

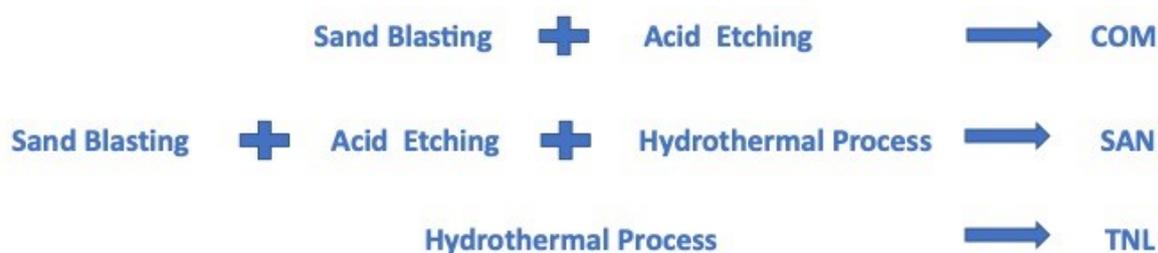
**Supporting Information (SI)**

**Superhydrophilic Multifunctional Nanotextured Titanium Dental Implants:**

**In Vivo Short and Long-term Response in a Porcine Model**

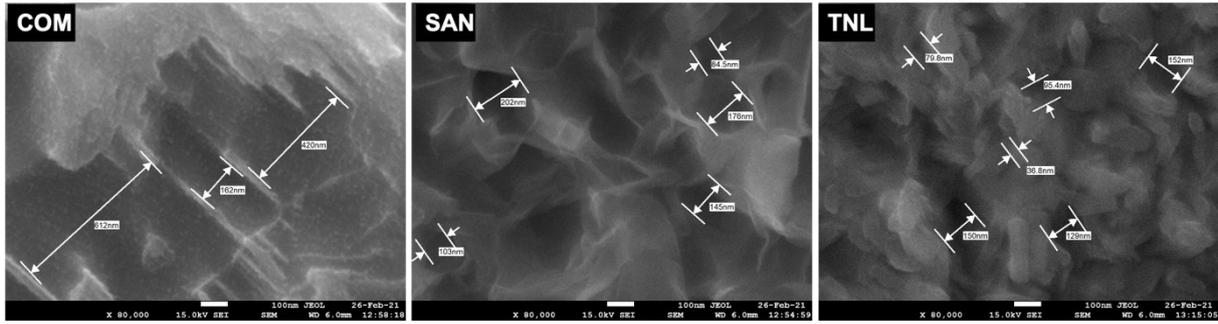
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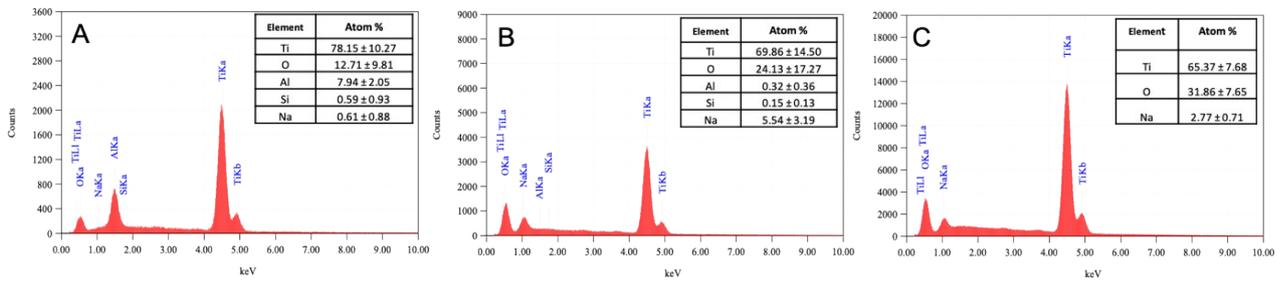


