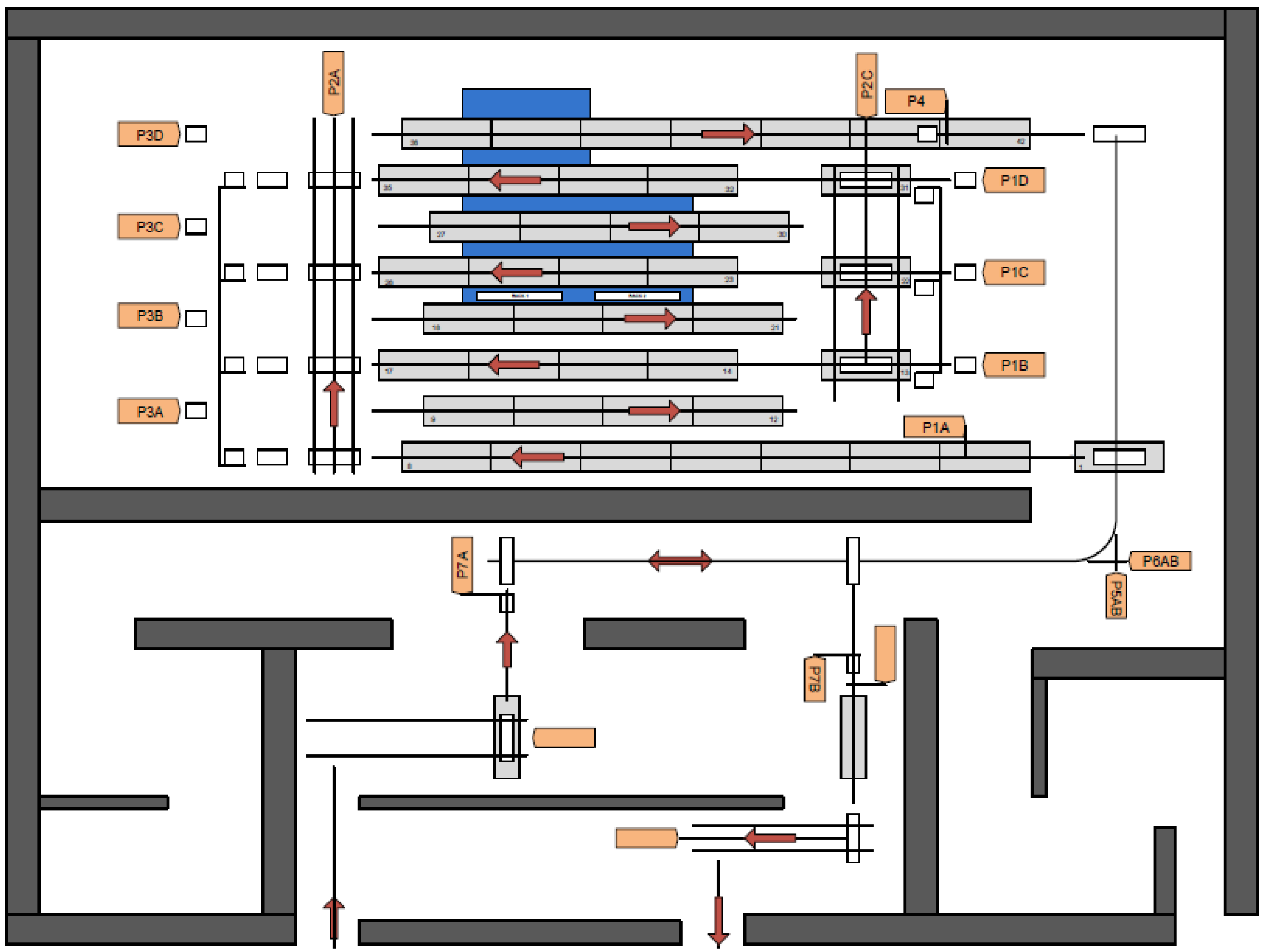
Modeling has many advantages

- Complement or supplement to actual dosimetry
- Reduce dosimetry monitoring locations
- Design of irradiation facilities
- Optimize dose distribution at existing facilities
- Reduce validation activities
- **Assess impact of changes in product composition, loading configuration and irradiator design on dose distribution**

