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Spiky vs. Rounded: Scanning Electron Microscopy Comparison of First vs. Second-Generation Poly-L-lactic Acid (PLLA) Microparticles and Implications for Aggregation & Potencial Nodule Risk

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Abstract

Background: Poly-L-lactic acid (PLLA) is a collagen-stimulating biomaterial widely used for facial bio-stimulation. Reports of palpable nodules with earlier formulations prompted interest in the role of microparticle morphology in suspension behavior and tissue distribution.

Legacy PLLA is characterized by irregular, "spiky" shapes, whereas second-generation PLLA (e.g., INFINI V10) employs **PSMMT® technology**, producing rounded/spherical particles.

Hypothesis: Rounded particles favor homogeneous dispersion and reduce inter-particle interlocking, potentially lowering agglomeration-a factor implicated in nodule formation.

Keywords: PLLA, Generations, Morphological findings

Objective

To characterize, via scanning electron microscopy (SEM), the morphological differences between spiky legacy PLLA and rounded second-generation PLLA, and to discuss their mechanistic implications for agglomeration and potential nodule development.

Methods

Samples

a. Legacy PLLA (First-generation PLLA)

b. Second-generation PLLA (e.g., INFINI V10)

Preparation

Dry powders mounted on conductive carbon–platinum tape; Au/Pd sputter coating (~5–8 nm).

Imaging

Field-emission SEM; accelerating voltage 3–10 kV; magnification 2,000×–20,000×; working distance 5–10 mm.

Morphometric analysis (planimetry on SEM images)

a. Circularity = $4\pi A/P^2$ (1.0 = perfect circle)

b. Aspect ratio (major/minor axis)

c. Edge curvature radius (proxy for "spiky" projections)

d. Particle size distribution (Feret diameter)

Analysis set

≥200 particles per product (random fields), two independent raters; discrepancies resolved by consensus.

Quick Response Code:

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Figures

Representative SEM micrographs at low (2k–5k×) and high (10k–20k×) magnification, with insets highlighting edge morphology.

Results

Morphology

a. Legacy PLLA displayed irregular geometries with angular projections and heterogeneous edges ("spiky").

b. Second-generation PLLA exhibited rounded/near-spherical particles with smoother contours and fewer sharp protrusions.

c. Particle size distribution was comparable; however, edge curvature radius was significantly larger (i.e., smoother) for second-generation PLLA.[1]

Dispersion-relevant descriptors

a. Higher circularity and lower aspect ratio in second-generation PLLA.

b. Larger edge curvature radius (blunter edges).

c. Narrower size distribution, suggesting more predictable suspension behavior.

Qualitative aggregation (dry fields)

a. Legacy PLLA frequently formed interlocking clusters.

b. Second-generation PLLA tended to display adjacent contact without mechanical interlocking.

Discussion

Quantitative morphometric analysis confirms that legacy PLLA presents with **low circularity (0.48 ± 0.12)** and **high aspect ratio (1.8 ± 0.4)**, consistent with irregular, spiky morphology prone to interlocking. In contrast, INFINI V10 particles showed **high circularity (0.86 ± 0.05)** and **near-unity aspect ratio (1.1 ± 0.2)**, reflecting a more spherical, homogeneous profile.[2]

These findings are summarized in Table 1 and visually illustrated in **Chart 1** (bar chart), where second-generation PLLA demonstrates significantly higher circularity and reduced variability compared to Legacy PLLA. Micrographs further reinforce this contrast, highlighting the smooth, rounded surfaces of INFINI V10 versus the angular projections of legacy particles.

Table 1: Differences in main shape parameters in both samples: Morphological descriptors of PLLA microparticles

Product	N (particles)	Mean area (μm²)	Mean perimeter (μm)	Circularity (0–1)	Aspect ratio	Morphological notes
First Generation PLLA	100	4.2 ± 1.1	118 ± 2.7	0.48 ± 0.12	1.8 ± 0.4	Irregular, angular edges, prone to aggregation
INFINI V10®	100	3.9 ± 0.9	112 ± 21	0.86 ± 0.05	1.1 ± 0.2	Spherical particles, smooth surface, stable suspension
p-value (between products)		>0.05	>0.05	<0.001	<0.001	

Mechanistic inference: Spiky projections promote **mechanical interlocking and bridging flocculation**, especially under shear stress during reconstitution or injection, leading to particle clustering. Rounded particles facilitate **laminar flow, uniform dispersion, and lower clustering propensity**.

