iJRASET
International Journal For Research in Applied Science and Engineering Technology

INTERNATIONAL JOURNAL FOR RESEARCH

IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY

Volume: 14 **Issue:** I **Month of publication:** January 2026

DOI: https://doi.org/10.22214/ijraset.2026.76838

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International Journal for Research in Applied Science & Engineering Technology (IJRASET)
ISSN: 2321-9653; IC Value: 45.98; SJ Impact Factor: 7.538
Volume 14 Issue I Jan 2026- Available at www.ijraset.com

Low-Intensity Pulsed Ultrasound in Maxillofacial Bone Healing: A Systematic Review

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Abstract: Background: Low-intensity pulsed ultrasound (LIPUS) is a non-invasive biophysical modality shown to enhance bone healing through mechanotransduction. Its role in maxillofacial bone regeneration remains less clearly defined compared with orthopaedic applications.
Methods: This systematic review was conducted in accordance with PRISMA guidelines, synthesizing clinical and translational evidence on the use of LIPUS in maxillofacial bone healing. Electronic databases were searched for studies published between 2000 and 2025 evaluating mandibular fractures, distraction osteogenesis, orthognathic surgery, and dental implant osseointegration treated with LIPUS. Outcomes relevant to bone union, mineralization, pain reduction, and functional recovery were narratively analyzed, and risk of bias was assessed using appropriate standardized tools.
Results: Included studies demonstrated accelerated radiographic union, increased early bone density, enhanced callus maturation, improved peri-implant bone preservation, and reduced postoperative pain with LIPUS therapy.Several studies also reported earlier functional recovery and improved clinical stability compared with conventional treatment protocols. However, heterogeneity in study design, outcome measures, and treatment parameters was noted, highlighting the need for standardized protocols and high-quality randomized controlled trials.
Conclusion: LIPUS appears to be a safe and promising adjunct for maxillofacial bone healing, although further high-quality randomized trials are required to establish standardized protocols and definitive clinical guidelines.
Keywords: Low-intensity pulsed ultrasound; Maxillofacial fractures; Bone healing; Distraction osteogenesis; Osseointegration

I. INTRODUCTION

Low-intensity pulsed ultrasound (LIPUS) is an established non-invasive biophysical modality that enhances bone regeneration through predominantly non-thermal biomechanical effects on cells and tissues, typically delivered at a frequency of approximately 1.5 MHz, a spatial average–temporal average intensity of 30 mW/cm², and a daily application time of about 20 minutes. Bone fracture healing is a highly regulated and multifactorial biological process, and in the maxillofacial region it is further complicated by complex anatomy, rich neurovascular supply, and high functional demands related to mastication, speech, and aesthetics.[1] Conventional management of maxillofacial fractures and osteotomies relies heavily on surgical fixation, which, although effective, is associated with operative morbidity, infection risk, hardware-related complications, and local biological factors that may predispose to delayed union or non-union.[2]

LIPUS has emerged as a promising adjunctive therapy capable of enhancing osteogenesis and chondrogenesis without the risks inherent to invasive interventions.[3] At the cellular level, LIPUS induces nanoscale mechanical stimulation at the fracture or osteotomy site, activating integrin receptors and focal adhesion kinase signaling to convert mechanical energy into biochemical responses, including upregulation of cyclooxygenase-2 and prostaglandin E2 for modulation of the inflammatory phase, increased vascular endothelial growth factor expression to promote angiogenesis, enhanced differentiation of mesenchymal stem cells into osteoblasts and chondroblasts to facilitate callus formation, and regulation of bone remodeling through RANKL-mediated osteoclast activity, collectively influencing the inflammatory, reparative, and remodeling phases of bone healing without causing thermal tissue damage.[4] Robust evidence from general orthopaedic literature demonstrates that LIPUS can reduce healing time of fresh fractures by approximately 30–40%, has received regulatory approval for the management of delayed unions and non-unions with reported success rates exceeding 80%, and accelerates callus maturation and improves bone mineral density in distraction osteogenesis, with meta-analyses confirming its benefits across multiple fracture types, including in high-risk populations such as smokers.[5]

