Adaptive Image Segmentation Detects Extensive Cortical Remodeling During Early Fracture Repair

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INTRODUCTION: Callus formation and cortical bone remodeling are integral to secondary bone healing. Previously, we used image analysis techniques to demonstrate cortical bone immediately adjacent to the fracture line undergoes remodeling in parallel with–not after–callus formation.[1] However, measuring remodeling over a large region of interest is challenging due to gradients in mineralization that cause errors in boundary detection when simple thresholding-based approaches are used. Accordingly, the technical objective of this study was to develop an automatic image segmentation algorithm for measuring the global remodeling throughout the entire bone.

METHODS: The image processing algorithm was developed and tested using data from 14 sheep with µCT scans of operated-contralateral limb pairs **(Figure 1-a**). Operated limbs had 3 mm tibia osteotomies stabilized by veterinary locking compression plates. After sacrifice at 9 weeks, both tibiae were µCT scanned with an isotropic resolution of 60.7 µm over the full length of the diaphysis. Axial registration of left-right limb pairs was achieved by matching the positions of the nutrient artery canal. We paired each contralateral slice image to an operated one, excluding slices from the osteotomy and those with screw holes. The endocortical and pericortical boundaries could be detected by a fixed threshold only in the absence of callus. However, the irregular shape and radiodensity of callus necessitated adaptive determination of thresholds in slices with callus. The required threshold for each boundary in each image was obtained by iterating it within a range until fulfilling a criterion or reaching a maximum threshold. The criterion for the endocortical boundary was an acceptable curve tortuosity, while for pericortical boundary, the paired image from the intact image was used to determine a target ratio for the endocortical to pericortical area. After segmentation, radiodensity data within the cortex was sampled over circumferential and radial paths, leading to the calculation of a (normalized) representative density for each slice image. Comparison of representative densities in each intact/operated image pair allowed for computation of a local and a global remodeling index. Variation of the local remodeling index over limb height was described by fitting a sigmoid function. Finally, the global remodeling intensity in each animal could concisely be reported by four parameters: remodeling zone height, maximum remodeling index, axial position of maximum remodeling, and summed total remodeling activity.

RESULTS: More than 17,000 operated and 33,000 contralateral images with a wide variety of callus volume and density from 13 animals were successfully segmented using the adaptive algorithm (**Figure 1-b/c**). One animal was so profoundly remodeled that it could not be analyzed using the same algorithm as the other sheep without changing the calibration constants, so its results are not reported together with the other 13. In the intact bones, the normalized representative density was highest at the midshaft. In the operated bones, the local remodeling index values were highest closest to the osteotomy and declined to negligible values at the proximal and distal ends of the diaphysis. Slices near screws demonstrated local porosification and microdamage-induced remodeling (**Figure 1-d/e**). On average, the remodeling zone height, maximum remodeling index, axial position of maximum remodeling, and summed total remodeling activity for the animals in this study were 70.7 mm (SD 14.4), 10.5% (1.7% SD), -6.8 mm (5.3 SD), and 5.3% (1.0% SD).

DISCUSSION: The introduction of an adaptive segmentation algorithm allowed us to investigate changes over the full diaphyseal segment, a much larger region of interest than in other prior studies. This revealed both global effects of remodeling related to the injury repair, which were clearly distinct from the localized effects near screws related to microdamage. Cortical remodeling was detectable far from the osteotomy, extending over approximately the middle 50% of each operated tibia and corresponding to the region where callus had formed.

SIGNIFICANCE/CLINICAL RELEVANCE: Cortical remodeling occurs rapidly during early bone healing over an extensive region of bone, suggesting that the cortical bone may be serving as a local source of the mineral needed to build callus.

REFERENCES: 1. Ren+ *Biomech Model Mechanobiol*. 2022;21(2):615-626. doi:10.1007/s10237-021-01553-2

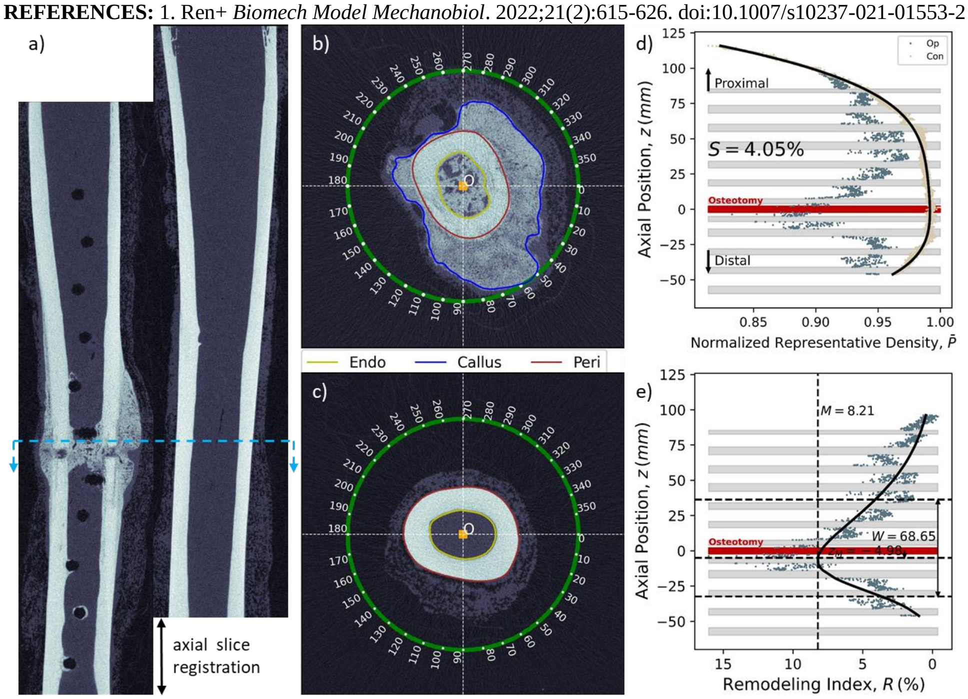

Figure 1. a) Operated and contralateral scans were axially registered to enable slice pairing. The algorithm successfully detected endocortical (yellow) and pericortical (red) boundaries in the operated (b) and intact (c) slices. Data resampling was used to generate a representative density (d) and a remodeling index (e) for each slice. Curve-fitting was used to obtain global remodeling parameters for each scan as shown in (e).