

**“CAROL DAVILA” UNIVERSITY OF MEDICINE AND  
PHARMACY IN BUCHAREST**



**PhD THESIS  
ABSTRACT**

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**2024**

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**ABSTRACT**

**IMPROVEMENT OF BONE INTEGRATION AND FIXATION OF GRAFTS  
AND IMPLANTS USED IN ANTEROLATERAL CRUCIATE LIGAMENT  
RECONSTRUCTION – A CLINICAL, IMAGING, AND EXPERIMENTAL  
STUDY**

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## **General part - current state of knowledge**

This section presents a detailed and comprehensive analysis of the latest discoveries and techniques used in the field of anterior cruciate ligament (ACL) surgery and the application of nanomaterials in this domain.

In **Chapter I**, titled "**Anterior cruciate ligament surgery: general data, classification, reconstruction and implantation methods, biocompatibility,**" the anatomy of the anterior cruciate ligament is explored, along with the etiology of injuries, modern diagnostic and treatment methods, as well as the complications and postoperative outcomes associated with the reconstruction of this crucial ligament for knee stability.

**Chapter II**, named "**Materials used in the fabrication of nanostructured coatings using the MAPLE technique,**" discusses the properties and applications of graphene oxide and silver nanoparticles in biomedicine, as well as the use of the MAPLE technique for the synthesis and application of nanomaterials in various medical and technological fields (medical devices and implants). This general part provides a solid foundation for understanding the complexity and importance of these subjects in modern medicine.

ACL reconstruction is a crucial area in modern orthopedic surgery, significantly impacting the quality of life for patients suffering from knee injuries. Since the 1970s, significant progress has been made in this procedure, particularly with the introduction of autologous grafts, which have significantly reduced complications and improved postoperative outcomes. However, the evolution of ACL reconstruction began much earlier, in the 1930s, when the first attempts involved using various materials, from ligaments harvested from animals to plastic and metallic materials. These methods were eventually abandoned due to the high rate of complications.

Technological advancements in the 1970s allowed the use of autologous grafts, such as the hamstring tendon, patellar tendon, and fascia lata, which established a new standard in ligamentoplasty due to their biological compatibility and quicker postoperative recovery. Modern techniques continue to evolve with the development of advanced surgical approaches and the use of cutting-edge technologies, such as sophisticated anchoring devices and complex sutures. In the future, advances in tissue engineering, the use of stem cells, and 3D printing technologies are expected to further transform this field, contributing to improved patient outcomes.

ALCL injuries are common among athletes and can lead to severe functional disabilities if not properly treated. Untreated, these injuries can progress to osteoarthritis and chronic knee

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instability. Initially, ALCL injury treatment involved primary ligament repair, but unsatisfactory results led to the development of more advanced reconstruction techniques. The first reconstruction attempts involved extra-articular techniques, but their outcomes were also below expectations. As knowledge of ALCL anatomy and function advanced, intra-articular reconstruction techniques were developed, proving to be more effective.

The anatomy of the ALCL is complex, being a ligament composed of dense connective tissue that attaches to the lateral femoral condyle and the anterior intercondylar fossa of the tibia. The vascularization of this ligament is provided by the middle genicular artery, and innervation is provided by branches of the tibial nerve, responsible for joint proprioception. ALCL injuries are common in sports involving sudden movements, such as rapid changes in direction or landings after jumps, with non-contact mechanisms being predominant.

Diagnosing ALCL injuries includes history-taking, physical examination, and imaging evaluation. Patients often describe a "popping" sensation in the knee, followed by a rapid increase in joint size, suggesting the presence of hemarthrosis. Physical examination is essential for assessing the integrity of the ligament and other associated structures, and stress tests, such as the Lachman test, are crucial for diagnosing ALCL ruptures. Magnetic resonance imaging (MRI) is considered the most accurate method for diagnosing ALCL injuries, with an accuracy of up to 100%.