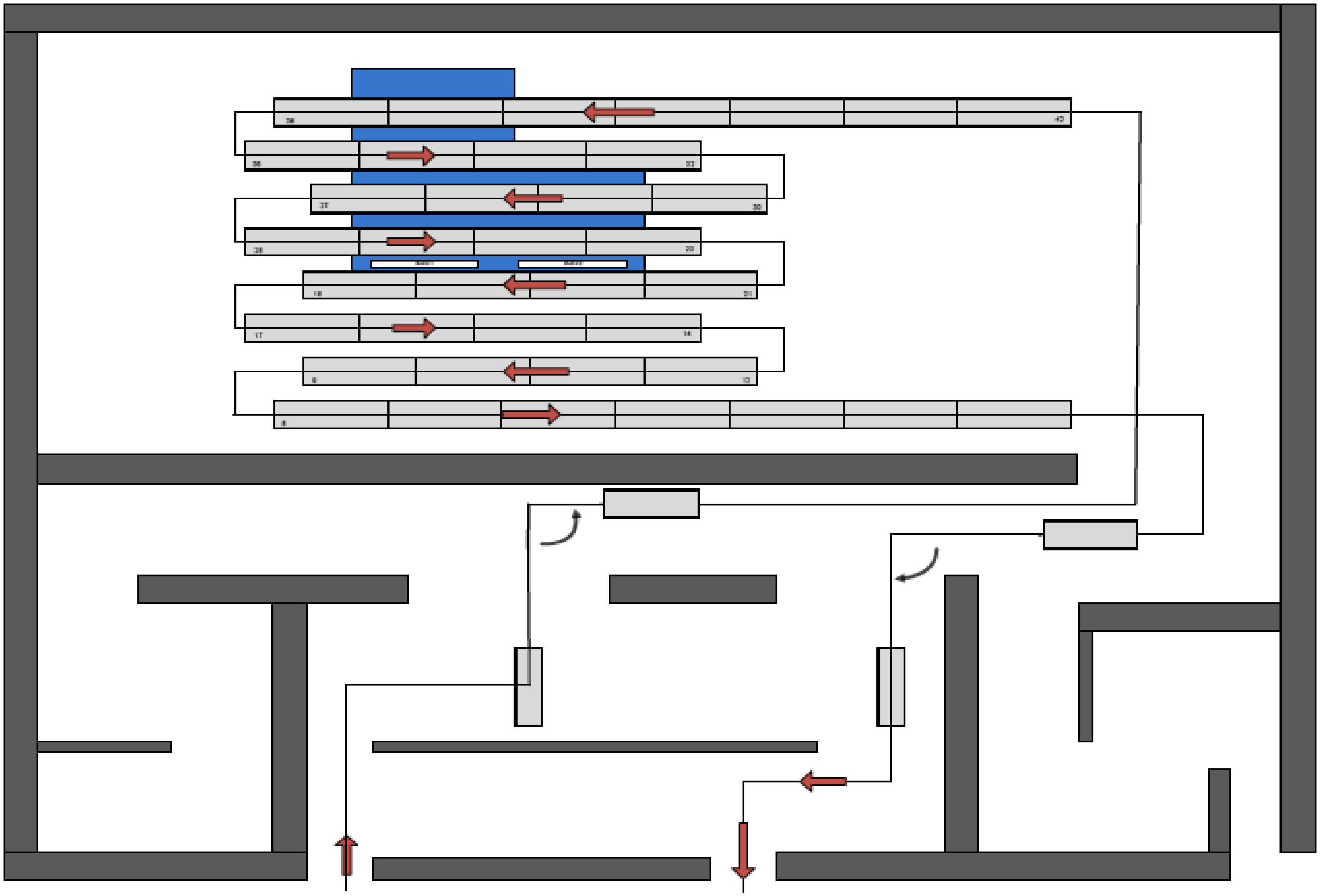
Overview - Sterilization Project

- Requalify Irradiator – after Machine Re-Design/Reload
  - Reload
  - Rail Replacement
  - Reverse Flow
  - No change to carriers or source rack
- Time Allotted by Production following OQ - 2 days
- Estimated Time to Complete – minimum 5,7 days
- Reduce Dosimetry Requirements
- Mathematical Modeling
- Resume Processing within 48 hours of OQ

Sterilizer Diagram – Pre Modifications



Sterilizer Diagram – Post Modification



Planning Stages

- Project Planning Begins

- Group Recommendation – Reload first and perform 2 OQ's
  - Like for Like Comparison - Does A = A?

- Enlist Support for Mathematical Modeling - Approved

- PQ – contingent on OQ results

Scope of Project and Timeline

Reload	2 days
OQ1 using Low and High density dunnage	1 day
Dosimetry Reading / Evaluation / Report	10 days available
Replace In-Cell Transit and Reverse Flow	2 weeks
OQ2 using Low and High Density Dunnage	1 day
Dosimetry Reading	24 hours
Dosimetry Evaluation and Report	2 days
Return to production	1 day

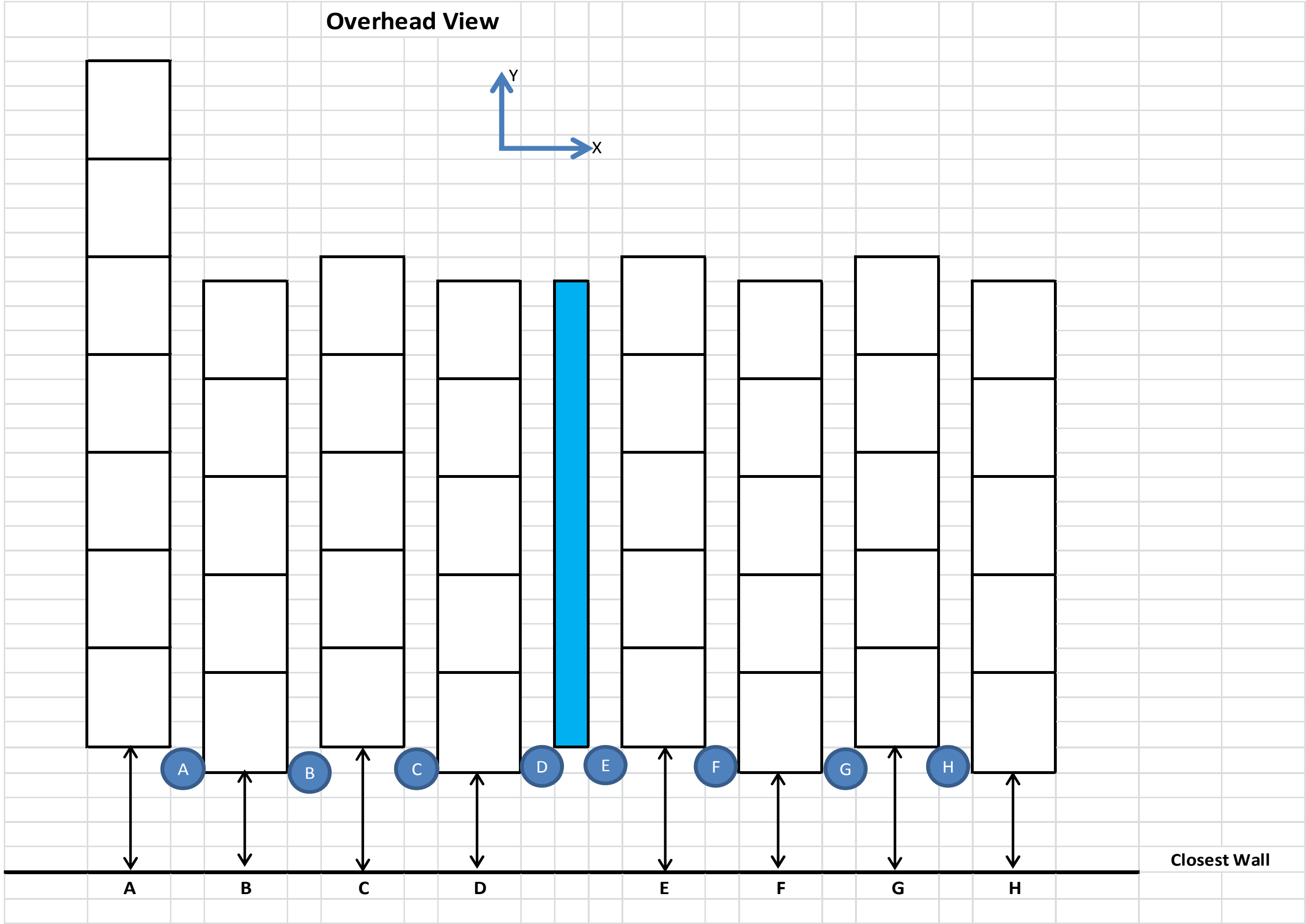
Pre-Work - Modeling Deliverables

- Review Cobalt pencil placement - Current and proposed load
- Review of available OQ/PQ data – previous 2 years
- Plant validation strategy - review protocols, provide suggestions
- Mathematical model, Simulations, and Interpretation
- Summary of load equivalence
- Goal for completion of all activities
- Future modeling

