

# The Biological Impact of Residual Aluminum Particles on Sand-Blasted Dental Implant Surfaces: A Systematic Review of Animal Studies

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**Abstract:** (1) Background: The use of alumina particles for surface treatment of dental implants is a common practice aimed at enhancing osseointegration. However, the biological effects of residual alumina particles on implant surfaces remain a subject of debate. This systematic review evaluates the impact of residual alumina particles on the osseointegration, biocompatibility, and bacterial adhesion of dental implants based on available in vivo experimental animal studies. (2) Methods: A comprehensive literature search was conducted across PubMed, Web of Science, and Scopus to identify relevant studies. The inclusion criteria focused on experimental animal studies that assessed the biological effects of alumina-blasted dental implants. Data extraction was carried out, and quality assessments were performed using the SYRCL risk-of-bias tool. (3) Results: Ten studies met the inclusion criteria, involving various animal models, such as rabbits, pigs, dogs, and sheep. The findings demonstrated that residual alumina particles did not negatively impact osseointegration. Some studies reported accelerated bone growth and improved osseointegration with residual alumina. Additionally, residual alumina showed potential bactericidal properties, reducing bacterial adhesion. (4) Conclusions: The available evidence from animal studies suggests that residual alumina particles do not adversely affect the osseointegration and biocompatibility of dental implants. These particles may even enhance bone growth and reduce bacterial adhesion. However, due to the scarcity of human studies and the impracticality of histological assessments in humans, further research, including long-term clinical trials, is necessary to confirm these findings.

**Keywords:** aluminum oxide; biological effects; dental implants; osseointegration; surface modification



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## 1. Introduction

Aluminum (Al) is the most abundant metal in the Earth's crust, naturally occurring as Al<sup>3+</sup> in various compounds, such as silicates, oxides, and hydroxides. Despite its ubiquity, Al has no known physiological role in human metabolism and can be toxic at high levels. The potential negative effects of Al on human health have been studied extensively. Notably, Igbokwe et al. [1] and Renke et al. [2] provided comprehensive reviews on the systemic toxicity of Al, highlighting its impact through various exposure routes, including environmental contamination and occupational hazards.

Al contamination arises from both natural processes, such as the weathering of rocks, and anthropogenic activities, including mining, recycling, and manufacturing. High exposure levels are particularly concerning in industrial areas where Al is processed, leading to

potential health risks for both humans and animals. Despite its widespread presence, Al ions can accumulate in the body, leading to conditions such as encephalopathy, especially in individuals with compromised renal function.

Al toxicosis has been linked to numerous health issues, including reproductive toxicity, pulmonary lesions, bone abnormalities, immunotoxicity, and neurological disorders. Chronic exposure can lead to significant tissue accumulation, exacerbating these conditions. The primary sources of Al exposure include air, drinking water, food, pharmaceuticals, and agrochemicals [1]. However, the potential impact of Al particles from biomedical devices, particularly dental implants, remains underexplored.

In the context of implantable devices, the concentration of aluminum particles and the rate of metabolism are critical factors influencing cytotoxicity. A critical threshold of aluminum concentration in tissues has not been defined, though it has been estimated that the level in healthy human bone tissue ranges from 5 to 10 mg/kg [1]. Higher concentrations of aluminum particles can lead to increased oxidative stress and inflammation around the implant site, potentially compromising the success of the implant. The metabolic rate of surrounding tissues, particularly in areas with high bone turnover, may exacerbate these effects, leading to greater cytotoxicity and potential implant failure. Safe concentrations of aluminum particles must be carefully controlled in dental materials to minimize adverse effects, ensuring biocompatibility and long-term stability of the implant.

Dental implants, first introduced by P-I Brånemark in the late 1960s, initially featured machined surfaces [3]. The milling, turning, or polishing processes used to manufacture these surfaces frequently led to lengthy healing periods and significant failure rates, especially in regions with low bone density, such as the posterior maxilla. Subsequent research indicated that moderate surface roughness could enhance osseointegration [4–7], leading to the development of techniques such as sandblasting and acid-etching (SAE).