The natural history of ALCL injuries can include the development of osteoarthritis and chronic knee instability, associated with significant changes in joint dynamics. Meniscal tears are frequently associated with acute ALCL injuries, with the lateral meniscus being most commonly affected. Patients who delay ALCL reconstruction are at an increased risk of osteoarthritis and secondary meniscal injuries.

Treatment for ALCL injuries ranges from non-operative options, suitable for patients willing to accept lifestyle changes to avoid activities that cause instability, to surgical interventions. Extra-articular reconstructions were initially used to create a restraint band on the lateral side of the knee, but these did not fully restore normal ALCL function. Intra-articular techniques, particularly those guided by arthroscopy, have significantly improved the treatment of ALCL injuries, providing rapid relief of postoperative pain and optimal functional recovery.

To better understand the complexity and innovation in this field, it is essential to explore other advanced materials used in modern medicine, such as graphene and nanoparticles. These

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materials not only enhance medical techniques but also open new horizons in diagnosis and treatment, with diverse applications in biomedicine and tissue engineering.

Graphene is a revolutionary material composed of a single layer of carbon atoms arranged in a two-dimensional sp<sup>2</sup> hybridized structure, forming a hexagonal lattice similar to a honeycomb. It is the thinnest known form of carbon, possessing unique properties including superior electrical and thermal conductivity, light absorption, and mechanical strength. Graphene can exist in various forms, including single-layer graphene, multilayer graphene, graphene oxide (GO), and reduced graphene oxide (rGO), each having specific applications depending on its distinct properties.

Graphene Oxide (GO) is particularly important due to its rich oxygen content and numerous functional groups on its surface, which confer stability in colloidal dispersions and facilitate surface chemical reactions. However, these functional groups reduce the mechanical and electrical properties of the material by creating defects in its structure. Although often seen as disadvantages, these defects can enhance the chemical reactivity of graphene, making it useful in various biological and technological applications.

The synthesis of graphene and its derivatives can be achieved through various methods, each with its advantages and disadvantages. Mechanical exfoliation was the first developed technique, involving the layered removal of graphite sheets. However, this method can generate structural defects, affecting graphene's electrical conductivity. Another effective method is chemical exfoliation, which transforms graphite from a colloidal suspension into graphene through a two-step process. Additionally, thermal epitaxial growth and chemical vapor deposition (CVD) are advanced techniques that enable the production of high-quality graphene on various substrates, including transition metals like copper and nickel.

Graphene has multiple applications in biomedicine due to its unique properties. It is used for drug delivery, facilitating the efficient loading and conjugation of hydrophobic drugs, thereby improving their solubility and therapeutic efficacy. Moreover, graphene can be used in cellular imaging due to its stability and the ability to be functionalized as an efficient biosensor.

Photodynamic and Photothermal Therapy are other promising applications of graphene, particularly in cancer treatment. Graphene-based materials have superior optical absorption in the NIR (near-infrared) region and high photothermal conversion, making them ideal for phototherapy. In photodynamic therapy, photosensitizers exposed to a specific light wavelength produce reactive oxygen species (ROS), which are toxic to cancer cells. In photothermal therapy,

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graphene-based materials absorb NIR light and convert it into heat, leading to the destruction of cancer cells.

Tissue Engineering is another field where graphene plays a crucial role. In the form of foam, graphene can act as a scaffold for the growth of neural stem cells, supporting their proliferation and differentiation. Additionally, due to its remarkable electrical properties, graphene is used as a chemical matrix for sensors and biosensors, enabling the specific detection of DNA sequences or other biomolecules.

Silver Nanoparticles (AgNPs) are another nanostructured material with exceptional antimicrobial properties. These nanoparticles are widely used in the medical industry due to their ability to destroy a broad spectrum of pathogenic microorganisms, being integrated into dressings, catheters, and other medical devices. The antimicrobial properties of silver have been known for centuries, and silver nanoparticles have demonstrated superior efficacy in inhibiting bacterial growth, including antibiotic-resistant strains.