Sand Blasting	Acid Etching				Hydrothermal Process
<p>Alumina-110 microns Distance-35 mm 20 secs at 6 points</p>	Hydrofluoric acid (15%) 1 min	Water 2 min	Sodium bicarbonate 90mg/ml 0.5 min	Water 2 min	<p>Temperature (200°C) Time (~ 4h) pH (13-14 using NaOH)</p>
	Sulphuric acid (96%) 3 min	Water 2 min	Sodium bicarbonate 90mg/ml 0.5 min	Water 2 min	
	Hydrochloric acid (37%) 3 min	Water 2 min	Sodium bicarbonate 90mg/ml 0.5 min	Water 2 min	

**Figure S1: Schematic of the different processing steps involved in fabricating COM, SAN, TNL samples**



**Figure S2: High magnification SEM images (80,000X) of COM, SAN, TNL obtained on Titanium plates**



**Figure S3: EDS Spectra of (A) COM, (B) SAN and (C) TNL samples. Inset shows the atomic percentage of individual elements present on the samples**

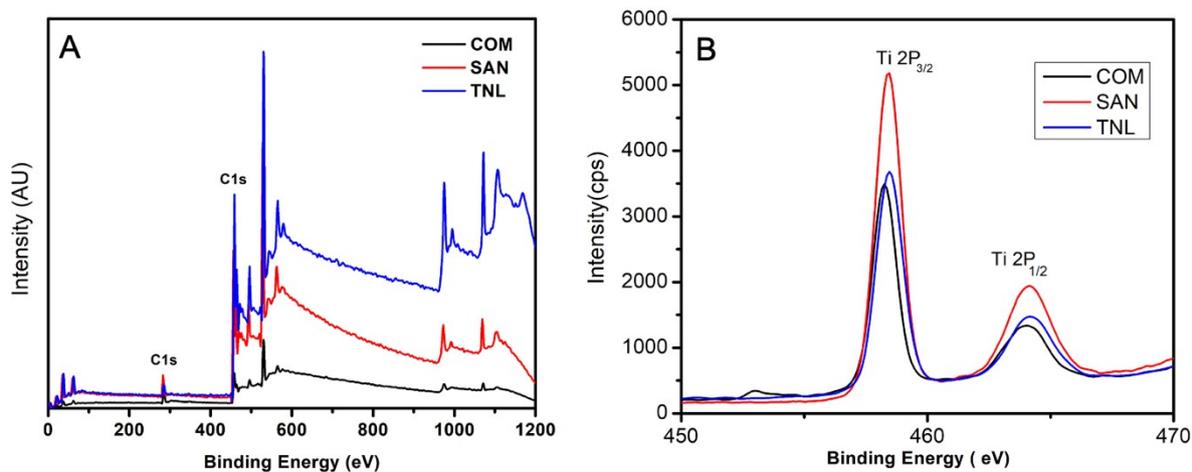


Figure S4: X-ray photoelectron spectra of COM, SAN and TNL samples. (A) Wide spectra and (B) High resolution spectra

