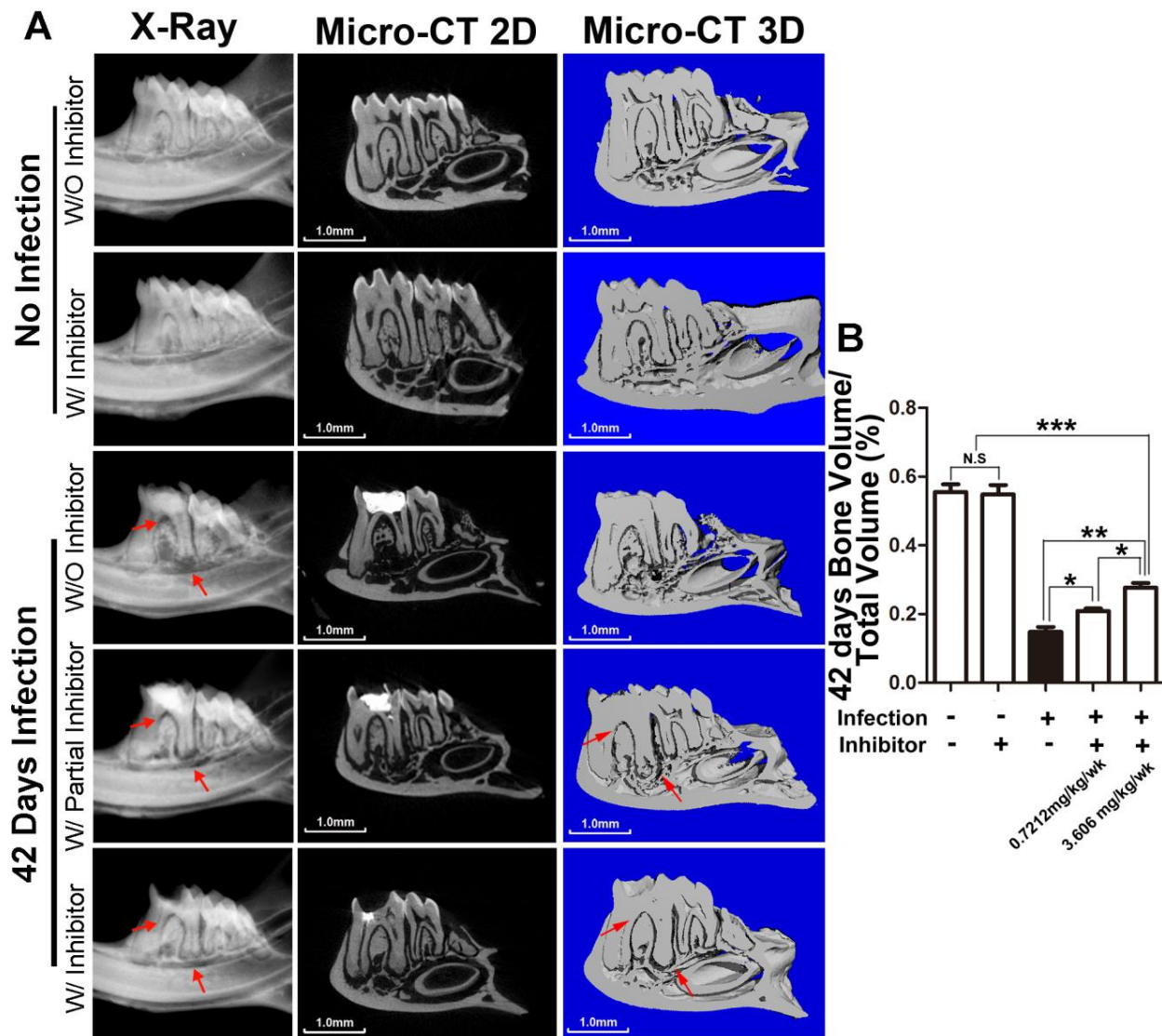


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2 **Figure S1. Inhibition of Ctsk by specific inhibitor of normal group in endodontic**
3 **and furcation area at different time points by X-ray analysis. (A-C)** X-ray imaging of
4 the first molar tooth of the normal group without inhibitor at different time points (7, 21
5 and 42 days). **(D-F)** X-ray imaging of the first molar tooth of the normal group with
6 inhibitor (3.606 mg/kg/wk) at different time points (7, 21 and 42 days). There was no
7 reduced bone density area in the normal group. N = 3, repeated three times.

