How clean do sterile implants have to be?

Analysis and clinical relevance of factory-related contaminations

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The initial phase of the biological response to a placed implant is primarily determined by the implant's surface characteristics. The properties of any implant surface are an essential factor of its non-irritant integration into surrounding tissue structures.[1] Undisturbed osteoblast proliferation and osteoblast differentiation at the implant surface depend decisively on the microstructure of the surface.[2] Since the 1980s, however, there have also been growing demands for flawless cleanliness of the implant systems used.[3] In this context, it is a logical step not only to look at current analytical techniques but also to take a critical look at the clinical significance of avoidable contamination on brand-new sterile-packaged implants.

SEM imaging

Imaging in the material contrast mode of a scanning electron microscope (SEM) has proved to be very useful for the analysis of particulate and film-like contaminants on sterile-packaged dental implants. Back-scattered electrons from the implant surface have typical energy of up to 10 keV. The intensity of these signals depends on the average atomic number of the sample material in focus. Compared with titanium or zirconium, heavier elements, such as iron or nickel, show more intense back scattering so that corresponding image areas appear bright (Fig. 1). In contrast, locations with lighter elements, such as carbonaceous plastic particles, are displayed darker than areas with titanium or zirconium (Fig. 2).

The image generated by the back-scattered electron detector thus allows conclusions regarding the distribution of foreign materials or elements in the imaged section of the implant surface. For a valid assessment of the particle load of an implant, a SEM image of the entire implant should always be acquired. In order

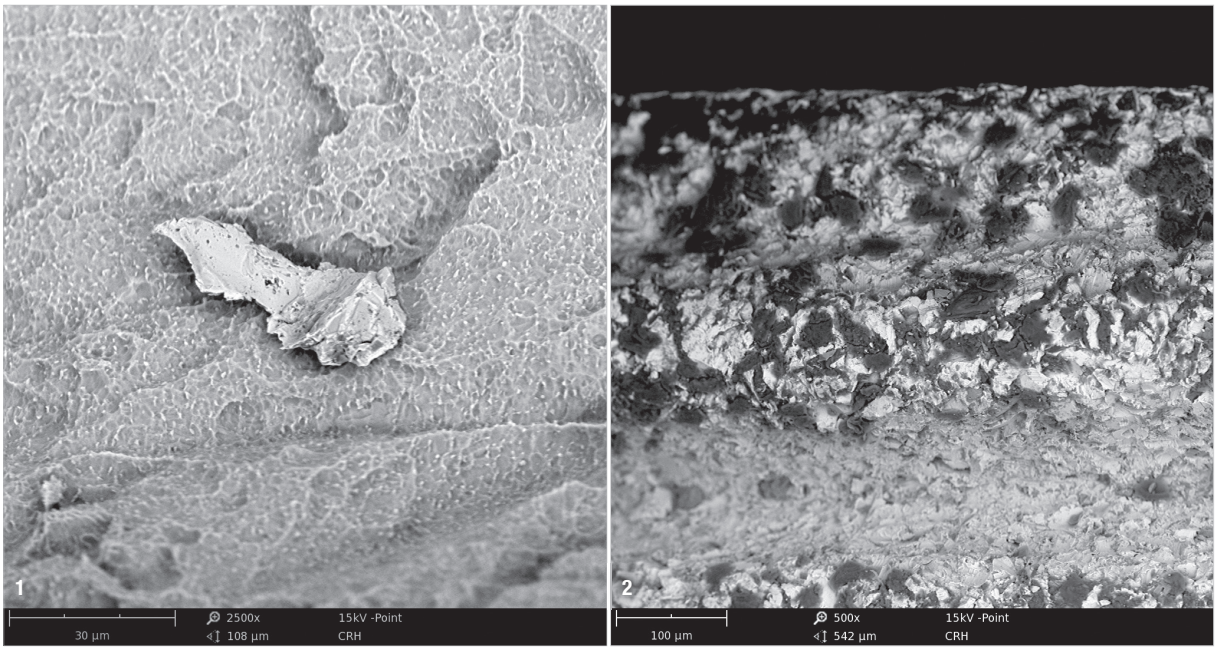

Fig. 1: Metal particle of iron, chromium and nickel on the surface of a titanium implant (Adin). SEM 2,500× magnification. **Fig. 2:** Numerous organic particles on the entire implant shoulder (OCO Biomedical). SEM 500× magnification.