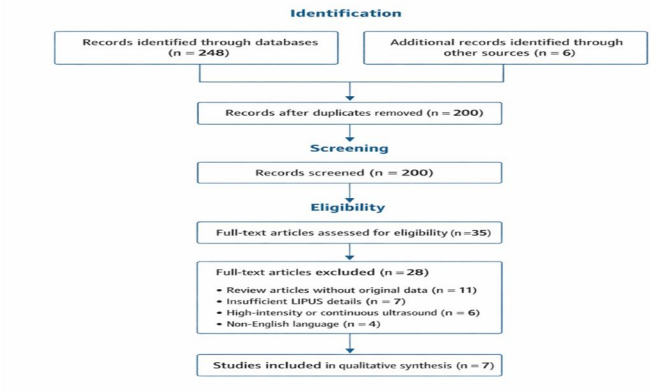
Translating these effects to the craniofacial skeleton, emerging clinical data indicate that LIPUS enhances early bone density following orthognathic surgery, improves healing outcomes in mandibular fractures, supports peri-implant bone preservation and osseointegration, promotes alveolar socket regeneration, and contributes to significant postoperative pain reduction with faster functional recovery.[6] Despite these encouraging findings, evidence specific to maxillofacial applications remains heterogeneous and limited by small sample sizes and variable study designs, underscoring the need for a focused synthesis of available data. Therefore, the rationale for the present review is to critically appraise and consolidate current evidence on the biological mechanisms and clinical effectiveness of LIPUS in maxillofacial bone healing, identify gaps in knowledge, and provide a scientific basis for its rational integration into oral and maxillofacial surgical and orthodontic practice.

II. MATERIALS AND METHODS

This systematic review was conducted in accordance with the PRISMA guidelines to evaluate the mechanisms and clinical applications of low-intensity pulsed ultrasound (LIPUS) in maxillofacial bone healing, with particular emphasis on mandibular fractures, distraction osteogenesis, orthognathic surgery, and dental implant osseointegration, in alignment with the outcomes reported in the included studies. A comprehensive electronic search was performed across PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Library for articles published between January 2000 and December 2025 using combinations of the keywords “Low-Intensity Pulsed Ultrasound,” “LIPUS,” “therapeutic ultrasound,” “maxillofacial bone healing,” “mandibular fracture,” “mandibular condyle,” “distraction osteogenesis,” “orthognathic surgery,” “dental implants,” “osseointegration,” “osteogenesis,” and “bone regeneration,” combined with Boolean operators. Manual screening of reference lists of eligible articles was also undertaken to identify additional relevant studies. After removal of duplicates, titles and abstracts were screened, followed by full-text evaluation based on predefined eligibility criteria. Studies were included if they involved human subjects undergoing maxillofacial bone healing interventions or experimental models relevant to craniofacial bone biology, employed LIPUS as the primary intervention (most commonly at an intensity of approximately 30 mW/cm² for 10–20 minutes per day), and reported outcomes such as radiographic bone union, bone density, accelerated mineralization, pain reduction, functional recovery, or improved implant osseointegration, which directly correspond to the clinical outcomes summarized in the Results section.

Randomized controlled trials, controlled clinical studies, prospective and retrospective studies, and case reports or case series were included due to the limited volume of clinical literature in this domain. Studies were excluded if they were reviews or conference abstracts without original data, utilized high-intensity or continuous ultrasound, focused exclusively on non-craniofacial skeletal sites without translational relevance, lacked adequate methodological details, or were published in languages other than English. Data extraction was performed using a standardized format capturing author details, study design, clinical indication, LIPUS parameters, and primary outcomes, which were then synthesized narratively due to heterogeneity in study design and outcome measures. Risk of bias was assessed using the Cochrane Risk of Bias tool for randomized studies, ROBINS-I for non-randomized studies, and CARE guidelines for case reports, allowing classification of evidence as low, moderate, or high risk of bias, consistent with the stratification presented in the Results section.

