Signafuse®: Biomechanical Validation of Fusion in a PLF Rabbit Model

The posterolateral spine fusion (PLF) rabbit model has been widely used to evaluate bone graft substitutes for spine fusion procedures in comparison to ICBG autograft [1]. These studies typically determine fusion using radiographic and histological evaluations in conjunction with manual palpation. Manual palpation most closely replicates direct surgical exploration of psuedarthrosis, and has been validated in this animal model by comparison with biomechanical range of motion (ROM) data under simulated physiologic loading conditions [2]. Range of motion measurements in the flexion-extension plane provide an objective physical indicator of fusion solidity that can be directly correlated to manual palpation data and compared to ICBG autograft data obtained in similar published animal studies that used identical loading conditions [2]. Further, spine fusion clinical studies have utilized lateral flexion-extension radiographs to assess biomechanical stability, where less than $5°$ ($< 5°$) of angular motion is a determinant of spine fusion effectiveness. This established fusion criteria provides a clinically relevant functional benchmark by which biomechanical animal fusion data can be correlated to clinical outcomes [2,3].

As part of a rabbit fusion analysis submitted to the FDA, flexion-extension ROM data measured at 12 weeks was presented as a determinant of solid fusion, as compared to the range of motion threshold ($< 5°$) described above. The Signafuse treated animals revealed a fusion rate of 80% (8/10 rabbits fused) compared to 44% (4/9 rabbits fused) for Actifuse ABX, and 63% (5/8 rabbits fused) reported for ICBG autograft (Figure 1).
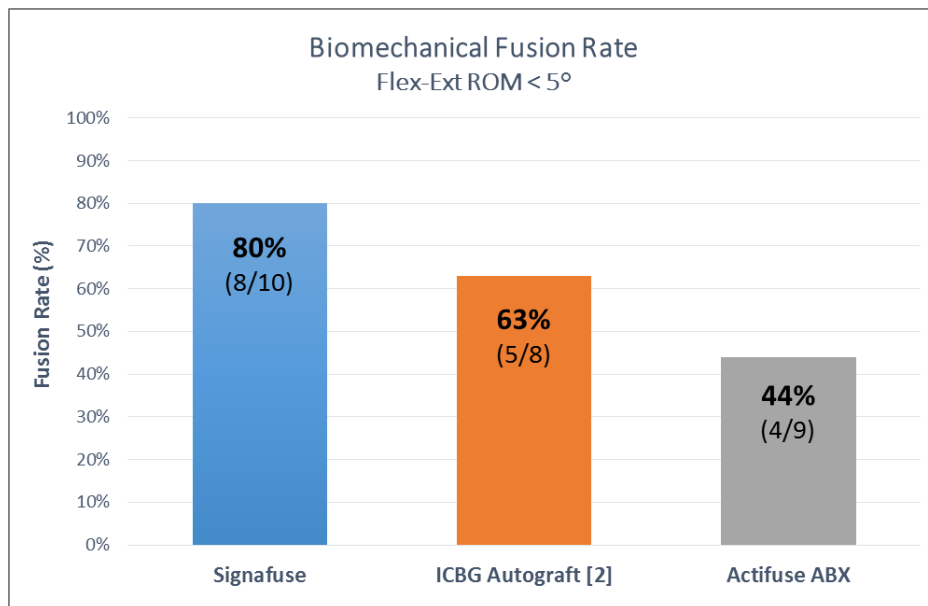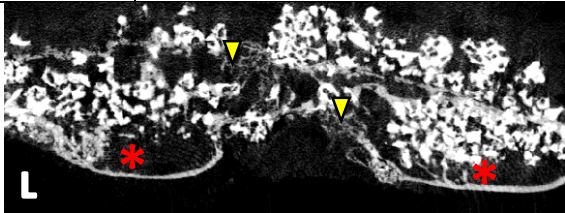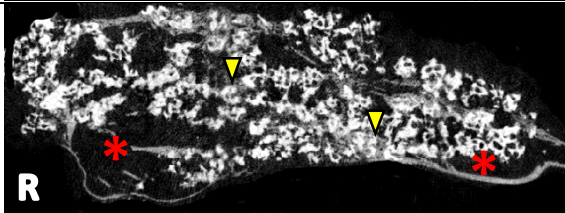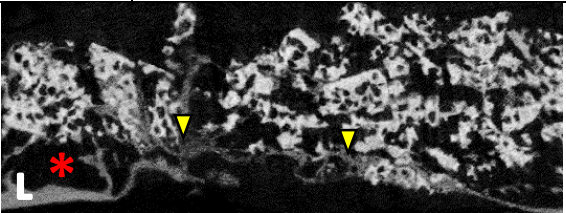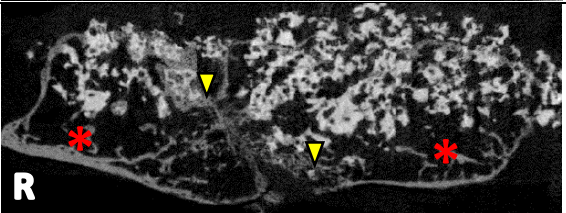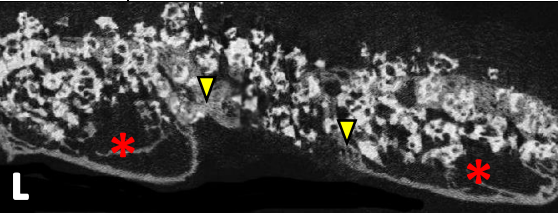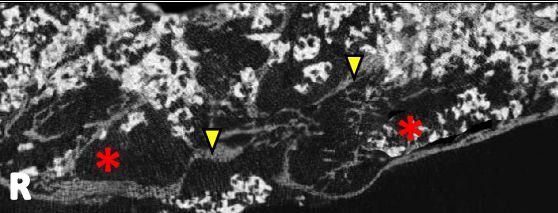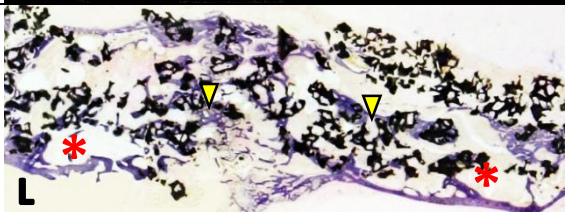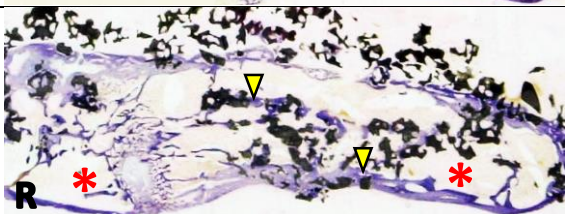