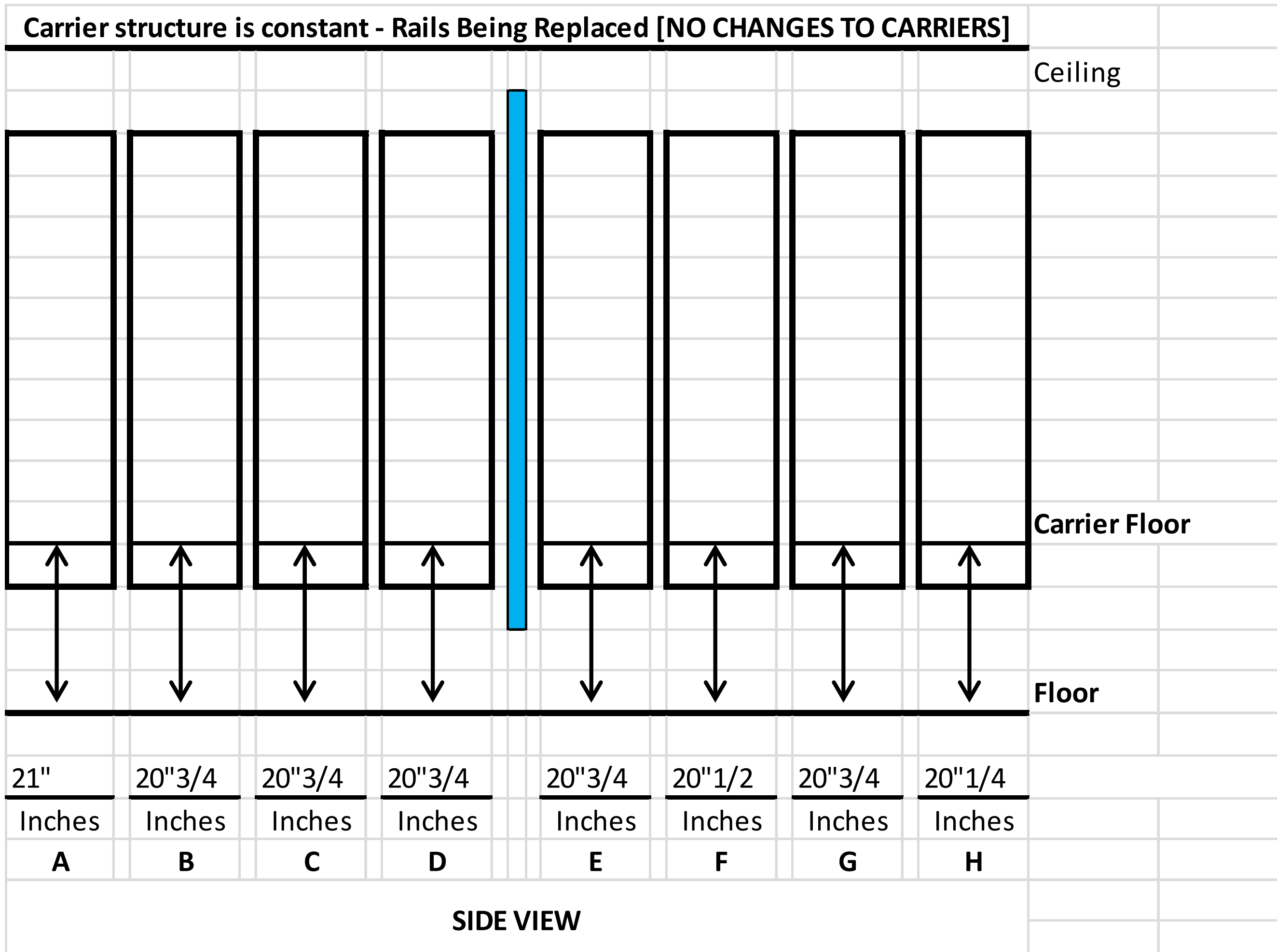
Pre-Work - Building the Model

- Critical Measurements and Source Load
  - Distance between carriers (X)
  - Relative Measurement – Carrier to nearest wall (Y)
  - Floor of Carrier to Floor of Cell (Z)
  - Width of Source Rack
  - Current Source Load (Nordion)

Pre-Work – Building the Model
Critical Measurements



Pre-Work – Building the Model
Critical Measurements



Pre-Work - Dosimetry

- Dosimeter Placement - emphasize anticipated regions of minimum and maximum absorbed dose – Based on previous 2 OQ's

- Dosimeter Reduction – Fewer dosimeters on intermediate areas

- 2 previous loads were determined to be equivalent

- Additional dosimeters – selected in order to confirm the presence of absorbed dose values between expected dose minima and maxima (energy deposition gradients)