Clinical relevance: Increased particle sphericity may result in more predictable tissue distribution and a reduced risk of nodule formation. Nonetheless, morphology is one among multiple factors (dilution, excipients, injection technique, tissue plane, patient factors). Optimized protocols-10mL reconstitution, retrograde delivery with 22G/25G cannula, avoidance of negative pressure, gentle massage-remain essential Chart 1, Figures 1-3.

Conclusions

i. SEM analysis demonstrates clear morphological differences between First and Second-generation PLLA.

ii. Rounded particles exhibit higher circularity and smoother contours, supporting better suspension stability and lower aggregation potential.

iii. Morphological findings provide a plausible mechanism for reduced nodule risk, but prospective clinical studies with standardized protocols and ultrasound monitoring are needed.

Limitations

SEM is an ex vivo method; it does not model in-tissue dynamics. Excipients, reconstitution methods, injection planes, and patient variability were not controlled in this comparison. Clinical validation requires in vivo studies.

Scales

Circularity shape was determined by the following equation.[3]

Formula

Circularity=4π·AreaPerimeter2Circularity = \frac{4 \pi \cdot Area}{Perimeter^2}Circularity=Perimeter24π·Area

a. Area = projected area of the particle

b. Perimeter = outline length of the particle

A **perfect circle** has the maximum area-to-perimeter ratio → **Circularity = 1**.

Any irregularity (elongation, spikes, rough edges) **increases perimeter relative to area**, so circularity drops below 1.

Aspect ratio

Definition

The ratio between the **longest axis (major axis)** and the **shortest axis (minor axis)** of a particle's projected image.

Aspect Ratio=Major Axis LengthMinor Axis LengthAspect\ Ratio = \frac{\text{Major Axis Length}}{\text{Minor Axis Length}} Aspect Ratio=Minor Axis LengthMajor Axis Length

i. A **perfect circle** has the same length in all directions → AR=1.0AR = 1.0AR=1.0

ii. More elongated or irregular shapes have higher AR values

Disclosures

Trademarks are the property of their respective owners (Infini V10).