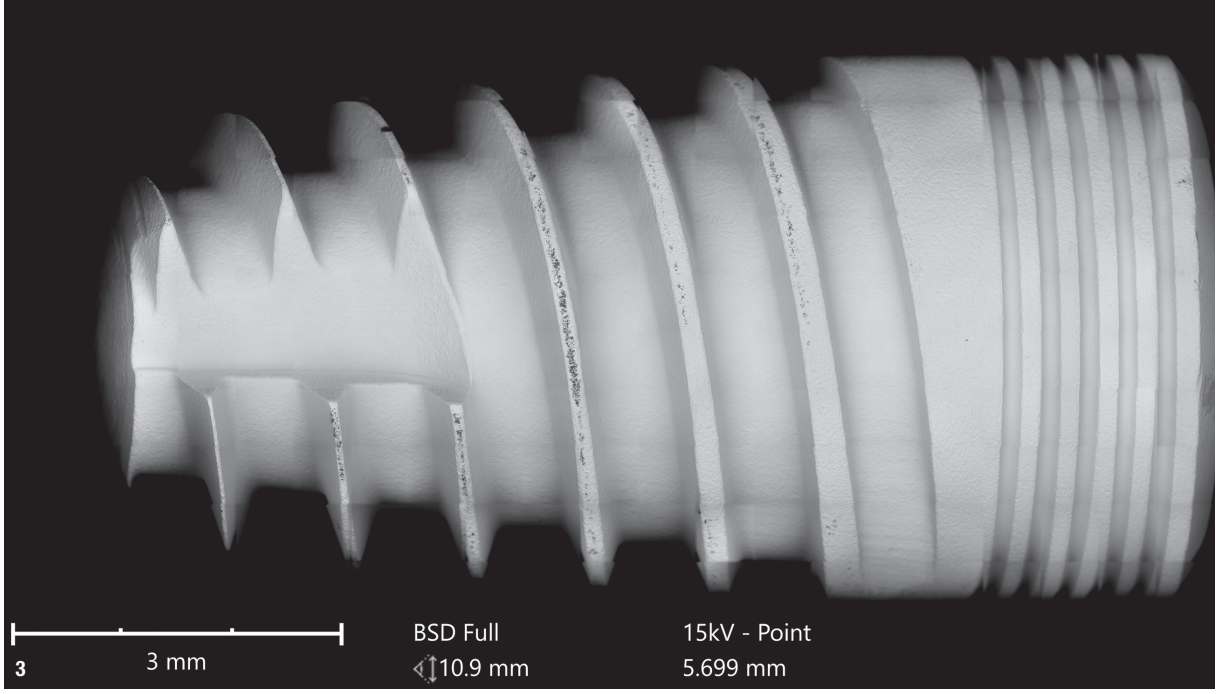

Fig. 3: Factory-related contamination of entire implant threads (Ritter Implants). Full-size SEM image of the implant electronically compiled from hundreds of single images at 500× magnification using the material contrast technique (back-scattered electron mode).

to depict details at high magnification without pixelation, up to 600 individual SEM images must be electronically stitched together in high resolution for these comprehensive overview images. The resulting SEM image in material contrast provides a detailed overview and allows the quantitative detection of individual particles (Fig. 3).

Identification of impurities

Energy-dispersive X-ray spectroscopy (EDS) provides information about the exact elemental composition of an impurity and thus provides hints about its origin. When fast electrons hit the sample surface, X-rays are emitted inter alia. The energy of these X-rays is characteristic of each chemical element present in the sample or contaminant. The energy and the number of X-ray quanta emitted in this way are measured over a defined time and output as an EDS spectrum.

Time-of-flight secondary ion mass spectrometry (ToF-SIMS) provides even more precise information about the chemical composition of an impurity. The method provides information on the atomic and molecular structure of the uppermost monolayers of a substrate on an analysis area of $500 \times 500\,\mu m^2$ with sensitivity in the parts per million range and a lateral resolution of up to 100 nm. Comparison of the spectra with known substances allows precise material determination of the respective contamination (Fig. 4).

