Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.
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Supporting Information

Influence of strontium ions incorporated nanosheet-pore topographical titanium substrates on osteogenic differentiation of mesenchymal stem cells *in vitro* and osseointegration *in vivo*

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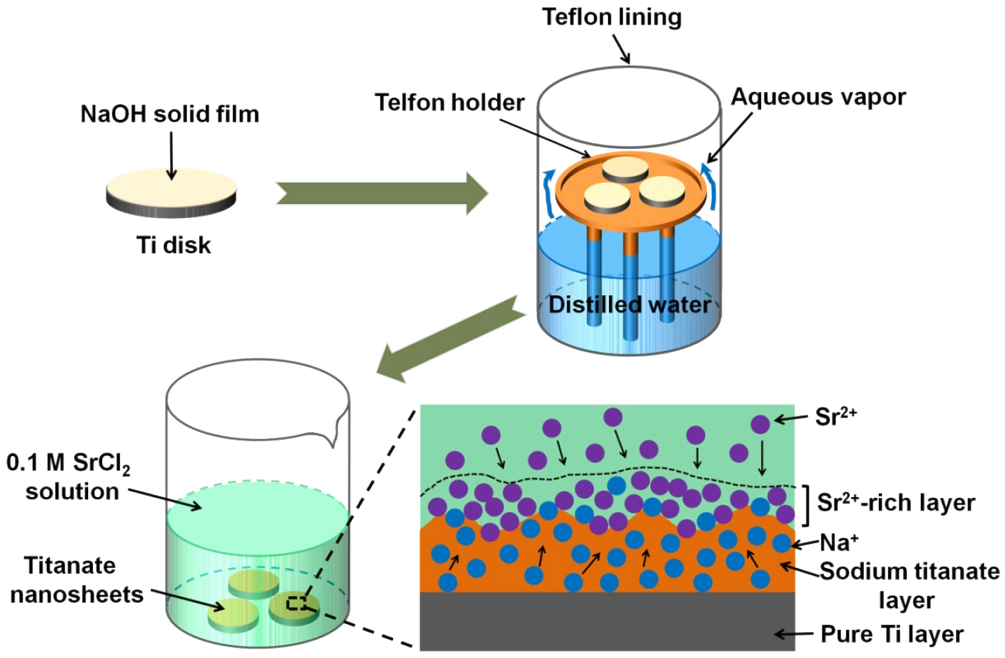


Figure S1. Illustration of the sample fabrication process.

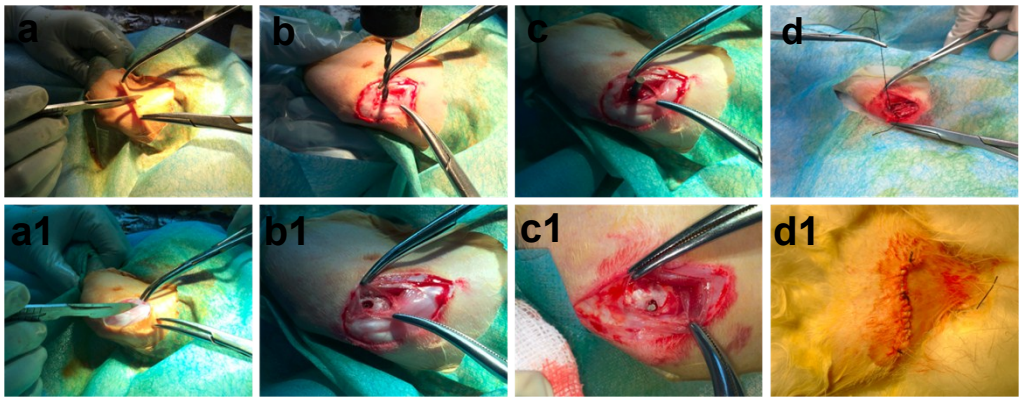


Figure S2. Surgical procedure: (a & a1) the upper legs of rabbits were shaved and disinfected with iodophor, then the femurs were exposed and periosteum was separated; (b & b1) a hole was made on the planar surface of femur with a tryphine drill; (c & c1) a prepared implant was gently inserted into the hole, and the end of samples should keep parallel with bone surface; (d & d1) wound bed was closed in layers with sutures and disinfection treatment was performed.

