IMPLANT STUDY 2017/2019

“On Cleanliness of Sterile Dental Implants - A Global Quality Assessment of Implant Surfaces by SEM/EDS Analysis”

PRELIMINARY STUDY REPORT

Name of Manufacturer:
Bego Implant Systems GmbH

Analyzed Product(s):

Semados TiPure+ LOT 038485 0917 valid 2022-09

Scientific Advisory Board:

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1 Background and Aim

The CleanImplant Foundation was established as a non-profit organization in 2016 with the aim of providing information on possible impurities on sterile-packaged implants sold throughout the world, and their potential clinical significance.

Residues on sterile-packaged implants, in particular organic particles originating in the production or packaging process, are suspected of being responsible for cases of incomplete osseointegration of implants or early bone loss. Studies have shown that neither the CE mark nor the US FDA clearance is a reliable indicator of the purity of dental implants surfaces.

In three consecutive SEM studies conducted by the University Clinic of Cologne and the Charité University Medicine Berlin, over 250 implants in sterile packaging were analyzed using the same protocol over the past ten years [Duddeck, 2009: Duddeck et al., 2013; Duddeck et al., 2015]*. Results from the most recent study, with data on 135 implants, and a comparison with previous studies, have shown a significant increase in the number of implants with conspicuous residues. Despite the fact that it is technically possible to produce residue-free implants, these residues remain.

Residue-free medical devices are invariably the result of very considerable technological efforts during the production process and a consistent quality management approach. If, by contrast, adequate quality assurance testing is not performed during production, inferior medical devices will be the inevitable result — a fact that no formal marketing authorization can distract from. As a continuation of the three studies cited above, the aim of this study is to investigate improvements in manufacturing and quality management, and determine any increases in the quality level of the participating manufacturers and implant companies.

In order to provide a setup which complies with the highest standards of scientific research, the process of analysis in this study will be performed by the mmri-Test Laboratory according to DIN EN ISO/IEC 17025.

The unpacking of the implants themselves, the fixation of the samples on a charge-reduction specimen holder and even the scanning electron microscope analysis will take place in an environment that meets class 100 cleanroom requirements according to United States Federal Standard (US FS) 209 and ISO class 5 according to DIN EN ISO 14644-1 (see 2.2).

A digitally composed high-resolution SEM image (FSHR) shows the complete surface of an implant in an angle of view of 120° (see 2.5). Thus, the detailed report of every implant shows not only single sections of the sample but always a precise overview of the implant´s surface.

*) Reprints of various publications and poster-presentations available on request

2 Material and Method / Study Protocol

2.1 Scanning Electron Microscope

The scientific workstation is a Phenom proX Scanning Electron Microscope, equipped with a high-sensitivity backscattered electron detector that allows compositional and topographical imaging modes. Energy Dispersive X-ray Spectroscopy (EDS) analysis is performed with a thermoelectrically cooled Silicon Drift Detector (SDD). Active area: 25mm2; Energy resolution Mn Kα ≤ 140 eV; Processing capabilities: Multi-channel analyzer with 2048 channels at 10 eV/ch; Max. input count rate: 300,000 cps

2.2 ISO Class 5 Cleanroom Environment DIN EN ISO 14644-1

In order to avoid artifacts on the unpacked implant samples during the transfer into the SEM all implants have to be unpacked and analyzed in the scanning electron microscope under cleanroom conditions according Class 100 US Fed. 209 and ISO class 5 (DIN EN ISO 14644-1).

2.3 SEM Analysis Accreditation - DIN EN ISO/IEC 17025

All collected samples are subjected to the same quality analysis protocol performed by independent laboratories that apply a Quality Management System according to DIN EN ISO/IEC 17025 (general requirements for the competence of testing and calibration laboratories)*. All commissioned laboratories have to implement a quality system aimed at improving their ability to consistently produce valid results.

This includes the quality standard according to DIN EN ISO 9001:2015 as well as implementation of international standards for microbeam analysis – scanning electron microscopy such as

- ISO 16700:2016 Guidelines for calibrating image magnification
- ISO 14595:2014 Guidelines for the specification of certified reference materials
- ISO 22309:2015 Quantitative analysis using energy-dispersive spectrometry EDS

The laboratories undergo regular audits and multiannual re-assessments by external, independent accreditation bodies (e.g. DAkkS).

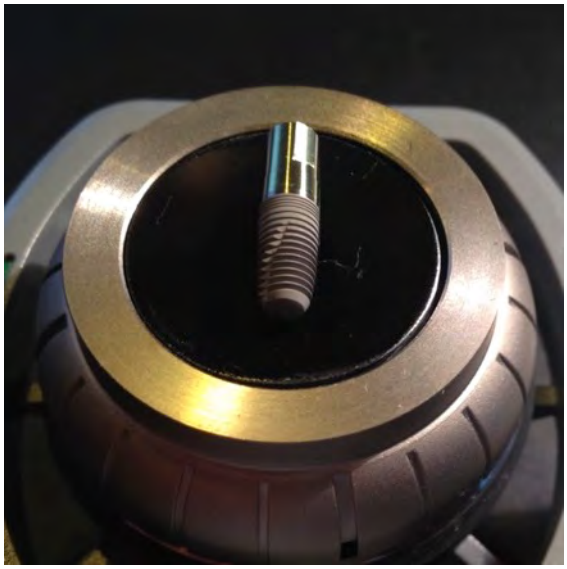
*) DAkkS accreditation number for this analysis is D-PL-21057-01-00

Workstation with Phenom proX Scanning Electron Microscope

2.4 Unboxing of Samples

Unboxing and mounting of the implant on the SEM charge-reduction sample holder and the transfer to the SEM vacuum chamber is performed inside a cleanroom environment using cleanroom suitable gloves.

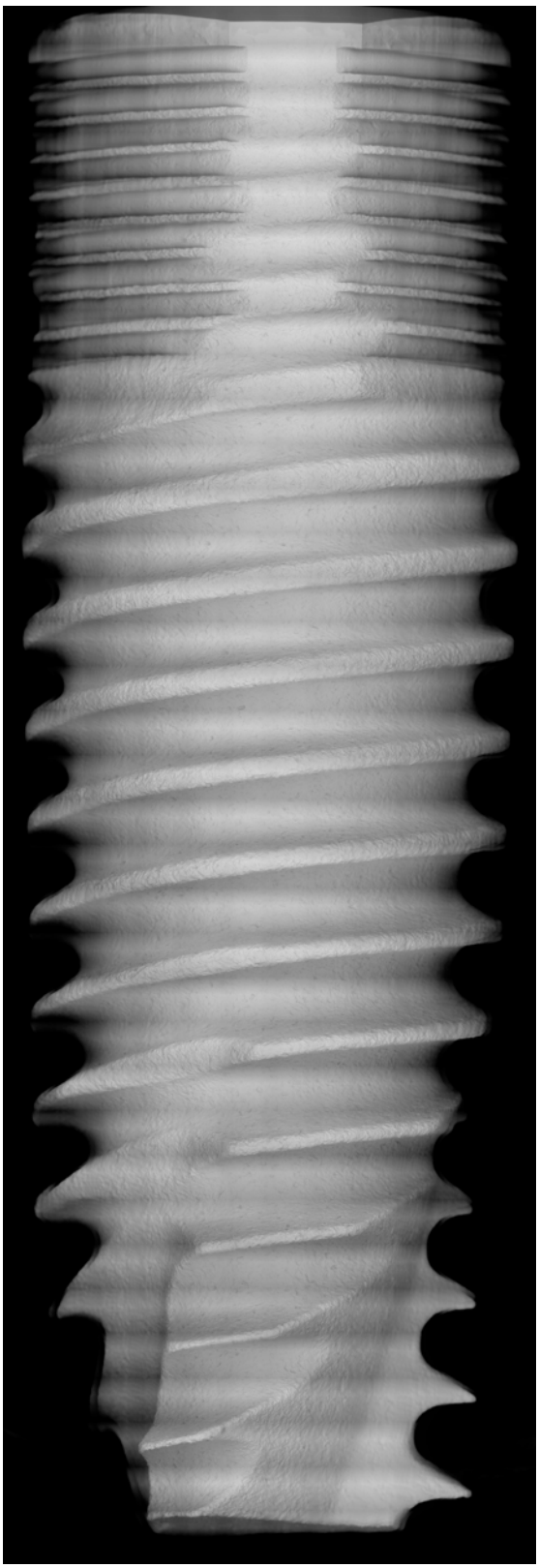
Without touching the surface, each implant will be taken out of the package with sterile forceps and fixed on the sample holders. During this procedure the implant surface that is to be analyzed will not be in contact with any other material. After the vacuum is generated in the electron microscope imaging and EDS-analyses will be completed.



