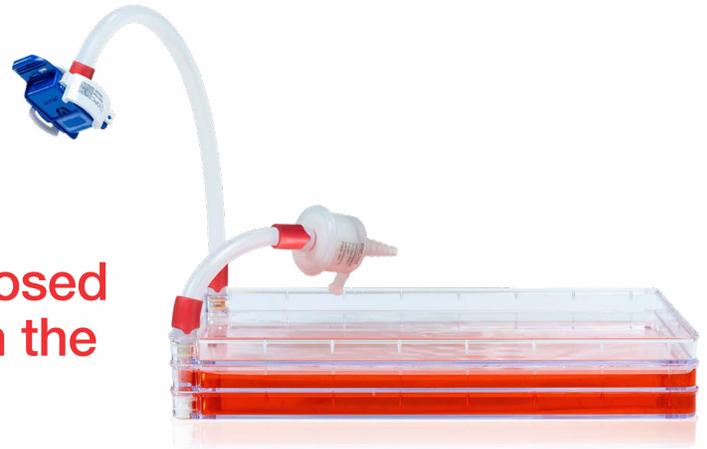


Bioprocessing

Reducing risks of leaks in a closed Nunc Cell Factory system with the BioTitan Retention Device



Abstract

Thermo Scientific™ Nunc™ Cell Factory™ systems are an excellent choice for expanding adherent cells. Configuring them as closed systems reduces contamination risk and helps reproducibility, both of which are crucial in a high-stakes bioprocessing environment. However, leaks in a closed system can lead to contamination and the loss of valuable cells. To mitigate this risk, we have incorporated Thermo Scientific™ BioTitan™ Retention Devices into the ports of a Nunc Cell Factory system. These devices create a 360° seal to help prevent leaks. We verified the performance of the BioTitan Retention Devices on the barbed ports of the Nunc Cell Factory system through fit checks and pressure testing after irradiation. Each tubing-to-barb configuration underwent a submergence pressure test from 1 to 80 psi, and all tests exceeded the required minimum pressure rating without leaks. Helium integrity testing on the samples tested further confirmed a secure, leak-free seal, and computed tomography (CT) imaging showed full engagement across all barbs on the Nunc Cell Factory port, forming a 360° seal that can help limit the likelihood of leakage.

Introduction

Growing large numbers of adherent cells can be challenging due to their need to attach to the surface of the growth vessel. Nunc Cell Factory systems address this challenge by offering a multilayered design with less space between layers compared to stacks of typical flasks, significantly expanding the growth surface area in a given height. These systems feature the same high-quality Thermo Scientific™ Nunclon™ Delta cell culture

surface as Thermo Scientific™ Nunc™ plates and flasks. The Nunclon Delta surface is a fully synthetic, chemically modified surface that enhances the hydrophilicity of the otherwise hydrophobic polystyrene, facilitating cell attachment and growth. These systems maintain the same growth kinetics as laboratory-scale cell culture products.

The ports of the Nunc Cell Factory systems allow for easy customization and closure, with custom tubing assemblies that facilitate venting, filling, and harvesting. Configuring these systems as closed aseptic systems using tubing, a peristaltic pump, or bagged media helps reduce contamination risk and improves reproducibility.

To further enhance the integrity of closed systems, BioTitan Retention Devices have been added to the ports to help reduce the risk of leaks. The BioTitan Retention Device provides a 360° seal, allowing even compression at connection points. It is used in most Thermo Scientific™ bioprocessing fluid transfer systems, including Thermo Scientific™ Single-Use BioProcess Containers (BPCs).

Following fit checks and pressure testing to confirm performance, we conducted helium integrity testing. Helium testing is a standard method for detecting leaks due to its high sensitivity and accuracy, allowing even the smallest leaks to be identified. This is crucial for maintaining the integrity of bioprocessing systems, preventing contamination, and helping to ensure the safety and efficacy of the final product.

Helium integrity testing

Helium integrity testing—an industry-standard method for verifying the leak-tightness of sterile assemblies—was used to evaluate BioTitan Retention Devices on the barbed ports of a Nunc Cell Factory system. Using the Q010 leak check station (third party-sourced), the assembly first undergoes a pressure check to confirm all connections are secure. The chamber is then evacuated until background helium is no longer detected, after which a controlled helium concentration is introduced into the fill line and allowed to reach system pressure. A mass spectrometer measures any helium entering the vacuum chamber; leak rates above the established rejection limit indicate a failed seal.