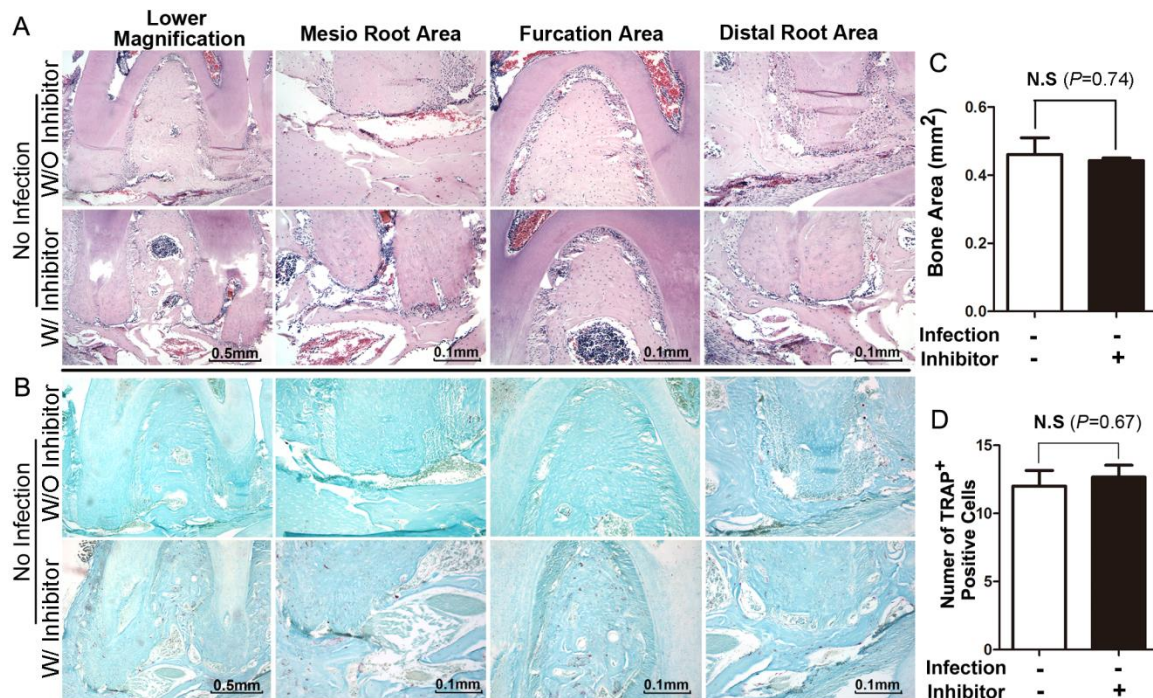


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17 **Figure S2. Inhibition of Ctsk by specific inhibitor of different dose reduced infection-**
 18 **stimulated endodontic bone resorption by Micro-computed tomography (μ CT)**
 19 **analysis. (A) μ CT analysis of endodontic area of normal group without or with inhibitor**
 20 **(3.606 mg/kg/wk) at 42 days. (B) μ CT analysis of endodontic lesion area of bacterial**
 21 **infected group with inhibitor (3.606 mg/kg/wk) or (0.7212mg/kg/wk) at 42 days. (C)**
 22 **Quantification of bone volume/total volume measured for periapical lesion area from**
 23 **bacteria infected group without and with inhibitor (3.606 mg/kg/wk) or (0.7212mg/kg/wk)**
 24 **at 42 days. *: $P < 0.05$, **: $P < 0.01$, ***: $P < 0.001$. N.S: No Significance. N = 3, repeated**
 25 **three times. Left column of panel A are X-ray images. Middle column of panel A are**