Fixed implant (example) on the sample holder

2.5 FSHR SEM-Image

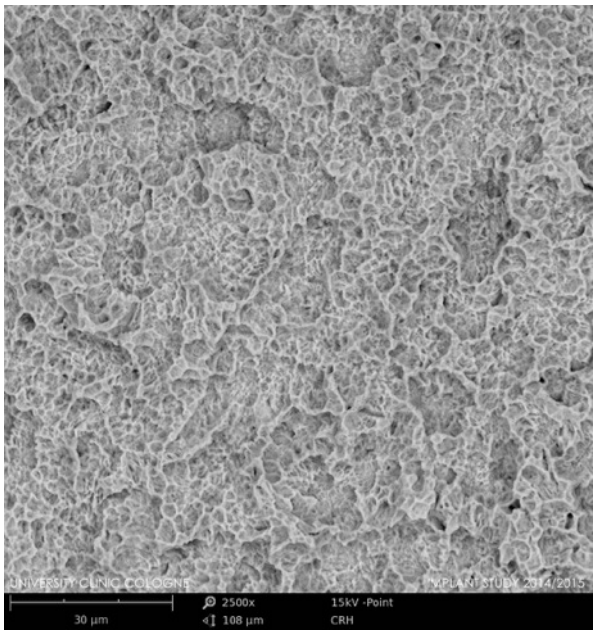
In order to achieve a complete overview of the sample and comprehensive surface quality information in high resolution, implants are scanned at a magnification of 500x in the “Image-Mapping” mode. This technique produces more than 360 single high-resolution SEM images that are digitally composed to one large image with an extreme high resolution, the FSHR image (Full-Size High-Resolution). The composed SEM image makes it possible to count particles in the visible field and identify areas of interest for a subsequent spot-analyses.



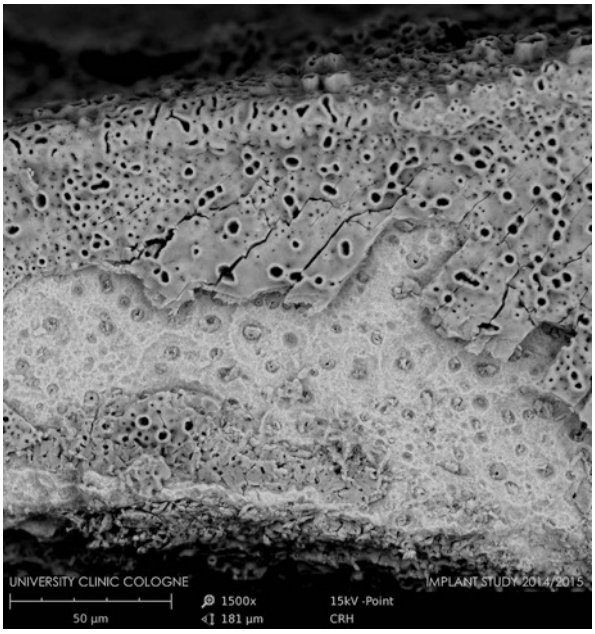
More than 360 single SEM images are digitally composed for one FSHR image (example).

2.6 SEM-imaging of the implant surface

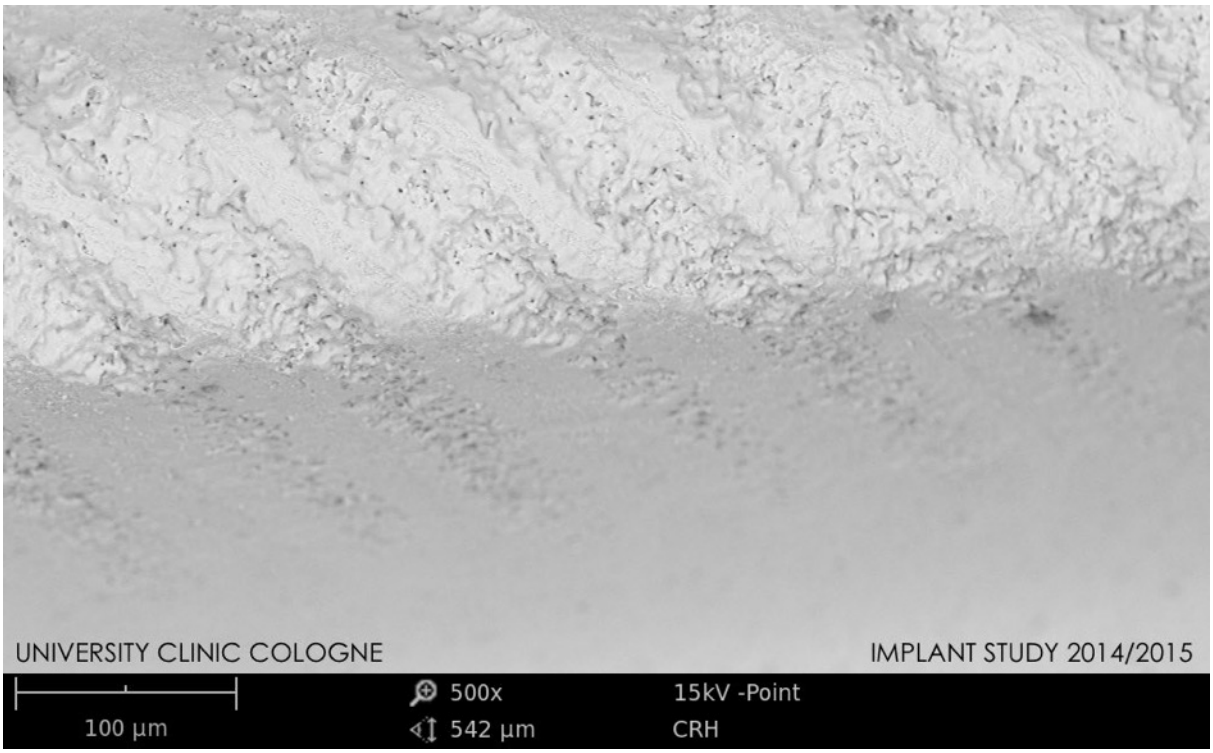
Scanning electron microscopy (SEM) enables the topical evaluation of the implant surface. The high-sensitivity backscattered electron (BSE) detector generates material-contrast images to a magnification of 10.000x. Thus, additional information about the sample e.g. the chemical nature and allocation of different remnants or contaminations on the sample material is provided.



