INTRODUCTION
Articular cartilage, although a remarkably durable tissue, has a limited capacity to heal and can lead to premature arthritis when it is damaged due to injury or disease. Arthritis is a major health issue that is predicted to increase as our population ages. As such, there is considerable interest in the development of techniques to repair or reconstruct damaged cartilage.

The injections were made into the subperiosteal region of the medial proximal rabbit tibia. 6-8 rabbits received subperiosteal injections similar to the method of Critchlow et al. [1]. 10 µl containing 20 or 200 ng TGF-β1 or vehicle (200 ng) were injected into each rabbit (Fig. 1A). One limb of each rabbit received growth factor while the other limb was injected with vehicle. The injections were made into the subperiosteal region of the medial side of the proximal tibia. Four injections were made in each limb spaced apart in a manner to center them over the four 2x3mm areas normally used to harvest periosteal explants for periosteal in vitro chondrogenesis. After 1, 3, 5, or 7 days, the rabbits were sacrificed and periosteal explants (8 per rabbit, 2x3mm) were harvested from the injection sites by sharp elevation. A total of 512 explants were harvested and cultured for 6 weeks with DMEM 10% FBS in agarose suspension with 10 ng/ml TGF-β1 for the first two days of culture. The explants were then weighed, embedded in paraffin, sectioned and stained with Safranin O/fast green [2]. The cartilage yield (% area) and total cartilage (in mg) in the explants was determined using established computerized histomorphometry methods [2, 3]. Results were analyzed using 1, 2 or 3-factor ANOVA and means contrast comparisons where appropriate. All data are presented ± SE.

RESULTS
Substantial swelling and periosteal thickening was seen in the medial proximal tibiae of the limbs that were injected with TGF-β or IGF-1. While periosteal explants were being harvested from these tibiae, it could be clearly seen that the periostem was markedly thicker in these growth-factor-treated regions (Fig. 1B). Evidence of this could still be seen after 6 weeks of culture in the weight data. ANOVA growth factor dose (high, low or none), and the delay duration between injection and explant harvest (1, 3, 5, or 7 days) all had a significant effect on periosteal wet weight (p < 0.0001 and p < 0.023 respectively). More importantly, growth factor dose and the delay duration also had a significant effect on cartilage yield (i.e. % area cartilage) and total cartilage produced (in mg) (p < 0.0003) (Fig. 2). The highest outcomes in total cartilage, cartilage yield and wet weight were seen with the high dose injection of TGF-β1 (200 ng/ml) (p < 0.05) (Fig. 3). The injection of IGF-1 did not have a significant impact on periosteal chondrogenesis or explant cartilage weight.

DISCUSSION
These findings suggest that it is indeed possible to increase the chondrogenic potential of periosteal prior to explantation. Further work is being done to examine the effects on subperiosteal injections on the cellular level as well as examining the effects of TGF-β and IGF-1 combined. Ongoing studies include detailed histological examination of the injection site and the injection of older rabbits (1 and 2 yr). Future studies will include in vivo defect repair. Beyond articular cartilage repair, these studies have the potential to impact the use of periosteum for other applications such as tissue engineering of bone. In addition, by eliminating the need for cell culture expansion facilities and expertise, the cost of this approach should be considerably less thereby making cartilage repair more globally accessible.

REFERENCES

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