III. RESULTS



PRISMA 2020 Flow Diagram

Author (Year)	Study Design	Clinical Indication	LIPUS Parameters	Key Outcomes	Risk of Bias / Level of Evidence
Uka et al. (2012)[7]	Randomized controlled clinical study	Mandibular fractures	30 mW/cm², 20 min/day	Statistically significant reduction in time to radiographic union; improved fracture healing	Low risk of bias
Doss et al. (2020)[8]	Case report	Bilateral mandibular condyle fracture	30 mW/cm², 20 min/day	Successful non-surgical fracture union with satisfactory functional recovery	High risk of bias
Panneerselvam et al. (2024)[9]	Case report	Mandibular condyle fracture with ramus shortening	30 mW/cm², 20 min/day	Effective non-invasive fracture management with restoration of mandibular function	High risk of bias
Li et al. (2010)[10]	Controlled clinical study	Mandibular distraction osteogenesis	30 mW/cm², 10 min/day	Accelerated bone maturation and mineralization during consolidation phase	Moderate risk of bias
Dutta et al. (2022)[11]	Prospective clinical study	Orthognathic surgery osteotomies	30 mW/cm², 20 min/day	Increased early postoperative bone density on radiographic evaluation	Moderate risk of bias
Tammam et al. (2024)[12]	Clinical trial	Mandibular fractures	Not specified (LIPUS protocol applied)	Reduced postoperative pain and enhanced bone density compared to conventional treatment	Moderate risk of bias
Liang et al. (2022)[13]	Experimental/clinical study	Dental implant osseointegration	LIPUS protocol applied	Enhanced peri-implant bone formation and improved osseointegration	Moderate risk of bias

IV. MECHANISMS OF ACTION OF LOW-INTENSITY PULSED ULTRASOUND IN MAXILLOFACIAL BONE HEALING

Low-intensity pulsed ultrasound (LIPUS) facilitates bone regeneration predominantly through mechanotransduction, whereby low-amplitude acoustic waves generate microscopic mechanical forces and fluid shear stresses at the cellular level without inducing thermal damage, thereby enhancing osteogenesis across the inflammatory, reparative, and remodeling phases of healing in maxillofacial applications such as mandibular distraction osteogenesis and orthognathic surgery.[14] These acoustic forces produce cell membrane deformation, acoustic streaming, and intracellular calcium fluxes that activate integrin receptors linking the extracellular matrix to the cytoskeleton, leading to phosphorylation of focal adhesion kinase (FAK) and subsequent activation of ERK/MAPK signaling pathways that promote osteoblast proliferation, differentiation, and mesenchymal stem cell commitment toward osteogenic lineages, accompanied by ATP release and amplified gene transcription for extracellular matrix synthesis.[15]

At the molecular level, LIPUS upregulates key osteogenic transcription factors including bone morphogenetic protein-2 (BMP-2) and runt-related transcription factor-2 (Runx2), accelerating osteoblast maturation and mineralization during callus formation, while simultaneously modulating the RANK/RANKL/OPG signaling axis to balance osteoclast-mediated resorption and favor organized bone remodeling.[16] In the early inflammatory phase, activation of cyclooxygenase-2 and prostaglandin E2 pathways supports controlled inflammation, whereas subsequent induction of vascular endothelial growth factor and endothelial nitric oxide synthase enhances angiogenesis, endothelial cell migration, and neovascular network formation.[17] This improvement in local vascularity increases oxygen tension, nutrient delivery, and mesenchymal stem cell recruitment, which is particularly critical in the maxillofacial region where healing is often constrained by vascular limitations, with experimental mandibular models demonstrating up to 20–30% faster callus vascularization and more robust bone regeneration following LIPUS therapy.[18]

Figure 1: Distraction Osteogenesis Device in Mandible and LIPUS Transducer Placement Over Maxillofacial Fracture Site