Clean Implant surface; 2.500x



Anodized implant, damaged oxide layer; 1.500x

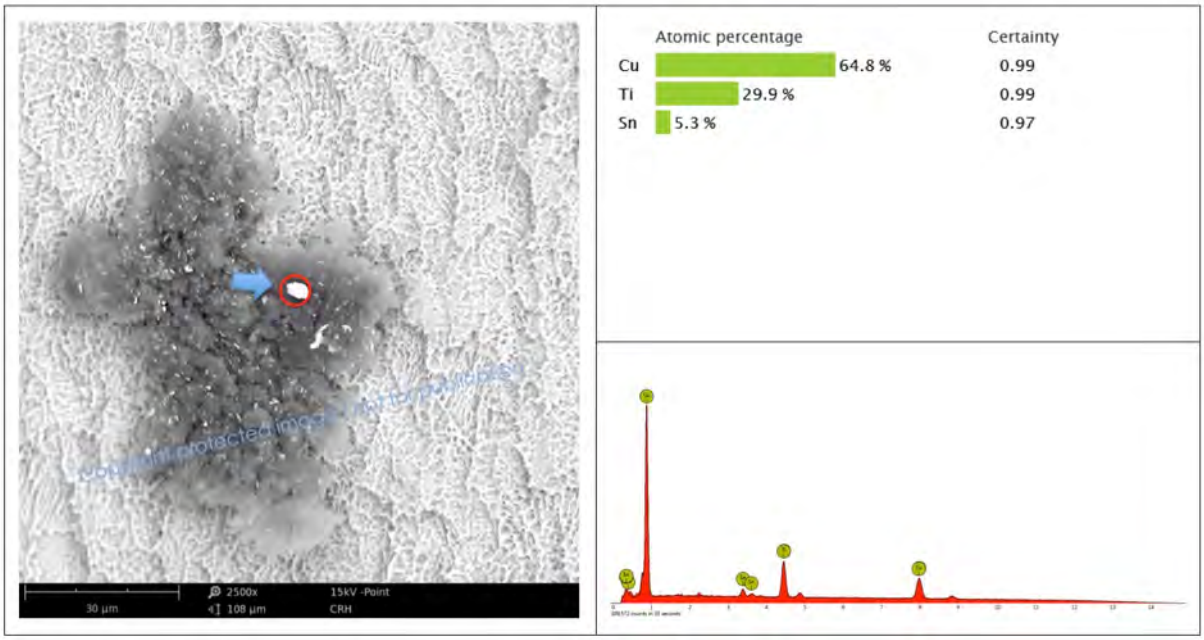


Thread flank of a clean zirconia implant; 500x

2.7 Elemental analysis (EDS)

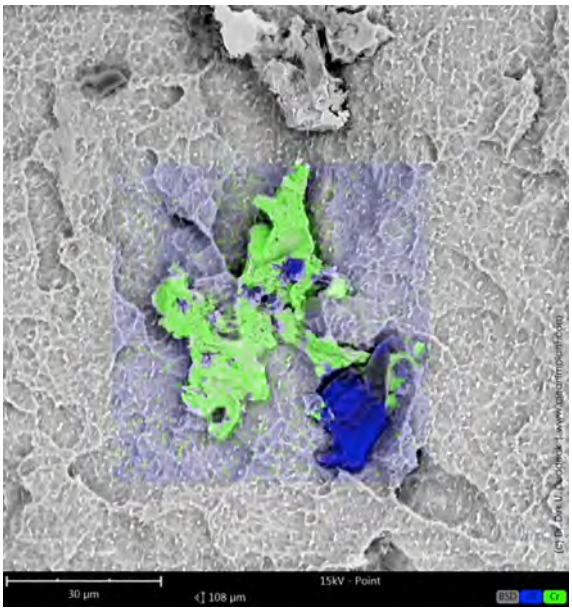
Energy Dispersive X-ray Spectroscopy (EDS) analyzes X-rays generated by the electrons of the electron beam (CeB_6 electron source) while they are interacting with the sample. Each element emits specific X-ray peaks. The element identification software identifies even hidden elements within the sample via the spot mode analysis. All results are verified using iterative peak stripping deconvolution.

An area-analysis and one or more spot analyses are performed for each tested implant (analysis of spots and areas by EDS). An area-analysis covers the entire implant area in the focus of the microscope. For a spot analysis, the electron beam is focused on a specific area to get information about selective accumulations on the implant surface.



Remnants with traces of copper and tin (white particle) embedded in organic residue (black), 2.500 x

If necessary, elemental mapping reveals the distribution of elements within the sample. Selected elements can be mapped. Compiling these elements with the backscattered image gives a clear insight into the distribution of elements within the sample. Line scan allows analysis to be performed over a selected line. A line profile of every selected element is displayed on the screen.



Example of EDS mapping
(stainless steel particles and Al_2O_3 particles):
green = Signals originated by chrome;
blue = signal originated by aluminum; x 2,500

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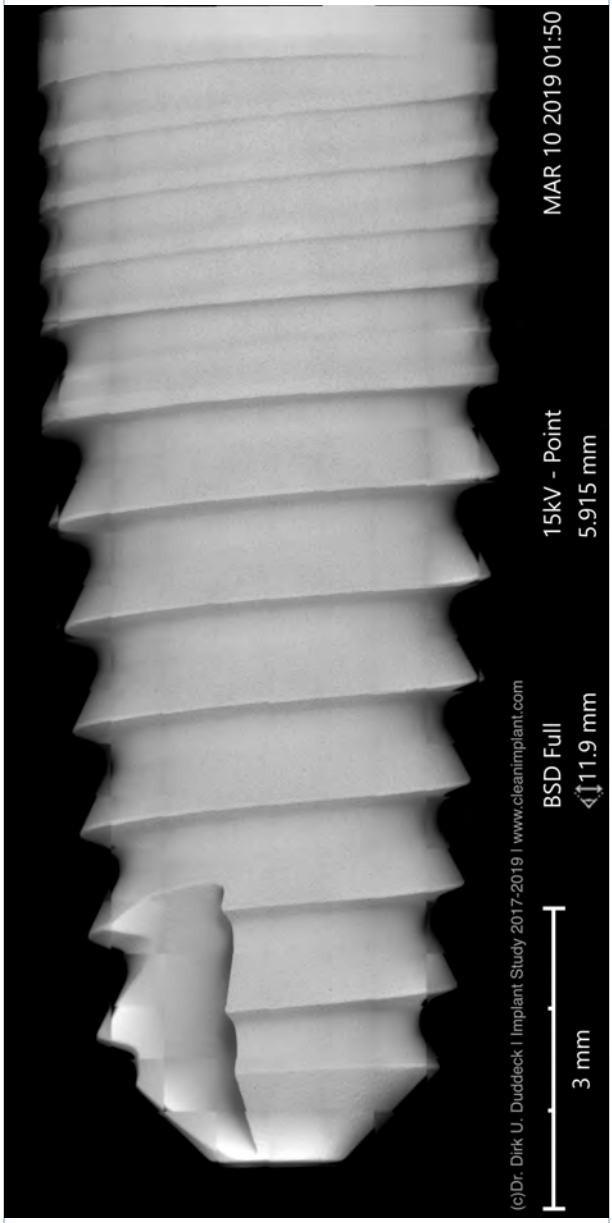
3.1 Full-Size High-Resolution SEM Image



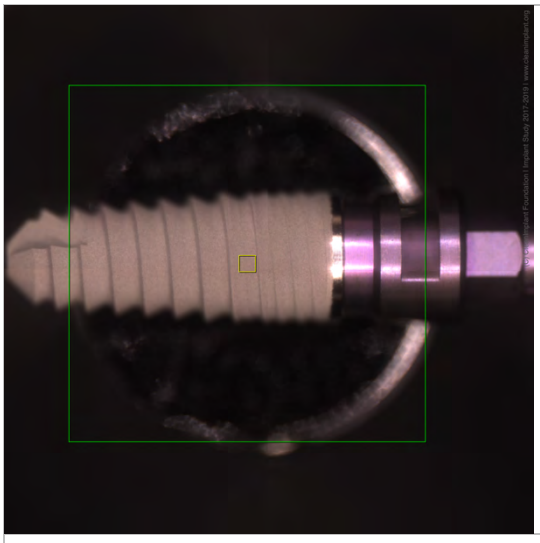
FSHR-SEM image (digitally composed, approx. 500x)