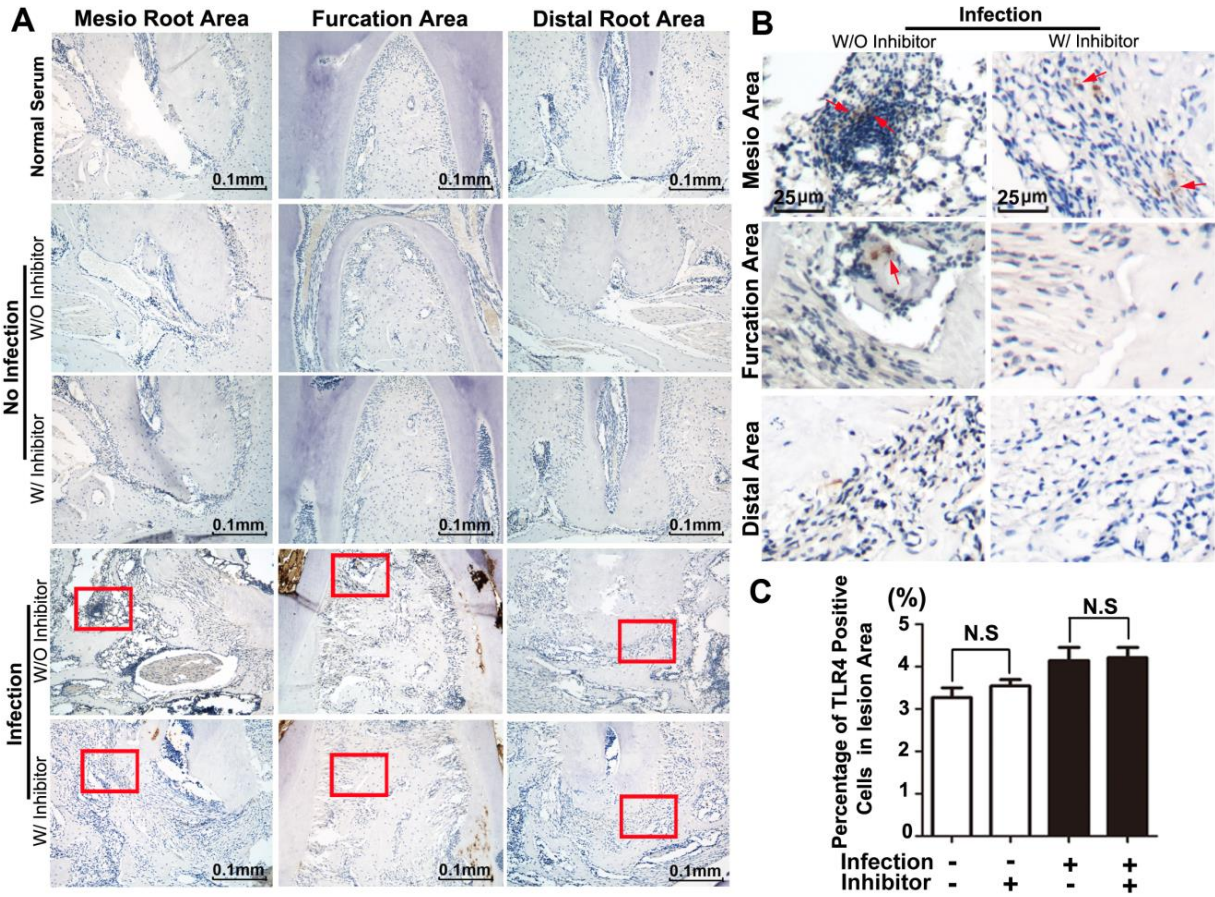
26 typical slice 2D μ CT images, while the right column of panel **A** are 3D reconstitutions
27 images.

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 58 **Figure S3. H&E and TRAP stain of periapical and furcation area of normal group. (A)**
 59 H&E staining of the periapical mesio, distal root sections and furcation area sections
 60 from normal group with or without inhibitor (3.606 mg/kg/wk) at day 42. **(B)** TRAP
 61 staining of the periapical mesio, distal root sections and furcation area sections from
 62 normal group with or without inhibitor (3.606 mg/kg/wk). **(C)** Quantification of bone area
 63 at normal group with or without inhibitor (3.606 mg/kg/wk). **(D)** Quantification of TRAP⁺
 64 cells at normal group with or without inhibitor (3.606 mg/kg/wk). N.S: No Significance. N
 65 = 3, repeated three times.