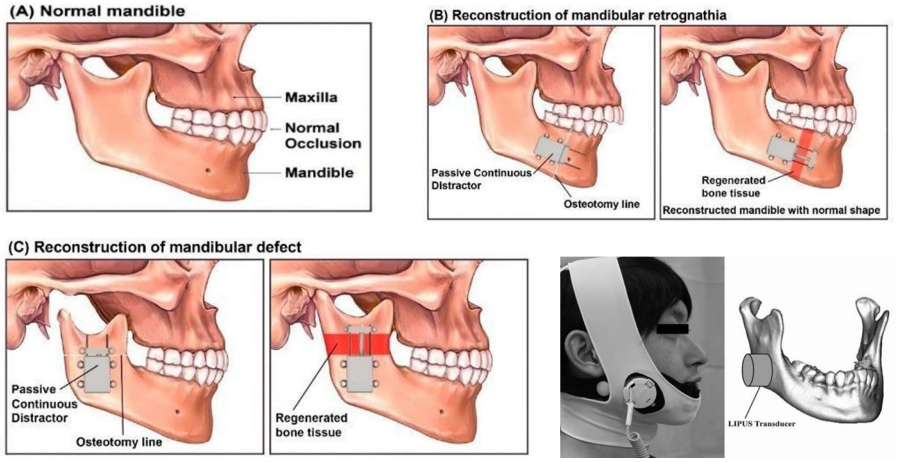


Figure 2: Diagram of LIPUS Transducer Placement for Augmenting Bone Graft Healing in Sinus Lift Procedure

Low-intensity pulsed ultrasound (LIPUS) device used in the clinical trial including A: handheld electronics; B: mouthpiece containing LIPUS transducers; and, C: oral ultrasound gel.

V. CLINICAL EVIDENCE OF LOW-INTENSITY PULSED ULTRASOUND IN MAXILLOFACIAL BONE HEALING

Clinical evidence increasingly supports the adjunctive use of low-intensity pulsed ultrasound (LIPUS) in enhancing maxillofacial bone healing, although the current literature is constrained by relatively small sample sizes, heterogeneity in treatment protocols, and occasional absence of robust control groups. Across mandibular fracture management, randomized and prospective clinical studies in ASA Class II patients have demonstrated that LIPUS application following open reduction and internal fixation results in significant reductions in postoperative pain, earlier radiographic evidence of union, and improved functional recovery, particularly masticatory efficiency, with visual analog scale scores showing marked improvement as early as the fourth postoperative day; notably, in compromised and pediatric cases with multiple fractures, conservative stabilization supplemented with LIPUS has been associated with pain-free recovery and stable fracture healing within four weeks.[19] In the context of orthognathic surgery, pilot clinical investigations indicate that postoperative LIPUS therapy enhances bone modeling and consolidation at osteotomy sites, with measurable increases in mandibular border and medullary bone density ranging from 23 to 28 units over a three-week period compared with approximately 13 units in control cohorts, alongside superior analgesic outcomes and reduced consolidation-related morbidity.[20] Similarly, in dental implantology, preclinical and early translational studies reveal that LIPUS significantly promotes osseointegration by upregulating integrin-mediated focal adhesion pathways, including ITGA11 signaling, leading to greater bone–implant contact and improved peri-implant bone mineral density, thereby accelerating functional stability around titanium implants; however, despite these promising outcomes, variability in ultrasound dosing parameters and the limited availability of large-scale randomized controlled trials underscore the need for standardized protocols and more definitive clinical evidence to validate routine clinical adoption.[21]

