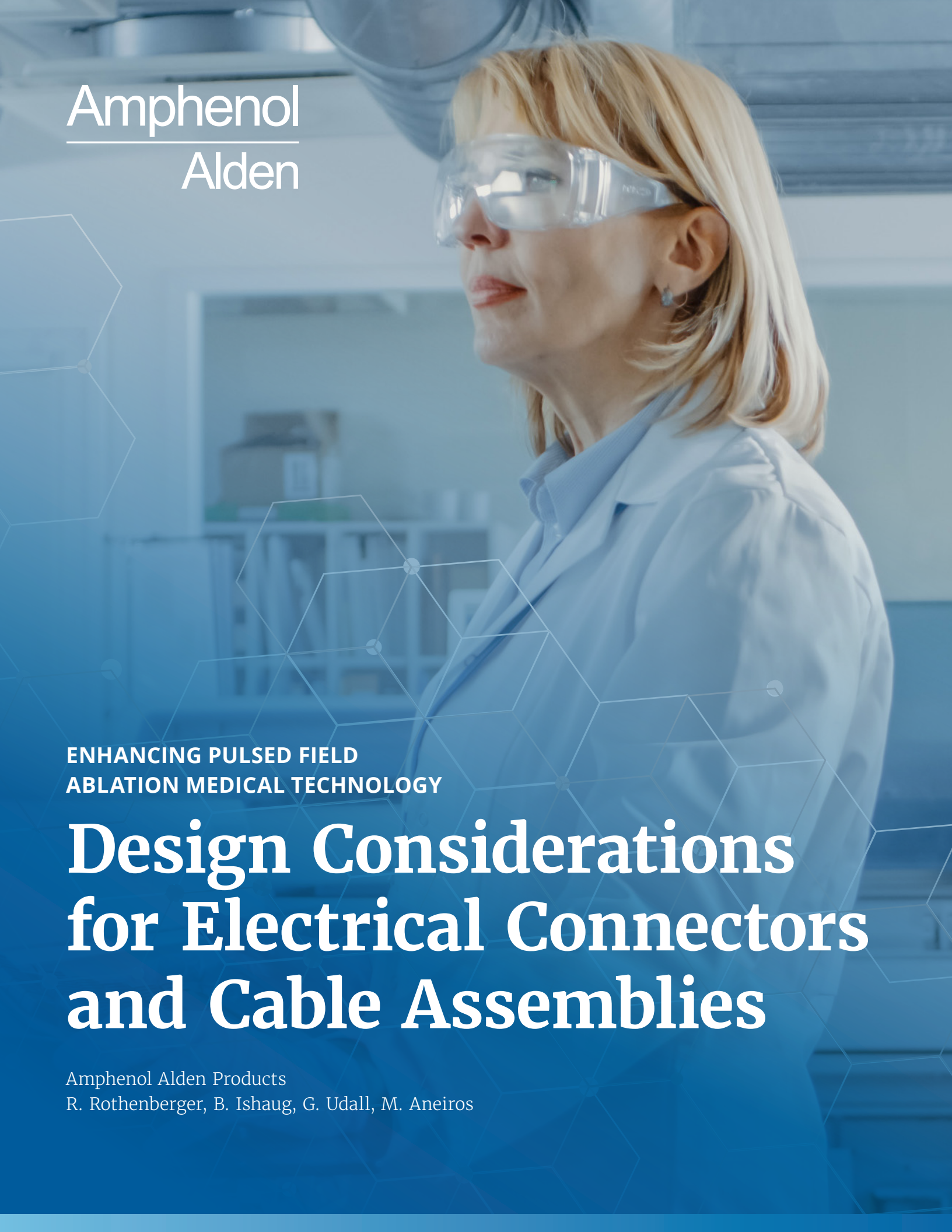

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ENHANCING PULSED FIELD
ABLATION MEDICAL TECHNOLOGY

Design Considerations for Electrical Connectors and Cable Assemblies

Amphenol Alden Products
R. Rothenberger, B. Ishaug, G. Udall, M. Aneiros

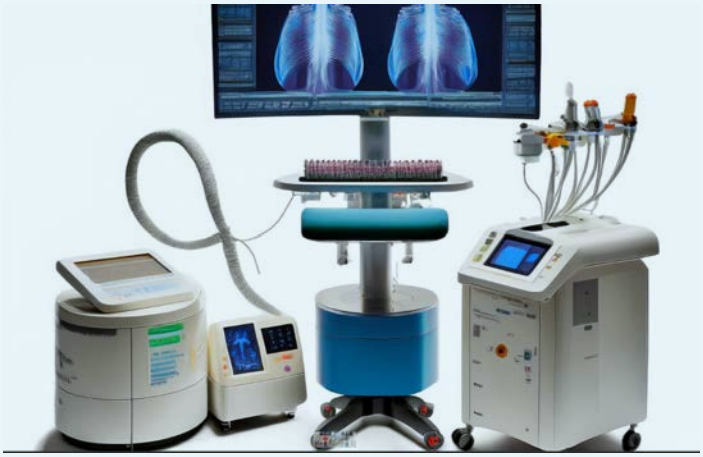
Abstract

This white paper delves into the critical factors influencing the development of connectors and cable assemblies for the rapidly advancing fields of pulsed field ablation (PFA) and pulsed electric field (PEF) therapies, along with their integration into diagnostic, mapping, ablative, and therapeutic catheters, generators, and umbilical cable assemblies. Addressing the intersection of technology, innovation and clinical need, the paper highlights design considerations such as proper electrical isolation, procedural safety, regulatory compliance, and optimizing product geometry for user-ergonomics and other human factors that mitigate risk and improve the end-user experience. By exploring these key elements, this paper provides insights into the design challenges and opportunities in developing interconnect solutions to support the next generation of pulsed field ablation medical devices.

Introduction

In the rapidly evolving landscape of cardiac electrophysiology, tumor ablation, and other adjacent practices, the integration of new therapy delivery methodologies, such as pulsed field ablation (PFA) and pulsed electric field (PEF) technologies hold immense promise for revolutionizing treatments and improving patient outcomes. Successful implementation of these cutting-edge therapies hinges on the development of new connector and cable assemblies that are designed for the unique functional requirements associated with these treatments.

This paper explores the pivotal factors that must be considered when engineering next-generation connector and cable assemblies tailored to the unique requirements of the PFA and PEF medical ablation, heart mapping, diagnostics, and related therapy markets. From ensuring safe and reliable high voltage isolation to optimizing user ergonomics, this paper delves into the intricacies of designing interconnect solutions that integrate the capital equipment and catheters with the technicians who use them, saving and improving the lives of the patients under their care.



Typical PFA System image

What is a PFA system and what differentiates it from traditional Radio Frequency (RF) ablation systems?