The action mechanism of silver nanoparticles involves interacting with functional protein groups in membranes, leading to protein denaturation and bacterial cell destruction. Additionally, silver nanoparticles can damage bacterial genetic material, inhibiting DNA replication and transcription. These properties make silver nanoparticles a vital tool in infection treatment and tissue regeneration.

Silver nanoparticles are also used in non-medical applications, such as drinking water purification and in the textile industry, due to their ability to generate surface plasmon resonance (SPR). In this context, nanoparticles are integrated into various consumer products, including cosmetics, food, and water purification equipment.

MAPLE technique (Matrix-Assisted Pulsed Laser Evaporation) is an advanced thin-film synthesis technique derived from the conventional pulsed laser deposition (PLD) method. It was developed to allow the deposition of soft materials, such as organic polymers and biomaterials, offering precise control over deposition parameters such as film thickness, roughness, and homogeneity. A major advantage of the MAPLE technique is its versatility in fabricating nanostructures.

MAPLE is widely used in various fields, including microelectronics, tissue engineering, and the pharmaceutical industry. For example, the MAPLE technique enables the deposition of thin polymeric films for optoelectronic and chemical sensors, as well as the production of active

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protein films and carbon nanotube-based composites. This technique is also applicable in the deposition of biological materials on substrates, with significant potential for use in molecular printing.

Despite its advantages, the MAPLE technique has some drawbacks, including high costs and the need for specialized knowledge to operate the equipment. Additionally, selecting the solvent and solution concentration for the MAPLE technique involves adhering to precise criteria to ensure the efficiency and quality of thin film deposition.

### **Special part - personal contributions**

The **Special part** of the doctoral thesis is a fundamental section where the author presents in detail the objectives and aims of the studies, as well as the original research conducted. This part includes two chapters.

**Chapter I**, titled "**Clinical study of autograft fixation in ACL reconstruction**," focuses on investigating the effectiveness and safety of autograft fixation techniques used in anterior cruciate ligament (ACL) reconstruction. It highlights the performed interventions, the analysis methods, and the outcomes obtained from the clinical evaluation of patients.

**Chapter II**, named "**Advanced nanostructures for enhancing biocompatibility and reducing microbial susceptibility of medical devices used in knee surgery**," explores the use of innovative nanomaterials, such as graphene oxide and silver nanoparticles, in developing nanostructured coatings for orthopedic devices. This chapter analyzes their performance in terms of biocompatibility and protection against infections. These contributions represent a significant step forward in orthopedic surgery and nanostructured materials, opening new perspectives for improving clinical outcomes and reducing postoperative complications.

The first major objective of the thesis was to analyze the efficacy and safety of ACL reconstruction, with a focus on functional outcomes, the incidence of postoperative complications, and factors influencing the success of interventions. A comparison was made between two types of autografts used—hamstring tendons and patellar tendon—to determine which method offers superior results.

The second objective was aimed at developing and characterizing advanced antimicrobial nanostructures, specifically silver nanoparticles and graphene oxide, applied to medical devices used in knee surgery. These nanostructures were synthesized and evaluated for biocompatibility and antimicrobial efficacy using advanced laboratory methods such as scanning and transmission

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electron microscopy, X-ray diffraction, and biological tests. The studies included tests on cellular viability and evaluation of the inhibition capacity of bacterial biofilm formation, essential for preventing postoperative infections.

*Chapter I. Clinical study of autograft fixation in ACL reconstruction* offers a detailed analysis of anterolateral cruciate ligament (ALCL) injuries, a common condition in sports activities that can have severe consequences if not properly treated, including functional disability and the development of osteoarthritis. The treatment of these injuries has significantly evolved, with notable advances in surgical techniques and rehabilitation programs aimed at optimizing recovery and preventing further complications. Over the years, reconstruction techniques have varied from the initially used extra-articular methods, which had unsatisfactory results, to intra-articular techniques that proved more effective, such as the use of autografts like bone-patellar tendon-bone and hamstring tendon grafts.