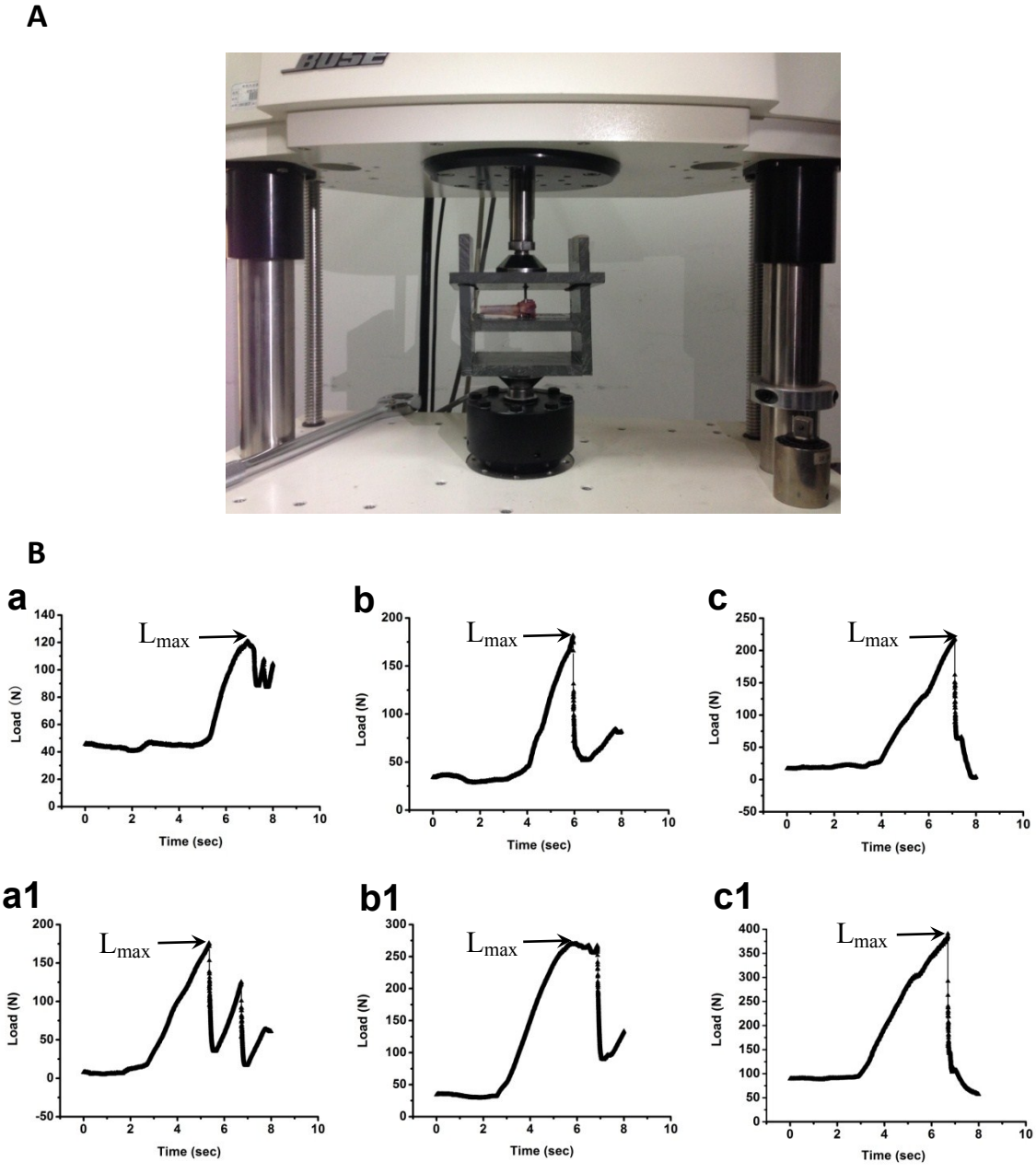


Figure S3. (A) The photo of instrument for push-out test; (B) The Representative push-out load -time curve of pure Ti (a & a1), TNSs (b & b1) and Sr120-TNSs (c & c1) implants after implantation for 4 (a, b & c) and 12 (a1, b1 & c1) weeks. The samples

were pushed out along the long axis at a loading rate of 5 mm/min. L_{max} (N) was the maximum push-out load.