Testing was performed on a 2-layer Nunc Cell Factory system with BioTitan Retention Devices installed on both ports, including a configuration exposed to a double dose of sterilizing gamma radiation (2×25 kGy). Both the pre- and post-irradiated assemblies exhibited leak rates well below the acceptance threshold of 4.05×10^{-3} mBar-L/sec, confirming a robust, leak-free seal (Figure 1). The gamma-irradiated configuration showed slightly higher variability, consistent with normal test-to-test variation and the expected material effects of exposure to gamma radiation, but the configuration still passed with a wide margin.

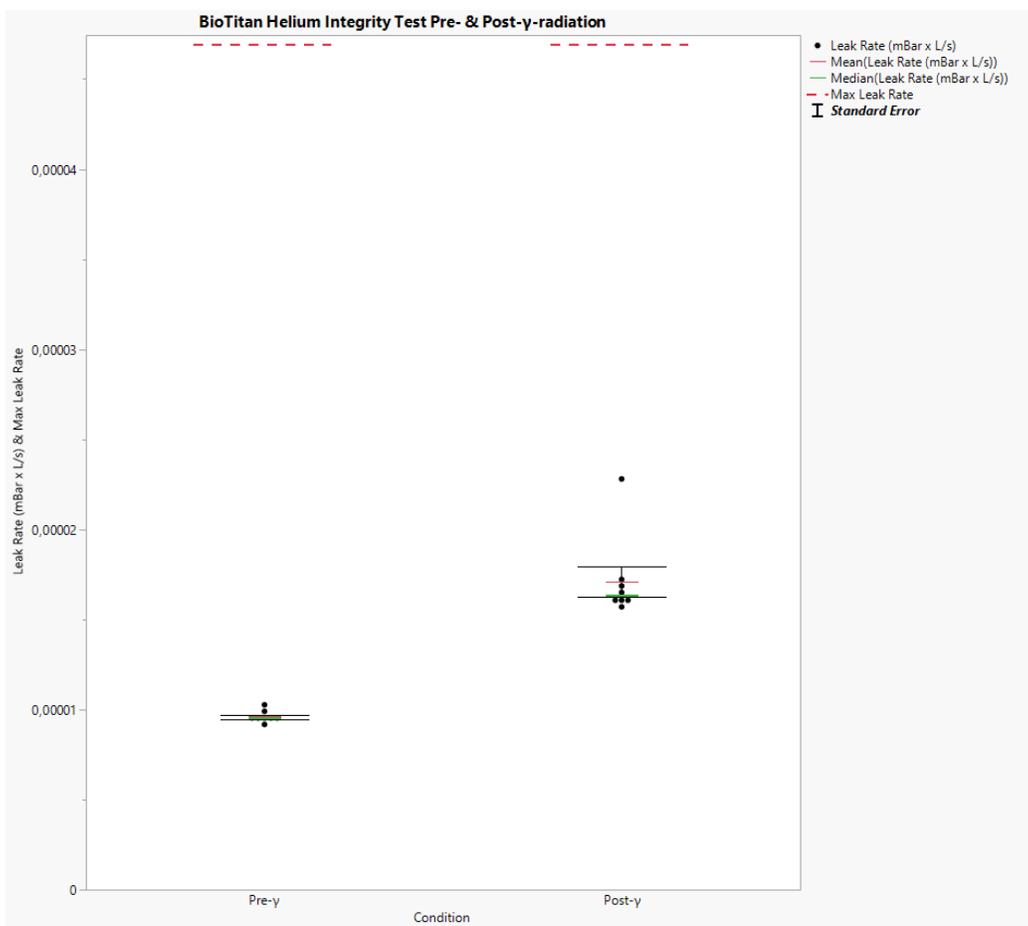


Figure 1. Helium integrity testing of a 2-layer Nunc Cell Factory system. Results show all units passing well below leak-rate limits before and after gamma irradiation, confirming robust sealing performance of the BioTitan Retention Devices.

Confirmation of barb contact

To confirm that the BioTitan Retention Devices engaged all barbed ports of the Nunc Cell Factory system, CT scans were taken of a tubing set on a Nunc Cell Factory barbed port that was mounted in a Nunc Cell Factory tray and secured using a BioTitan collar. Scans were taken from three different angles (Figures 2A–C) demonstrating how the BioTitan Retention Device helps to tighten the grip between the tubing and port, engaging all the barbs of the port. Figure 2D shows a 3D rendering of the barbed port alone placed in the same orientation as in the CT scans. Engagement of the barbs is consistent at all angles, suggesting a 360° seal.