The study was conducted as a retrospective analysis, evaluating a sample of 54 patients who underwent ALCL reconstruction surgery between 2018 and 2023. Among this population, 38 patients were male and 16 were female, aged between 20 and 50 years. Patients were distributed across different age categories, with the majority being young and active, aged 21 to 40 years—a group particularly prone to ligament injuries due to intense sports activities.

Regarding the surgical interventions, most patients (51 out of 54) were treated with hamstring tendon grafts, while only three patients received patellar tendon grafts. The choice of graft was influenced by factors such as reduced donor site morbidity and more comfortable postoperative recovery associated with the use of hamstring tendons. The grafts were folded into four parts to enhance the strength and stability of the reconstructed ligament.

Graft fixation was performed using resorbable interference screws, a significant advancement over the use of metal screws, which required removal in case of interference with magnetic resonance imaging (MRI). The size of the screws used ranged from 9 to 10 mm, and the tibial and femoral tunnels were appropriately sized to ensure optimal fixation. The choice of resorbable screws eliminated the need for subsequent surgeries to remove implants, thereby reducing the risk of postoperative complications and improving the overall patient experience.

A central aspect of the study was the analysis of postoperative complications, with hemarthrosis being the most common, affecting 38 out of 54 patients. Hemarthrosis, defined as the accumulation of blood in the joint after surgery, can compromise the functional recovery of

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the knee, prolonging rehabilitation and increasing the risk of complications such as arthrofibrosis. Although hemarthrosis was more frequent in patients with hamstring tendon grafts, only two cases of postoperative infections were documented, both being superficial infections successfully treated with antibiotic therapy. Graft degradation was a rare complication, observed in only one case through arthroscopy five months postoperatively, suggesting that continuous monitoring is essential in the early months after surgery to detect any signs of graft failure.

Postoperative joint mobility was evaluated using the Lysholm score, which indicated good functional recovery in most cases. Patients with hamstring tendon grafts had slightly higher Lysholm scores compared to those with patellar tendon grafts, suggesting a possible superiority of this technique regarding short- and medium-term knee function. Knee stability was assessed using the pivot-shift and Lachman tests, both indicating satisfactory joint stability in most cases in the long term.

Regarding the subjective sensation of knee instability reported by patients at 1, 2, and 5 years postoperatively, the results showed a slight increase in the sensation of instability over time, which may be attributed to gradual graft weakening or external factors such as joint overuse.

The statistical methods applied included frequency and distribution analysis, the Chi-square test for evaluating the relationship between categorical variables (e.g., graft type and incidence of hemarthrosis), and linear regression analysis for exploring the relationship between continuous variables such as screw size and postoperative mobility scores. The results of these analyses provided valuable insights for optimizing surgical and rehabilitation techniques.

The study's conclusions suggest that the use of hamstring tendon grafts offers good functional outcomes but requires special attention in managing the risk of hemarthrosis. Additionally, the size of the fixation screws plays a crucial role in the mechanical stability of the graft and the functional recovery of patients. Overall, the study contributes to a deep understanding of the factors influencing the success of ALCL reconstruction and provides a solid foundation for improving surgical and recovery strategies to optimize functional outcomes and minimize postoperative complications.

***Chapter II: Advanced nanostructures for enhancing biocompatibility and reducing microbial susceptibility of medical devices used in knee surgery*** provides an in-depth analysis of recent advances in nanotechnology applied in the context of knee surgery, with a focus on the use of advanced nanostructures to improve the performance of implantable medical devices.

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The section *Nanostructured coatings of silver/graphene oxide for modulating the microbial susceptibility of fixation devices used in knee surgery* highlights how nanomaterials, such as silver nanoparticles and graphene oxide, can be used to create nanostructured coatings on fixation devices used in knee ligament reconstruction. These coatings have the potential to reduce microbial susceptibility, prevent biofilm formation, and improve biocompatibility, thus providing effective protection against postoperative infections.