SAE involves blasting the implant surface with ceramic particles (e.g.,  $\text{Al}_2\text{O}_3$ ) to create micro-craters, followed by acid treatment to remove residual particles and further modify the surface [8]. It is difficult to completely remove blasting particles despite these efforts, which raises questions regarding the possibility of residual Al remaining on the implant surface.

It has been widely demonstrated that with the use of a blasting material, such as  $\text{Al}_2\text{O}_3$ , a potential risk of contamination by remnants of blasting particles with dissolution of aluminum ions into the host tissue cannot be excluded [9,10]. It has also been reported that Al ions may inhibit normal differentiation of bone marrow stromal cells and normal bone deposition and mineralization [11,12], and aluminum has been shown to induce net calcium efflux from cultured bone [13]. Moreover, aluminum may compete with calcium during the healing of the implant bed. Aluminum has also been shown to accumulate at the mineralization front and in the osteoid matrix itself [14].

There is little evidence to support the hypothesis that the presence of Al particles on the implant surface causes poor osseointegration or other harmful consequences *in vivo*, even in the context of interactions with biological structures. Some experimental studies suggest no significant differences in bone response between pure titanium and Al-containing alloys [15]; yet, the presence of residual Al still raises concerns due to its possible contribution to tissue breakdown and inflammatory responses [16].

The aim of this systematic review was to evaluate and synthesize the available *in vivo* evidence on the biological effects of residual Al particles on dental implant surfaces compared to implants without residual Al particles. This review seeks to determine how the presence of residual Al particles influences osseointegration, cellular response, inflammatory response, and overall implant success rates. The null hypothesis was that the presence of residual Al particles on the implant surface has no detrimental effects on the biological response of peri-implant tissues and on systemic health following implant installation.

## 2. Materials and Methods

This systematic review was designed to investigate the biological effects of residual Al particles on dental implant surfaces. The review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [17] to ensure a comprehensive and unbiased evaluation of the existing literature. This systematic review was registered in PROSPERO (No. CRD42024562169).

### 2.1. Search Strategy

A comprehensive search was conducted across multiple databases, including PubMed, Scopus, and Web of Science. The search strategy employed a combination of MeSH terms and free-text keywords to identify relevant studies. The search strings used for all databases are shown in Table 1.

**Table 1.** Search strings and retrieved number of articles for each database searched.

Database	Search String	Records
PubMed	("Dental Implants" [MeSH Terms] OR "Dental Implants" [Title/Abstract] OR "Titanium Implants" [Title/Abstract]) AND ("Aluminum Particles" [Title/Abstract] OR "Alumina Oxide" [Title/Abstract]) AND ("Surface Properties" [MeSH Terms] OR "Surface Contamination" [Title/Abstract] OR "Surface Modification" [Title/Abstract]) AND ("Osseointegration" [MeSH Terms] OR Biocompatibility OR "Biological Effects" [Title/Abstract])	88
Scopus	(TITLE-ABS-KEY ("Dental Implants") OR TITLE-ABS-KEY ("Titanium Implants")) AND (TITLE-ABS-KEY ("Aluminum Particles") OR TITLE-ABS-KEY ("Alumina Oxide")) AND (TITLE-ABS-KEY ("Surface Properties") OR TITLE-ABS-KEY ("Surface Contamination") OR TITLE-ABS-KEY ("Surface Modification")) AND (TITLE-ABS-KEY ("Osseointegration") OR TITLE-ABS-KEY ("Biocompatibility") OR TITLE-ABS-KEY ("Biological Effects"))	1320
Web of Science	(TS = ("Dental Implants" OR "Titanium Implants")) AND (TS = ("Aluminum" OR "Aluminum Particles" OR "Alumina Oxide")) AND (TS = ("Surface Properties" OR "Surface Contamination" OR "Surface Modification")) AND (TS = ("Osseointegration" OR "Biocompatibility" OR "Biological Effects" OR ""))	114

The search was restricted to articles published in English, from inception to the date of the search (20 June 2024).