The goal of both PFA and RF-ablation systems is to induce targeted, controlled, cellular death in the tissue under treatment. The mechanisms through which they achieve this goal, however, are vastly different and PFA can deliver significant advantages over traditional RF-ablation systems.

In an RF-ablation system, energy is transmitted in electrical pulses operating in the MHz frequency range. This energy induces heat-rise at the catheters' electrode initiating cellular death in the tissue contacted by the energized electrode. Although well understood, RF-ablation presents inherent risks to surrounding tissues such as unintended damage or death to adjacent healthy tissue, leading to longer patient recovery times and potentially requiring additional procedures.[1] PFA systems, however, take a different approach.

Typically, PFA systems deliver short-duration, high-voltage pulses with rapid rise times to create localized electric fields within the myocardium or other biologic tissue. The pulse duration, amplitude, and frequency are carefully controlled to induce irreversible electroporation (IRE). The electrical current characteristics of PFA pulses are tailored to minimize energy dissipation and collateral tissue damage while ensuring effective therapeutic benefit. Through its different approach to energy delivery, PFA mitigates the risks associated with RF-ablation and may have relatively shorter recover times for the patients.[2]

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Typical Low Voltage and High Voltage Pin Arrangement

Interconnect and Cable Assembly Requirements and Challenges

Pulsed Field Ablation (PFA) catheter cable assemblies present multifaceted requirements and challenges, demanding meticulous attention to engineering, design, and manufacturing.

First and foremost, there is the need for robust isolation of multiple high-voltage lines from each other as well as any adjacent low-voltage lines. Sufficient high-voltage isolation is paramount to limit electrical leakage current and prevent high voltage arcing, ensuring patient and technician safety while preserving the signal integrity of ancillary circuits.

The combination of low-voltage signal/power lines and high-voltage ablation lines in catheter cable assemblies serve vital roles in ablation and other medical procedures. The signal lines enable, among other things, the detection of cardiac signals and tissue characteristics, facilitate logic-level power and signals for data processing, and support ground and shield connections. Additionally, specialized electronics for catheter identification could streamline procedural setup and enhance efficiency in navigating catheters during ablation therapy.

