



## Review article

## Immune response to foreign materials in spinal fusion surgery

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## ABSTRACT

Spinal fusion surgery is a common procedure used to stabilize the spine and treat back pain. The procedure involves the use of foreign materials such as screws, rods, or cages, which can trigger a foreign body reaction, an immune response that involves the activation of immune cells such as macrophages and lymphocytes. The foreign body reaction can impact the success of spinal fusion, as it can interfere with bone growth and fusion. This review article provides an overview of the cellular and molecular events in the foreign body reaction, the impact of the immune response on spinal fusion, and strategies to minimize its impact. By carefully considering the use of foreign materials and optimizing surgical techniques, the impact of the foreign body reaction can be reduced, leading to better outcomes for patients.

## 1. Introduction

## 1.1. Brief explanation of spinal fusion and the use of foreign materials in the procedure

Overview of the foreign body reaction and its impact on spinal fusion.

Spinal fusion is a surgical procedure that involves joining two or more vertebrae in the spine to treat conditions such as degenerative disc disease [1], spinal stenosis [2], or spondylolisthesis. The procedure is intended to stabilize the spine and relieve pain by eliminating motion between the fused vertebrae [3]. Foreign materials such as metal implants [4], bone grafts [5], or synthetic materials [6] are often used in spinal fusion procedures to promote bone growth and fusion between the vertebrae [7]. These materials are intended to provide stability and support to the spine as it heals [8]. However, the use of foreign materials in spinal fusion procedures can trigger a foreign body reaction [9], which is an immune system response to the presence of foreign materials in the body [10]. The foreign body reaction can cause inflammation, tissue damage, and impair the healing process of the spine [11]. The impact of the foreign body reaction on spinal fusion can lead to complications such as implant failure [12], non-union (lack of bone growth and fusion) [13], and chronic pain [14]. Therefore, it is important for medical professionals to carefully evaluate the use of foreign materials in spinal fusion procedures and consider alternative approaches to promote successful fusion while minimizing the risk of a foreign body reaction. Despite the great success of artificial implants for the human body, they are not without their limitations. One major issue is the foreign body reaction, which is an immune reaction of the organism to the implant. However, researchers have found a way to avoid or decrease the foreign body reaction by modifying the surface of the artificial implant with condensed aromatic structures containing free radicals. This modification allows for covalent attachment of host proteins in their native conformation,

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resulting in total protein coverage that prevents direct contact of immune cells with the implant surface. As a result, the immune response of the organism is not generated, and the artificial implant is not isolated from the tissue, resulting in low activity of macrophages, low cell proliferation, and low inflammatory activity. This promising approach could help to address some of the major health problems associated with artificial implants [15].

The specific types of foreign materials used in spinal fusion procedures and how they trigger the foreign body reaction.