Pre-Work - Dosimetry

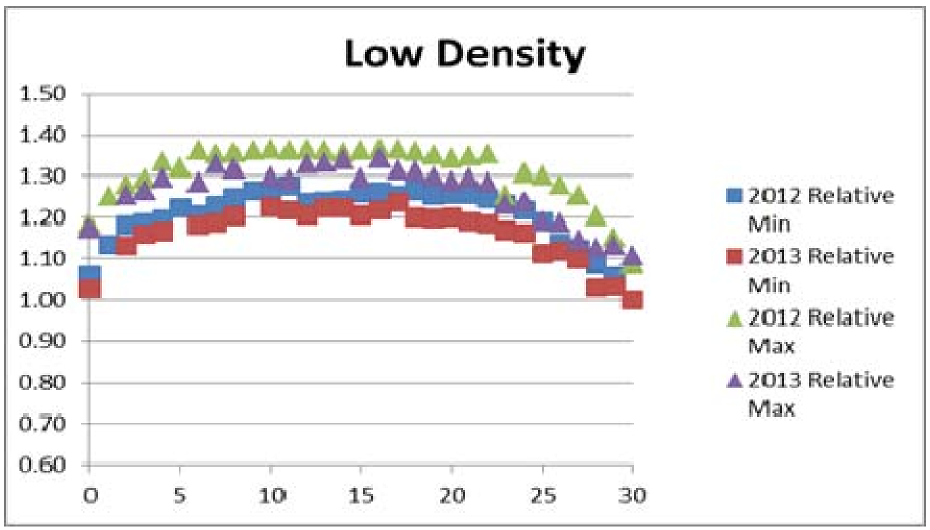
- **Diagram - Locations Monitored**

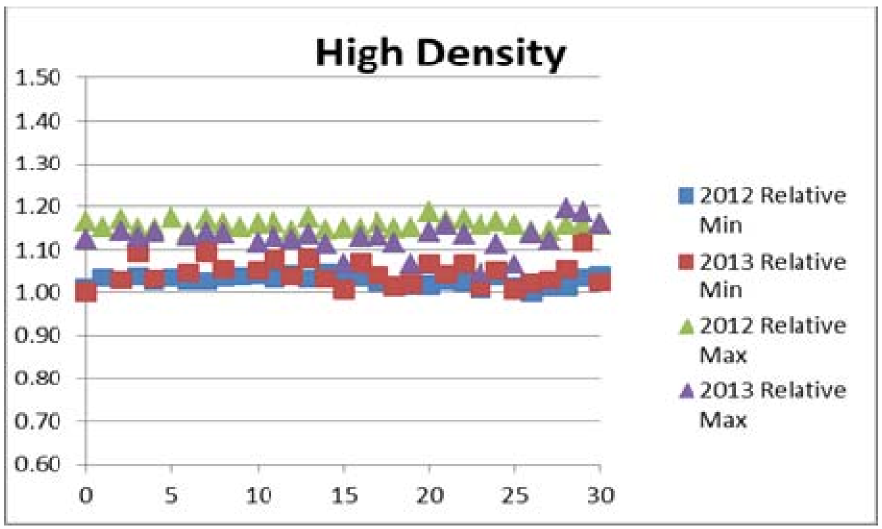
- **Preparation of Dosimeter Boards**
  - Follow Diagram
  - Create a grid on dose board
  - Planes
  - Locations
  - Levels

	Plane A					Plane B					Plane C				
	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
0		X		X	X	X	X	X	X	X		X		X	X
1								X							
2	X	X	X	X	X			X			X	X	X	X	X
3	X		X								X		X		
4	X	X	X	X	X			X			X	X	X	X	X
5															
6		X		X	X			X				X		X	X
7	X		X								X		X		
8		X		X	X			X				X		X	X
9															
10	X	X	X	X	X			X			X	X	X	X	X
11	X		X								X		X		
12		X		X	X			X				X		X	X
13	X		X								X		X		
14		X		X	X			X				X		X	X
15						X	X	X	X	X					
16		X		X	X							X		X	X
17	X		X					X			X		X		
18		X		X	X	X	X	X	X	X		X		X	X
19						X	X	X	X	X					
20	X	X	X	X	X						X	X	X	X	X
21	X		X					X			X		X		
22	X	X	X	X	X						X	X	X	X	X
23						X	X	X	X	X					
24		X		X	X							X		X	X
25						X	X	X	X	X					
26		X		X	X	X	X	X	X	X		X		X	X
27						X	X	X	X	X					
28		X		X	X	X	X	X	X	X		X		X	X
29	X		X								X		X		
30	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

OQ 1 Acceptance Criteria

- Training to the Protocol Complete - ✓
- Carrier absorbed dose distribution is evaluated via a minimum of triplicate carrier-based measurements -✓
- Dose values shall be within calibration limits of the dosimeters ✓
- Absorbed dose minima and absorbed dose maxima are identified and relative doses are plotted and compared with previous - ✓





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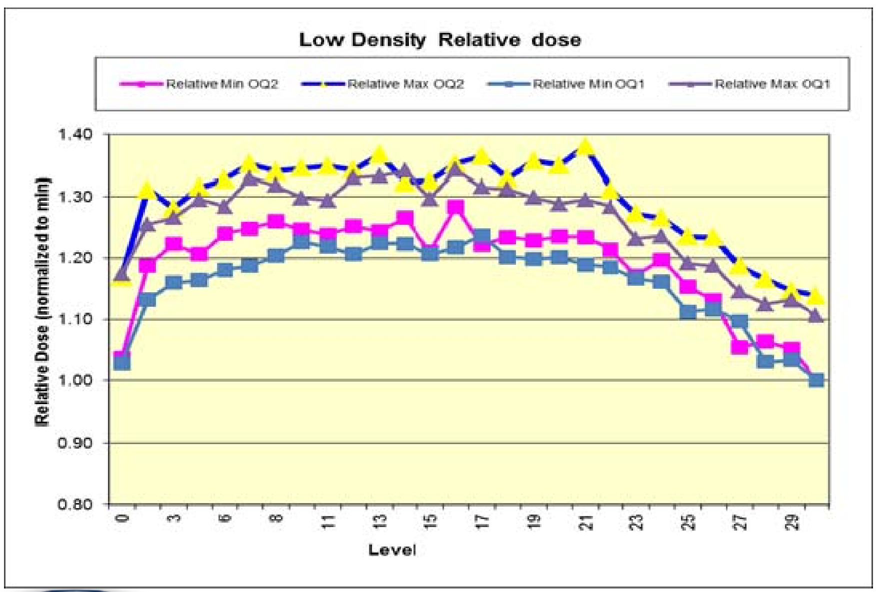
OQ 1 Acceptance Criteria