### 2.2. Inclusion and Exclusion Criteria

Inclusion Criteria:

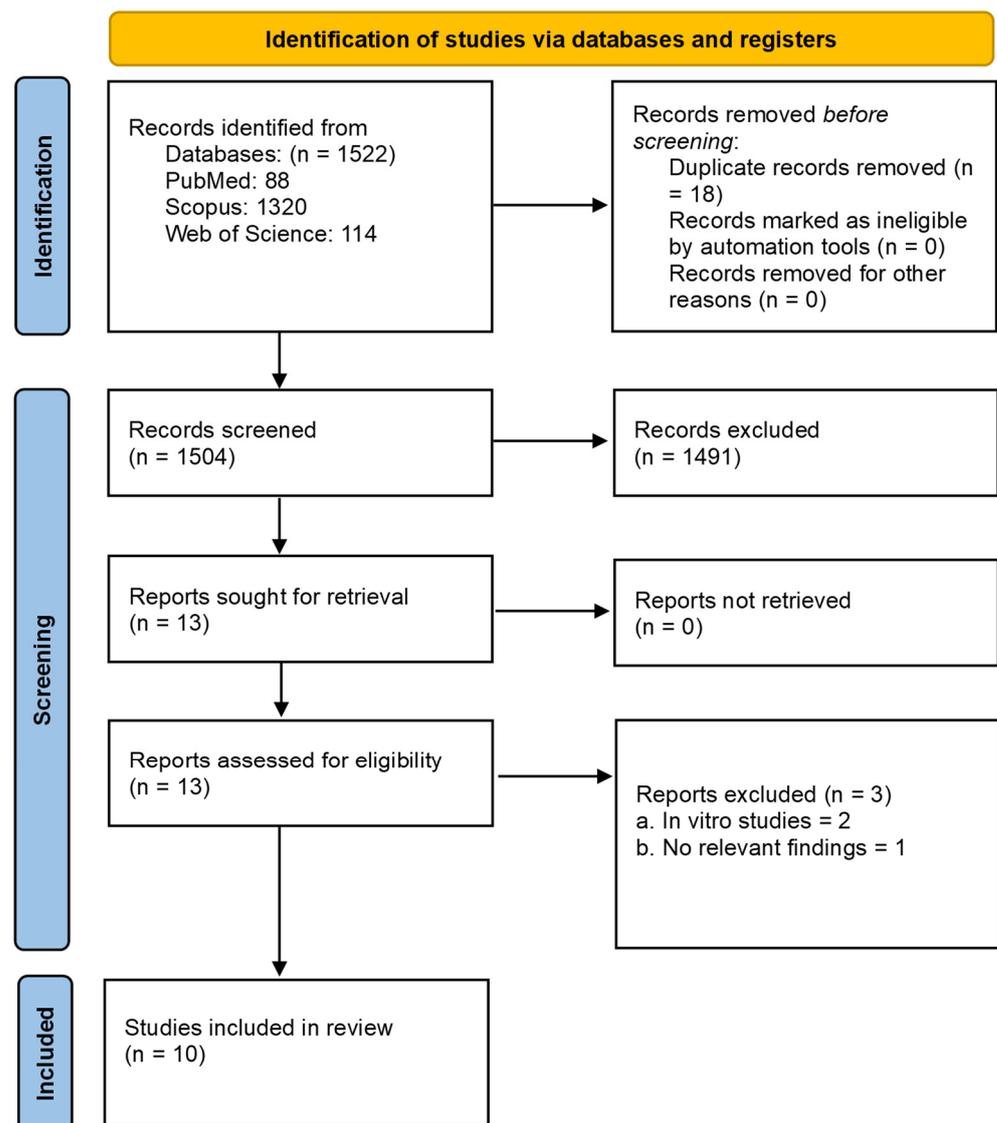
- In vivo experimental animal studies evaluating the biological effects of residual Al particles on Al<sub>2</sub>O<sub>3</sub>-blasted dental implant surfaces.
- Studies published in peer-reviewed journals.
- Articles available in English.

Exclusion Criteria:

- Studies not involving dental implants.
- Reviews, editorials, and opinion pieces without original data.
- Studies not focusing on Al particles or residual Al contamination.