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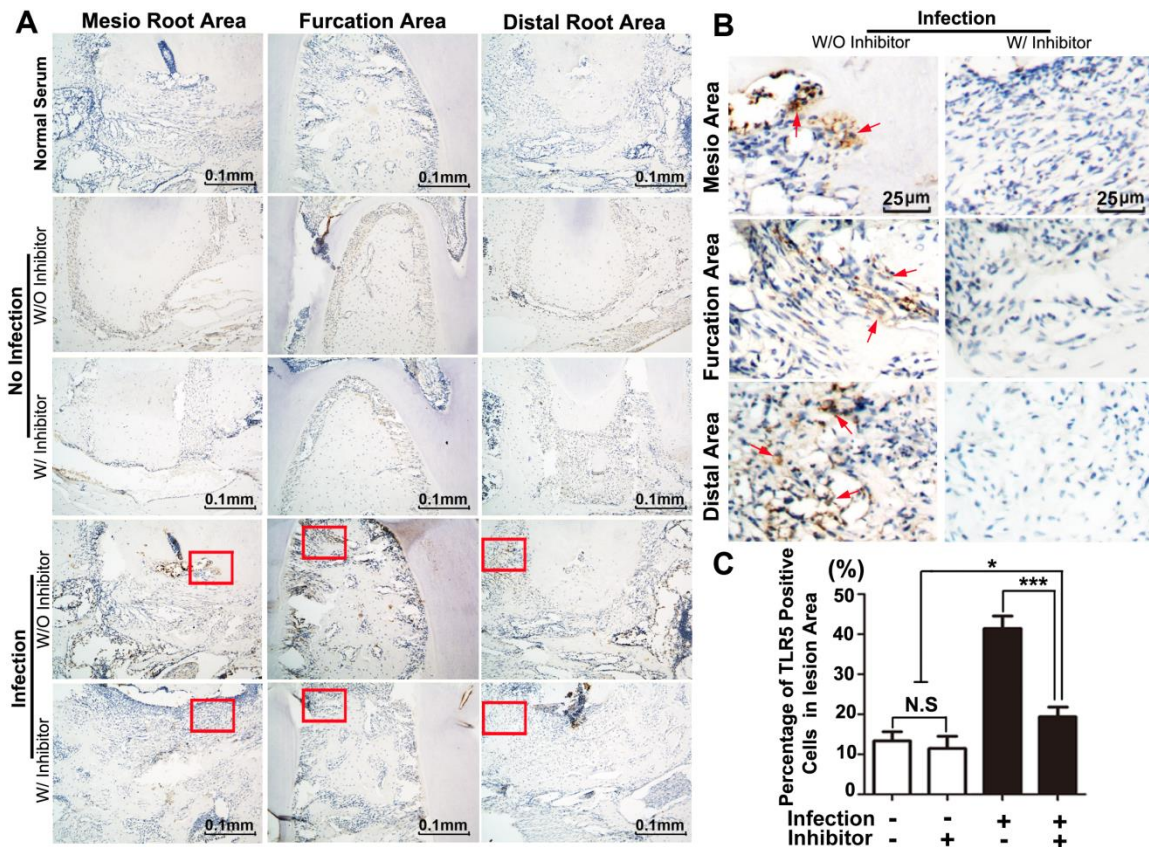
75 **Figure S4. Inhibition of Ctsk by specific inhibitor showed no effect on expression of**
 76 **TLR4 in periapical lesion area at 42 days by immunohistological analysis. (A)**
 77 **Immunohistochemistry stains of TLR4⁺ (Brown) cells areas in normal group and**
 78 **bacterial infected group with or without inhibitor (3.606 mg/kg/wk) at 42 days. Normal**
 79 **serum served as negative control. (B) Higher magnification view of infection disease**
 80 **group and ODN treated disease group at 42 days. Red arrows indicated TLR4⁺ cells.**
 81 **(C) Quantification of TLR4⁺ cells in frucation, mesio and distal periapical area of normal**
 82 **group and bacterial infected group with or without inhibitor (3.606 mg/kg/wk) at 42 days.**
 83 **N.S: No Significance. N = 3, repeated three times.**

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89 **Figure S5. Inhibition of Ctsk by specific inhibitor showed reduced expression of**
 90 **TLR5 in periapical lesion area at 42 days by immunohistological analysis. (A)**
 91 **Immunohistochemistry stains of TLR5⁺ (Brown) cells areas in normal group and**
 92 **bacterial infected group with or without inhibitor (3.606 mg/kg/wk) at 42 days. Normal**
 93 **serum served as negative control. (B) Higher magnification view of infection disease**
 94 **group and ODN treated disease group at 42 days. Red arrows indicated TLR5⁺ cells.**
 95 **(C) Quantification of TLR5⁺ cells in frucation, mesio and distal periapical area of normal**
 96 **group and bacterial infected group with or without inhibitor (3.606 mg/kg/wk) at 42 days.**
 97 ***: $P < 0.05$, ***: $P < 0.001$. N.S: No Significance. N = 3, repeated three times.**

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103 **Table S1. Primers used for qRT-PCR**

Gene Symbol	Primers used for qRT-PCR	
	Forward Primers (5'-3')	Reverse Primers (5'-3')
<i>Ctsk</i>	ATACGTTACTCCAGTCAAGAACCAG	TAATTCTCAGTCACACAGTCCACA
<i>TNFα</i>	AGGGTCTGGGCCATAGAACT	CCACCACGCTCTTCTGTCTAC
<i>IL6</i>	CTCTGCAAGAGACTTCCATCCAGT	GAAGTAGGGAAGGCCGTGG
<i>IL23</i>	ATGCTGGATTGCAGAGCAGTA	ACGGGGCACATTATTTTTAGTCT
<i>TLR4</i>	ACCTGGCTGGTTTACACGTC	CTGCCAGAGACATTGCAGAA
<i>TLR5</i>	GCCACATCATTTCCACTCCT	ACAGCCGAAGTTCCAAGAGA
<i>TLR9</i>	TTCTCAAGACGGTGGATCGC	GCAGAGGGTTGCTTCTCACG

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