Recent progress in the field of spinal fusion has highlighted the importance of understanding the specific types of foreign materials used in these procedures and how they trigger the foreign body reaction [16]. One technique that has gained traction in recent years is the use of bioactive materials, which can enhance the biological response and promote faster and more complete fusion [17]. However, these materials can also trigger a more severe foreign body reaction compared to traditional materials such as titanium and stainless steel [18]. Bioactive materials, such as ceramics and calcium phosphate-based materials, can release ions that stimulate immune cells and trigger the foreign body reaction [19]. Additionally, some bioactive materials can induce fibrosis, which can further contribute to implant failure [20]. Therefore, careful consideration of the specific types of foreign materials used in spinal fusion procedures is necessary to minimize the risk of a foreign body reaction and ensure successful fusion [21]. In addition to bioactive materials, other foreign materials used in spinal fusion procedures can also trigger the foreign body reaction [22]. Metallic materials can corrode and release metal ions, which can cause an inflammatory response and lead to implant failure [23]. Synthetic materials, such as polymers, can also trigger the foreign body reaction due to their chemical and mechanical properties [16]. Therefore, it is crucial to carefully select the appropriate foreign materials for spinal fusion procedures and consider their potential impact on the foreign body reaction [24]. Researchers are exploring different strategies to minimize the foreign body reaction, such as surface modifications and coatings that can reduce immune cell activation and fibrous capsule formation [25]. Further research is needed to identify the most effective approaches to minimize the foreign body reaction and improve the long-term success of spinal fusion procedures [24]. In recent years, there has been growing interest in developing biomaterials that can better integrate with the host tissue and minimize the foreign body reaction [26]. One promising approach is the use of biodegradable materials that can gradually degrade and be replaced by the host tissue [27], minimizing the formation of a fibrous capsule and reducing the immune response [28]. Natural materials, such as collagen and chitosan, have also been explored for their ability to mimic the extracellular matrix of the host tissue and promote cellular attachment and proliferation [29]. Additionally, researchers are investigating the use of stem cells and growth factors to enhance the biological response and promote faster and more complete fusion [30]. By carefully selecting and designing foreign materials for spinal fusion procedures, it may be possible to minimize the foreign body reaction and improve the long-term success of these procedures [24]. One major concern with spinal fusion procedures is the immune response of the patient to the foreign materials used in the procedure [31]. The immune response can lead to the formation of a fibrous capsule, which can compromise the stability of the implant and interfere with the fusion process [22]. In addition, the immune response can cause chronic pain and other complications that can reduce the quality of life of the patient [32]. To address this concern, researchers are exploring different strategies to modulate the immune response and minimize the foreign body reaction [24]. One approach is the use of immunosuppressive drugs, which can reduce the activity of immune cells and minimize the formation of a fibrous capsule [33]. However, this approach is not without its risks, as it can increase the risk of infection and other complications [34]. Therefore, researchers are also exploring the use of immune-modulating biomaterials that can interact with the immune system in a more controlled and targeted manner [35]. By carefully balancing the immune response to the foreign materials used in spinal fusion procedures, it may be possible to improve the long-term success of these procedures and reduce the risk of complications [36]. Table 1 provides a summary of examples of foreign materials used in spinal fusion procedures and their potential impact on the foreign body reaction. By carefully selecting and designing foreign materials for spinal fusion procedures [37], it may be possible to minimize the foreign body reaction and improve the long-term success of these procedures (see Table 1).

## 2. Cellular and molecular events in the foreign body reaction

The foreign body reaction is a complex process that involves the interaction between the implant and the host tissues, leading to a series of cellular and molecular events [38]. Upon implantation, the body initiates an inflammatory response to the presence of the foreign material [39], which is characterized by the recruitment of immune cells such as macrophages and neutrophils to the site of implantation [39]. These immune cells phagocytose and degrade the implant material, releasing cytokines and growth factors that can stimulate the proliferation and differentiation of fibroblasts [40]. These fibroblasts then produce extracellular matrix components such as collagen [41], which can lead to the formation of a fibrous capsule around the implant [41]. The fibrous capsule acts as a barrier

**Table 1**  
Examples of foreign materials used in spinal fusion procedures and their potential impact on the foreign body reaction.

Material	Potential impact on foreign body reaction
Titanium [28,136–138]	Low immune response and fibrous capsule formation
Stainless steel [28,138,139]	Low immune response and fibrous capsule formation
Cobalt-chromium [23,140,141]	Moderate immune response and potential for metal ion release
Bioactive ceramics [142–144]	High immune response and fibrosis
Calcium phosphate [144–146]	High immune response and potential for fibrosis
Biodegradable polymers [25,147,148]	Gradual degradation and minimal fibrous capsule formation
Collagen [149–151]	Mimics host tissue and promotes cellular attachment
Chitosan [152–154]	Mimics host tissue and promotes cellular attachment

between the implant and the surrounding tissues [42] and can inhibit the exchange of nutrients and cells between the implant and the surrounding tissues [43], leading to implant failure. In addition to the recruitment of immune cells and the formation of a fibrous capsule, the foreign body reaction is also characterized by the activation of signaling pathways that regulate the immune response and inflammation [44]. These pathways can modulate the magnitude and duration of the foreign body reaction, as well as the formation of the fibrous capsule around the implant [45].