Too many implants of inferior quality

In a study from 2017 to 2020, the CleanImplant Foundation, a non-profit organisation based in Berlin in Germany, analysed sterile-packaged implants from various manufacturers. In cooperation with Charité—Universitätsmedizin Berlin in Germany, a total of 14 ceramic implant systems and 86 implant systems made of titanium and its alloys were examined under the SEM. The protocol of analysis used in this quality assessment study was published in a 2019 pilot study by Duddeck et al.[4] The samples were examined for contaminants under the SEM in a testing laboratory accredited according to the DIN EN ISO/IEC 17025:2018 standard. For the study, the implants were unpacked in a particle-free environment (Class 5 clean room according to the DIN EN ISO 14644-1 standard) and subsequently scanned in the same clean room to exclude any laboratory interference with the test samples. To an unexpected extent, that is, in more than one-third of the samples examined, the analysis revealed factory-related residues and contamination. SEM imaging identified not only carbonaceous contaminants in significant quantities (Fig. 5) but also foreign metals such as chromium, iron, tungsten, nickel, copper and tin. Implants made of titanium and zirconium dioxide were affected, regardless of price, market position, size of the manufacturer or production location. Subsequent to the SEM/EDS analysis, selected contaminated implant samples were additionally examined by a detailed ToF-SIMS analysis. Polysiloxanes, that is, synthetic polymers (Fig. 6), thermoplastics and residues of dodecylbenzene sulphonic acid were found on the implant surfaces. This cytotoxic surface-active chemical is one of the most aggressive components in many cleaning agents and is classified as a hazardous substance.

Clinical relevance

In particular, organic carbonaceous foreign materials have been associated with initial bone loss or even peri-implantitis in the literature.[5] Increased osteoclast activity associated with a possible foreign-body reaction, resulting in peri-implant bone resorption, could be the cause.[6] Exposure to foreign particles induces macrophages to secrete tumour necrosis factor-α, interleukin-1β, interleukin-6 and prostaglandin E2, which in turn stimulates the differentiation of osteoclast precursors into mature osteoclasts. This response would explain clinically striking bone loss during the initial healing phase or the early onset of peri-implantitis. All particles found in the study

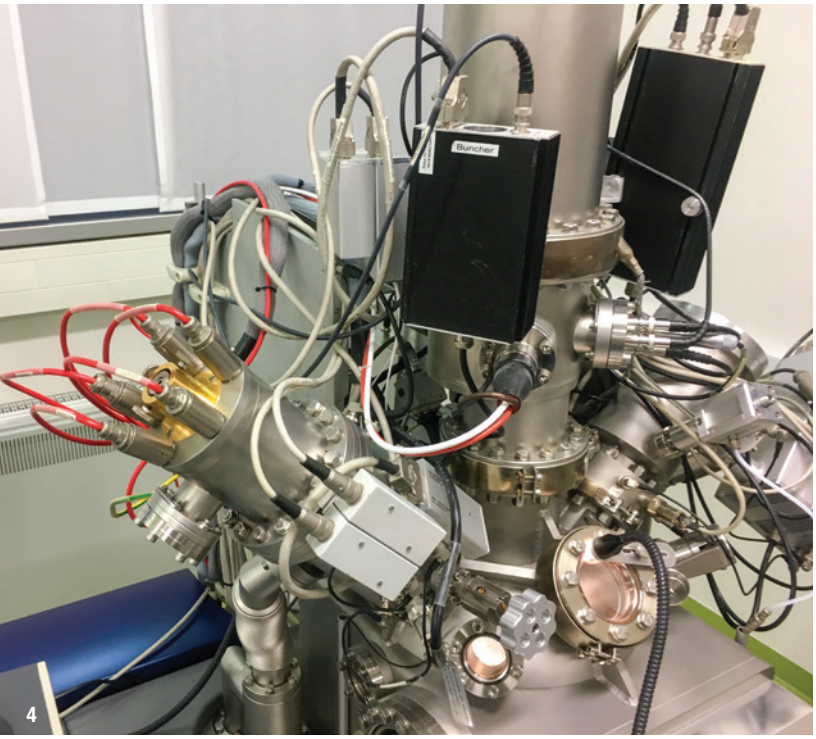

Fig. 4: Time-of-flight secondary ion mass spectrometry instrument (tascon).