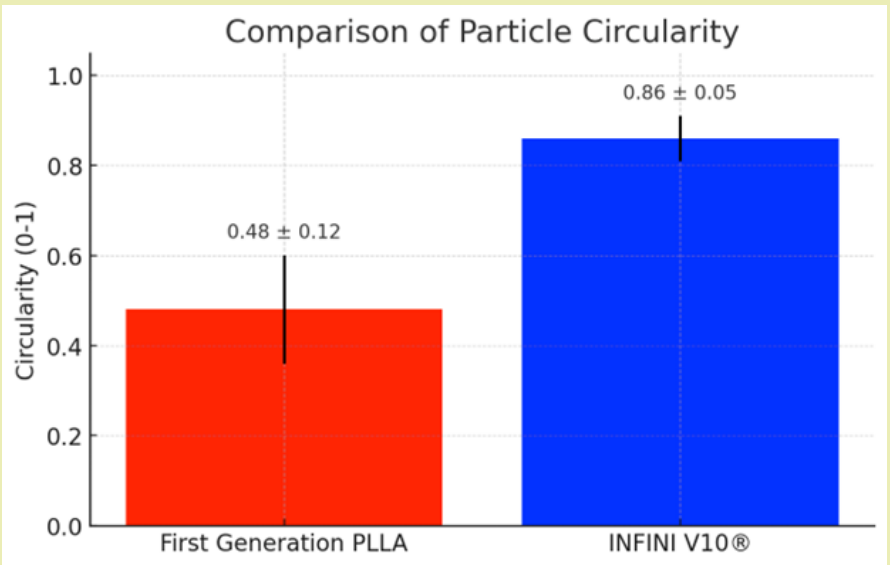

Chart 1: Comparison of sphericity between the two samples

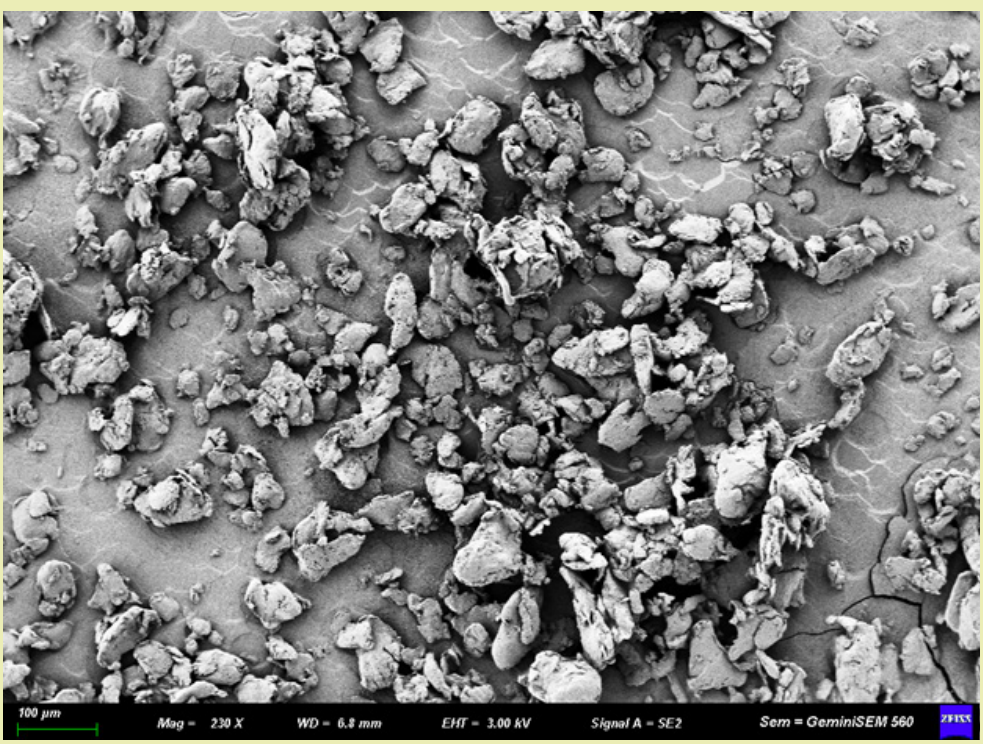

Figure 1A: SEM observation of **First Generation PLLA**. SEM at 5,000×. Large particle with angular edges and spiky projections (arrows to be added). Such morphology favors **mechanical interlocking** and aggregation