Label

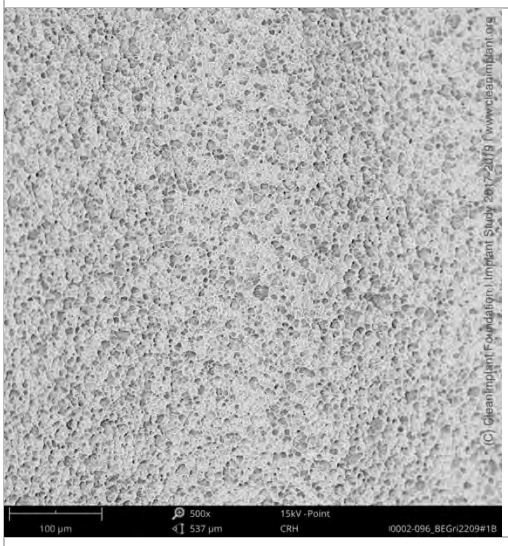
Sample mounted on sample holder

3.2 SEM - Results | mmri report no. 18-00002-096

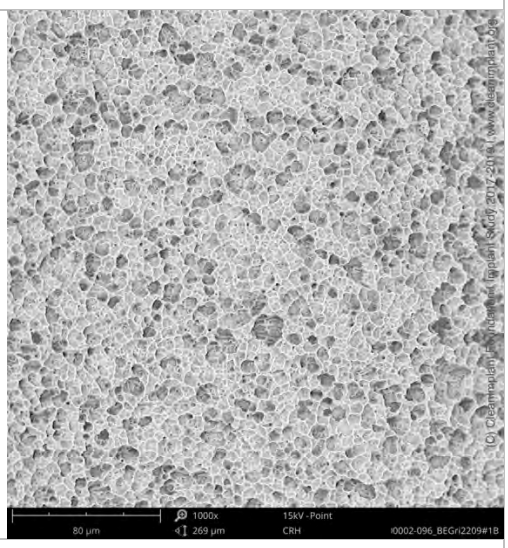
3.2.1 SEM Images Implant Body



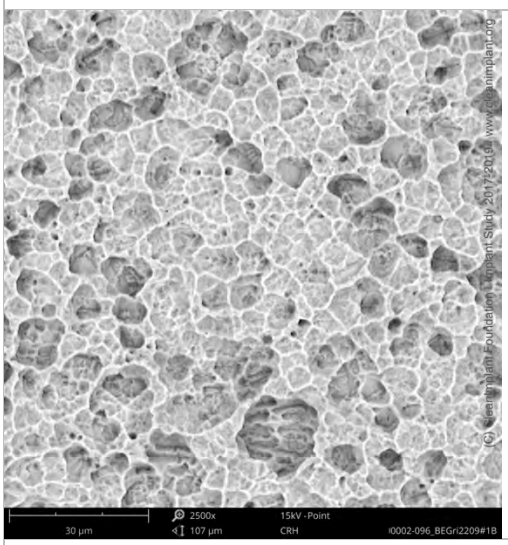
Phenom camera



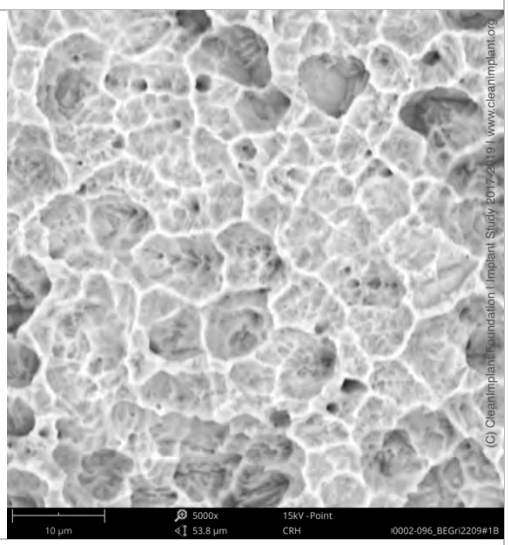
500x



1.000x

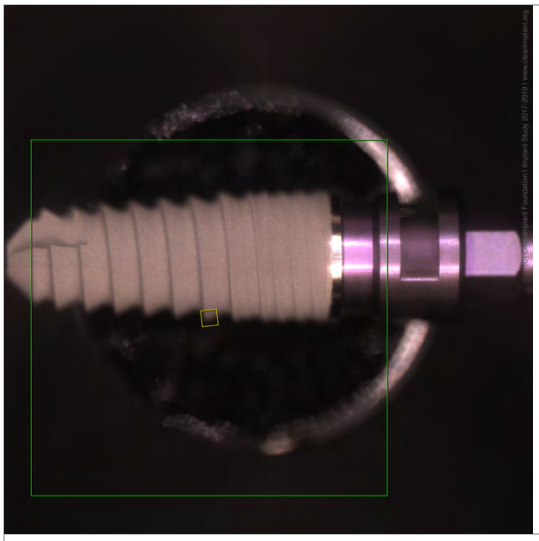


2.500x

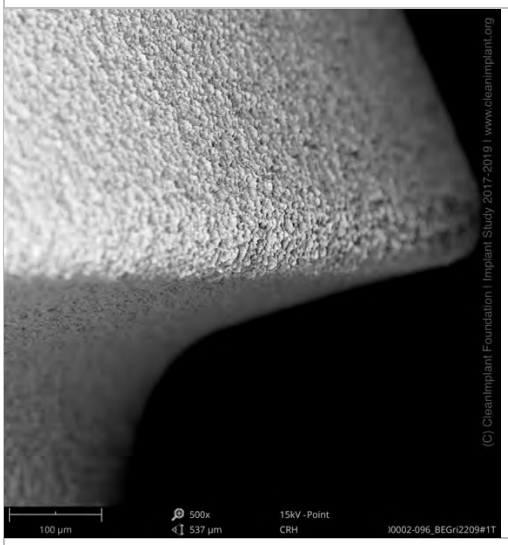


5.000x

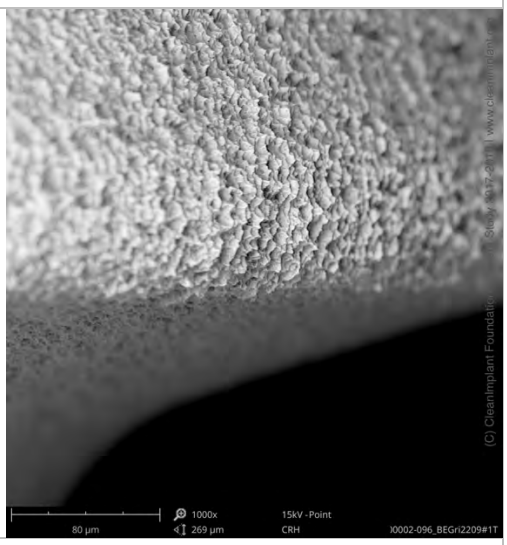
3.2.2 SEM Images Implant Thread



Phenom camera



500x



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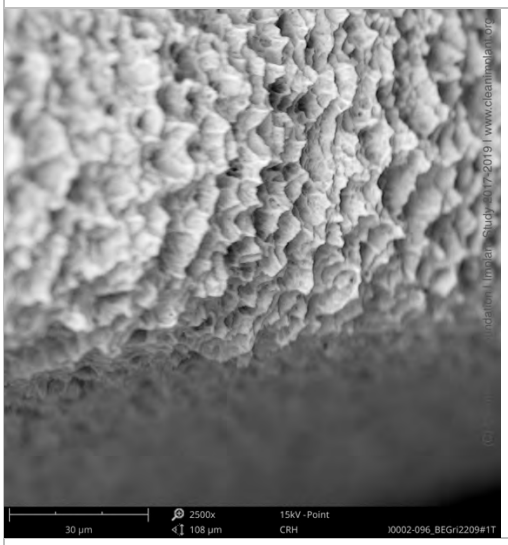
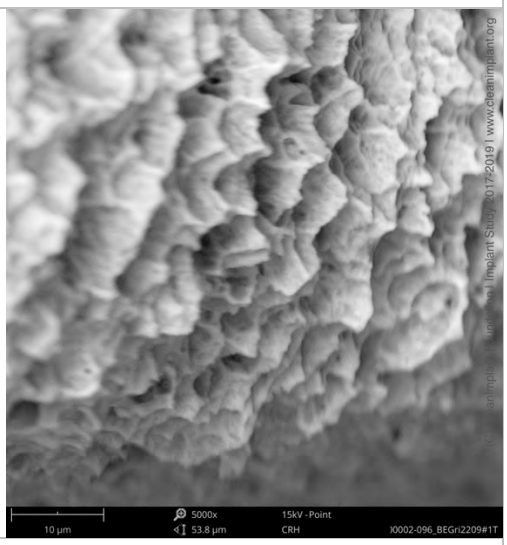
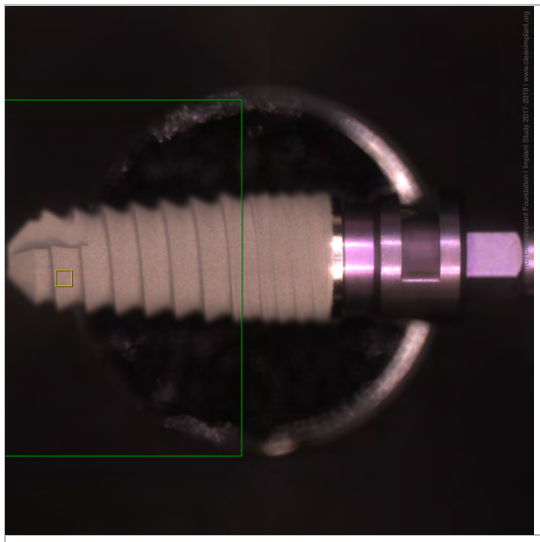