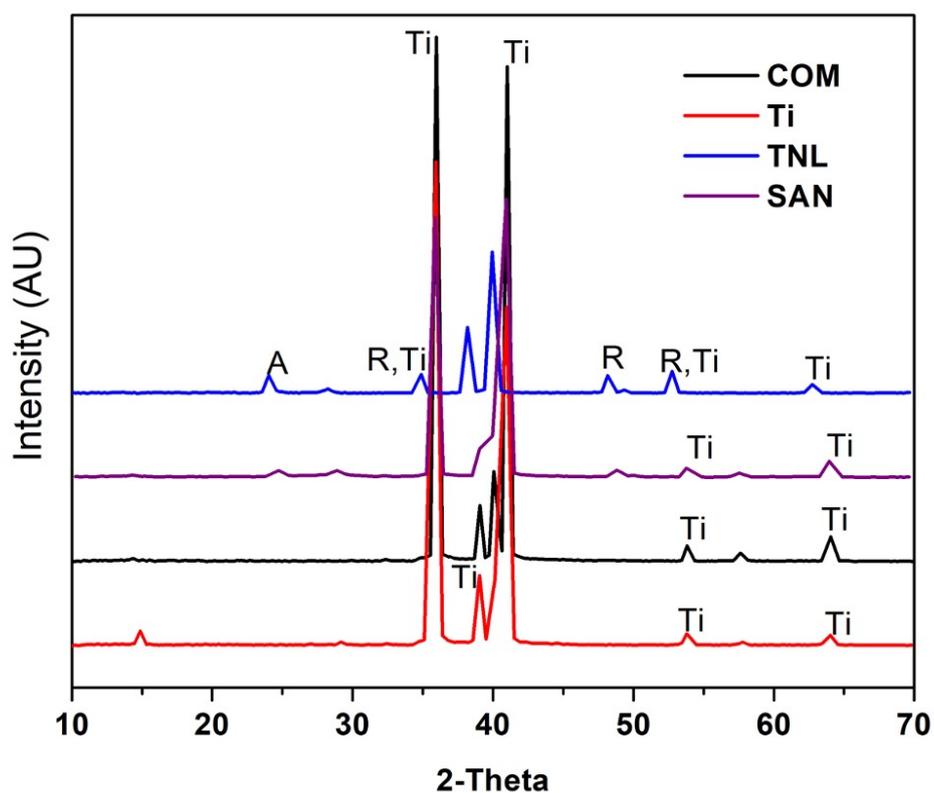
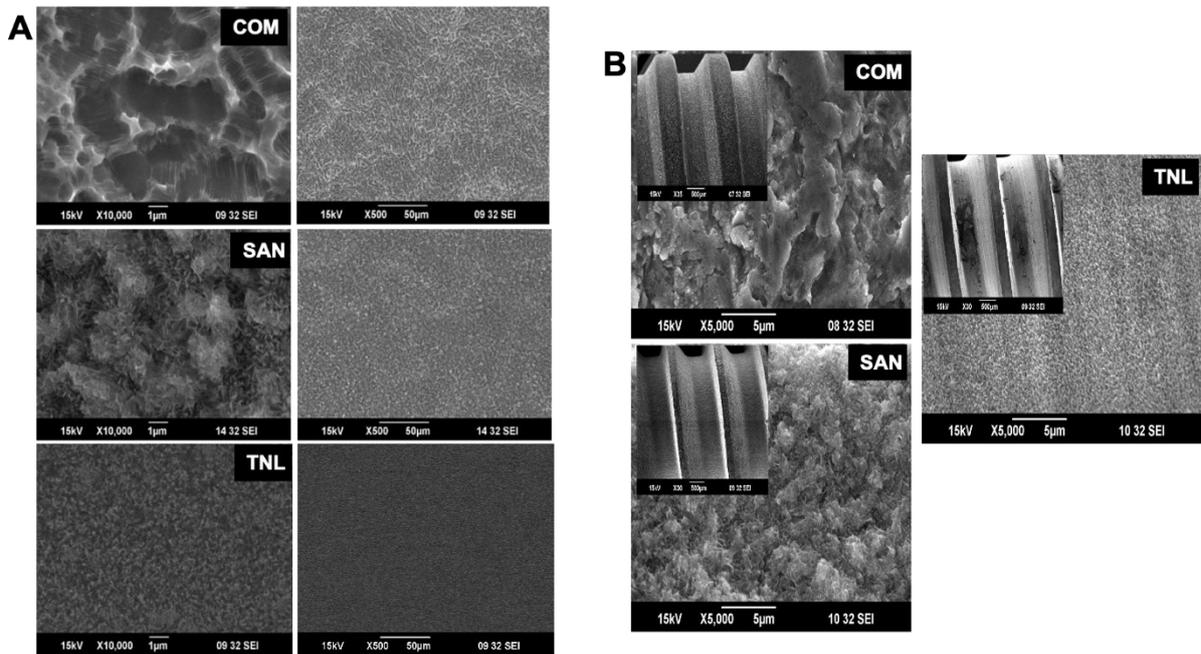
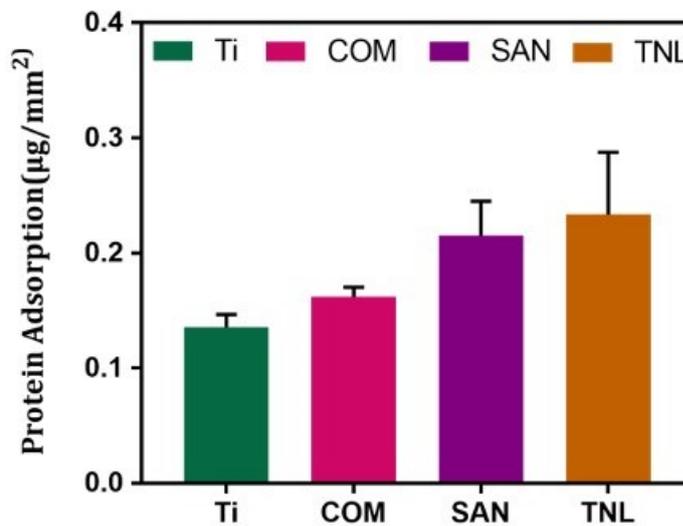