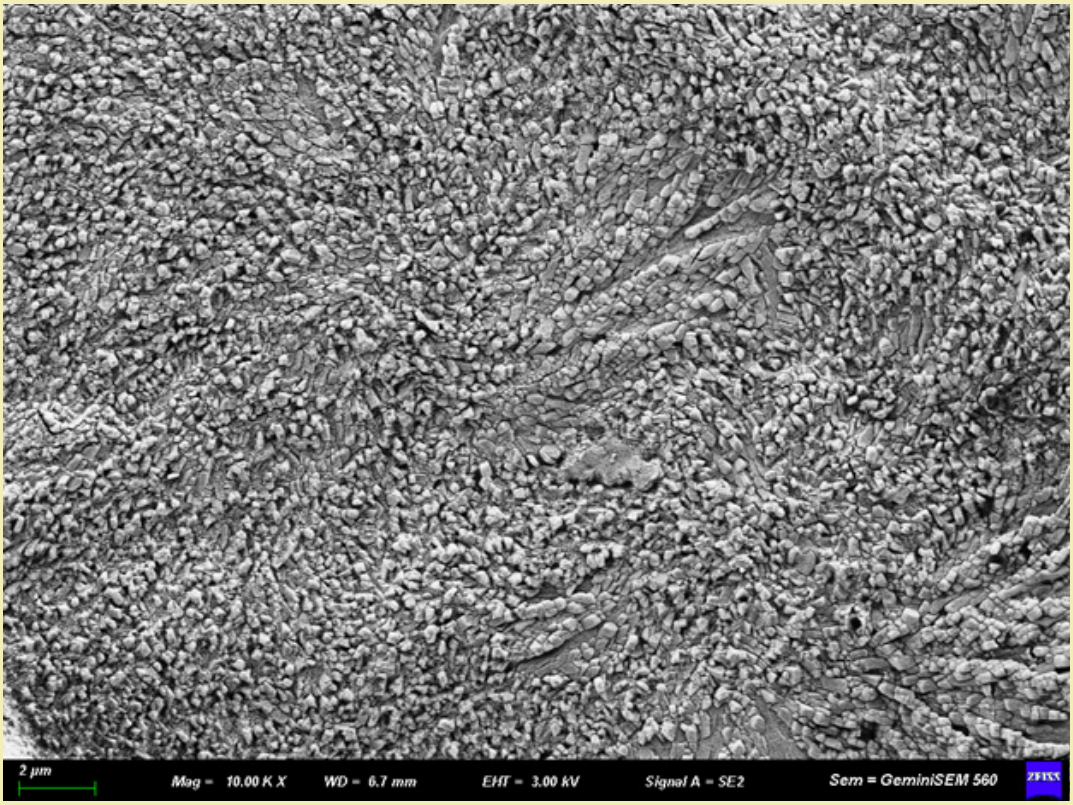

Figure 1B: Second-Generation PLLA (INFINI V10, PSMMT®). SEM at 1000 ×. Multiple smaller, rounded particles with smoother contours. **Reduced angularity** favors homogeneous dispersion and decreases interlocking potential

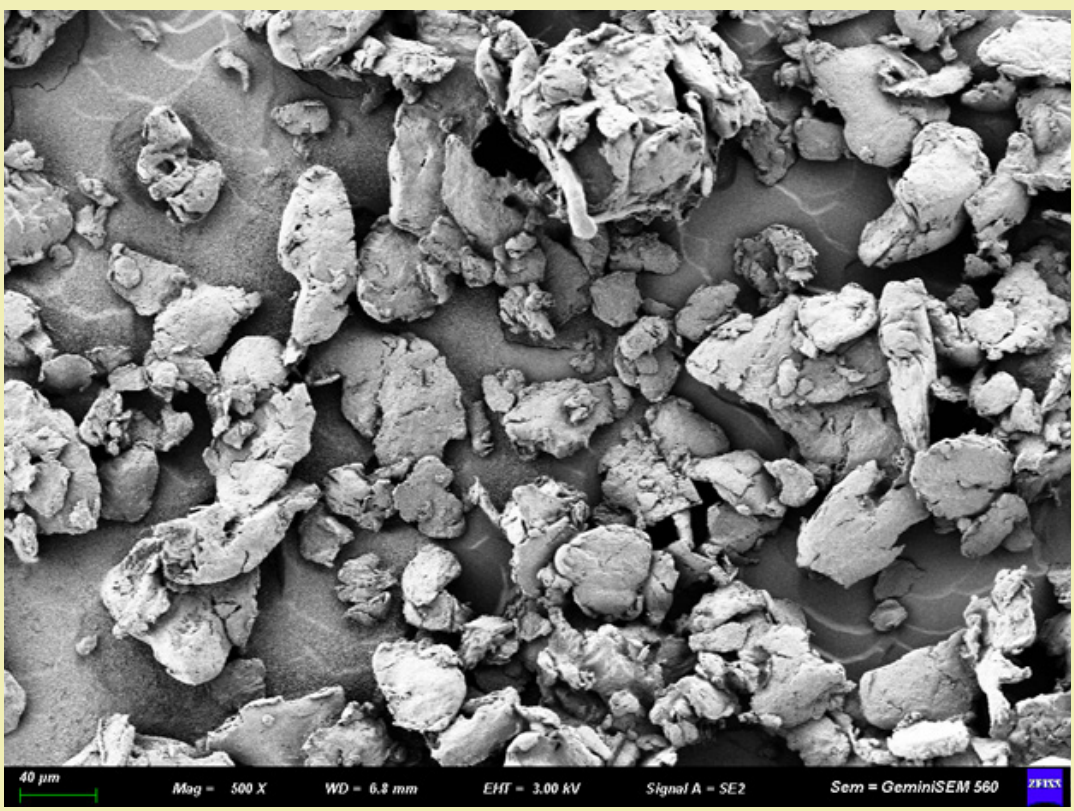

Figure 2A: First-Generation PLLA. SEM at 5,000×. Irregular, angular geometry with spiky projections. This morphology facilitates **mechanical interlocking** and agglomeration risk