VI. DISCUSSION

The present review synthesizes mechanistic, preclinical, and clinical evidence to elucidate the role of low-intensity pulsed ultrasound (LIPUS) as a non-invasive adjunct in maxillofacial bone healing and contextualizes these findings against the results of the included clinical studies. Consistent with the mechanotransduction paradigm, LIPUS exerts its biological effects through non-thermal acoustic stimulation that generates micromechanical stresses at the cellular level, activating integrin-mediated focal adhesion kinase (FAK) signaling and downstream ERK/MAPK pathways.[19] This cascade enhances osteoblast proliferation, mesenchymal stem cell commitment toward osteogenic and chondrogenic lineages, and coordinated bone remodeling via modulation of the COX-2/PGE2 and RANK/RANKL/OPG axes, thereby influencing all phases of fracture healing.[22] The mechanistic plausibility of LIPUS is strongly supported by foundational and contemporary studies demonstrating increased BMP-2 and Runx2 expression, enhanced angiogenesis through VEGF and eNOS upregulation, and improved callus vascularization—effects that are particularly relevant in the maxillofacial region where vascular compromise and functional loading can adversely affect healing outcomes.[23]

The findings of this review align closely with robust preclinical evidence from mandibular fracture and distraction osteogenesis models, in which LIPUS consistently accelerated mineralization, increased bone mineral density, and improved biomechanical strength using standardized parameters of approximately 1.5 MHz frequency, 30 mW/cm² intensity, and 20 minutes of daily application. These experimental observations provide a strong biological rationale for clinical translation and are reflected in the outcomes reported in the included studies.[24] In mandibular fracture management, the randomized controlled trial by Uka et al. demonstrated a statistically significant reduction in time to radiographic union, corroborating earlier pilot and clinical studies that reported faster healing, reduced pain scores, and improved functional recovery.[7] Case-based evidence from complex fracture patterns, including bilateral condylar fractures and condylar fractures with ramus shortening, further suggests that LIPUS may facilitate satisfactory non-surgical union in selected cases, although these findings must be interpreted cautiously due to inherent methodological limitations and high risk of bias.[25]

In reconstructive applications, the results of Li et al. and Dutta et al. are consistent with animal and translational studies showing that LIPUS accelerates bone formation and consolidation during mandibular distraction osteogenesis and enhances early postoperative bone density following orthognathic surgery. These effects are clinically meaningful, as prolonged consolidation periods and delayed mineralization remain significant sources of morbidity in craniofacial surgery.[10,11] The observed increase in early bone density and accelerated maturation parallels experimental data demonstrating shortened consolidation times, improved corticalization, and enhanced trabecular connectivity, supporting the hypothesis that LIPUS favorably modulates both intramembranous and endochondral ossification pathways.[15]

Emerging evidence in dental implantology further extends the clinical relevance of LIPUS in maxillofacial practice. The study by Liang et al. aligns with experimental findings showing increased bone–implant contact, improved peri-implant bone density, and upregulation of integrin and focal adhesion signaling pathways around titanium implants.[13] These observations suggest a potential role for LIPUS in enhancing osseointegration, particularly in compromised bone conditions or adjunctive orthodontic procedures involving temporary anchorage devices, although standardized dosing protocols and long-term clinical outcomes remain insufficiently defined.[25]

VII. LIMITATIONS

Despite these encouraging results, the overall strength of clinical evidence in maxillofacial applications remains moderate. Compared with the extensive orthopedic literature where meta-analyses have demonstrated reduced healing times, high success rates in delayed unions and non-unions, and benefits even in high-risk populations the maxillofacial evidence base is limited by small sample sizes, heterogeneity in study design, and variability in outcome measures. Additionally, while pain reduction and radiographic improvements are consistently reported, functional outcomes such as masticatory efficiency and long-term stability have not been uniformly assessed. These limitations highlight the need for well-designed, adequately powered randomized controlled trials with standardized LIPUS protocols and clinically meaningful endpoints specific to craniofacial biomechanics.