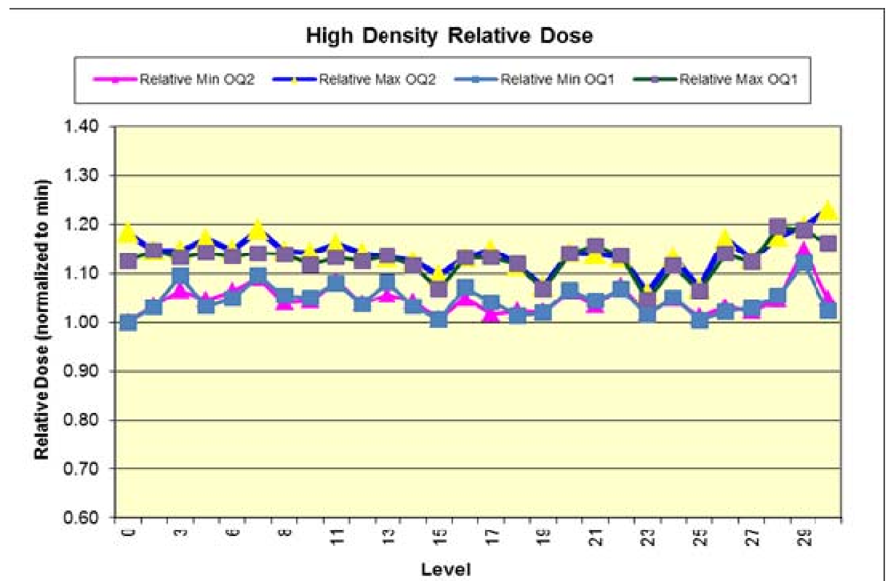
- Dose uniformity for low/high density established
  - If greater than ±5%, a PQ will be performed.
  - Dose Uniformity Ratio was the same for high density and within the required 5% for the low density ✓
  - No PQ required - Product Dose Uniformity remains as determined in the last PQ ✓

- Low/High density CV's are found to demonstrate a reproducible delivery of absorbed dose to specified ACE positions
  - CV's exceeding 3% re-examined
    - High density had 7 of 207 data points that exceeded 3%. Overall average % cv was 1.5 ✓
    - Low density had 9 of 207 data points that exceeded 3%. Overall average % cv was 1.7

OQ 2 Acceptance Criteria

- Training to the Protocol Complete ✓
- Carrier absorbed dose distribution is evaluated via a minimum of triplicate carrier-based measurements ✓
- Dose values shall be within calibration limits of the dosimeters ✓
- Absorbed dose minima and local absorbed dose maxima are identified and relative doses are plotted and compared with OQ 1 - ✓





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OQ 2 Acceptance Criteria

- Dose uniformity for low/high density established
  - If greater than ±5%, a PQ will be performed.
  - Dose Uniformity Ratio was within the required 5% for the low and high density ✓
  - Product Dose Uniformity remains as determined in the last PQ ✓

- Low/High density OQ – CV's are found to demonstrate a reproducible delivery of absorbed dose to specified ABC positions ✓
  - CV's exceeding 3% re-examined
    - High density had 6 of 207 data points that exceeded 3%. Overall average % cv was 1.8
    - Low density had 1 of 207 data points that exceeded 3%. Overall average % cv was 1.5