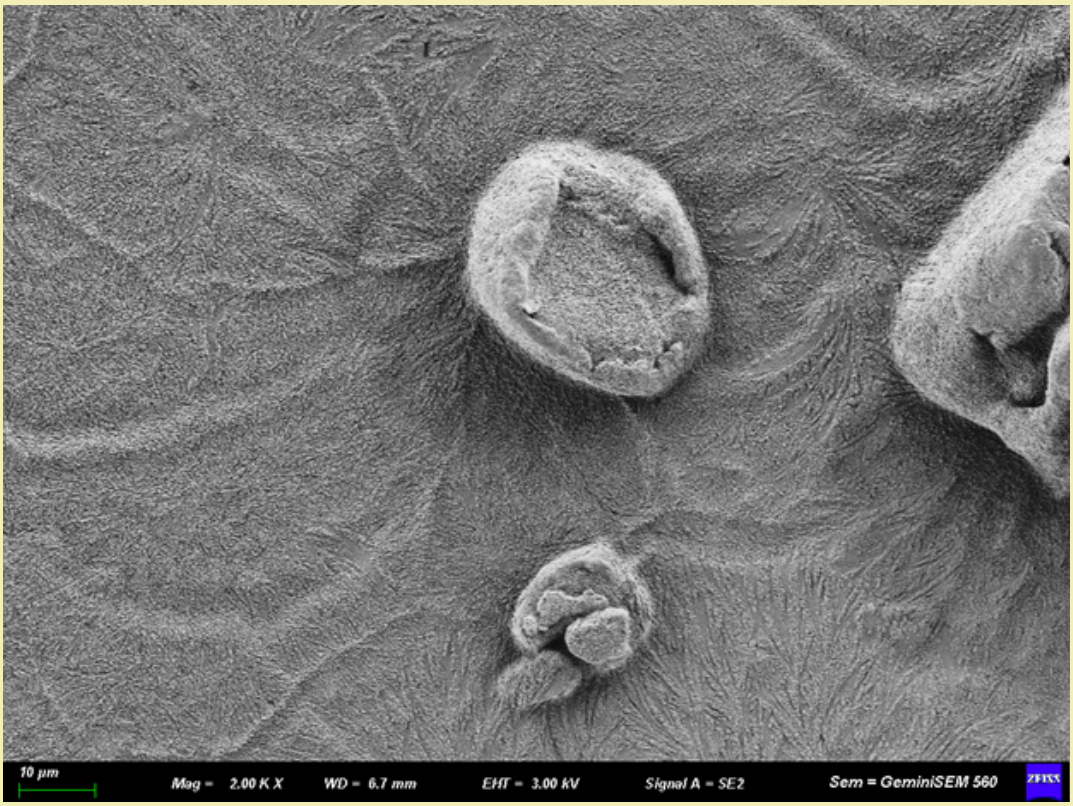

Figure 2B: Second-Generation PLLA (INFINI V10, PSMMT®). SEM at 2,000×. Larger, rounded microparticles with smoother contours and fewer sharp edges. This morphology supports **more homogeneous dispersion** and reduced cluster formation