2.500x

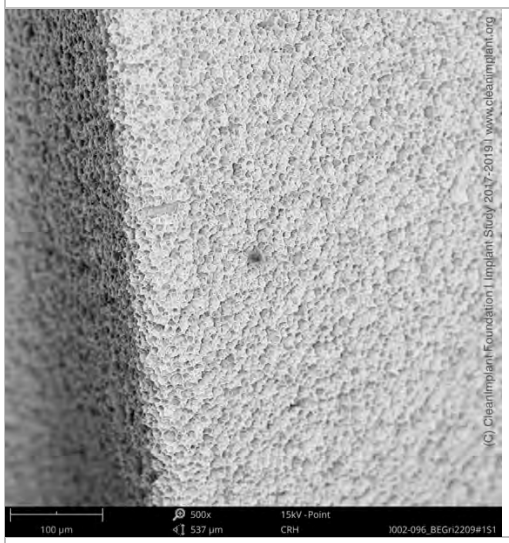


5.000x

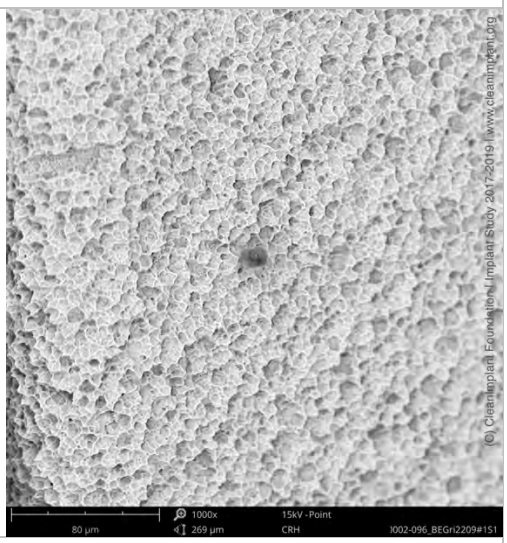
3.2.3 SEM Images Spot_1



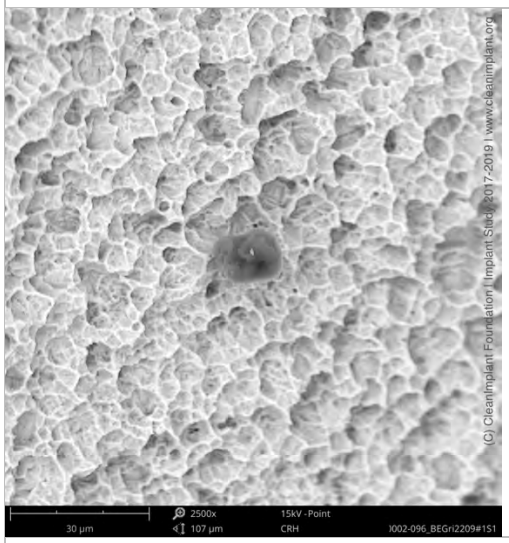
Phenom camera



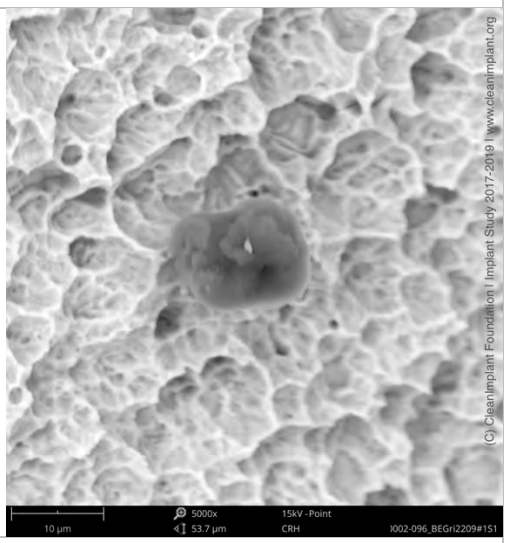
500x



1.000x



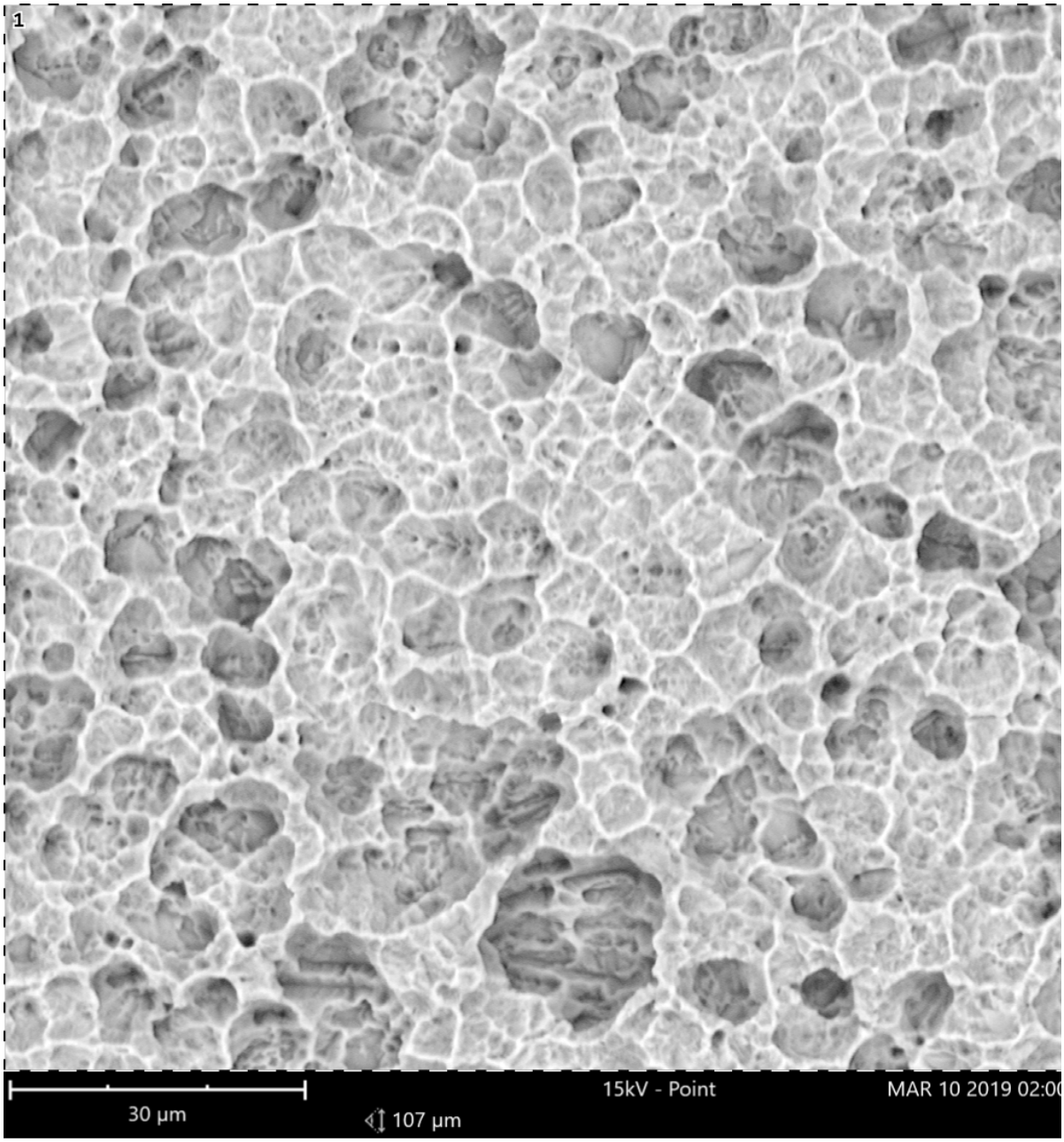
2.500x



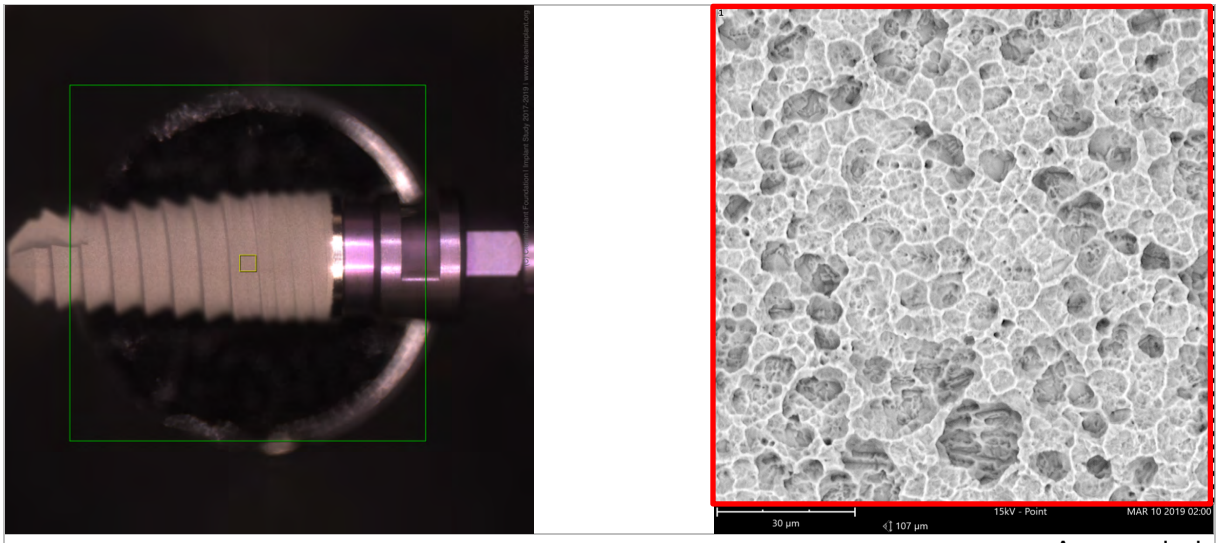
5.000x

3.3 Elemental Analysis (EDS)

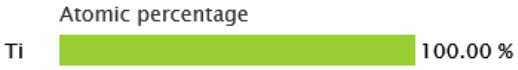
3.3.1 EDS Analysis Area (Overview)