### 3. Cellular and molecular events in the foreign body reaction

The foreign body reaction is a complex process that involves the interaction between the implant and the host tissues [38], leading to a series of cellular and molecular events. Upon implantation, the body initiates an inflammatory response to the presence of the foreign material [46], which is characterized by the recruitment of immune cells such as macrophages and neutrophils to the site of implantation [47]. These immune cells phagocytose and degrade the implant material, releasing cytokines and growth factors that can stimulate the proliferation and differentiation of fibroblasts [48]. These fibroblasts then produce extracellular matrix components such as collagen [49], which can lead to the formation of a fibrous capsule around the implant [50]. The fibrous capsule acts as a barrier between the implant and the surrounding tissues [51] and can inhibit the exchange of nutrients and cells between the implant and the surrounding tissues [52], leading to implant failure [53]. In addition to the recruitment of immune cells and the formation of a fibrous capsule [54], the foreign body reaction is also characterized by the activation of signaling pathways that regulate the immune response and inflammation [55]. These pathways can modulate the magnitude and duration of the foreign body reaction [56], as well as the formation of the fibrous capsule around the implant [57].

#### 3.1. Inflammatory responses, tissue damage, and bone resorption during the foreign body reaction

The fibrous capsule that forms around the implant in response to the foreign body reaction can have different fates [58], depending on various factors such as the size, shape, and composition of the implant [59], as well as the patient's immune system. In some cases, the fibrous capsule can lead to successful spinal fusion, as it helps to stabilize the implant and promotes the fusion process [60]. However, in other cases, the fibrous capsule can inhibit the fusion process by acting as a barrier between the implant and the surrounding tissues [61], preventing the exchange of nutrients and cells needed for fusion [62]. In addition, the fibrous capsule can also lead to implant failure by causing stress shielding, which is characterized by the transfer of stress from the vertebral bodies to the implant [63], leading to implant failure [64]. The fibrous capsule can also lead to other complications such as pain, stiffness, and implant loosening [65], which can result in the need for revision surgery [66]. Therefore, it is important to understand the fate of the fibrous capsule around the implant in order to optimize the outcome of spinal fusion and minimize the risk of complications [67].

### 4. Impact of the foreign body reaction on spinal fusion

The foreign body reaction can have a significant impact on the success of spinal fusion [68]. The formation of a fibrous capsule around the implant in response to the foreign body reaction can lead to successful spinal fusion in some cases [69], as it helps to stabilize the implant and promotes the fusion process [70]. However, in other cases, the fibrous capsule can inhibit the fusion process by acting as a barrier between the implant and the surrounding tissues [61], preventing the exchange of nutrients and cells needed for fusion. The foreign body reaction is a complex process that involves various signaling pathways and cellular mechanisms [11]. When an implant is placed in the body, it is recognized as a foreign object by the immune system [46], which triggers a series of events aimed at removing the foreign material [71]. This process is initiated by the activation of innate immune cells, such as macrophages and neutrophils [72], which engulf the implant and release pro-inflammatory cytokines and chemokines to recruit more immune cells to the site of injury [73]. The activation of immune cells is mediated by various signaling pathways, such as the toll-like receptor (TLR) pathway [74], which recognizes pathogen-associated molecular patterns (PAMPs) [75] and damage-associated molecular patterns (DAMPs) on the surface of the implant [76]. This leads to the activation of transcription factors, such as nuclear factor kappa B (NF- $\kappa$ B) [77], which induce the expression of pro-inflammatory cytokines, such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF- $\alpha$ ) [78]. The pro-inflammatory cytokines attract more immune cells to the site of injury [79], which further amplify the immune response [80]. In addition to the activation of innate immune cells, the foreign body reaction also involves the activation of adaptive immune cells [81], such as T cells and B cells [82]. These cells recognize specific antigens on the surface of the implant and mount an antigen-specific immune response [83]. The foreign body reaction can also affect the mechanical stability of the implant by inducing the formation of a fibrous capsule around the implant [58]. The formation of the fibrous capsule is mediated by various signaling pathways, such as the transforming growth factor beta (TGF- $\beta$ ) pathway [84], which promotes the differentiation of fibroblasts into myofibroblasts and the deposition of extracellular matrix proteins [85]. Stress shielding is another complication that can result from the foreign body reaction [86]. This occurs when the implant absorbs a significant portion of the load that would normally be borne by the surrounding bone [87], leading to bone resorption and implant loosening [88]. The mechanisms underlying stress shielding are complex and involve various signaling pathways, such as the RANK/RANKL/OPG pathway [89], which regulates osteoclast differentiation and bone resorption [90]. In summary, the foreign body reaction is a complex process that involves various signaling pathways and cellular mechanisms. The impact of the foreign body reaction on spinal fusion can vary depending on various factors, such as the size, shape, and composition of the implant, as well as the patient's immune system. A better understanding of the mechanisms underlying the foreign body reaction is essential for optimizing the outcome of the procedure and minimizing the risk of complications. One important subcluster of cells involved in the foreign body reaction are macrophages [91]. Macrophages play a