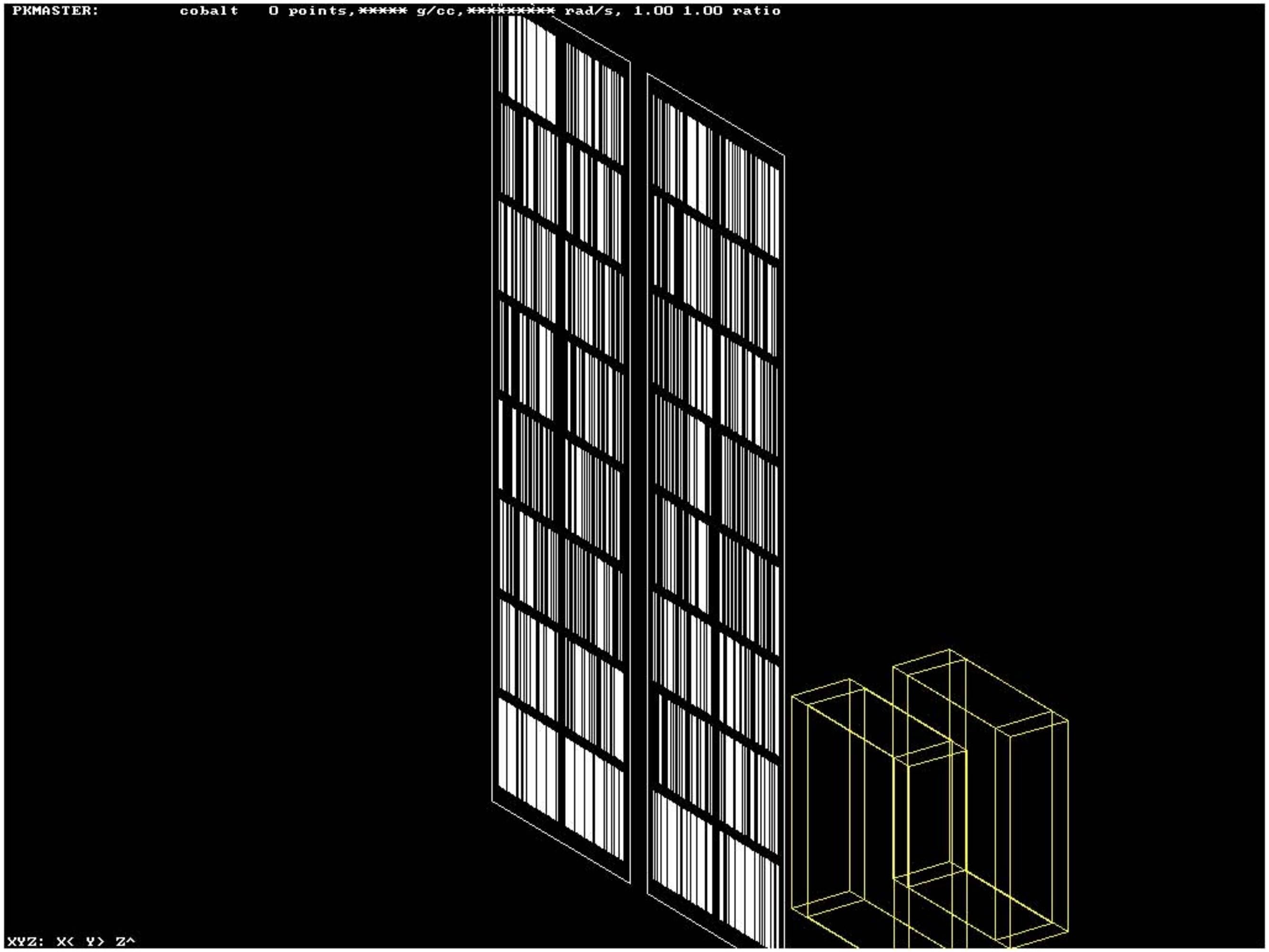
BD

Mathematical Modeling

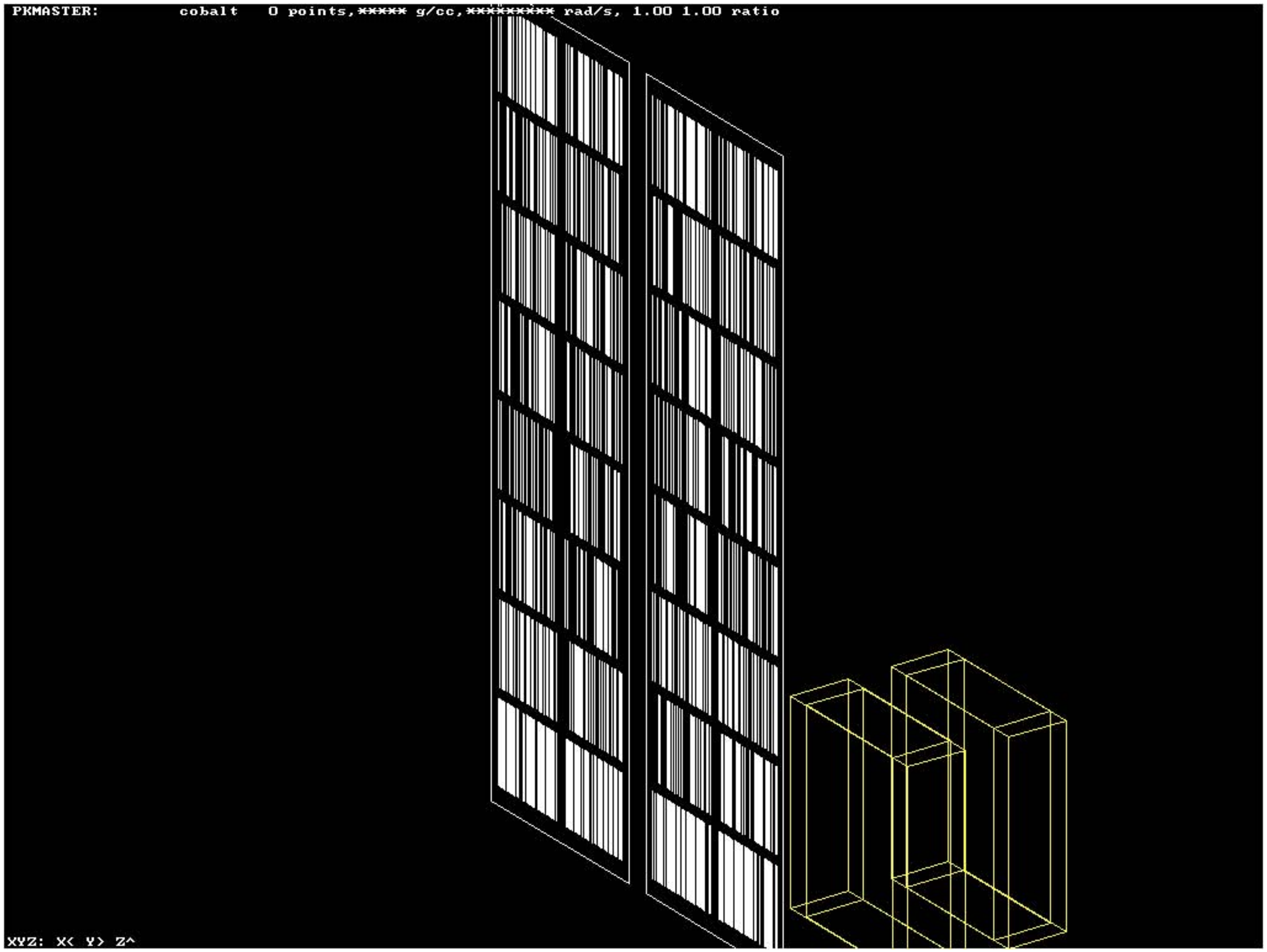
- Changes to the Percent Contribution - Insignificant
  - Previous to current
  - Pre-modification to Post-modification
  - Verified by Independent BD Dosimetry

Row Number		Loading No. 25 (L25) [Pre-Mod]	Loading No. 25 (L25) [Post-Mod]	Loading No. 24 (L24)	Difference
1		14.29	14.29	14.29	0
2		12.21	12.21	12.21	0
3		11.39	11.39	11.4	-0.01
4		11.4	11.4	11.39	0.01
5		11.38	33.38	11.39	-0.01
6		11.39	11.39	11.38	0.01
7		12.2	12.2	12.21	-0.01
8		15.72	15.72	15.73	-0.01
	Total	100%	100%	100%	