appear to have survived the wet chemical cleaning procedures in the manufacturing process or contaminated the implant in the handling and packaging process. Especially foreign particles with a size of 0.2–7.2 µm are classified as pro-inflammatory.[7–9] If they detach from the surface during the insertion of the implant, macrophages take up the particles by phagocytosis and subsequently release pro-inflammatory cytokines. The result is an expanding zone of soft-tissue damage and inflammation.[6]

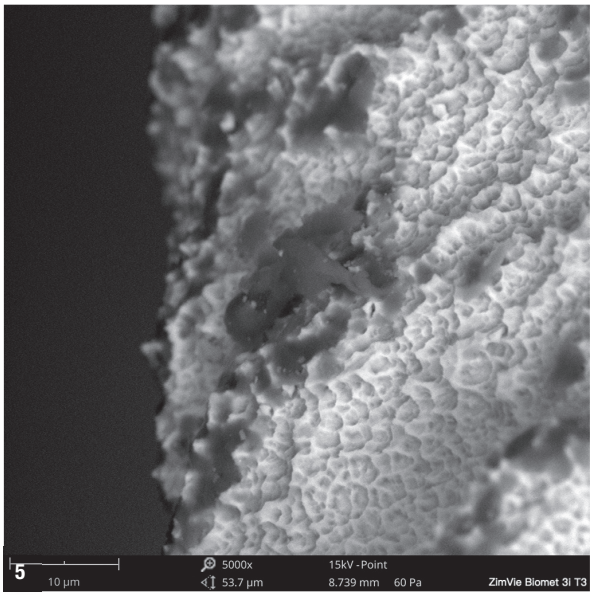

Fig. 5: Carbonaceous particles (polysiloxanes) on a titanium implant at the implant apex of a titanium implant (T3, ZimVie). SEM 500× magnification.

Independent test procedure provides safety for dentists

All implants examined in the recent quality assessment study, including those significantly contaminated, showed the CE mark on the packaging or carried the U.S. Food and Drug Administration logo for marketing clearance on the US market. With the introduction of a worldwide quality seal for clean implants, the "Trusted Quality" mark, the CleanImplant Foundation addressed this issue years ago. Criteria for implants that are largely free of foreign particles were defined in a guideline in 2017 and published as a consensus paper involving renowned scientists such as Prof. Tomas Albrektsson, Prof. Ann Wennerberg, Prof. Hugo de Bruyn, Prof. Florian Beuer, Prof. Jaafar Mouhyi, Dr Michael Norton, and Dr Luigi Canullo.[10] These scientists also form the foundation's scientific advisory board, which ultimately decides on the awarding of the above-mentioned quality seal. For the testing procedure of an implant system, a total of five samples are included. A maximum of three implants are obtained from the respective manufacturer and at least two implants from implantology practices. This procedure ensures random selection during sampling and reliably prevents the acquisition of potentially specially treated test samples. The independent and thorough analysis of the samples must be renewed every two years in specially accredited testing laboratories. The same protocol of analysis described in the *Journal of Clinical Medicine* in 2019 is to be applied.[4]

Before the seal can be awarded, proof of a multi-annual survival rate of at least 95% must be provided for the respective implant system, as well as proof of the absence of a significant number of particles. The results of the analysis and the sufficiently reliable clinical documentation of a system are always checked independently by two members of the scientific advisory board in a peer-review process and compared with the requirements of the guideline. Not until all criteria are met can an implant system be awarded the seal for a period of two years. To date, the following systems have been awarded the foundation's "Trusted Quality" seal after rigorous peer review (in alphabetical order): AnyRidge and BLUEDIAMOND (MegaGen), blueSKY (bredent medical), CONELOG (CAMLOG), ICX-PREMIUM (medentis medical), In-Kone (Global D), Kontact S (Biotech Dental), NobelActive (Nobel Biocare), Patent/BioWin! (Zircon Medical/Champions), Prama (Sweden & Martina), SDS1.2 and SDS2.2 (SDS Swiss Dental Solutions), T6 (NucleOSS) and UnicCa (BTI). Other implant systems are currently undergoing the testing process of the foundation.