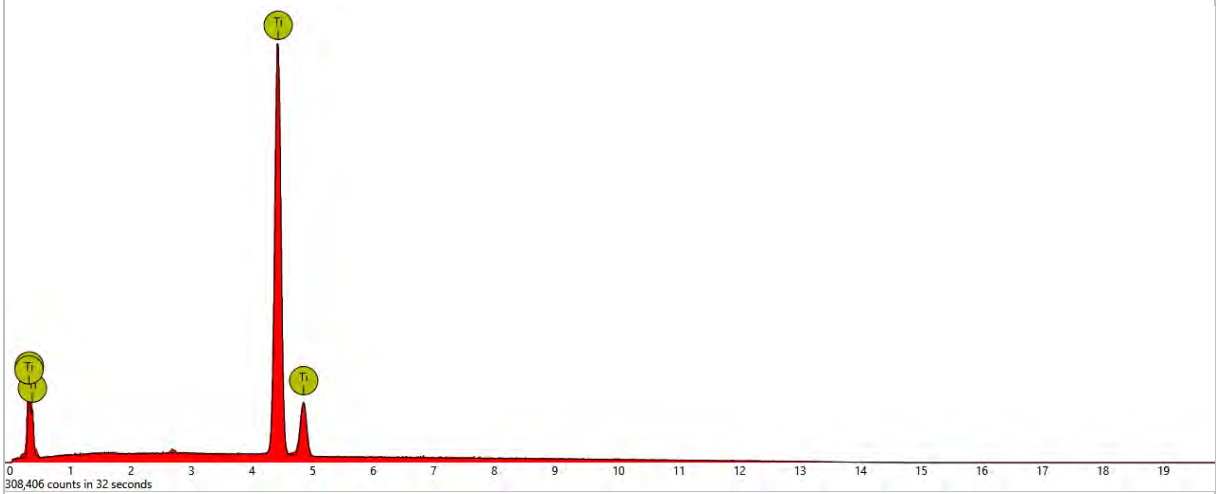
EDS Area Analysis



Area analysis



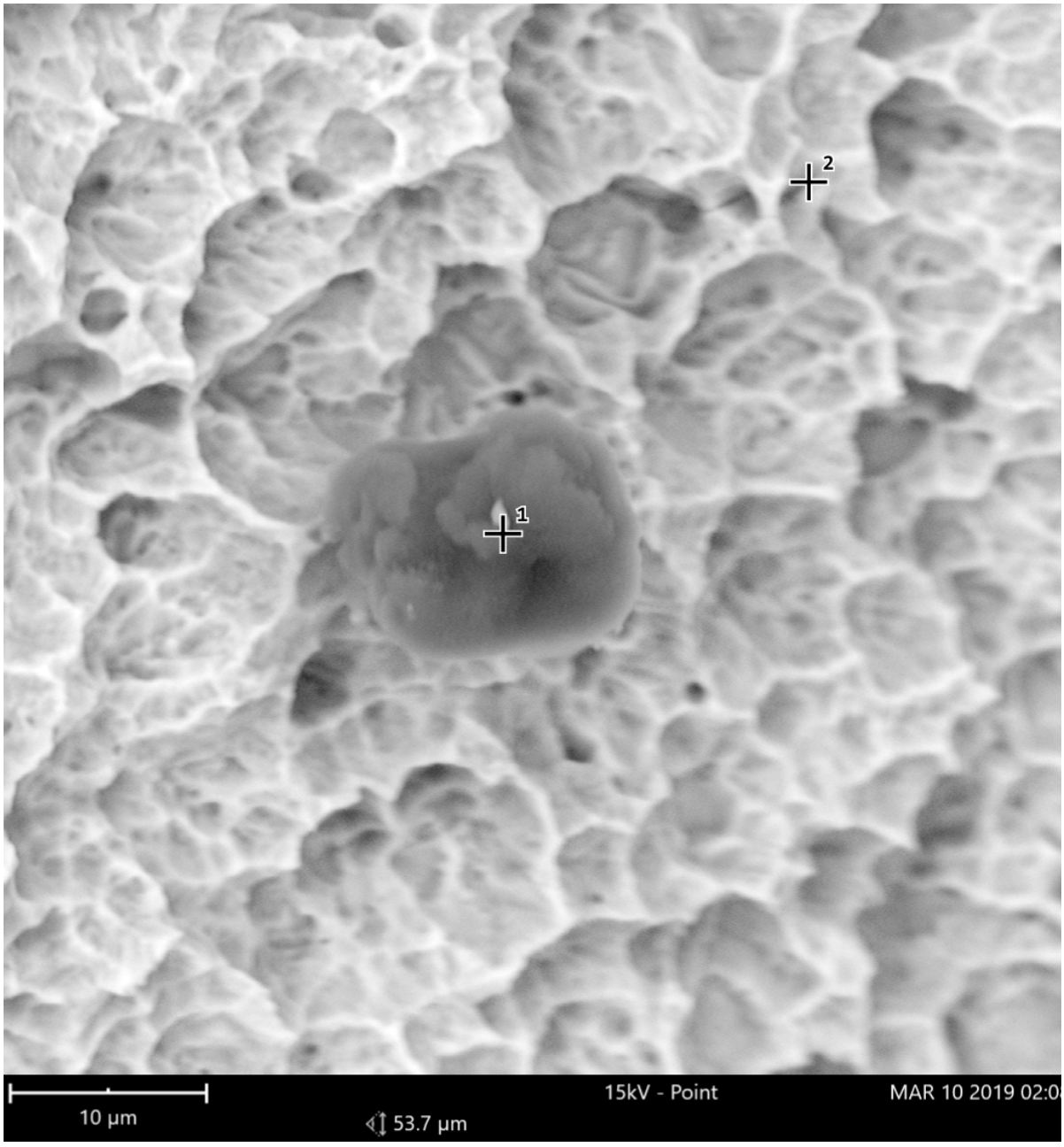
Quantitative elemental analysis



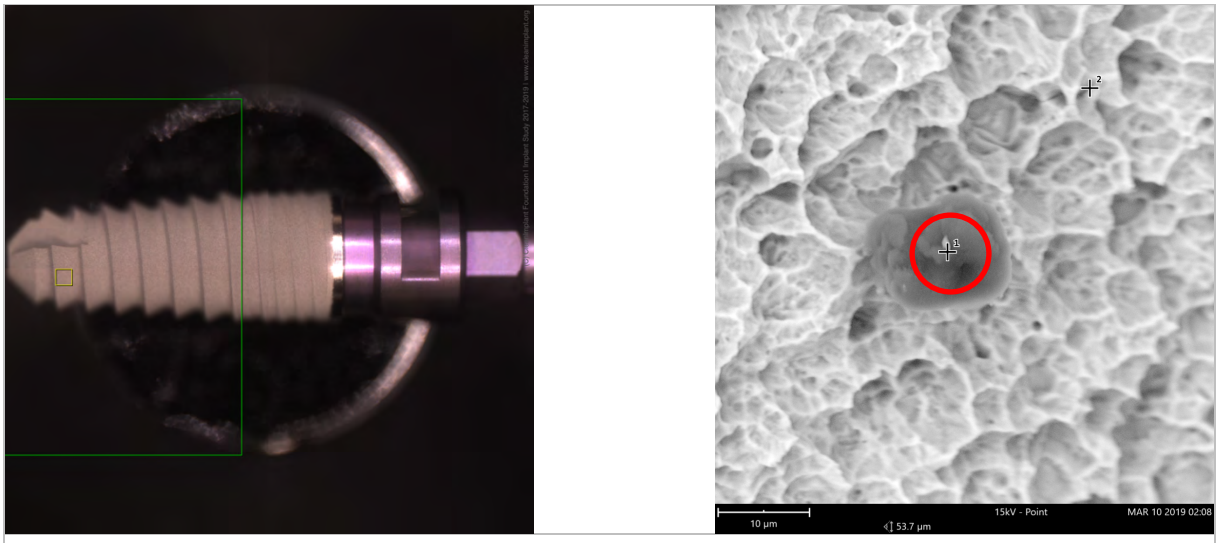
Qualitative elemental analysis

3.3.2 EDS Analysis Spot_1

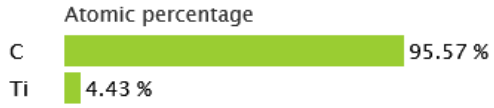
Overview



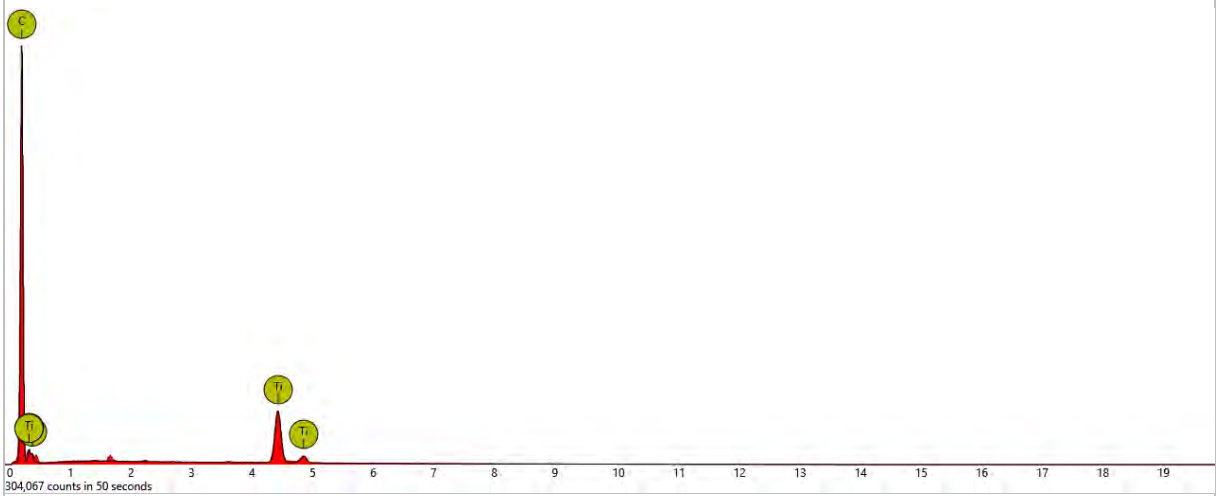
EDS Analysis Spot_1



Spot reading #1

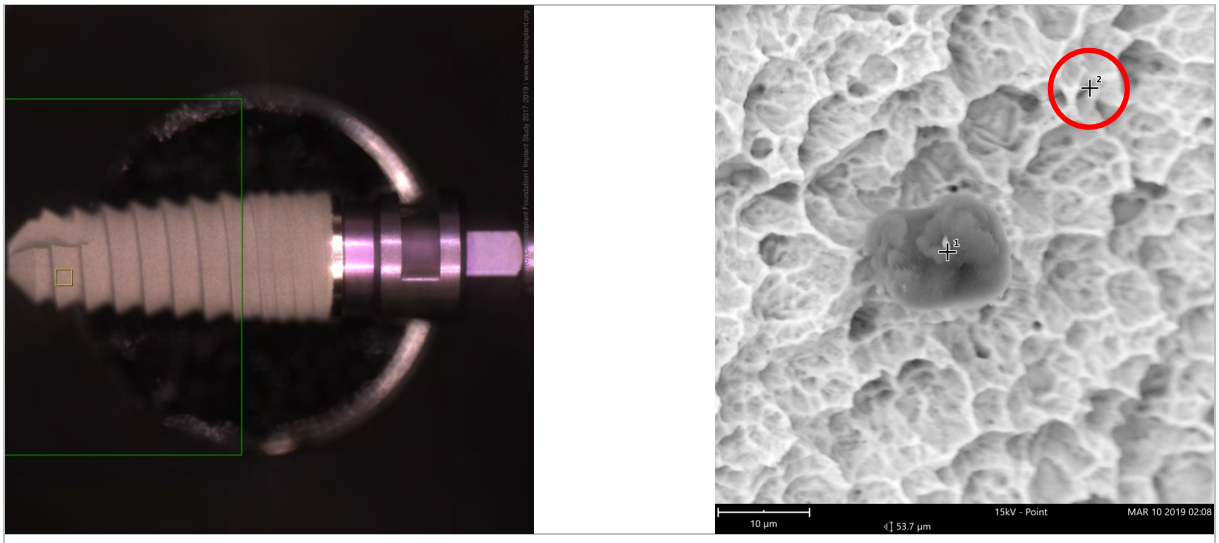


Quantitative elemental analysis

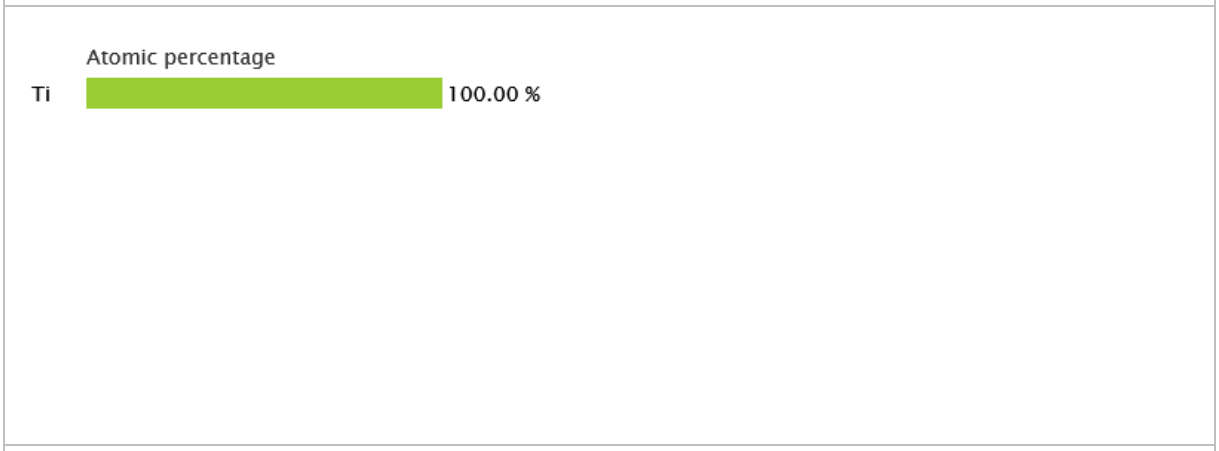


Qualitative elemental analysis

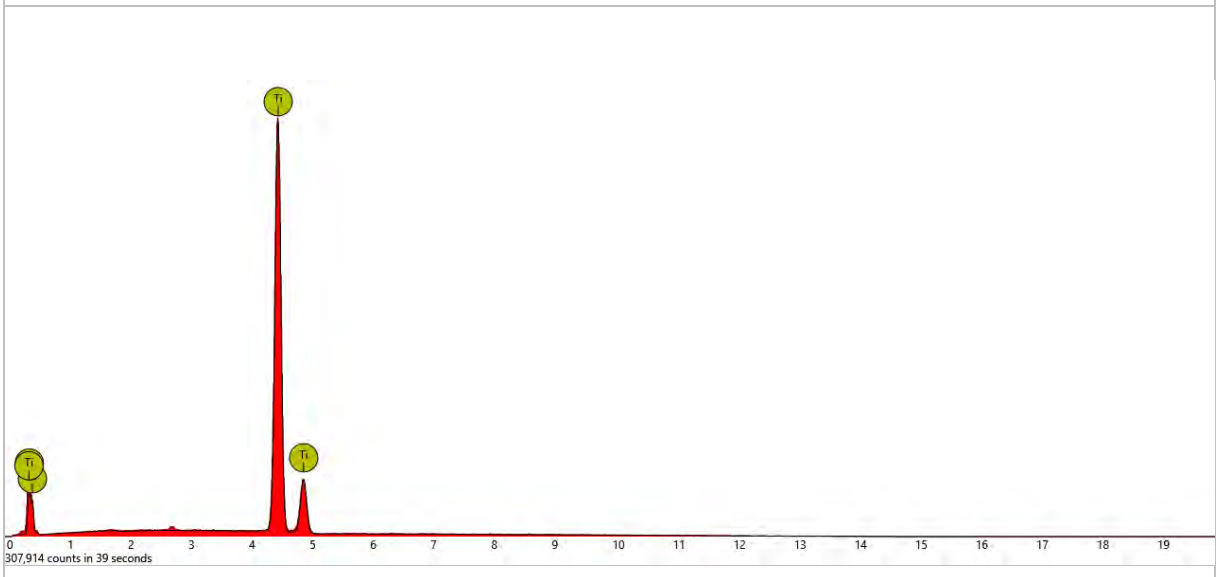
EDS Analysis Spot_1



Spot reading #2

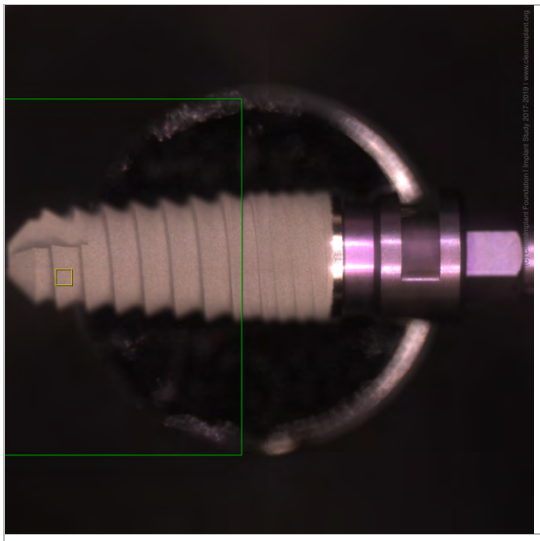


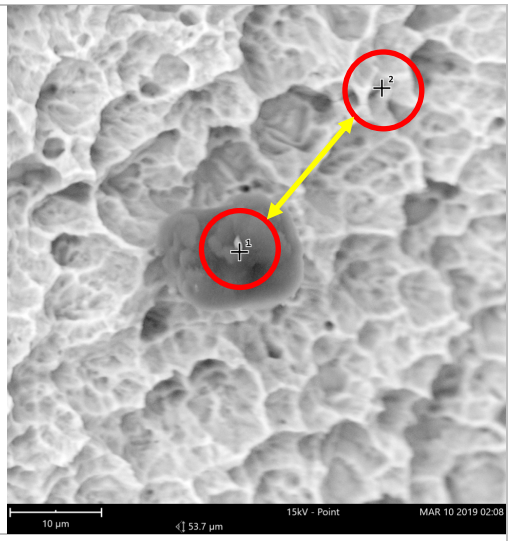
Quantitative elemental analysis



Qualitative elemental analysis

EDS Analysis Spot_1 (Differential Spectrum)





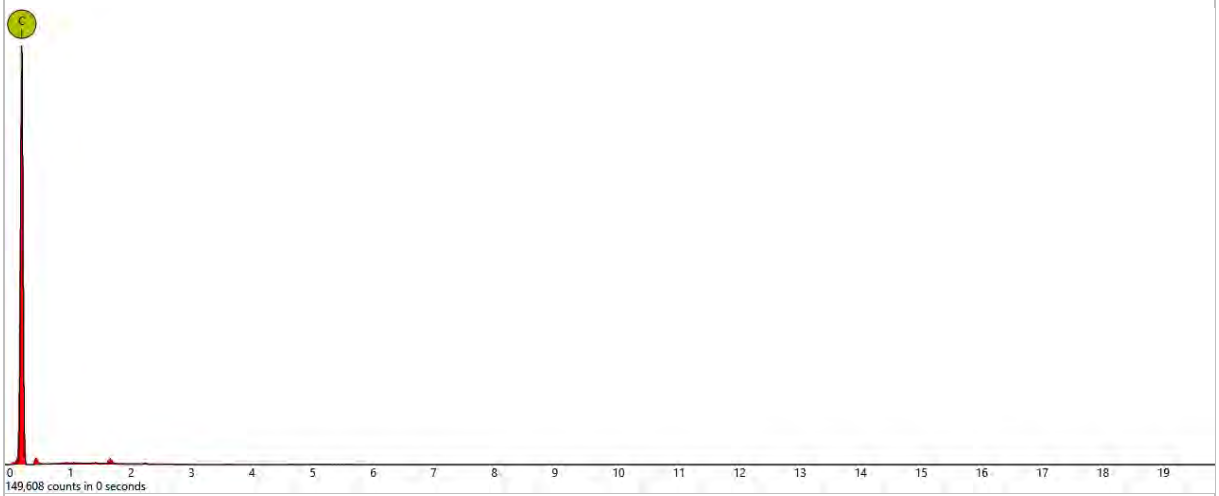