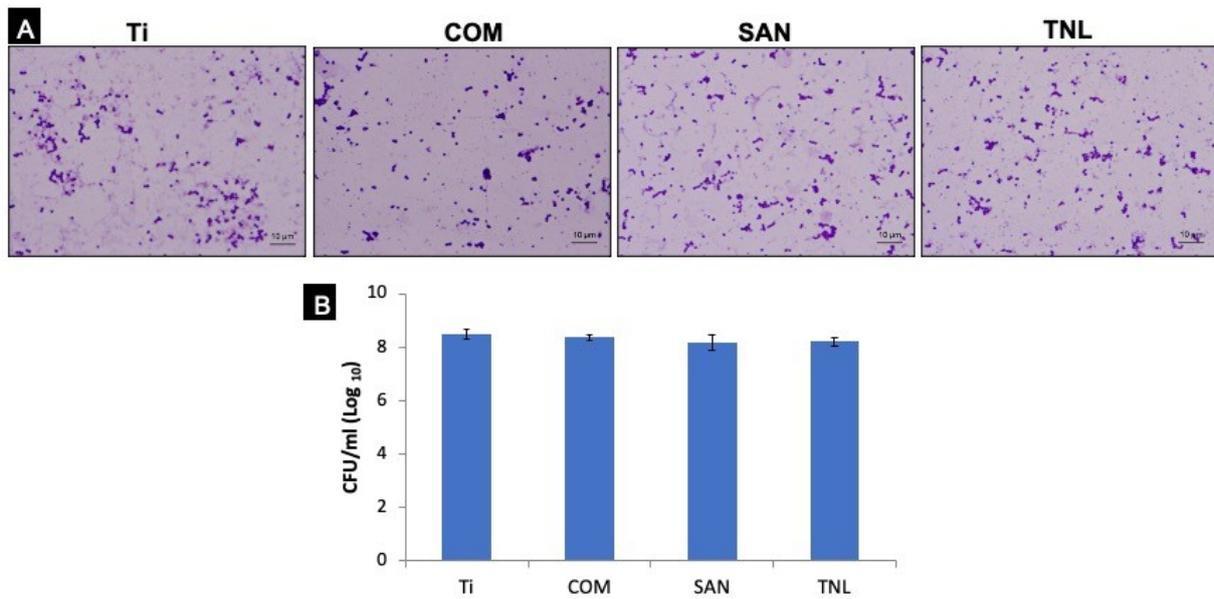
Figure S5: XRD spectra of COM, SAN and TNL samples in comparison to Ti