Discussion

The evaluation of the CleanImplant quality assessment study revealed both light and shadow with regard to the current quality level and sustainable quality control of dental implants. This creates a problem for the careful

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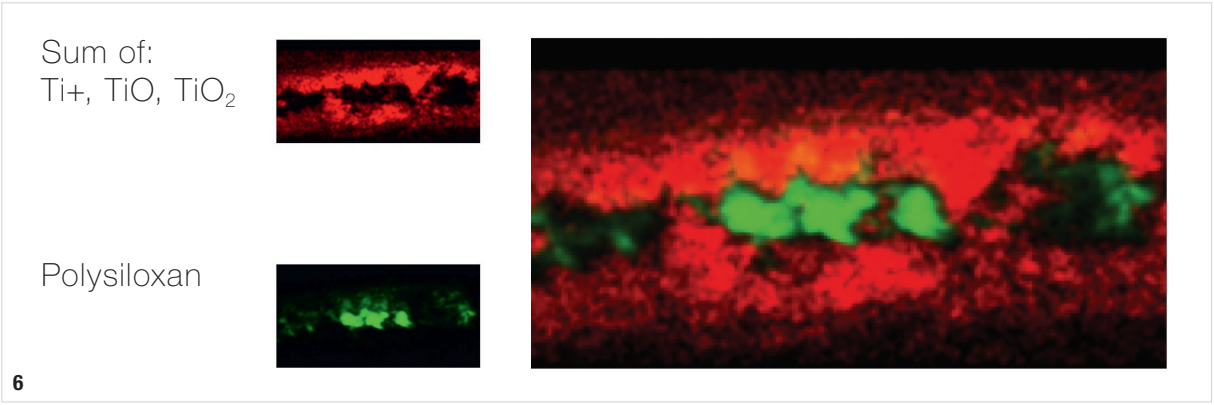

Fig. 6: Time-of-flight secondary ion mass spectrometry detection of polysiloxane on a titanium implant.

practitioner: he or she usually does not know whether the implant system of his or her choice has already been contaminated at the factory. This is because information or warnings about possible foreign particles that could cause peri-implantitis or about residues of cleaning agents is not provided on the implant packaging or on the package insert.

Fig. 7: Significant plastic material (polyacetal) on the shoulder of a ceramic implant (vitaclinical, VITA Zahnfabrik) from abrasion from the packaging.

Unfortunately, implant systems do not have consistent, comparable quality, as summarised in 2020 by Dr Norton, a past president of the Academy of Osseointegration, in an opinion piece in the *British Dental Journal* that is well worth reading.[11] The use of factory-contaminated implants not only may lead to inferior clinical outcomes but also carries the risk of legal implications. The problem of possible factory-related contamination concerns not only implants made of titanium or titanium alloys but also ceramic implants, as scientists from the universities of Gothenburg, Malmö and Berlin impressively described in a study published in 2021.[12] The bottom line of the study is that just because the material of ceramic implants is white does not necessarily mean that they are clean (Fig. 7).

Suppose a clinician chooses a ceramic implant as a metal-free alternative and it has been demonstrably contaminated by packaging residues across batches. In that case, he or she is, unwittingly, doing a disservice to precisely those patients who place great value on particularly biocompatible materials in their bodies. In a remarkable article decades ago, Wahl and Tuschewitzki employed an apt term for factory contamination of dental implants: they referred to it as “sterile dirt”.[3]

Conclusion

The placement of foreign metals and packaging residues or cleaning agent residues in the osseous site of an implant can lead to an uncontrolled foreign-body reaction, resulting in bone recession and even the loss of implants. Contamination of sterile-packaged dental implants can be largely avoided by the manufacturer. However, if individual manufacturers, when asked, say that they consider the amounts of foreign particles found on their products to be harmless according to their own judgement, it would be appropriate for them either to scientifically verify this or to warn users and patients accordingly.

about the author

Dr Dirk U. Duddeck studied biology and dentistry and specialised in oral implantology. He is a guest researcher at Charité—Universitätsmedizin Berlin and founder and head of the non-profit organisation CleanImplant Foundation, both in Berlin in Germany.

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Literature

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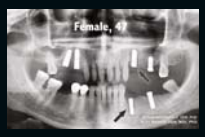

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