### 2.3. Study Selection

Two independent reviewers (M.D.F. and S.P.) screened the titles and abstracts of the retrieved articles for eligibility. Full-text articles of potentially relevant studies were then assessed based on the inclusion and exclusion criteria. Disagreements between reviewers were resolved through discussion or consultation with a third reviewer (M.T.). The study selection process is provided in Figure 1.



**Figure 1.** Study selection flow chart.

#### 2.4. Data Extraction

Data were extracted using a standardized form. The extracted data included: study author(s); year of publication; comparison groups; number of animals per group; follow-up duration; type of dental implant; location of implant placement; surface modification technique used for sandblasting; technique for detection of the presence and quantification of residual Al particles and other surface contaminants; biological effects observed (e.g., osseointegration, cell adhesion, and inflammatory response), and any additional relevant findings.

#### 2.5. Quality Assessment

The quality of the included studies was assessed using the SYRCLE (Systematic Review Centre for Laboratory animal Experimentation) risk-of-bias tool. This tool is specifically designed for assessing bias in animal studies and covers ten domains: sequence generation (selection bias), baseline characteristics (selection bias), allocation concealment (selection bias), random housing (performance bias), blinding (performance bias), random outcome assessment (detection bias), blinding (detection bias), incomplete outcome data (attrition bias), selective outcome reporting (reporting bias), and any other sources of bias.

Each domain was rated as having a low, unclear, or high risk of bias based on the information provided in the study reports. A summary chart was created to visualize the risk of bias across all included studies, facilitating a quick assessment of the overall quality and potential biases present in the evidence.

### 2.6. Data Synthesis

Data from included studies were synthesized qualitatively. Due to the heterogeneity in study designs, methodologies, and outcome measures, a meta-analysis was not feasible. Instead, a narrative synthesis was conducted, summarizing the key findings and identifying trends and gaps in the literature.

## 3. Results

This systematic review evaluated the biological effects of residual alumina ( $\text{Al}_2\text{O}_3$ ) particles on dental implant surfaces. The comprehensive search of all digital databases yielded 1522 records. After removing duplicates, 1504 records were screened based on the title and abstract. Full-text assessment was performed for 12 records, out of which 3 records were excluded based on the predefined inclusion and exclusion criteria.

A total of ten animal experimental studies [15,18–26] were included, encompassing a range of experimental designs and methodologies. The studies primarily involved *in vivo* experiments using animal models (minipigs, rats, dogs, and rabbits), and they varied in terms of implant types, surface treatments, and outcomes assessed. The characteristics of the included studies are provided in Table 2. The risk of bias of the included studies is reported in Table 3.

The included studies collectively indicated that residual alumina particles on dental implant surfaces do not negatively impact osseointegration, with some studies even suggesting beneficial effects. Gil et al. in two studies [19,20] demonstrated that residual alumina did not affect osseointegration, and accelerated bone growth and improved osseointegration in minipigs, respectively, highlighting potential bactericidal properties due to reduced bacterial adhesion. These findings support what was previously reported by Wennerberg et al. 1996 [26], who showed that implants blasted with 75  $\mu\text{m}$  alumina particles exhibited significantly higher bone-to-metal contact after 12 weeks compared to machined implants.

Comparative studies by Gehrke et al. [22] and Yurttutan et al. [23] found no significant differences in osseointegration between alumina-blasted implants and those treated with alternative materials, such as titanium dioxide ( $\text{TiO}_2$ ) or bio-ceramics. This indicated that both alumina and these other materials are effective for surface enhancement. Ríos-Carrasco et al. [21] also confirmed that alumina-blasted implants achieved high osseointegration rates, comparable to acid-etched implants.

In terms of biocompatibility, Rürger et al. [24] reported that alumina-free implants had increased bone–implant contact, although they exhibited lower shear resistance compared to those with residual alumina. This suggests that while removing residual alumina might enhance bone–implant contact, it may also compromise mechanical stability.

Piattelli et al. [15] and Abdulla et al. [18] found no adverse effects of residual alumina on the cellular response. Piattelli et al. [15] observed newly formed bone and active osteoblasts in close contact with alumina-blasted implants, while Abdulla et al. [18] noted consistent and ongoing bone growth around alumina-blasted implants in dogs.