crucial role in the initial recognition and removal of the implant by engulfing the foreign material and releasing pro-inflammatory cytokines and chemokines to recruit more immune cells to the site of injury [92]. Macrophages can also differentiate into different subtypes depending on the microenvironment and signals they receive [93]. In the context of the foreign body reaction, macrophages can differentiate into two main subtypes: M1 and M2 macrophages. M1 macrophages are classically activated and secrete pro-inflammatory cytokines such as IL-1, IL-6, and TNF- $\alpha$  [94], which amplify the immune response and promote the clearance of the foreign material [95]. M1 macrophages are important in the early stages of the foreign body reaction. In contrast, M2 macrophages are alternatively activated and secrete anti-inflammatory cytokines such as IL-10 [96], which dampen the immune response and promote tissue repair and remodeling. M2 macrophages are important in the later stages of the foreign body reaction when tissue repair and remodeling are necessary to restore normal tissue function [97]. The transition from M1 to M2 macrophages is regulated by various signaling pathways, such as the TGF- $\beta$  pathway [98]. The balance between M1 and M2 macrophages is important for the resolution of the foreign body reaction and the restoration of tissue function [99]. Imbalance between these subtypes can lead to chronic inflammation, fibrosis, and implant failure. Therefore, strategies that modulate the polarization of macrophages towards the M2 phenotype may be beneficial for minimizing the foreign body reaction and promoting tissue repair and regeneration. T cells also play an important role in the foreign body reaction. T cells are a type of adaptive immune cell that recognizes specific antigens on the surface of the implant [100] and mount an antigen-specific immune response [101]. This response is mediated by various signaling pathways, such as the T cell receptor (TCR) pathway, which leads to the activation of transcription factors and the production of cytokines [102]. In addition to recognizing antigens on the surface of the implant, T cells can also interact with other immune cells, such as macrophages and dendritic cells, and modulate their function [103]. For example, T cells can secrete cytokines such as interferon-gamma (IFN- $\gamma$ ), which activates macrophages and enhances their phagocytic activity [104]. T cells can also secrete cytokines such as IL-4 and IL-13, which promote the differentiation of macrophages towards the M2 phenotype [105]. The balance between different subtypes of T cells is also important in the foreign body reaction. For example, regulatory T cells (Tregs) are a subset of T cells that suppress immune responses and promote tissue repair and regeneration [106]. Tregs can secrete cytokines such as IL-10 and transforming growth factor beta (TGF- $\beta$ ), which dampen the immune response and promote tissue repair [107]. The balance between Tregs and other T cell subsets, such as Th1 and Th17 cells, is important in maintaining immune homeostasis and preventing chronic inflammation and tissue damage [108]. In addition to T cells, other immune cells such as B cells, neutrophils, and mast cells are also involved in the foreign body reaction. B cells can produce antibodies against the implant [100], which can contribute to the formation of the fibrous capsule [108]. Neutrophils can release reactive oxygen species and proteases [109], which can damage the surrounding tissue and contribute to chronic inflammation [110]. Mast cells can release histamine and other pro-inflammatory mediators [111], which can amplify the immune response and contribute to tissue damage [112]. In summary, T cells and other immune cells play a crucial role in the foreign body reaction. The balance between different subtypes of immune cells is important in maintaining immune homeostasis and promoting tissue repair and regeneration. Strategies that modulate the immune response and promote tissue repair may be beneficial for minimizing the foreign body reaction and improving the outcome of implant surgery.