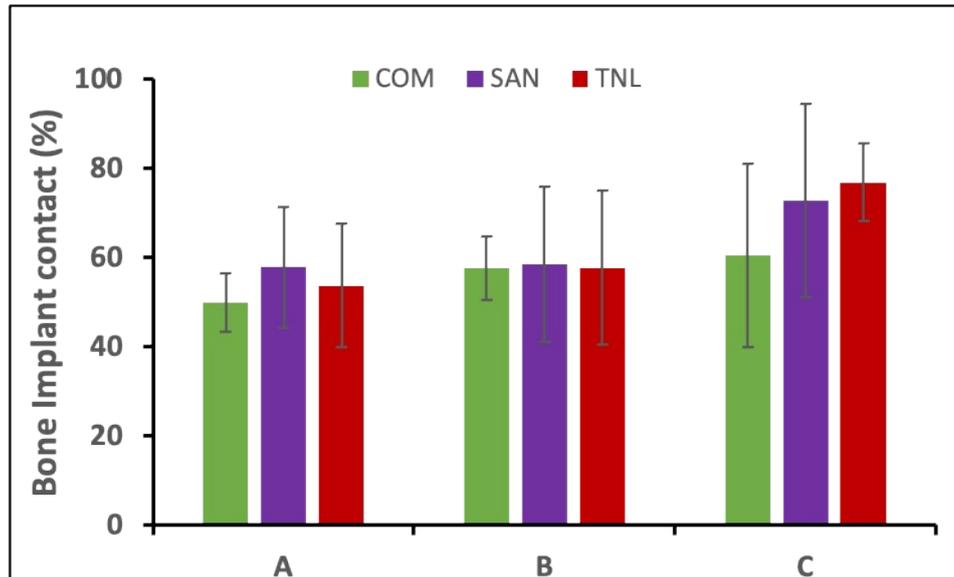
**Figure S6: (A) COM, SAN and TNL samples after ion leaching experiments for a duration of 8 weeks and (B) SEM images of ex vivo COM, SAN and TNL implants retrieved from the osteotomy sites after implantation, showing stability of the surface structures**



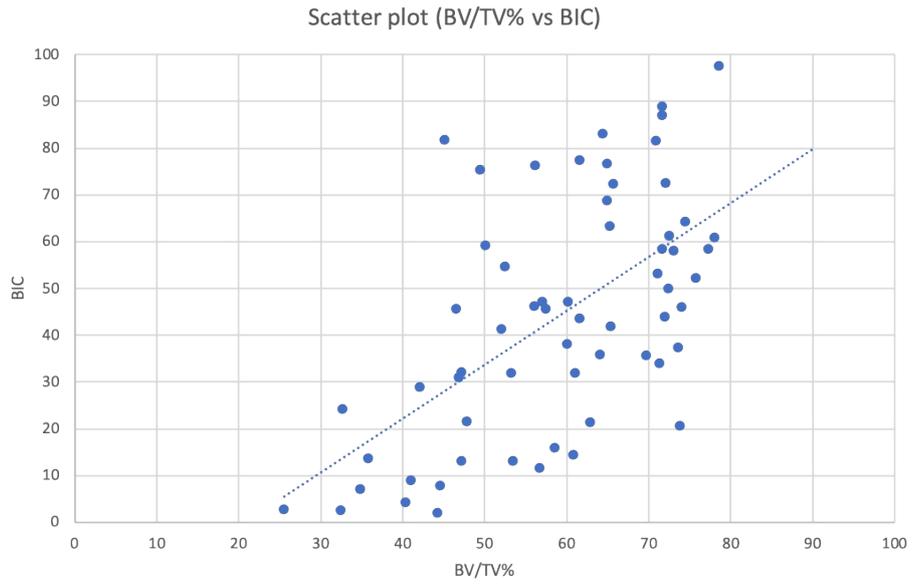
**Figure S7. Protein adsorption on polished Ti, COM, SAN and TNL samples after 1 h of incubation with Fetal Bovine Serum, measured by BCA assay.**



**Figure S8. (A) Gram staining showing no significant anti-bacterial activity on polished Ti, COM, SAN and TNL samples and (B) Anti-bacterial activity plot showing the total number of bacteria on different samples after 48 h.**



**Figure S9: Graph representing the variations in percentage bone implant contact (BIC) of the three implants at time points A (pre-loaded), B and C (loaded)**