In recent decades, nanotechnology has opened new perspectives in modern medicine, especially in the development of nanomaterials applicable to medical devices. These nanostructures enable precise modulation of the interactions between implantable materials and the biological environment, contributing to infection prevention and optimizing the integration of fixation devices used in knee surgery. The chapter explores the use of nanomaterials such as silver nanoparticles (AgNPs) and graphene oxide (GO) in the development of nanostructured coatings for medical devices, with the primary goal of preventing microbial contamination and promoting biocompatibility.

Silver nanoparticles were synthesized through a chemical reduction protocol using silver nitrate and glucose as reducing agents. Graphene oxide nanostructures were obtained via a modified Hummers protocol, which involved the oxidation of graphite layers to produce graphene nanosheets. The nanostructured coatings were applied to medical fixation devices using the Matrix-Assisted Pulsed Laser Evaporation (MAPLE) technique, which allows precise control over the structure and composition of the coatings. These coatings were subsequently characterized using various physico-chemical methods, including X-ray diffraction (XRD), transmission electron microscopy (TEM), scanning electron microscopy (SEM), and thermal analysis.

Physico-chemical characterization of the silver nanoparticles and graphene oxide showed that the synthesized nanoparticles had uniform sizes and a cubic crystalline structure, with an average particle size of approximately 54 nm. The obtained graphene oxide was characterized by a folded structure and a uniform distribution of nanosheets. Coatings obtained via MAPLE at an optimal laser fluence of 400 mJ/cm<sup>2</sup> exhibited a porous and homogeneous surface with a thickness of approximately 2 μm.

Biocompatibility evaluation of the coatings revealed that Ag@C18-nGO coatings supported the adhesion and proliferation of MC3T3-E1 cells (murine preosteoblasts) without inducing significant cytotoxicity or oxidative stress. Tests demonstrated that the nanostructured

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coatings enhanced cell proliferative activity and reduced membrane damage compared to uncoated substrates, suggesting that these nanostructures could provide a more favorable environment for tissue healing and regeneration.

Microbiological evaluation of the nanoparticles and coatings showed that silver nanoparticles had significant antimicrobial efficacy, inhibiting the growth of resistant bacterial strains such as *Escherichia coli* and *Staphylococcus aureus*. Ag@C18-nGO coatings demonstrated a sustained capacity to inhibit bacterial biofilm development, reducing microbial populations by at least one order of magnitude after 48 hours of exposure.

The section demonstrates that the use of advanced nanostructures, such as Ag@C18-nGO coatings, can be an effective solution for preventing postoperative infections and improving the biocompatibility of fixation devices used in knee surgery. These nanomaterials not only provide antimicrobial protection but also support tissue regeneration, making them promising candidates for future biomedical applications. The efficiency of coatings processed via MAPLE suggests that this technology can be adapted for various clinical applications, contributing to the development of safer and more effective medical devices.

The section *Nanostructured graphene oxide-based coatings for managing periprosthetic infections* focuses on the use of advanced nanotechnologies to improve the performance of implantable medical devices used in knee surgery, particularly in the context of preventing periprosthetic infections and enhancing their biocompatibility.

Postoperative infections are a major challenge in orthopedics, affecting between 1% and 5% of orthopedic implants, leading to considerable morbidity and significant medical costs. Traditional materials such as metals used in fixation devices pose an increased risk of infection and other complications, including corrosion and chronic toxicity. Therefore, there is an urgent need to develop more effective solutions for infection prevention and biocompatibility improvement.

A key focus of this section is the fabrication of nanostructured coatings based on graphene oxide (nGO) and polylactide (PLA) intended for use on the surface of implantable medical devices. These coatings were developed using the Matrix-Assisted Pulsed Laser Evaporation (MAPLE) technique, which allows for precise and controlled application of nanostructures to medical devices. Study results have shown that PLA-nGO-Zin coatings (a broad-spectrum cephalosporin

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antibiotic) are extremely effective in preventing bacterial biofilm formation and have excellent biocompatibility.