Figure 1: Biomechanical fusion rates of Signafuse, ICBG autograft and Actifues ABX in the rabbit posterolateral spine fusion model.

Using precise biomechanical measurements and clinical relevant fusion criteria, Signafuse demonstrated a 46% higher fusio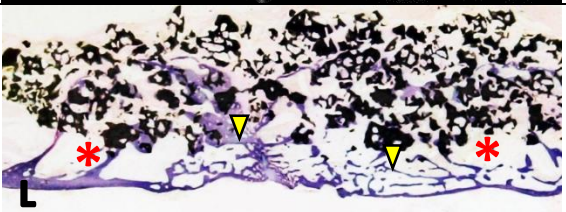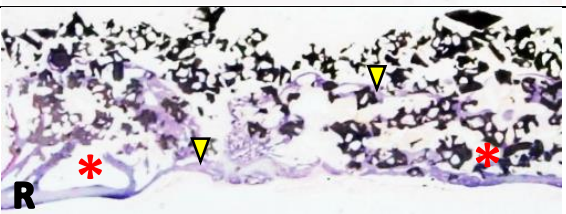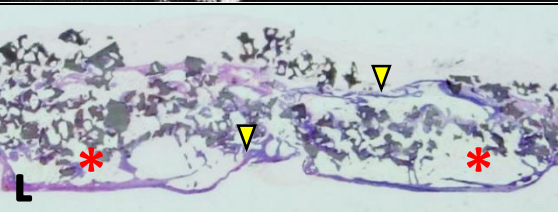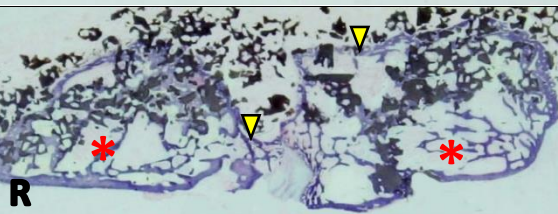n rate than Actifuse ABX and a 17% higher fusion rate than reported for ICBG autograft under identical loading conditions. The greater biomechanical performance is strongly supported by microCT and histological observations, which consistently show new bridging bone and developed marrow spaces spanning across the transverse processes (Attached). The prevalence of structurally mature fusion development in the 12 week Signafuse animals observed across clinically relevant endpoints is superior to Actifuse ABX and historical ICBG autograft data in this validated PLF rabbit model, indicating that Signafuse elicits an effective healing response that is amenable to the functional demands of spine fusion healing.

1. Riordan AM, Rangarajan R, Balts JW, Hsu WK, Anderson PA. Reliability of the Postero-Lateral Fusion Model: A Meta-Analysis. J Orthop Res. 2013 Aug; 31(8):1261-9. doi: 10.1002/jor.22359. Epub 2013 Apr 18.
2. Erulker JS, Grauer JN, Patel TC, Panjabi MM. Flexibility analysis of posterolateral fusions in a New Zealand white rabbit model. Spine (Phila Pa 1976). 2001 May 15;26(10):1125-30.
3. James Kang, MD, Howard An, MD, Alan Hilibrad, MD, Tim Yoon, MD, PhD, Eoin Kavanagh, MD, Scott Boden, MD. Grafton and Local Bone Have Comparable Outcomes to Iliac Crest Bone in Instrumented Single-Level Lumbar Fusions. Spine. 2012;37:1083-1091.

Signafuse MicroCT & Histology Results Correlating to Flexion-Extension ROM Data – Representative Animals at 12 Weeks

Endpoint	Animal #	Flexion-Extension ROM (°) (< 5° = Fused)	Animal #	Flexion-Extension ROM (°) (< 5° = Fused)	Animal #	Flexion-Extension ROM (°) (< 5° = Fused)
	4998	0.882 (Fused)	5001	0.856 (Fused)	5004	1.592 (Fused)
MicroCT (Sagittal)						
Histology (Sagittal)						

▽ = New bridging bone

✱ = Transverse process