The particle size of alumina used in surface treatment also influences outcomes. Wennerberg et al. [26] observed better osseointegration with implants blasted with 75  $\mu\text{m}$  particles compared to those blasted with 25  $\mu\text{m}$  particles or machined surfaces, indicating that larger particles might enhance the biological response.

**Table 2.** Main features and findings of the included studies.

Study Author	Study Year	Study Type (Animal Model)	Number and Features of Animal Used	Dental Implant Number and Type; Location of Placement	Groups	SLA Technique Used	Residual Al	Biological Effects	Study Findings	Comments/Notes
Abdulla et al. [18]	2024	Experimental (Dogs)	24 healthy, mature adult, local breed male dogs, aged 1–1.5 years and weighing $22 \pm 3$ kg	72 commercially pure, standard screw-type Titanium dental implants; mandible	G1: SLA surface G2: 50 $\mu$ m $Al_2O_3$ -blasted G3: Laser-treated G4: Propolis-coated	Air-abraded with 50 $\mu$ m $Al_2O_3$ particles for 15 s at 0.6 MPa, 6 bars of pressure	Present	Good bone response with sufficient new bone development along the implant surface.	Uniform and ongoing pattern of bone growth and many osteoblasts, with few osteocytes within lacunae in new bone trabeculae.	$Al_2O_3$ showed no negative effect on osseointegration.
Gil et al. [19]	2022	Experimental (Minipig)	20 twelve-year-old female minipigs	240 commercially pure grade 3 titanium dental implants (3.8 mm-wide, 12 mm-long); mandible and maxilla	G1: As-received (CTR) G2: $TiO_2$ -blasted G3: $Al_2O_3$ -blasted	G2–G3: Grit-blasted with 600- $\mu$ m size particles and 0.25 MPa blast pressure. All samples AE with HCl/ $H_2SO_4$ for 15 s	Present	The presence of residual blasting of $Al_2O_3$ and $TiO_2$ did not affect the osseointegration of titanium dental implants.	Osseointegration of $Al_2O_3$ -blasted implants is higher than the control and $TiO_2$ -blasted implants, with BIC values twice as high (63% vs. 38%) at 6 weeks follow-up.	Blasting with $Al_2O_3$ favors the osseointegration of titanium dental implants compared with $TiO_2$ .
Gil et al. [20]	2022	Experimental (Minipig)	8 twelve-year-old female minipigs	110 cylindrical, commercially pure grade 3 titanium dental implants (3.8 mm-wide, 12 mm-long); mandible	G1: No blast G2: $Al_2O_3$ -blasted G3: $Al_2O_3$ -blasted and special cleaning	Shot-blasted with $Al_2O_3$ particles with a size range of 212–300 $\mu$ m at a pressure of 2.5 MPa until saturation	Present and removed	Residual Al accelerated bone growth and reduced bacterial adhesion.	In vivo studies demonstrated the beneficial effects of residual Al on bone growth and bactericidal properties	Presence of residual blasting of $Al_2O_3$ favors the osseointegration of titanium dental implants.
Ríos-Carrasco et al. [21]	2021	Experimental (Rabbit)	6 New Zealand white rabbits of 6 months of age weighing 3 to 4 kg	24 commercially pure titanium grade 4 dental implants, 4.0 mm-wide $\times$ 8.0 mm-long and a neck section of 1.5 mm in height; tibia	G1: $Al_2O_3$ -blasted G2: $Al_2O_3$ -blasted, and acid-etched	Shot-blasted with $Al_2O_3$ particles of 425 to 600 $\mu$ m	Present	No negative impact on osseointegration.	The bone-to-implant contact ratio (BIC%) showed a similar tendency, with $55.18 \pm 15.67$ and $59.9 \pm 13.15$ for SB and SB + AE implants.	Both surfaces of implants studied showed high osseointegration.

Table 2. Cont.