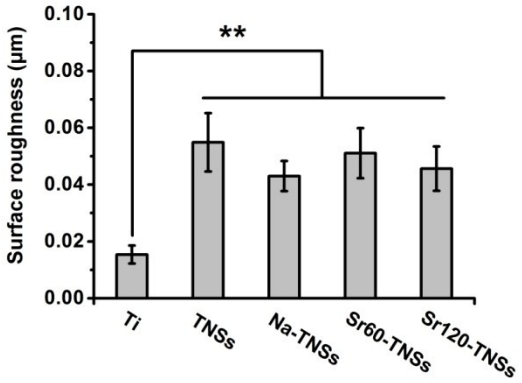


Figure S4. Surface average roughness (Ra) of Ti, TNSs, Na-TNSs, Sr60-TNSs and Sr120-TNSs substrates. Error bars represent means ± SD for n=6, **p<0.01.

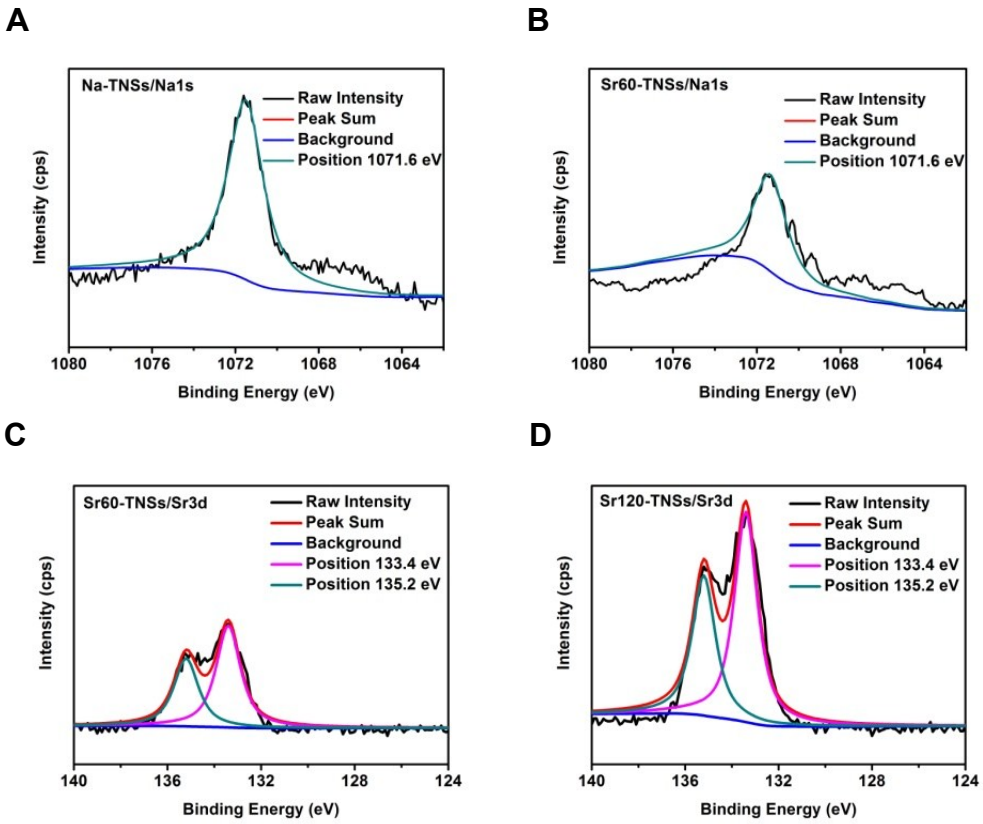


Figure S5. High-resolution XPS spectra of Na1s and Sr3d detected from Na^{+}-incorporating and/or Sr^{2+}-incorporating titanium surfaces: (A) Na1s of Na-TNSs substrates. (B) Na1s of Sr60-TNSs substrates. (C) Sr3d of Sr60-TNSs substrates. (D) Sr3d of Sr120-TNSs substrates.