#### Overview of Specific Types of Foreign Materials Used in Spinal Fusion Procedures.

Spinal fusion procedures involve the use of foreign materials to promote bone growth and stability [31]. The types of foreign materials used in spinal fusion procedures can vary depending on the specific procedure and the patient's individual needs [113]. Metallic materials such as titanium, stainless steel, and cobalt-chromium alloys have traditionally been used due to their strength and biocompatibility [114]. However, they can still trigger the foreign body reaction and may require additional coatings or modifications to minimize this response [115]. Bioactive materials, such as ceramics and calcium phosphate-based materials, have been developed to enhance bone growth and fusion [116]. However, these materials can trigger a more severe immune response compared to traditional materials. Biodegradable materials, such as polymers, are also being explored as an alternative to permanent foreign materials [117]. They can gradually degrade over time and be replaced by host tissue, minimizing the foreign body reaction [26]. By understanding the types of foreign materials used in spinal fusion procedures and their potential impact on the foreign body reaction [24], researchers and medical professionals can make informed decisions regarding material selection and optimize the outcome of these procedures [118]. Table 2 provides a summary of the different types of foreign materials used in spinal fusion procedures, including their potential benefits and drawbacks. By carefully selecting and designing foreign materials for spinal fusion procedures, it may be possible to

**Table 2**  
Types of foreign materials used in spinal fusion procedures.

Material	Description	Potential benefits	Potential drawbacks
Titanium [155–157]	A biocompatible metal commonly used in spinal fusion procedures	Strong and lightweight material	May still trigger the foreign body reaction
Stainless steel [158–160]	A durable metal commonly used in spinal fusion procedures	Biocompatible and strong material	May still trigger the foreign body reaction
Cobalt-chromium alloys [157,161,162]	A metal alloy commonly used in spinal fusion procedures	Biocompatible and strong material, less likely to corrode	May still trigger the foreign body reaction, potential for metal ion release
Bioactive ceramics [163, 164]	Ceramic materials designed to enhance bone growth and fusion	Can enhance bone growth and fusion	May trigger a more severe immune response compared to traditional materials
Calcium phosphate [116, 165,166]	A synthetic material that can enhance bone growth and fusion	Can enhance bone growth and fusion	May trigger a more severe immune response compared to traditional materials
Biodegradable polymers [27,167,168]	Materials that can gradually degrade and be replaced by host tissue	Can minimize the foreign body reaction and promote tissue integration	May not provide sufficient strength or stability for some spinal pathologies

minimize the foreign body reaction and improve the long-term success of these procedures [24](see Table 2). Medical professionals can use this information to make informed decisions regarding material selection and optimize the outcome of spinal fusion procedures.