Study Author	Study Year	Study Type (Animal Model)	Number and Features of Animal Used	Dental Implant Number and Type; Location of Placement	Groups	SLA Technique Used	Residual Al	Biological Effects	Study Findings	Comments/Notes
Gehrke et al. [22]	2018	Experimental (Rabbit)	8 New Zealand white adult rabbits weighing approximately 4 kg	48 cylindrical titanium dental implants; tibia	G1: Al <sub>2</sub> O <sub>3</sub> microparticles G2: TiO <sub>2</sub> microparticles	Sandblasting with Al <sub>2</sub> O <sub>3</sub> and TiO <sub>2</sub>	Present	No significant differences in osseointegration between Al <sub>2</sub> O <sub>3</sub> and TiO <sub>2</sub> .	Histological analysis showed a complete bone organization and mineralization at 8 weeks in both groups. The BIC% did not show statistical differences.	Both Al <sub>2</sub> O <sub>3</sub> and TiO <sub>2</sub> can be used effectively for surface blasting.
Yurttutan et al. [23]	2018	Experimental (Sheep)	4 two-year-old female sheep, weighing 45 kg	64 cylindrical titanium dental implants, 4.0 mm-wide and 10 mm-long; tibia	G1: Al <sub>2</sub> O <sub>3</sub> -blasted G2: TiO <sub>2</sub> -blasted G3: SiO <sub>2</sub> -blasted G4: Machined	Sand-blasted with Al <sub>2</sub> O <sub>3</sub> particles of 180 to 200 µm	Present	Better osseointegration with implants blasted with Al <sub>2</sub> O <sub>3</sub> particles.	Although there were no statistically significant differences between the groups, the implants sandblasted with Al <sub>2</sub> O <sub>3</sub> showed a higher Implant Stability Quotient (ISQ) and removal torque value at the end of the 1st and 3rd months.	The results demonstrate that Al <sub>2</sub> O <sub>3</sub> is superior to other sand particles.
Rüger et al. [24]	2010	Experimental (Rabbit)	38 adult female New Zealand white rabbits	Cylindrical implants of either commercial pure titanium (ISO5832-2) or Ti <sub>6</sub> Al <sub>7</sub> Nb (ISO5832-11), 10 mm, the outer diameter 5 mm, and the inner diameter 2 mm, with a threaded bore; distal femoral metaphysis	G1: 20 µm Al <sub>2</sub> O <sub>3</sub> grit blasting G2: Al <sub>2</sub> O <sub>3</sub> free (acid-etched)	Grit-blasting with 20 µm Al <sub>2</sub> O <sub>3</sub> , followed by a special cleaning procedure rinse in ammonium bifluoride and nitric acid (<1 min each)	Present and removed	Improved biocompatibility and increased bone-implant contact, and lower shear resistance.	Al <sub>2</sub> O <sub>3</sub> -free implants exhibited increased bone-implant contact but lower shear resistance.	Indicates that removing residual Al particles may enhance bone-implant contact.

Table 2. Cont.