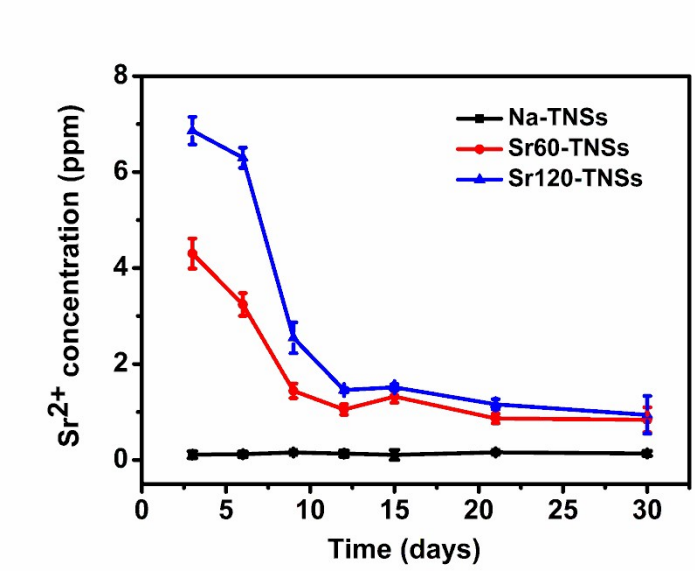


Figure S6. Release profiles of Sr^{2+} from Na-TNSs, Sr60-TNSs, and Sr120-TNSs substrates at different time points after immersion into SBF solution for 30 days.

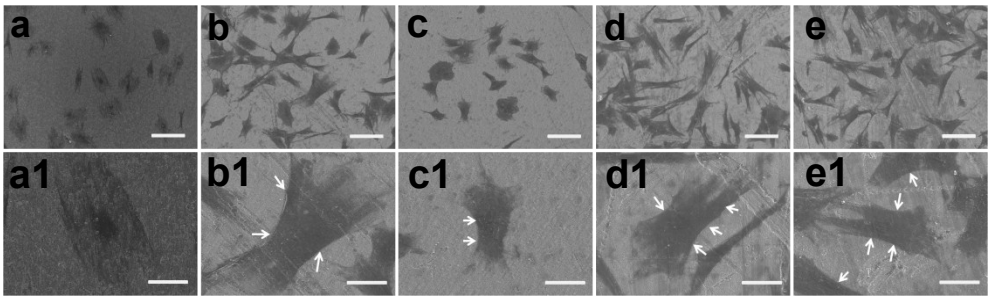


Figure S7. Representative SEM images of MSCs cultured onto different Ti substrates: Ti (a & a1), TNSs (b & b1), Na-TNSs (c & c1), Sr60-TNSs (d & d1), Sr120-TNSs (e & e1) (scale bar: 100 μm for a, b, c, d and e, 30 μm for a1, b1, c1, d1 and e1).

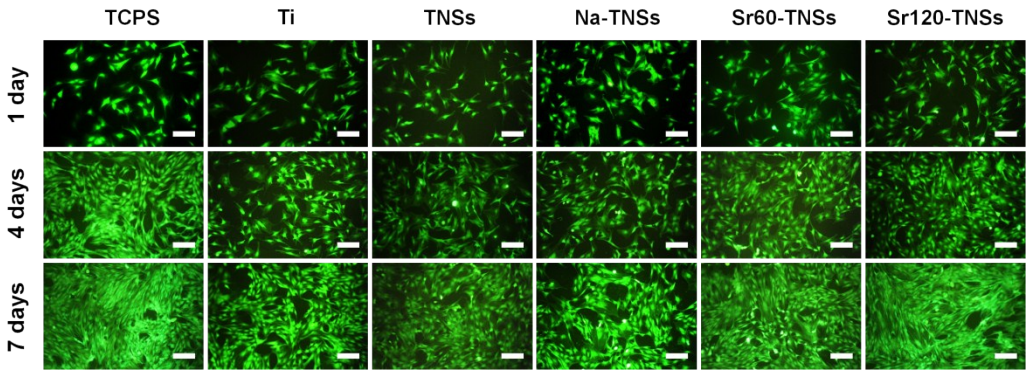


Figure S8. Representative fluorescence microscopy images of MSCs grown onto these five kinds of different samples and TCPS, which was observed by a stereoscopic microscope (MVX10, Olympus) after staining with fluorescein diacetate (FDA) (scale bar, 200 μm).