**Figure S10: Correlation analysis of the results of  $\mu$ -CT (BV/TV value) and histology (BIC values)**

**Table S1: Acid etching protocol for indigenous blasted etched surface**

Etchant	Hydrofluoric acid (15%)	Water	Sodium bicarbonate 90mg/ml	Water
Time	1 min	2 min	0.5 min	2 min
Etchant	Sulphuric acid (96%)	Water	Sodium bicarbonate 90mg/ml	Water
Time	3 min	2 min	0.5 min	2 min
Etchant	Hydrochloric acid (37%)	Water	Sodium bicarbonate 90mg/ml	Water
Time	3 min	2 min	0.5 min	2 min

**Table S2. Chemical composition of fresh and aged COM, SAN and TNL surfaces obtained by XPS analysis**

Sample	C content (C 1s) Atomic Conc %	O content (O 1s) Atomic Conc %	Ti content (Ti 2p) Atomic Conc %
Ti - fresh	36.98	51.79	11.23
Ti – 6 months	61.86	32.72	5.42
COM - fresh	61.45	30.40	8.15
COM – 6 months	52.44	43.80	3.76
SAN - fresh	24.20	58.44	17.36
SAN – 6 months	26.28	59.21	14.51
TNL - fresh	25.95	57.52	16.53
TNL – 6 months	30.66	53.26	16.08

**Table S3: Bone Implant contact of COM, SAN and TNL at different time points measured by histomorphometry, \*p< 0.05 is considered statistically significant.**

<b>Time point</b>	<b>Group</b>	<b>N</b>	<b>Mean</b>	<b>Median</b>	<b>p value</b>
<b>14 days</b>	COM	2	2.57±0.72	2.57	0.153
	SAN	3	7.96±1.03	7.81	
	TNL	2	7.18±3.45	7.18	
<b>28 days</b>	COM	2	11.90±6.97	11.90	0.368
	SAN	2	12.41±0.97	12.41	
	TNL	2	22.72±11.71	22.72	
<b>Group A</b>	COM	4	49.84±6.61	50.17	0.779
	SAN	4	57.74±13.50	58.28	
	TNL	6	53.62±13.89	48.61	
<b>Group B</b>	COM	4	57.43±7.14	59.64	0.736
	SAN	5	58.55±17.43	54.81	
	TNL	4	57.61±17.28	52.07	
<b>Group C</b>	COM	5	60.33±20.54	59.23	0.309
	SAN	3	72.70±21.69	61.95	
	TNL	4	76.76±8.72	74.57	

**Table S4: Table representing the variations in (A) bone volume percentage – BV/TV (B) mineral density of region of interest – BMD (au) and (C) tissue mineral density of the three different implants at all time points obtained from micro CT analysis. \*p< 0.05 is considered statistically significant.**

**Table S4A**

<b>Time point</b>	<b>Group</b>	<b>N</b>	<b>Mean±SD</b>	<b>Median</b>	<b>p value</b>
<b>14 days</b>	COM	2	40.04±5.96	40.04	0.555
	SAN	3	43.99±2.73	44.54	
	TNL	2	42.24±0.31	42.24	
<b>28 days</b>	COM	2	33.73±1.55	33.73	0.779
	SAN	3	39.98±7.37	40.28	
	TNL	2	36.14±15.03	36.14	
<b>Group A</b>	COM	7	66.01±5.01	65.29	0.055
	SAN	4	73.96±1.52	74.02	
	TNL	6	70.11±12.51	71.61	
<b>Group B</b>	COM	6	69.32±6.65	68.90	0.808
	SAN	4	72.26±0.58	72.21	
	TNL	5	70.58±11.40	66.21	
<b>Group C</b>	COM	4	57.05±	56.60	0.034*
	SAN	3	75.15±	77.21	
	TNL	5	64.60±	64.86	