Study Author	Study Year	Study Type (Animal Model)	Number and Features of Animal Used	Dental Implant Number and Type; Location of Placement	Groups	SLA Technique Used	Residual Al	Biological Effects	Study Findings	Comments/Notes
Piattelli et al. [15]	2003	Experimental (Rabbit)	12 New Zealand white mature male rabbits	24 threaded screw-shaped, machined grade 3 commercially pure titanium dental implants; tibia	G1: Al <sub>2</sub> O <sub>3</sub> -blasted G2: Saline-treated	Sandblasted with 100–120 µm Al <sub>2</sub> O <sub>3</sub> particles at a 5 atm pressure for 1 min	Present	Newly formed bone was found in contact with the implant surface. Bone trabeculae were in close contact with the implant surface. Newly formed blood vessels were observed. Some osteoblasts were actively secreting osteoid matrix directly on the implant surface.	Found no statistically significant differences in bone–implant contact, number of multinucleated cells, and osteoclasts between groups.	Residual Al oxide particles on implant surface do not affect osseointegration.
Mueller et al. [25]	2003	Experimental (Rabbit)	27 female adult Chinchilla rabbits, strain CH bb-CH, body weight 3–4 kg	63 commercially pure titanium cylinders (8 mm in length and 4 mm in diameter); distal femur epiphysis	G1: Untreated G2: 110 µm Al <sub>2</sub> O <sub>3</sub> -blasted G3: 50 µm bio-ceramic-blasted	Blasted with Al <sub>2</sub> O <sub>3</sub> particles (carborundum) with a particle size of 110 µm	Present	No untoward or negative effects from Al ions found on implant surfaces.	A dense ring of bone was developed, similar to cortical bone regarding density and development of Haversian canals with all surfaces after 84 days.	The MBC showed a tendency for more bone after bio-ceramics were used as a blasting material, compared to Al <sub>2</sub> O <sub>3</sub> .
Wennerberg et al. [26]	1996	Experimental (Rabbit)	10 adult (9–11 months old) male New Zealand white rabbits	60 screw-shaped, commercially pure titanium implants of length 6mm, diameter 3.75 mm, and pitch height 0.6 mm; tibia	G1: Machined surface G2: TiO <sub>2</sub> -blasted G3: 25 µm Al <sub>2</sub> O <sub>3</sub> -blasted G4: 75 µm Al <sub>2</sub> O <sub>3</sub> -blasted	Sandblasting with 25 µm and 75 µm Al <sub>2</sub> O <sub>3</sub> particles	Present	No untoward or negative effects from Al ions found on implant surfaces.	Comparing implants blasted with 75 µm Al <sub>2</sub> O <sub>3</sub> particles to as-machined implants, the blasted specimens exhibited a statistically significant higher bone-to-metal contact after 12 weeks in the rabbit bone.	Implants blasted with 75 µm Al <sub>2</sub> O <sub>3</sub> particles showed better osseointegration than 25 µm particles.



Overall, the evidence suggests that residual alumina particles on dental implant surfaces support osseointegration, enhance bone growth, and reduce bacterial adhesion, while it is unclear if there is an effect on mechanical stability. The positive effects on osseointegration are comparable to other surface treatment materials, making alumina a viable option for dental implant surface modification.

#### 4. Discussion

The present systematic review aimed to evaluate the biological effects of residual Al particles on dental implant surfaces compared to implants without such residues, and/or to different blasting materials, in animal models. The studies published so far on this topic encompass a range of experimental *in vitro* and *in vivo*, clinical, and review papers, providing a comprehensive overview of the current understanding of this issue.

The studies indicate that residual Al particles on dental implant surfaces do not significantly impair osseointegration or biocompatibility. For instance, Piattelli et al. [15] found no statistically significant differences in osseointegration between implants with and without residual Al particles in an experimental rabbit model. Similarly, Wennerberg et al. [26] observed no adverse effects from Al ions on implant surfaces in both *in vitro* and *in vivo* studies.

Interestingly, some studies suggest potential benefits associated with residual Al particles. Gil et al., 2022 [20] reported that implants with residual Al particles demonstrated accelerated bone growth and reduced bacterial adhesion compared to cleaned implants. This finding aligns with the hypothesis that the physicochemical properties imparted by residual Al particles may enhance specific biological responses.

The cleanliness of dental implant surfaces is a critical factor for successful osseointegration. The reviewed literature highlights the importance of controlling surface contamination during the manufacturing process. For instance, R uger et al., 2010 [24] showed that removing residual Al particles resulted in increased bone–implant contact, although it also reduced shear resistance. Bone–implant contact (BIC) is defined as the percentage of implant surface that is in contact with newly formed bone. The BIC estimates the ability of a surface to induce bone formation around implants, and it is measured histologically and is related to implant surface roughness [27]. The association between surface roughness and osseointegration is well known [4]. A rough implant surface may be considered as a series of pits (peaks) and valleys, with different density (number per area), height, and sharpness [27]. Some biomechanical studies in the past observed that there is a range of pit size (normally in the micrometer range) and density that is related to high shear strength [28]. Within this range, when increasing the pit density, the shear strength increases, while below or above this range, a decrease in mechanical retention is observed. The presence of alumina may further increase the surface roughness, which can contribute to improving mechanical implant–bone interlocking. Several studies also found a correlation between BIC and the mechanical stability of implants [29,30]. These findings suggest that while surface cleanliness is desirable, residual Al particles may not necessarily be detrimental to implant osseointegration and could potentially offer some benefits.