Physico-chemical characterization of graphene oxide nanostructures revealed that nGO nanosheets were successfully synthesized using a modified Hummers methodology. These nanosheets exhibited a highly folded and textured structure, with oxygen-rich functional groups, confirmed by XRD and TEM analysis. Coatings created by MAPLE were continuous, compact, and had an irregular surface, giving them superior mechanical and biological properties.

Biocompatibility evaluation of PLA-nGO-Zin coatings demonstrated that they are highly hemocompatible, with a hemolytic index below 5%, classifying them as non-hemolytic. Additionally, it was observed that the coatings significantly reduced the expression of pro-inflammatory cytokines IL-1 $\beta$ , IL-6, and IL-8, suggesting significant anti-inflammatory potential. These results indicate that PLA-nGO-Zin coatings are not only well tolerated by human tissues but can also modulate inflammatory responses, which is essential for implantable medical devices.

The antimicrobial efficacy of the coatings was evaluated by testing their ability to inhibit long-term bacterial biofilm formation. Studies showed that PLA-nGO-Zin coatings are extremely effective against bacterial biofilm formed by *Staphylococcus aureus* and *Escherichia coli*, maintaining their antimicrobial efficacy for up to 72 hours. Notably, the coatings were particularly effective against the *Pseudomonas aeruginosa* strain in the early stages of biofilm formation, inhibiting its development by nearly four orders of magnitude.

The study concludes that these nanostructured coatings have significant potential for use in preventing periprosthetic infections due to their combination of antimicrobial and biocompatible properties. These PLA-nGO-Zin coatings not only improve the mechanical performance of implantable devices but also offer protection against infections, thus reducing the need for systemic antibiotics and contributing to the prevention of microbial resistance development. Overall, these nanostructured coatings represent a promising strategy for enhancing the safety and efficacy of medical devices used in knee surgery.

The section ***Graphene oxide-based coatings prepared by maple for enhanced orthopedic screws used in knee surgery*** aimed to develop and evaluate nanostructured coatings based on graphene oxide (GO) and polycaprolactone (PCL) to improve the performance of orthopedic screws used in knee surgery.

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Orthopedic screws are essential for securing implants to the bone, and the traditional materials from which they are made, such as titanium alloys and stainless steel, have significant disadvantages, including corrosion risk, excessive stiffness, inflammatory reactions, and, most critically, periprosthetic infections caused by bacterial colonization. These infections can lead to severe complications, including the need for revision surgeries.

To address these challenges, the study proposes using GO and PCL-based coatings applied via the MAPLE technique. These coatings have the potential to improve biocompatibility and provide antimicrobial protection, thereby reducing the risk of postoperative infections and promoting better implant integration into the bone.

Physico-chemical characterization of the coatings showed that the PCL/GO composite structure is well-defined, with a homogeneous distribution of components on the surface of the screws. SEM images and Raman analysis confirmed the presence of graphene oxide in the polymer matrix, and FT-IR tests revealed the retention of essential functional groups in the materials. These coatings not only improve surface adhesion and hardness but also provide significant protection against corrosion, extending the lifespan of implants.

Microbiological evaluation demonstrated the antimicrobial efficacy of the coatings, particularly against Gram-positive (*Staphylococcus aureus*) and Gram-negative (*Escherichia coli*) bacteria. The coatings significantly inhibited biofilm formation, a key factor in preventing periprosthetic infections. Although biofilm formation was not completely prevented, the coatings significantly delayed its development, maintaining high antimicrobial efficacy during the first 48 hours after implantation.

Biocompatibility of the coatings was evaluated through *in vitro* tests, which showed good compatibility with human osteoblasts. The PCL/GO/MRP coatings did not induce cellular toxicity, demonstrating comparable cell viability to uncoated control surfaces. These results suggest that the coatings are effective in preventing infections and support bone regeneration, making them suitable for use in orthopedic implants.