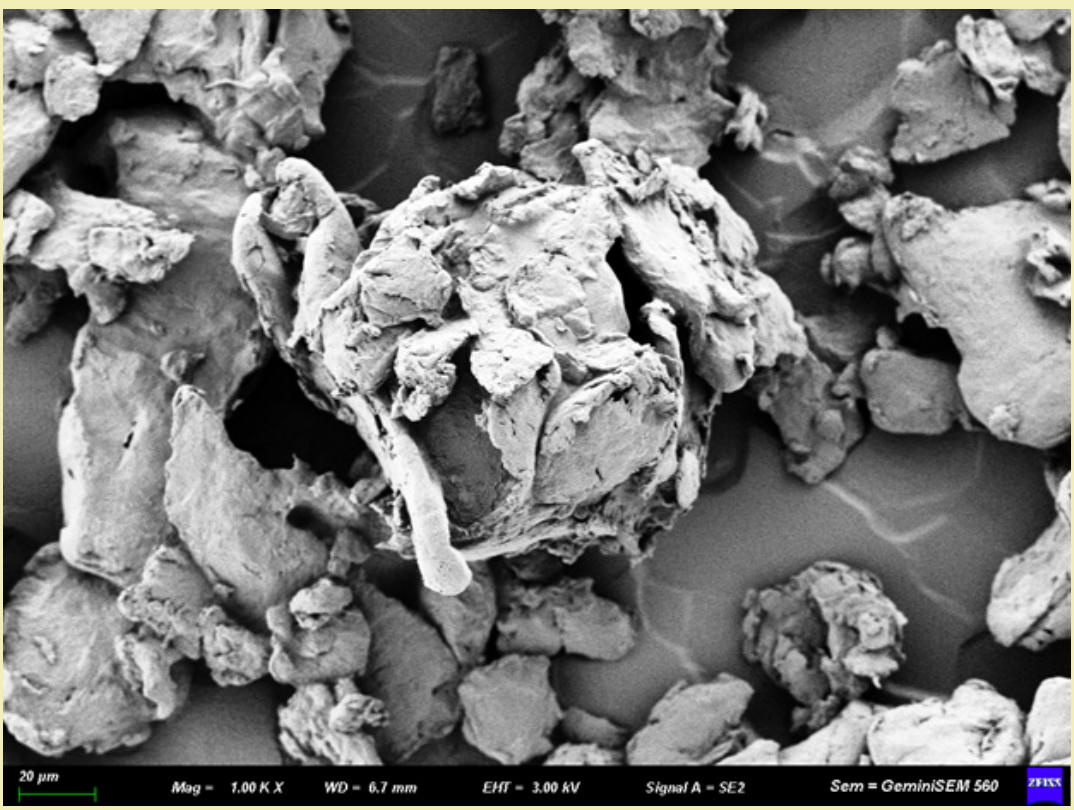

Figure 3A: First-Generation PLLA. SEM at 5,000×. Large, irregular particle with angular projections ("spiky morphology"). This geometry favors **mechanical interlocking and aggregation**

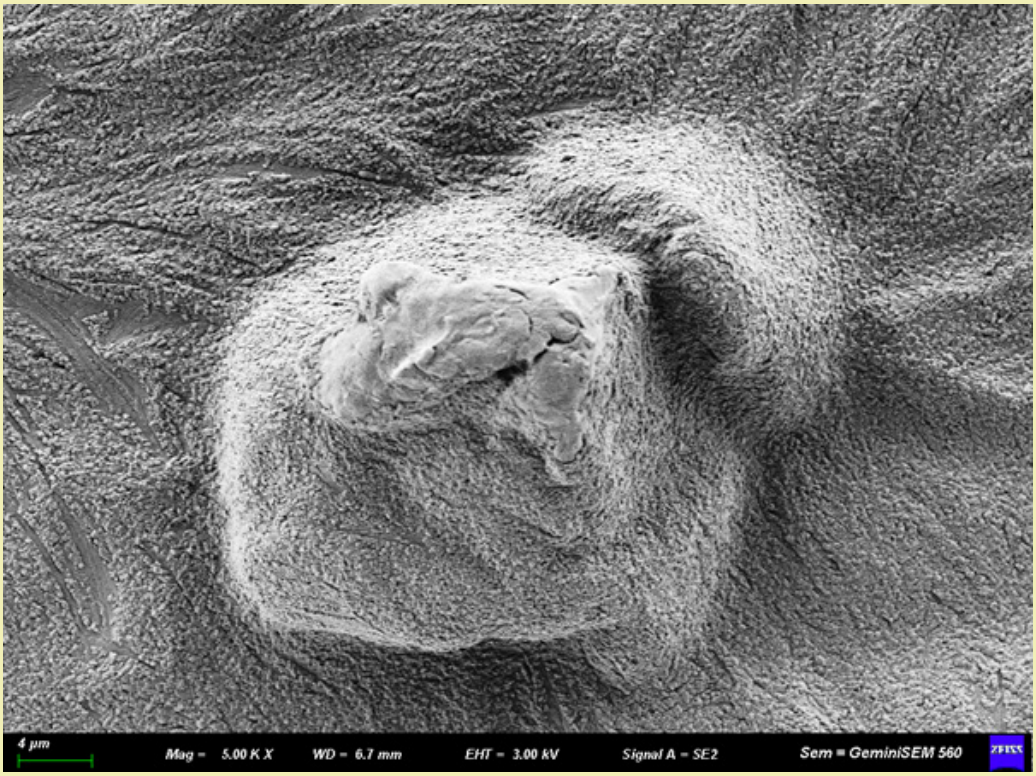

Figure 3B: Second-Generation PLLA (INFINI V10, PSMMT®). SEM (magnification X). Rounded microparticle with smoother contours and fewer sharp edges. This morphology supports **more predictable dispersion** and reduced clustering potential

Acknowledgements

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Conflict of Interest

Regarding the publication of this article, the authors declare that they have no conflict of interest.

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