Mathematical Modeling
Pencil Diagram



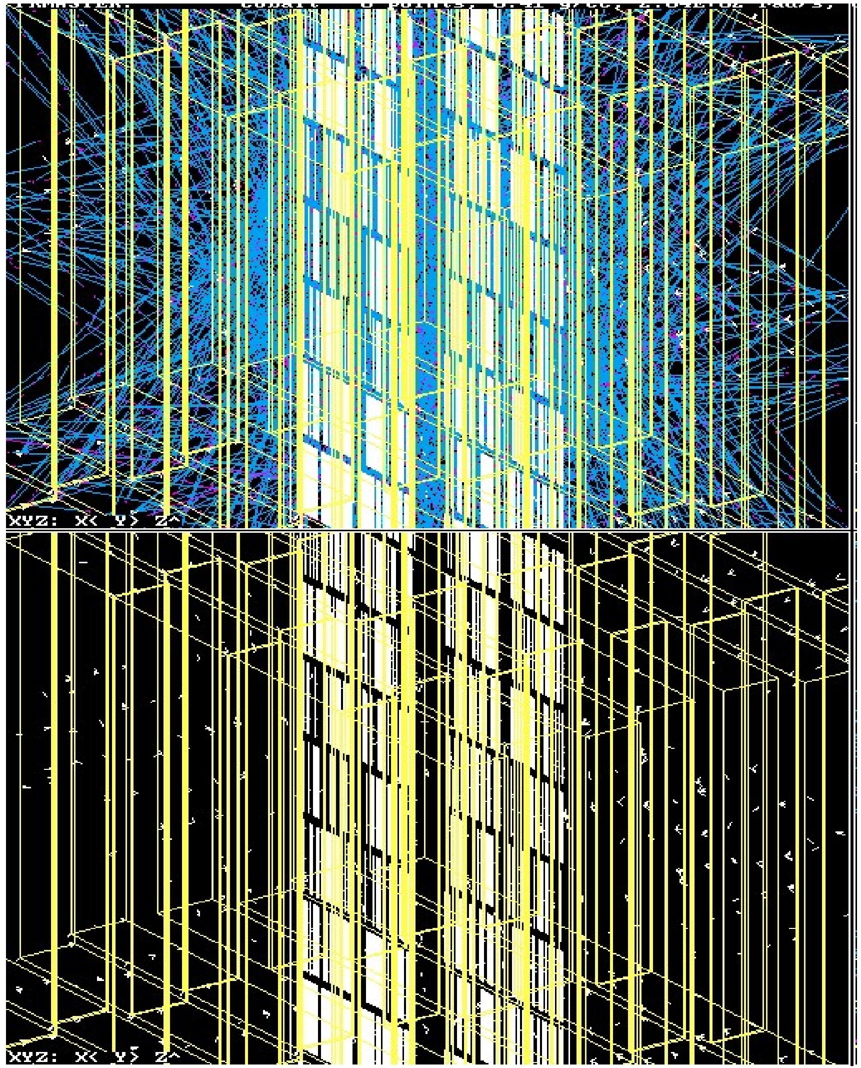
Mathematical Modeling
Pencil Diagram



Mathematical Modeling
Cherenkov

- Cherenkov radiation - The characteristic blue glow in the cobalt pool

Mathematical Modeling
Simulated Dosimetry

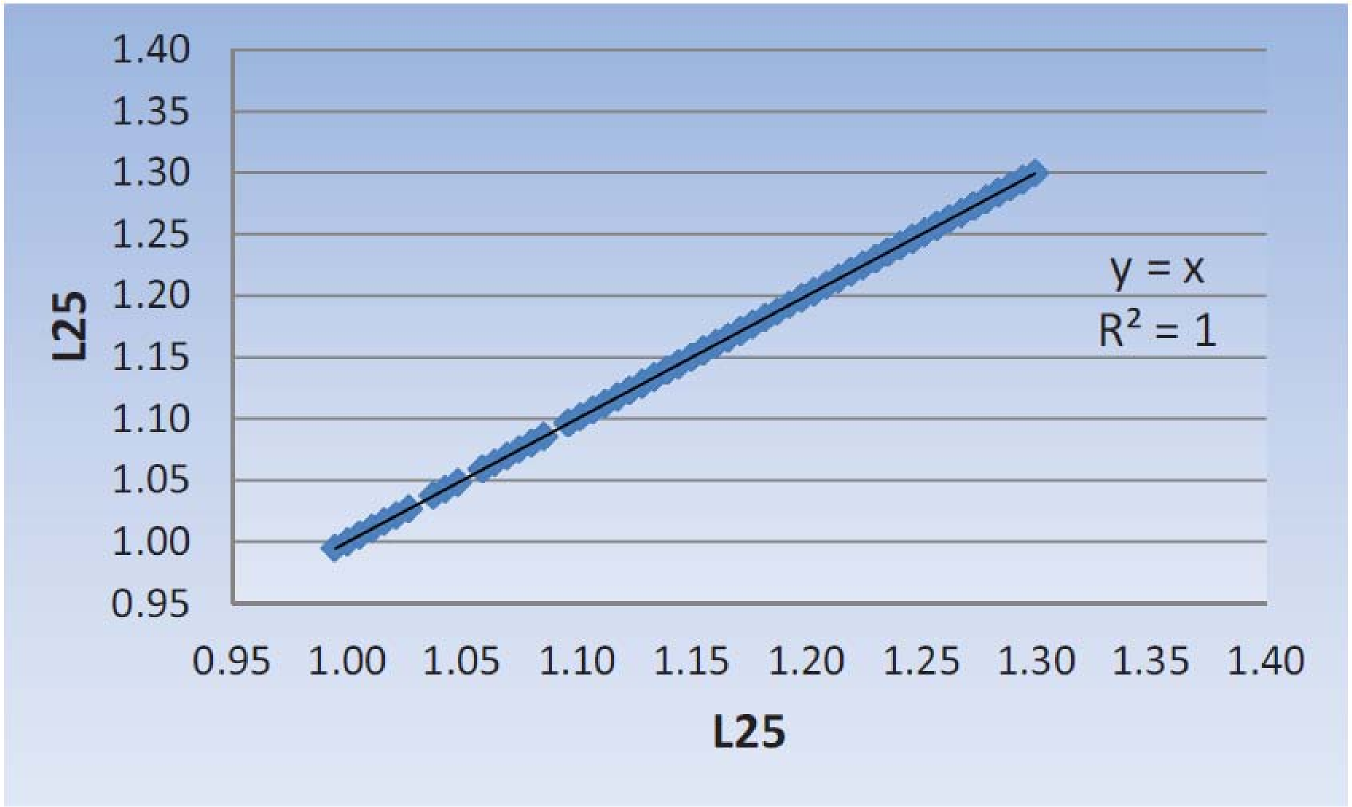


Mathematical Modeling Dosimetry

- Theoretical performance of the irradiator used a point kernel-based mathematical model and simulation was performed
- Theoretical (simulated) and experimental (actual) dosimetry for OQ1 and OQ2 were evaluated
- The energy deposition prior to and following the modification was as expected, demonstrating functional equivalency as per the acceptance criteria
- The simulation results demonstrated good-to-excellent functional equivalency pre/post modification
- Dosimetry data generated from actual dosimetry results confirmed equivalence

