INTRODUCTION
Tendon-bone insertion or junction (TBJ) acts as interface for force transmission from tendon to bone as well as a stress absorber during mechanical loading. Chronic injuries and delayed healing are often observed at TBJ. A delayed TBJ healing model by shielding the healing interface for 4 weeks was developed recently[1]. Extracorporeal shock wave (ESW) therapy (0.43 mJ/mm², 4Hz, 1500 impulses) promoted osteogenesis, regeneration of fibrocartilage zone, and remodeling in delayed TBJ healing[2,3]. However, no dosing studies were conducted to identifying optimal dose for ESW application for TBJ healing. In our previous in vitro study using human periosteal cells, low-intensity ESW (0.12 mJ/mm², 1250 impulses) enhanced cell proliferation, cell viability, and calcium deposition compared with high-intensity ESW (0.5 mJ/mm², 300 impulses)[4]. During the early phase of the treatment, high intensity ESW also caused more detrimental effect than low intensity ESW on human periosteal cells in vitro[4]. Therefore, we hypothesized that low dose of ESW can enhance the TBJ healing quality and have a similar effect compared to high dose ESW.

METHOD
Partial patellectomy with shielding was performed on 48 female New Zealand White Rabbits according to our established protocol to mimic delayed TBJ healing [1-3]. The rabbits were separated into three different groups (Control, Low Dose (LD)-ESW (0.06 mJ/mm², 4Hz, 1500 impulses), and High Dose (HD)-ESW (0.43 mJ/mm², 4Hz, 1500 impulses) and two different time points (8 and 12 weeks after partial patellectomy). ESW was applied two weeks after the removal of shielding placed between tendon and bone after partial patellectomy at week 4. New bone area and volume were measured using anteroposterior radiographs and µCT respectively. As the end-point assessment of the integration of the TBJ healing interface, the tensile strength was evaluated mechanically. One-way analysis of variance with Bonferroni post hoc test was used to detect differences between difference dosages of ESW and control group. Significance level was set at p < 0.05.

RESULTS SECTION
Radiographic assessments showed that the new-formed bone area was larger in both LD-ESW (59% with p=0.024 and 80% with p=0.003) and HD-ESW (63.3% with p=0.004 and 61.1% with p=0.003) at week 8 and week 12 respectively (Figure 1A). The new-formed bone volume measured by using µCT showed that LD-ESW and HD-ESW were 50.9% and 85% (p=0.045) larger than control at week 12 (Figure 1B). This enhancement in new bone formation was confirmed histologically (Figure 2A). There was no significant difference between LD-ESW and HD-ESW with respect to new-formed bone area and volume.

The overall healing quality of the TBJ healing interface was assessed with respect to the tensile strength. Both LD-ESW (30.9% with p=0.049) and HD-ESW (37.7% with p=0.038) showed higher failure load than control group at week 12 (Figure 3A). However, the failure load and ultimate strength did not showed significant difference between the two ESW-treatment groups.

DISCUSSION
Low dose ESW was found as effective as high dose ESW in promotion of the healing in delayed TBJ injuries. There was no statistical significant difference between LD-ESW and HD-ESW with respect to the radiological, histological, and mechanical assessments. Other randomized control trial studies also found no significance different between low dose and high dose ESW in treating shoulder pain and tendinosis calcarea of the rotator cuff[5].

ESW treatment enhanced the healing quality of the delayed TBJ repair. Both LD-ESW and HD-ESW showed enhanced osteogenesis and improved tensile properties when compared to control at both week 8 and week 12. Enhancement of osteogenesis in TBJ repair was also observed in our previous studies[2,3]. Enhanced osteogenesis at the healing interface by ESW might also be accounted for the enhanced the mechanical properties of the TBJ healing because the area and length of the new bone is correlated with the tensile strength of the TBJ healing complex[6]. The mechanism of ESW for the improved repair quality of TBJ might also be related the induction of micro-damage at the healing interface and the up-regulation of the related extracellular cytokines and growth factors, such as VEGF, BMP, and TGF-β, by ESW[7].

REFERENCES

ACKNOWLEDGEMENT
This project is supported by Competitive Earmarked Research Grant – Ref: CUHK4765/08.