Precise control over pulse duration is essential for delivering accurate energy pulses to the target tissue, requiring signal integrity management and insulation materials capable of withstanding extended high-voltage stress. Achieving the proper balance between the number of high-voltage and low-voltage lines within the assembly is crucial to optimizing system functionality while minimizing size and complexity of the interconnect solution, often requiring innovative cable construction techniques, connector designs, and assembly methodologies.

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Biocompatibility considerations, such as compliance with relevant sections of industry standard ISO 10993, are equally critical to ensuring that all materials used in the assembly are compatible with bodily tissues, preventing adverse reactions and ensuring patient well-being. Furthermore, significant thought must go toward an OEM's full reprocessing protocol, from cleaning and disinfection to sterilization. Understanding the materials, component geometries, and construction methods capable of withstanding various sterilization processes, including ETO, Autoclave, and Sterrad, without compromising performance is critical for PFA interconnects.

Finally, ergonomic design plays a vital role in enhancing user comfort and efficiency during prolonged procedures. Considerations such as cable flexibility, weight, size, and connector ergonomics can minimize operator fatigue and help ensure procedural success. Addressing these multifaceted, and often conflicting, requirements and challenges is crucial for the safe and effective performance of PFA catheter cable assemblies and connectors.

Interconnect and Cable Assembly Testing and Certification Requirements

The testing and certification of PFA cable assemblies is a multifaceted process critical to ensuring the products' safety, reliability, and regulatory compliance. In this section we will discuss some of the essential electrical, mechanical, and reprocessing tests required during design verification.

Electrical testing is conducted to verify the integrity and performance of electrical connections and signal transmission within the cable assembly, ensuring accurate energy delivery and reliable data transmission during procedures. Continuity, opens/shorts, and contact resistance verification ensures holistic functionality of the system. Dielectric withstand testing serves as a cornerstone in verifying high-voltage isolation, ensuring that

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Furthermore, cable durability testing is essential to assessing the mechanical robustness of cable assemblies. Subjecting the interconnect system to rigorous physical testing ensures they will withstand the demanding environments of clinical use. This testing evaluates the cable's ability to endure repeated flexing, torsion, tensile loads, and compression without compromising performance, electrical efficacy, or safety.

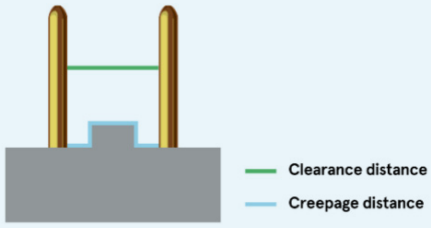
'Durability' also extends into confirming PFA product performance throughout repeated sterilization, reprocessing, and aging. Reprocessing protocols subject PFA cable assemblies to immersion in fluids, exposure to abrasive materials, aggressive chemicals, thermal cycling and negative pressure. Reprocessing methodologies include chemical wipe down, ultrasonic cleaner submersion, disinfectant washers, steam autoclave sterilization, and hydrogen peroxide plasma sterilization are typical methods used to disinfect and sterilize PFA cable assemblies. These stressors can impact a product in ways not traditionally found during mechanical or electrical testing.

Amphenol Alden's in-house sterilization test lab

Many of the electrical, mechanical, and environmental requirements mentioned previously are driven by compliance with required regulatory standards. Meeting these requirements is imperative for market approval, ensuring that cable assemblies meet stringent safety, performance, and quality standards before being introduced for clinical use. Overall, rigorous testing and certification processes are essential to validate the safety, reliability, and regulatory compliance of PFA cable assemblies, ultimately enhancing patient outcomes and ensuring the efficacy of PFA therapy in cardiac electrophysiology and beyond.

Material Selection and Design Considerations

To achieve the required high voltage performance of Pulsed Field Ablation (PFA), the selection process for connector and cable assembly materials is critical, coupled with the proper design of component geometries necessary to meet the desired creepage and clearance distances. Another important factor is the utilization of robust and validated product assembly processes.



Creepage and Clearance Distances

With PFA therapy, high-voltage isolation is paramount. Materials such as medical-grade silicone, fluoropolymers, epoxies, and other high dielectric materials are commonly used in interconnect solutions for this market due to their excellent electrical insulation properties.

Additionally, designing the required creepage and clearance distances between conductive elements is crucial to prevent arcing and ensure compliance with safety standards. This requires careful consideration of connector and cable geometry, insulation thicknesses, spacing between conductors, and proper selection of a combination of dielectric materials.