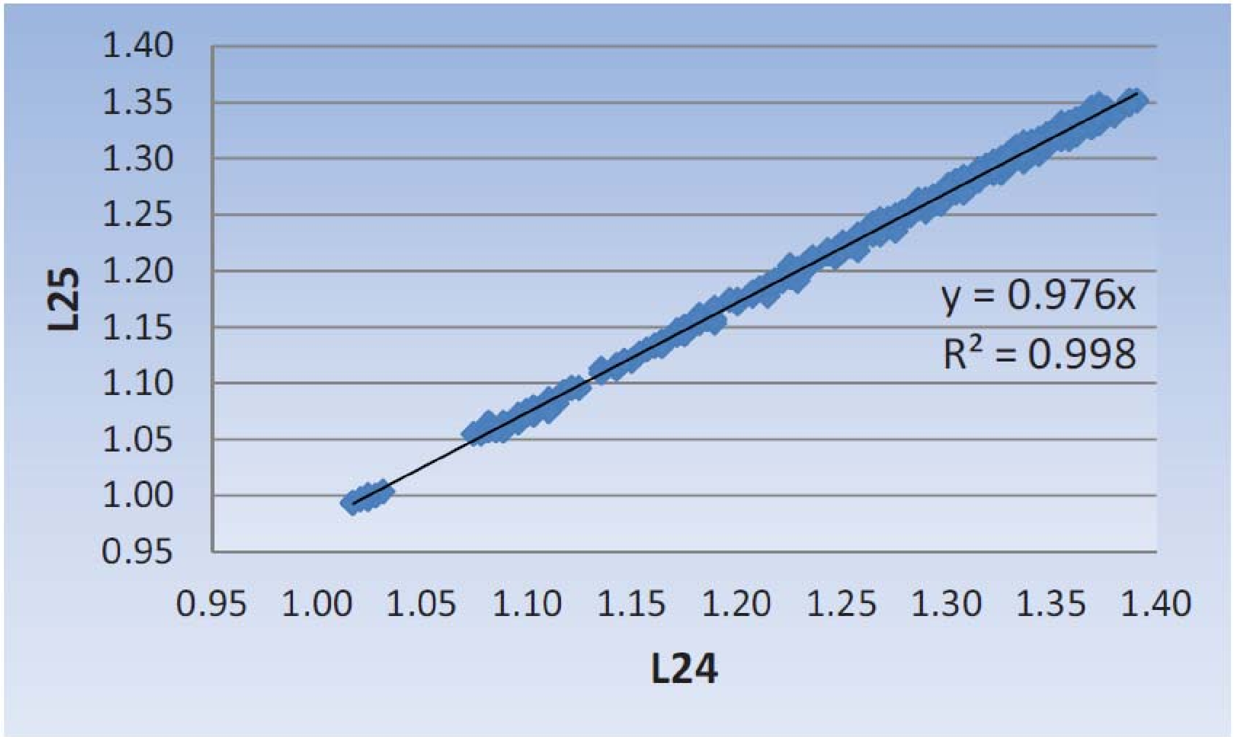
Theoretical Equivalence

- Simulated Absorbed Dose Ratio – scaled to 0B3



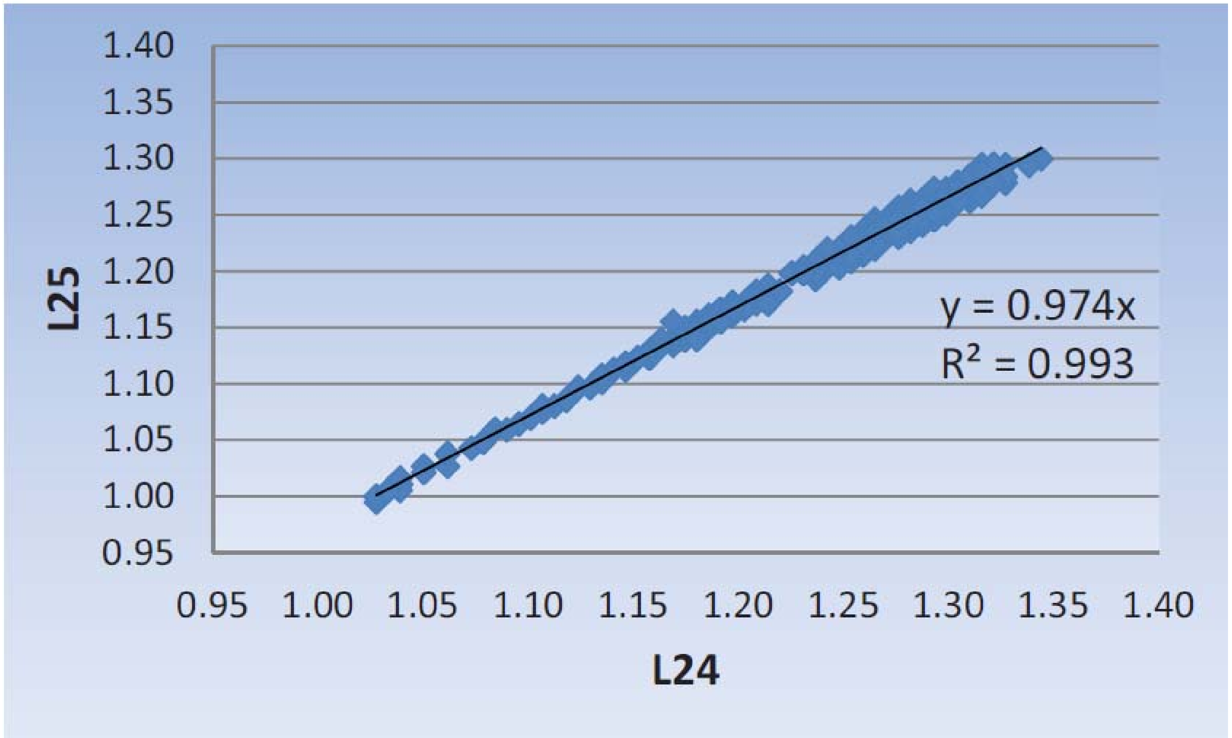
Theoretical Equivalence

- Simulated Absorbed Dose Ratio – Low Density



Theoretical Equivalence

- Simulated Absorbed Dose Ratio – High Density



Summary

- Project was Successful – Authorization to Process within Goal of 48 hours
- Theoretical Evaluation
  - Load 2 is equivalent to Load 1
- Theoretical Evaluation
  - Load 3 is equivalent to Load 2
- Experimental Dosimetry – Absorbed Dose Delivery
  - Load 3 is equivalent to Load 2
  - Post-modification absorbed dose is equivalent to Pre-modification absorbed dose
- Functional Evaluation
  - Replacement of the transport rails and the redirection of the carriers through the cell - Functionally Equivalent A = A

No Questions