Differential measurement: #1 minus #2

Atomic percentage

C 100.00 %

The differential spectrum deducts X-ray quanta from the core material and focuses on signals from the superficial material.

Quantitative elemental analysis



Qualitative elemental analysis

4 Synopsis

Name of Manufacturer:	Bego Implant Systems GmbH
Analyzed Product(s):	Semados TiPure+ LOT 038485 0917 valid 2022-09 based up on mmri report no.18-00002-096
Investigator/s:	Dr. Dirk U. Duddeck
Analyses carried out by:	mmri.berlin - medical materials research institute Test Laboratory according DIN EN ISO/IEC 17025
Analysis period:	March 2019
Methodology:	Phenom proX Scanning Electron Microscope, equipped with high-sensitivity backscattered electron detector; EDS Analysis detector type: Silicon Drift Detector (SDD) Thermoelectrically cooled (LN_2 free), Detector active area: 25 mm^2, Ultra-thin Silicon Nitride (Si_3N_4) X-ray window allowing detection of elements C to Am, Energy resolution Mn Kα ≤ 140 eV, Max. Input count rate: 300,000 cps
Summary/Conclusions:	The implant sample showed a single carbon-based particle with a diameter of 10-20 µm.

5 COORDINATING INVESTIGATOR(S) SIGNATURE(S)

TITLE: Preliminary Study Report: Implant Study 2017-2019
On Cleanliness of Sterile Dental Implants -
A Global Quality Assessment of Implant Surfaces
by SEM/EDS Analysis

AUTHOR OF REPORT: Dr. Dirk U. Duddeck

Principal Investigator and Managing Director CleanImplant Foundation
Guest researcher at the Charité University Medicine Berlin - Campus Benjamin Franklin
Department of Prosthodontics, Head: Prof. Dr. Florian Beuer

eMail: duddeck@cleanimplant.org

I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the analyses.

PRINCIPAL INVESTIGATOR: Dr. Dirk U. Duddeck

DATE: December 10, 2019