Amphenol Alden Cable Flex Tester

Mechanical durability, including repeated flexing, torsion, tension, and compression of the interconnect and cable is vital to withstanding the rigors of clinical use. Overall, the material selection and design process for PFA medical cable assemblies requires a comprehensive

understanding of electrical, mechanical, and regulatory requirements. Furthermore, the interplay and tradeoffs amongst those requirements is also critical to ensure the safe and effective delivery of PFA therapy.

Modification of Standard Product Platform or Full Custom Design

When embarking on a new product development project, customers often face the decision between selecting a standard product platform, and perhaps modifying it to meet their specific requirements, or starting from scratch with a full custom design.

Selecting a standard product platform, such as Amphenol Alden's P$_L$FA series of Pulse-Lok connectors, offers several advantages. These include reduced time to market, lower development costs, leveraging a proven design and materials, and benefiting from established manufacturing processes. However, in some cases, modifications may be necessary to tailor the product to unique specifications. This may include adjusting dimensions, contact count, customized keying, matching OEM's aesthetics and branding, and incorporating specialized components, all of which can be accommodated by the P$_L$FA series.

On the other hand, starting with a full custom design provides complete flexibility and control over every aspect of the product design, allowing for customization to the exact needs and preferences of the customer. While this approach offers maximum flexibility, it typically requires more time, resources, and expertise, as well as higher development and tooling costs.

Ultimately, deciding between a standard product platform, partially modified standard, or full custom design depends on factors such as project timeline, budget constraints, and technical complexity, all of which must be carefully evaluated to determine the most suitable approach for the customer's new product.

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Methods of terminating PFA interconnect solutions

Much has been said, to this point, regarding design and material considerations for PFA interconnect solutions with limited commentary on proper assembly of PFA connectors and cable bundles. Here, we will explore a few alternative assembly techniques that lend themselves to PFA interconnect assembly.

Without employing robust termination methodologies, PFA connectors and cable bundles cannot function as an assembly. Cable termination methods vary depending on the specific requirements and constraints of the design specifications, with options ranging from soldering individual wires to employing more sophisticated solutions such as flexible circuits or rigid PCBs.

Soldering individual wires provides a traditional yet reliable termination method offering simplicity and ease of implementation while ensuring secure connections. Alternatively, flexible circuits offer enhanced flexibility and durability, particularly suitable for applications requiring miniaturization. Rigid PCBs also provide a robust platform for terminating wires, offering precise control over signal routing and integration of components. All termination methods present their own value in the correct application, and skilled engineers can help provide guidance in selecting which approach is best for the application requirements.

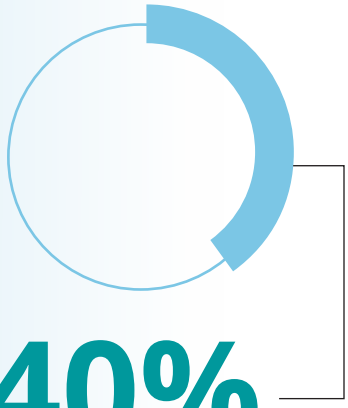
In a cable assembly, the wire termination methods discussed above are supported by additional cable assembly processes, such as over-molding, adhesive integration, and heat shrink tubing. These processing steps may be required to achieve isolated, secure, and sealed terminations tailored to the application's environmental, mechanical, electrical, and reprocessing requirements. When properly selected, the correct termination method and supporting assembly processes create unique advantages allowing for tailored solutions that meet the specific needs of the OEM.

"Without employing robust termination methodologies, PFA connectors and cable bundles cannot function as an assembly.

Automation for High Volume Manufacturing

If industry growth forecasts prove correct and that up to 40% of all cardiac EP procedures begin utilizing PFA therapy, the use of automation may be required to achieve cost and quality targets for high-volume catheter solutions. The effective use of automation is highly dependent on properly designing PFA interconnects and cable assemblies with these automated processes in mind.[3]

Design practices such as standardized component libraries and modular assembly techniques facilitate automation by simplifying the assembly process and ensuring compatibility between components.[4] Automation streamlines the manufacturing process, reducing labor costs and minimizes the potential for human error. Automated assembly equipment can precisely place components, terminate wires, and crimp connectors, ensuring consistent assembly quality and reliability across production batches.