In conclusion, the study suggests that PCL and GO-based coatings can be successfully used to improve the performance of orthopedic screws. These coatings provide both antimicrobial protection and support for osseointegration, reducing the risk of postoperative complications and contributing to a faster and more effective recovery for patients. The *in vitro* results are promising

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and suggest that these coatings could be implemented in future clinical practice; however, further studies are needed to confirm their efficacy in real-world conditions.

### **General conclusions of the special part**

Anterior cruciate ligament (ACL) reconstruction is one of the most common and complex surgical interventions in orthopedics, playing a crucial role in restoring knee stability and functionality, especially in athletes and individuals with an active lifestyle. The long-term success of this procedure depends on several essential factors, including the appropriate selection of grafts, fixation techniques, effective bone integration, and the prevention of postoperative complications such as infections and hemarthrosis. In the doctoral thesis titled **"IMPROVING BONE FIXATION AND INTEGRATION OF GRAFTS AND IMPLANTS USED IN ANTEROLATERAL CRUCIATE LIGAMENT RECONSTRUCTION – A CLINICAL, IMAGING, AND EXPERIMENTAL STUDY,"** attention is focused on exploring and optimizing these critical variables, with particular emphasis on using advanced nanotechnologies to improve biocompatibility and postoperative functional outcomes.

This thesis presents an extensive clinical, imaging, and experimental study investigating the effectiveness of ligament autografts, the impact of nanostructures on improving bone fixation and implant integration, and the analysis of postoperative complications. The general conclusions of this study highlight the importance of continuing research in this field and the need to integrate innovative technologies to optimize surgical outcomes and minimize associated risks.

#### **(i) Efficacy of anterolateral cruciate ligament (ALCL) reconstruction**

ALCL reconstruction is a complex surgical intervention aimed at restoring knee joint stability following severe ligament injury. This procedure is crucial for preventing long-term disabilities, including the development of osteoarthritis, a degenerative condition that can significantly impact patients' quality of life. The study demonstrates that using ligament autografts in ALCL reconstruction offers satisfactory functional outcomes with a relatively low incidence of major complications. However, the incidence of hemarthrosis, defined as the accumulation of blood in the joint, remains a challenge, negatively influencing the functional recovery of the knee and increasing the risk of arthrofibrosis. These findings underscore the need to improve surgical techniques and postoperative management to minimize risks and optimize long-term outcomes.

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## **(ii) Graft selection and fixation techniques**

The selection of autografts is a determining factor for the success of ALCL reconstruction. The study highlights a preference for using hamstring tendon grafts due to reduced donor site morbidity and less postoperative discomfort. These grafts, folded into multiple bundles, provide enhanced mechanical strength and excellent knee stability. While patellar tendon grafts, although less commonly used, offer faster bone integration and a reduced risk of hemarthrosis, they present increased risks of complications such as patellar tendinitis or stress fractures. Regarding fixation techniques, the size and type of interference screws used directly influence graft stability and postoperative recovery. The study showed that larger screws offer superior mechanical stability but may increase the risk of long-term complications, such as bone tunnel widening or mechanical discomfort. The material of the screws is also crucial, with bioabsorbable screws offering advantages in eliminating the need for subsequent removal surgery but posing risks of bone tunnel widening. These findings emphasize the need for a personalized approach in selecting grafts and fixation techniques based on the patient's needs and specific intervention goals.

## **(iii) Role of nanostructures in infection prevention and biocompatibility improvement**

Another significant aspect of this study is investigating the role of nanostructures in improving biocompatibility and preventing infections associated with implants used in ALCL reconstruction. Silver nanoparticles and graphene oxide have shown remarkable potential in preventing postoperative infections due to their strong antimicrobial properties. Graphene oxide, in particular, not only protects against infections but also contributes to creating a favorable environment for graft integration, promoting tissue healing and reducing inflammation. These innovations offer promising solutions for optimizing surgical interventions and minimizing associated risks, opening new perspectives in ligament reconstruction.