#### 4.1. Factors influencing the success of spinal fusion

The success of spinal fusion is influenced by a variety of factors, including the surgical technique, the type of implant used, and the patient's underlying medical conditions [119]. The surgical technique used for spinal fusion can impact the success of the procedure, as different techniques may result in varying levels of spinal stability and fusion rates [120]. For example, minimally invasive techniques, such as tubular retractor-assisted lumbar interbody fusion, have been shown to result in higher fusion rates compared to open techniques, such as posterolateral fusion [121]. The type of implant used for spinal fusion can also impact the success of the procedure, as different implants may have varying levels of biomechanical stability and biocompatibility [122]. For example, titanium implants have been shown to have higher biomechanical stability compared to polyetheretherketone (PEEK) implants, while PEEK implants have been shown to have a lower foreign body reaction compared to titanium implants [123]. Additionally, underlying medical conditions, such as osteoporosis, can also impact the success of spinal fusion, as they can weaken the vertebral bodies and reduce the stability of the implant [124]. Therefore, it is important to consider the various factors that can influence the success of spinal fusion in order to optimize the outcome of the procedure.

### 5. Strategies to minimize the impact of the foreign body reaction

There are several strategies that have been proposed to minimize the impact of the foreign body reaction on spinal fusion procedures. One approach is to modify the surface properties of the implant to reduce the foreign body reaction. This can be achieved by coating the implant with biocompatible materials or by modifying the surface roughness of the implant. Another approach is to use biologically active agents such as growth factors and cytokines to stimulate the fusion process and reduce the foreign body reaction. In addition, using minimally invasive surgical techniques, such as tubular retractor-assisted lumbar interbody fusion, has been shown to result in a lower foreign body reaction compared to open techniques, such as posterolateral fusion. Moreover, optimizing the patient's underlying medical conditions, such as osteoporosis, can also help to minimize the impact of the foreign body reaction on spinal fusion. Therefore, it is important to consider the various strategies that can be used to minimize the impact of the foreign body reaction in order to optimize the outcome of spinal fusion procedures.

#### 5.1. Use of biocompatible materials in spinal fusion

The use of biocompatible materials in spinal fusion has been proposed as a strategy to reduce the foreign body reaction and improve the success of the procedure [125]. Biocompatible materials are materials that are compatible with the host tissues and elicit a minimal foreign body reaction [126]. The use of biocompatible materials in spinal fusion can reduce the magnitude and duration of the foreign body reaction [127], leading to a smaller fibrous capsule and improved bone growth and fusion [128]. For example, biocompatible coatings, such as hydroxyapatite coatings, have been shown to reduce the foreign body reaction and improve the success of spinal fusion compared to uncoated implants [129]. Additionally, the use of biocompatible materials, such as PEEK, has been shown to result in a lower foreign body reaction compared to titanium implants [130]. Therefore, the use of biocompatible materials in spinal fusion can be an effective strategy to reduce the foreign body reaction and improve the success of the procedure.

#### 5.2. Optimization of surgical techniques to reduce tissue damage

Optimization of surgical techniques to reduce tissue damage is important in order to minimize the foreign body reaction and improve the success of spinal fusion [131]. Minimally invasive surgical techniques, such as tubular retractor-assisted lumbar interbody fusion, have been shown to result in reduced tissue damage compared to open techniques, such as posterolateral fusion [132]. Additionally, the use of smaller incisions and specialized instruments can help to reduce tissue damage and minimize the foreign body reaction [11]. Furthermore, the use of techniques such as nerve monitoring can help to minimize the risk of nerve damage during spinal fusion procedures [133]. The optimization of surgical techniques can help to reduce tissue damage and minimize the foreign body reaction, leading to improved outcomes and reduced risk of complications in spinal fusion procedures [134]. The underlying mechanism of minimizing the foreign body reaction in spinal fusion procedures is to reduce the interaction between the implant and the host tissues [135]. This can be achieved by reducing the magnitude and duration of the immune response, reducing the formation of a fibrous capsule around the implant, and improving the exchange of nutrients and cells between the implant and the surrounding tissues [65]. Minimizing the foreign body reaction can be achieved through various strategies, such as using biocompatible materials, optimizing surgical techniques, using biologically active agents such as growth factors and cytokines, and addressing underlying medical conditions such as osteoporosis [11]. By reducing the foreign body reaction, the success of spinal fusion can be improved by promoting bone growth and fusion, reducing the risk of implant failure, and minimizing the risk of complications such as pain, stiffness, and implant loosening.