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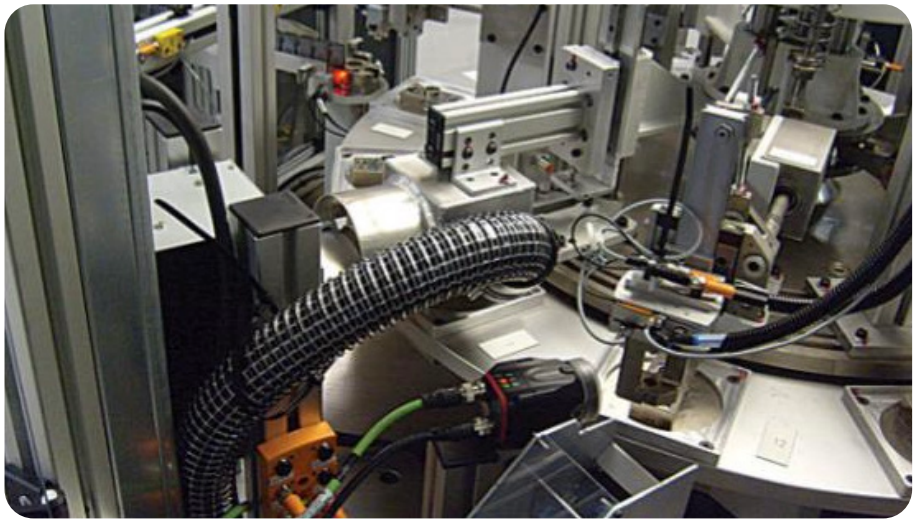
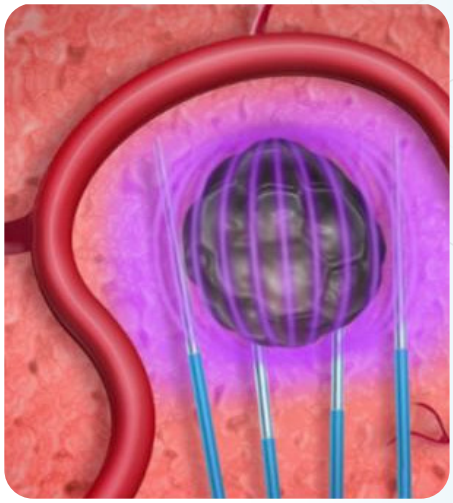


Amphenol Alden High Volume Automation

Future Trends and Other Applications of High Voltage Pulsed Therapies

The future of Pulsed Field Ablation (PFA) therapies and products, along with other therapies based on the use of pulsed field techniques, holds immense promise for revolutionizing the landscape of cardiac electrophysiology and other specialized treatment fields. Continued advancements in technology are expected to further refine PFA procedures, enhancing their efficacy, safety, and precision. This may include the development of more sophisticated catheter designs with improved energy delivery mechanisms, enhanced navigation capabilities, and integrated mapping functionalities. Additionally, research efforts are likely to focus on optimizing pulse parameters and treatment protocols to maximize therapeutic outcomes while minimizing procedural risks and patient discomfort.



Nano-second PEF Ablation[6]

Beyond PFA, pulsed field techniques are increasingly being explored for a wide range of medical applications, including cancer therapy, tissue regeneration, trans-cranial stimulation and drug delivery. As our understanding of pulsed field effects on biological tissues continues to evolve, we can anticipate innovative therapies and products that harness the potential of pulsed field techniques to address a diverse array of medical conditions, ultimately improving patient outcomes and quality of life.

For example, research in the area of nanosecond pulsed electric fields (nsPEFs) therapy represents a burgeoning field with promising potential in various medical applications. Nanosecond pulsed electric fields involve the application of extremely short-duration, high-voltage electric pulses to cells or tissues, resulting in unique biological effects.[5]

Studies have demonstrated that nsPEFs can induce reversible permeabilization of cell membranes, allowing for the targeted delivery of therapeutic agents such as chemotherapy drugs or genes into cells.

> Research efforts are likely to focus on optimizing pulse parameters and treatment protocols to maximize therapeutic outcomes while minimizing procedural risks and patient discomfort.

Moreover, nsPEFs have shown efficacy in selectively targeting cancer cells while sparing healthy tissue, offering a potentially groundbreaking approach to cancer treatment with reduced side effects compared to traditional therapies.

Furthermore, research indicates that nsPEFs may stimulate tissue regeneration and wound healing processes, presenting opportunities for applications in regenerative medicine and tissue engineering. Despite promising findings, further research is needed to fully understand the underlying mechanisms of nsPEFs and optimize[7] treatment parameters for various medical conditions.