**Table S4B**

<b>Time point</b>	<b>Group</b>	<b>N</b>	<b>Mean±SD</b>	<b>Median</b>	<b>p value</b>
<b>14 days</b>	COM	2	540.63±380.71	540.63	0.180
	SAN	3	890.44±263.17	935.69	
	TNL	2	1270.99±202.35	1270.99	
<b>28 days</b>	COM	2	465.11±83.79	465.11	0.915
	SAN	3	744.10±429.32	828.70	
	TNL	2	717.22±802.43	717.22	
<b>Group A</b>	COM	7	2554.11±538.42	2787.83	0.031*
	SAN	4	3422.87±119.39	3417.87	
	TNL	6	3283.34±1488.99	3063.05	
<b>Group B</b>	COM	6	2951.59±638.20	3012.13	0.570
	SAN	4	3253.58±287.48	3308.44	
	TNL	5	3133.37±970.56	2929.96	
<b>Group C</b>	COM	4	1856.61±707.41	1888.43	0.008*
	SAN	3	4003.70±489.05	4091.87	
	TNL	5	2988.64±254.19	3048.67	

**Table S4C**

<b>Time point</b>	<b>Group</b>	<b>N</b>	<b>Mean±SD</b>	<b>Median</b>	<b>p value</b>
<b>14 days</b>	COM	2	4667.92±72.57	4667.92	0.448
	SAN	3	4687.94±224.21	4592.54	
	TNL	2	4831.82±264.20	4831.82	
<b>28 days</b>	COM	2	4807.52±140.19	4807.52	0.779
	SAN	3	4694.86±2220.75	4637.00	
<b>Group A</b>	TNL	2	4771.57±351.58	4771.57	0.032*
	COM	7	4890.57±205.59	4784.56	
	SAN	4	5268.96±435.10	5144.81	
<b>Group B</b>	TNL	6	5506.16±671.61	5239.03	0.185
	COM	6	5104.88±255.11	5062.60	
	SAN	4	5149.98±480.58	5145.84	
<b>Group C</b>	TNL	5	4837.54±198.33	4807.85	0.046*
	COM	4	5039.95±334.92	4955.96	
	SAN	3	5771.90±248.94	5700.42	
	TNL	5	5350.77±446.71	5201.17	

**Table S5: Table representing the variations in percentage bone implant contact (BIC) of the three implants at different time points (14 days, 28 days, 4 months (Group A) preloaded, 3 months loaded (Group B) and 10 months loaded (Group C) obtained from  $\mu$ -CT analysis. \*  $p < 0.05$  is considered statistically significant.**

Time point	Group	N	Mean $\pm$ SD	Median	p value
14 days	COM	2	33.22 $\pm$ 2.67	33.22	0.292
	SAN	3	30.19 $\pm$ 12.92	28.83	
	TNL	2	45.01 $\pm$ 5.15	45.01	
28 days	COM	4	52.46 $\pm$ 7.97	52.56	0.618
	SAN	4	55.72 $\pm$ 6.20	53.77	
	TNL	4	56.73 $\pm$ 6.21	55.59	
Group A	COM	7	46.23 $\pm$ 12.22	47.18	0.553
	SAN	8	51.06 $\pm$ 17.45	57.21	
	TNL	5	53.56 $\pm$ 14.17	52.73	
Group B	COM	5	50.80 $\pm$ 4.63	53.38	0.284
	SAN	7	57.60 $\pm$ 6.43	56.72	
	TNL	5	58.99 $\pm$ 15.20	57.11	
Group C	COM	4	48.53 $\pm$ 13.91	45.57	0.231
	SAN	3	64.08 $\pm$ 10.14	60.20	
	TNL	4	64.99 $\pm$ 10.41	62.03	

**Table S6: Inflammatory response of COM, SAN and TNL after 10 months of loading assessed by histopathological evaluation of gingival tissue around the implant. \* p< 0.05 is considered statistically significant.**

<b>Histological features</b>	<b>Group</b>	<b>Grade 0</b>	<b>Grade 1</b>	<b>Grade 2</b>	<b>Grade 3</b>	<b>p value</b>
Inflammation	COM	0	0	2	2	0.355
	TNL	0	2	1	1	
	SAN	0	2	0	2	
Foreign Body	COM	4	0	0	0	-
	TNL	4	0	0	0	
	SAN	4	0	0	0	
Connective Tissue	COM	0	0	0	4	0.549
	TNL	0	0	1	3	
	SAN	0	0	1	3	