Application of anti-inflammatory agents to reduce the immune response.

## 6. Conclusion and future directions

The application of anti-inflammatory agents to reduce the immune response in spinal fusion procedures is an emerging strategy to minimize the foreign body reaction and improve the success of the procedure. Anti-inflammatory agents, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, have been shown to reduce the magnitude and duration of the immune response in spinal fusion procedures. Additionally, the use of biologic agents, such as cytokine inhibitors, has also been proposed as a strategy to reduce the immune response in spinal fusion procedures. However, further studies are needed to fully understand the mechanisms underlying the application of anti-inflammatory agents in spinal fusion and to determine the optimal dosing and administration of these agents. In conclusion, the foreign body reaction can have a significant impact on the success of spinal fusion procedures, and minimizing the foreign body reaction is essential to improve the outcome of the procedure. The use of biocompatible materials, optimization of surgical techniques, application of anti-inflammatory agents, and addressing underlying medical conditions are among the strategies that have been proposed to minimize the foreign body reaction in spinal fusion. Further research is needed to fully understand the mechanisms underlying these strategies and to determine the optimal approach to minimize the foreign body reaction and improve the success of spinal fusion procedures.

### 6.1. Summary of the key points

The application of anti-inflammatory agents to reduce the immune response in spinal fusion procedures is an emerging strategy to minimize the foreign body reaction and improve the success of the procedure. The foreign body reaction can have a significant impact on the success of spinal fusion, and minimizing the foreign body reaction is essential to improve the outcome of the procedure. Strategies to minimize the foreign body reaction include the use of biocompatible material, optimization of surgical techniques, application of anti-inflammatory agents and addressing underlying medical conditions such as osteoporosis. The application of anti-inflammatory agents, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, as well as biologic agents, such as cytokine inhibitors, have been proposed to reduce the immune response and minimize the foreign body reaction in spinal fusion. Further research is needed to fully understand the mechanisms underlying the application of anti-inflammatory agents and to determine the optimal approach to minimize the foreign body reaction and improve the success of spinal fusion procedures.

### 6.2. Discussion of future research directions and potential improvements in spinal fusion surgery

Future advancements in spinal fusion surgery aim to address the challenges posed by the foreign body reaction, which can negatively impact the success of the procedure. The development of biocompatible materials and the optimization of surgical techniques, such as minimally invasive surgical techniques, are among the strategies being explored to reduce tissue damage and minimize the foreign body reaction. The application of anti-inflammatory agents, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, as well as biologic agents, such as cytokine inhibitors, may also play a role in reducing the immune response and improving the success of spinal fusion. The potential use of regenerative medicine and tissue engineering represents another area of investigation for promoting the growth of new, functional tissue and improving the success of spinal fusion. However, further research is needed to fully understand these strategies and determine the optimal approach to improve the success of spinal fusion procedures. In recent years, there has been growing interest in exploring alternative approaches to spinal fusion procedures that can minimize the risk of complications and improve patient outcomes. One promising approach is dynamic stabilization, which uses flexible implants to stabilize the spine and preserve range of motion. This approach can help reduce the risk of adjacent segment disease and preserve patient mobility. Another alternative approach is disc replacement, which replaces the damaged disc with an artificial disc. This approach can preserve motion and reduce the risk of adjacent segment disease, although it is still a relatively new procedure and may require further research to establish long-term safety and efficacy. By providing more detailed information on alternative approaches to spinal fusion procedures and their potential benefits and drawbacks, medical professionals and patients can make more informed decisions about treatment options and optimize the outcomes of spinal fusion procedures.

### Author contribution statement

All authors listed have significantly contributed to the development and the writing of this article.

### Data availability statement

No data was used for the research described in the article.

### Additional information

No additional information is available for this paper.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to



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