## **(iv) Importance of the study in correlating nanotechnologies with ALCL**

The study represents an important step towards integrating nanotechnologies into orthopedic surgical practice, with direct applications in anterolateral cruciate ligament reconstruction. Integrating clinical and experimental data with innovations in nanomaterials opens new possibilities for significantly improving postoperative outcomes. The importance of this study lies in demonstrating that advanced nanostructures can be used not only to prevent complications such as infections but also to improve bone integration and the mechanical stability of grafts and implants.

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In conclusion, the integration of nanotechnologies in ALCL reconstruction represents a promising evolution in modern medicine, with the potential to transform current treatment approaches and significantly improve long-term surgical outcomes. This study provides a solid foundation for developing innovative treatment strategies to optimize the fixation and bone integration of grafts and implants, ensuring a complete and durable recovery for patients.

### **Research Perspectives**

These studies open new horizons in the development of advanced medical materials, offering promising perspectives for future research and clinical applications. The investigated nanomaterials, due to their antimicrobial and biocompatible properties, can be integrated not only in orthopedic surgery but also in other medical fields such as dental implantology, cardiovascular devices, and catheters. Expanding the applicability of these nanomaterials has the potential to significantly improve the safety and effectiveness of medical devices used across various branches of medicine.

In addition to antimicrobial and anti-inflammatory properties, future research could explore the integration of additional functionalities into coatings, such as osteoconductive and osteoinductive properties to support bone regeneration, or the incorporation of therapeutic agents for the controlled release of medications at the implantation site. This could lead to a significant improvement in the success rate of surgical interventions and patient recovery. For instance, nanomaterials could be used to create coatings that release anti-inflammatory drugs directly at the implantation site, thereby reducing the risk of infection and promoting faster and more effective healing.

It is essential that these materials undergo extensive clinical studies to evaluate their long-term safety and efficacy under real-world conditions. Monitoring patients using these implantable devices will provide valuable data on the performance of materials in the complex biological environment of the human body. These studies could include assessments of the immune response to nanomaterials, analyses of potential side effects, and measurements of the durability and resistance of materials over time.

Future research could investigate the optimization of synthesis and functionalization processes of nanomaterials to improve the uniformity and stability of coatings. The use of other advanced processing methods, such as 3D printing technologies, could be explored for the

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fabrication of these nanostructures. 3D printing technology allows for the creation of complex and customized structures that can be perfectly tailored to the specific needs of each patient, thereby reducing the risk of implant rejection and improving its integration into the body.

Combining silver nanoparticles and graphene oxide with other nanomaterials, such as nanoceria or carbon nanotubes, could create beneficial synergies and further enhance the properties of coatings. For example, nanoceria, due to its antioxidant properties, could protect tissues surrounding implants from oxidative stress, while carbon nanotubes would confer increased mechanical strength to the materials. Integrating these nanomaterials with advanced imaging and diagnostic technologies could allow real-time monitoring of biological responses and antimicrobial efficacy. This could include the use of nanoscale sensors to detect infections at early stages or to monitor the controlled release of drugs.

The development of guidelines and regulatory standards for the use of nanomaterials in medical devices represents an important direction for research. Ensuring compliance with international regulations will facilitate the approval and widespread adoption of these innovative technologies. It is necessary for regulatory authorities to collaborate with researchers and the industry to establish clear and rigorous criteria for evaluating the safety and efficacy of nanomaterials. Moreover, international standards should cover aspects such as production, handling, and disposal of nanomaterials to ensure environmental protection and public health.

Another essential aspect of developing and implementing nanomaterials in medicine is educating and training healthcare professionals. Doctors, surgeons, and other specialists must be well-informed about the properties and uses of nanomaterials, as well as the potential risks and benefits associated with them. Continuing education programs and specialized courses can play a crucial role in ensuring the safe and effective use of nanomaterials in medical practice.