The use of alternative blasting materials, such as titanium dioxide (TiO<sub>2</sub>), has been explored to avoid potential issues associated with Al particles. Gehrke et al., 2018 [22] compared the effects of Al<sub>2</sub>O<sub>3</sub> and TiO<sub>2</sub> microparticles and found no significant differences in osseointegration between the two materials. This suggests that TiO<sub>2</sub> could be a viable alternative to Al for implant surface modification, potentially eliminating concerns related to residual Al. Other studies found that blasting the implant surface with Al<sub>2</sub>O<sub>3</sub> produces better surface features (free energy, roughness, microhardness, residual stresses, and fatigue), as well as faster osseointegration and greater bone-to-implant contact, compared to surfaces blasted with TiO<sub>2</sub> [19,20].

From a clinical perspective, the SLA surface on dental implants does not appear to pose a significant risk to osseointegration or patient health. The findings from various studies indicate that current sandblasting and acid-etching techniques are effective in

maintaining implant biocompatibility [31–34]. However, the potential benefits observed in some studies suggest that residual Al particles might enhance specific biological responses, such as bone growth and antibacterial properties, as shown in this review.

This systematic review has several notable strengths. It comprehensively covered all the experimental studies on animals evaluating the biological effects of residual Al particles on dental implants. Furthermore, it critically evaluated the methodologies and findings of included studies, identifying both the benefits and potential concerns associated with residual Al particles on implant surfaces. Additionally, the review highlighted areas where further research is needed, guiding future studies to address unresolved questions and improve the understanding of implant surface modifications. The scarcity of evidence on the biological effects of residual alumina particles on dental implant surfaces in humans is a significant limitation in the current literature. This gap is primarily due to the ethical and practical challenges associated with conducting invasive histological assessments in human subjects. Such procedures are not feasible for routine clinical practice, as they would require biopsy or explantation of implants, which are invasive and carry potential risks for the patients. Consequently, animal experimental *in vivo* studies have been deemed appropriate and necessary to explore these biological effects. These studies provide valuable insights into the osseointegration process, biocompatibility, and cellular responses, which can be extrapolated to human scenarios with caution. The controlled environment of animal studies allows for precise manipulation of variables and thorough histological examination, offering a deeper understanding of the interactions between residual alumina particles and biological tissues.

However, this review also has limitations. The included studies varied significantly in design, methodologies, and outcome measures, which can make it challenging to draw definitive conclusions. Differences in the sandblasting and acid-etching protocols used across studies can influence the results, making it difficult to generalize findings to all types of dental implants. Studies comparing different implant brands using different protocols for sandblasting and acid-etching the implant surface showed wide variability in surface cleanliness, with potential different biological responses of tissues to implant insertion [35,36]. Additionally, there was a relatively small sample size of experimental animals involved in directly investigating the effects of residual Al particles across all studies. Despite a comprehensive search strategy, there is always a risk of selection bias. The diversity in outcome measures and uncontrolled confounding factors in many studies further complicates direct comparisons and interpretations of the results. Therefore, future research should address these limitations through standardized methodologies and long-term human studies to fully elucidate the impact of residual Al particles on dental implant success and patient health.

Future studies should focus on long-term *in vivo* studies to assess the chronic effects of residual Al particles, comparative studies involving a broader range of alternative blasting materials, and finally, investigations into the molecular mechanisms underlying the observed benefits of residual Al particles. Additionally, establishing standardized protocols for assessing and controlling surface contamination during implant manufacturing would be beneficial.

## 5. Conclusions

The evidence to date supports the safety and efficacy of Al<sub>2</sub>O<sub>3</sub>-blasted dental implants, despite the presence of residual Al particles. While Al ions pose potential risks, current manufacturing techniques appear to control these within safe limits. Ongoing research and improvements in surface treatment processes will be essential to maintaining and enhancing the biocompatibility and clinical success of dental implants.

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