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Conclusion

Pulsed field ablation (PFA) and Pulsed Electric Field (PEF) technologies are exciting new therapies that hold immense promise for revolutionizing treatments and improving patient outcomes. The topics explored in this technical paper encompass a wide range of considerations related to the field of medical cable assemblies for these technologies. From the design and engineering of cable assemblies to the intricacies of high-voltage isolation, signal integrity, and sterilization compatibility, each aspect plays a crucial role in ensuring the safety, efficacy, and regulatory compliance of medical devices used in this area.

As an emerging technology, discussions on manufacturing automation, best design practices, and future trends underscore the importance of innovation, collaboration, and value optimization in bringing to market products that enhance patient care. While challenges persist and the need for continued research and optimization of pulsed field therapies exists, the topics and expertise showcased in this paper pave the way for advancements that hold the potential to transform the landscape of medical interventions and improve outcomes for patients worldwide.

About the Author

For over 40 years Amphenol Alden has been a leading provider of medical cable assemblies and interconnect solutions to the market. Seamlessly integrating with our partners' engineering teams, we offer standard and custom-tailored solutions to meet the precise specifications provided by our OEM device partners.

Our Design Engineering team is dedicated to medical interconnect solutions, and we work in close collaboration with our partners' engineering teams during product design and development. Leveraging our on-site test lab, we assure the performance of all elements of our products, including robustness, safety, and compliance with industry standards and regulatory requirements, through in-house design-verification testing. These capabilities, along with our ISO13485 and FDA-registered global manufacturing footprint, offer unparalleled advantages to partners seeking to bring innovative products to market efficiently, effectively, and reliably.

With our extensive experience in manufacturing cable assemblies for Pulsed Field Ablation (PFA) devices, we are ready to support you from rapid prototyping to high-volume production. We achieve optimized product value through automated manufacturing, which enables inline visual inspection and electrical testing, to enhance quality control and reduce the risk of defects. This manufacturing approach allows for immediate detection of defects or inconsistencies, enabling prompt corrective actions which minimizes the likelihood of defective products reaching the market.

> **Contact us today** to see how Amphenol Alden Products can support your need for cable assemblies for Pulsed Field Ablation.

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1) Cappato, R. *et al.* Prevalence and causes of fatal outcome in catheter ablation of atrial fibrillation. J. Am. Coll. Cardiol. 53, 1798–1803 (2009)
2) Anic, A., Breskovic, T. & Sikiric, I. Pulsed field ablation: A promise that came true. Curr. Opin. Cardiol. 36, 5–9 (2021)
3) Sean Whooley, Catheter design was key for the Boston Scientific Farapulse pulsed field ablation system. Medical Design & Outsourcing (Feb 2024).
Jim, Boston Scientific initiates NAVIGATE-PF study of the Farawave Nav pulsed field ablation catheter and Faraview software module, Healthcare Global, cardiovascular (April 2024)
Verma A, Asivatham SJ, Deneke T, Castellvi Q, Neal RE II. Primer on pulsed electrical field ablation: understanding the benefits and limitations. Circ Arrhythm Electrophysiol 2021;14:e010086.
4) Todd Huston, Revolutionizing Solid Organ Tumor Ablation with High Voltage SolutionsPrimer on pulsed electrical field ablation: Advanced Energy, 2023; Aug 09
Yarmush ML, Golberg A, Serša G, Kotnik T, Miklavčič D. Electroporation-based technologies for medicine: principles, applications, and challenges. Annu Rev Biomed Eng 2014;16:295–320.
Ross, Christina L, et al. The Use of Pulsed Electromagnetic Field to Modulate Inflammation and Improve Tissue Regeneration: A Review. Bioelectricity Dec 2019;1(4):247-259.
5) Xie F, Varghese F, Pakhomov AG, Semenov I, Xiao S, Philpott J, et al. (2015) Ablation of Myocardial Tissue With Nanosecond Pulsed Electric Fields. PLoS ONE 10(12): e0144833. https://doi.org/10.1371/journal.pone.0144833
6) Friedrichs, Daniel: Applications of electrical energy in medicine: RF ablation and electroporation Medical Design and Outsourcing, Minnetronix (Dec 2022) Electrical energy in medicine: RF ablation, PFA and electroporation (medicaldesignandoutsourcing.com)
7) Friedrichs, Daniel: Applications of electrical energy in medicine: RF ablation and electroporation Medical Design and Outsourcing, Minnetronix (Dec 2022) Electrical energy in medicine: RF ablation, PFA and electroporation (medicaldesignandoutsourcing.com)