Conclusions

The addition of BioTitan Retention Devices to the barbed ports of a Nunc Cell Factory system provides a tight seal around the barbed port even after exposure to gamma radiation. Helium

testing demonstrated the ability to withstand pressure well beyond leak thresholds. CT scans at multiple angles showed that all barbs engaged to form a complete seal.

Expansion of adherent cells can be cumbersome. Changing growth surfaces or conditions adds time and cost to cell production. Nunc Cell Factory systems allow the expansion of adherent cells with the same type of surface and conditions as small-scale flasks. The addition of BioTitan Retention Devices to these systems help reduce the risk of leaks, contamination, and batch loss.

Design a Nunc Cell Factory system to meet your needs

Our experienced technical representatives can help you engineer systems to support cell expansion, including Nunc Cell Factory systems, fluid management systems, and more. Contact us for more information, or visit [thermofisher.com/cellfactory](https://www.thermofisher.com/cellfactory).

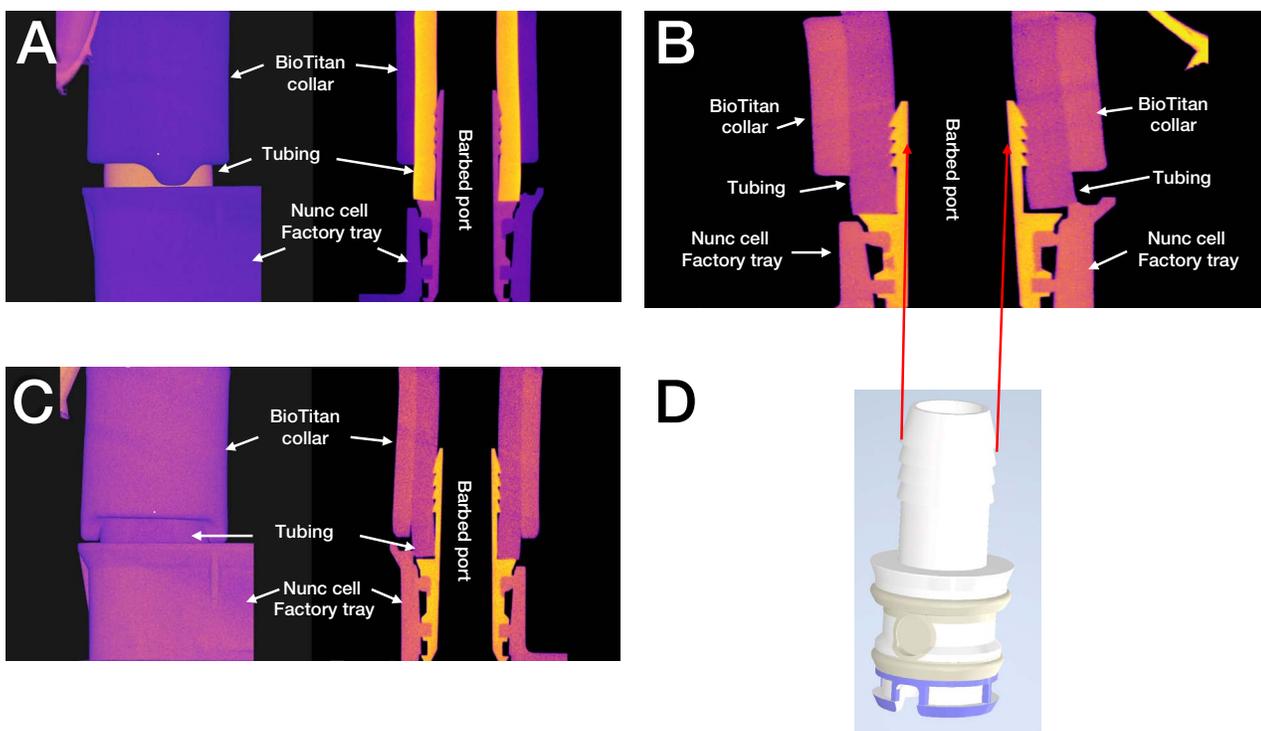


Figure 2. CT imaging of the secure seal of the BioTitan Retention Device. (A–C) CT scans from multiple angles show the BioTitan Retention Device securely engaging all barbs of the Nunc Cell Factory barbed port for a consistent, tight tubing connection. (D) 3D rendering of a barbed port in the same orientation.

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