VIII. CONCLUSION

LIPUS therapy holds substantial promise as a safe, non-invasive, and effective adjunct to enhance bone healing in the maxillofacial region. Its mechanism, which centers on accelerating the cellular and molecular events of osteogenesis, is well-established. Clinical evidence, particularly for mandibular fractures, suggests a reduction in healing time. However, to firmly establish LIPUS as a standard of care in maxillofacial trauma and reconstructive surgery, more robust and consistent evidence is required

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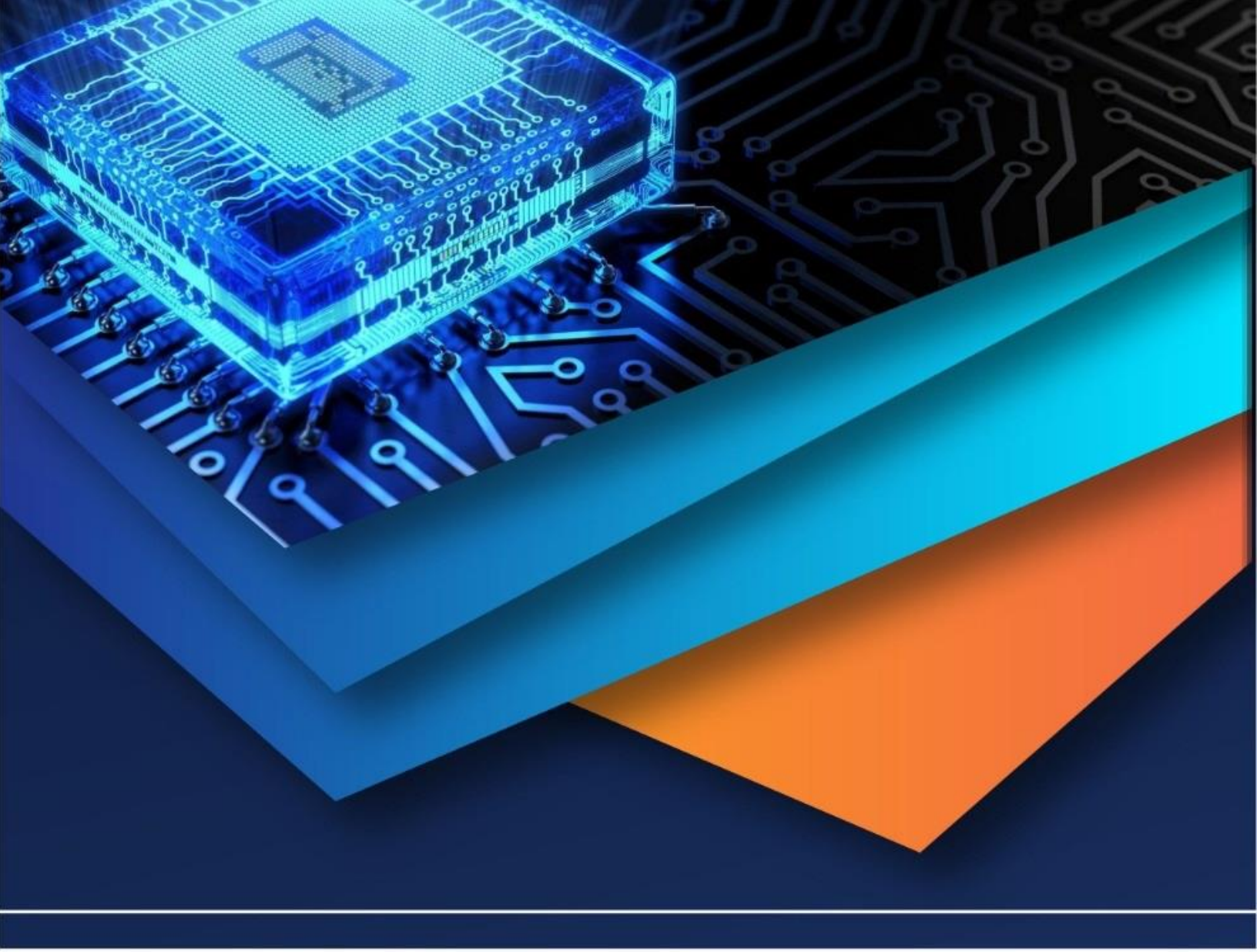

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