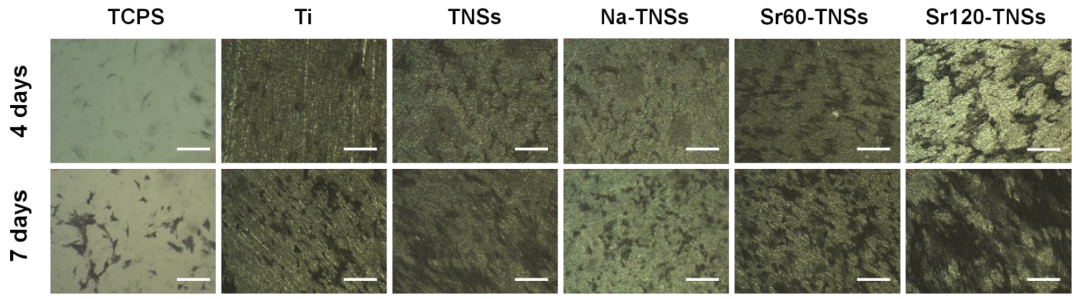


Figure S9. Representative ALP staining of MSCs cultured onto TCPS and different Ti substrates after incubation for 4 and 7 days (scale bar: 1 mm).

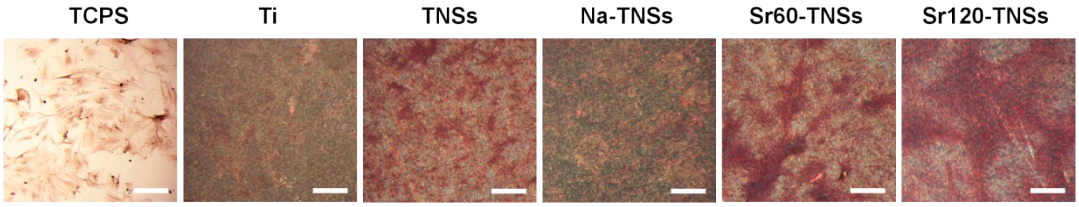
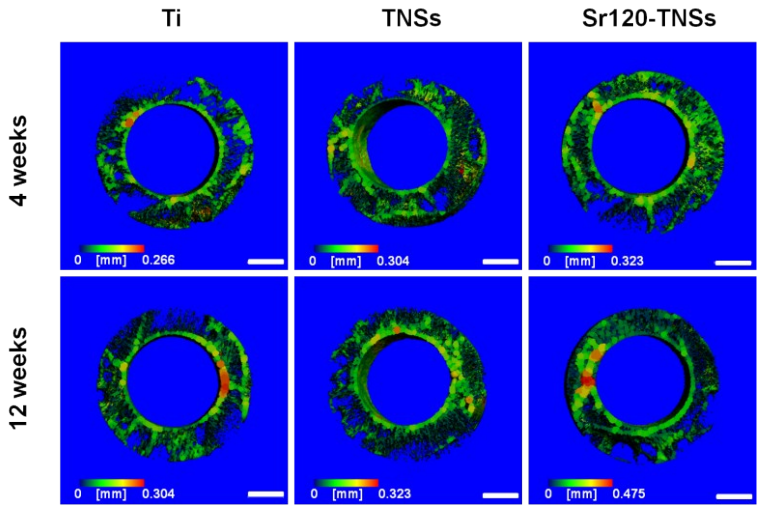


Figure S10. Representative optical images of ECM mineralization of MSCs adhered to different Ti substrates and TCPS for 3 weeks (scale bar: 1 mm).

Figure S11. Representative X-ray photographs of Ti, TNSs and Sr120-TNSs after implantation for 4 and 12 weeks.

A



B

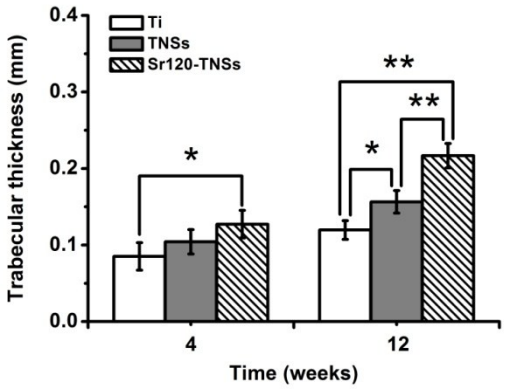


Figure S12. (A) Trabecular thickness of Ti, TNSs and Sr120-TNSs after implantation for 4 and 12 weeks (scale bar, 1 mm). (B) Quantitative analysis of the newly formed bone was performed for trabecular thickness. The above data were obtained according to the Micro-CT analysis. Error bars represent means ± SD for n=4, *p<0.05,

**p<0.01.