SALVIN OSS® Collagen

Xenograft + Collagen Bone Graft Material

SalvinOss® Collagen Xenograft Bone Graft Material
In Vivo Testing Summary

Summary Of In Vivo Use Of Bioresorbable Xenograft Bone Graft Materials
In The Treatment Of One-Walled Intrabony Defects In A Canine Model

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ABSTRACT:

The purpose of this study is to evaluate bone healing within a one-wall periodontal defect following treatment with two different bioresorbable xenograft bone graft materials. Thirteen (13) male beagle dogs at least one year of age (skeletally mature) had second and fourth pre-molars (P2 and P4) extracted from the mandible bilaterally. Radiographs were taken 8 weeks following extraction to assess adequate bone healing within the extracted root, with subsequent radiographs taken every two weeks until adequate bone healing was achieved, which was deemed to be at 12 weeks. One-wall critical sized defects were then created at the extraction sites to yield four mandibular defect sites per dog. Treatment of defects were randomly assigned to receive SalvinOss® Collagen Xenograft Bone Graft Material or Bio-Oss® Collagen Xenograft Bone Void Filler. Following implantation with bone graft materials, the defects were covered with Bio-Gide® dental membrane, and the gingiva was closed. Evaluations were conducted using Radiographic, Histologic, and MicroCT analysis at 10, 16, and 24 weeks post-implantation. SalvinOss® Collagen devices, presenting with 20% more porosity than that of Bio-Oss Collagen® devices, demonstrated greater ridge height and ridge width compared to the Bio-Oss Collagen® device throughout the study. Both devices had similar radio-density at the study's conclusion at 24 weeks post implantation. Microscopic evaluations confirmed that the SalvinOss® Collagen devices allowed the defect site to remodel with similar volumes of woven and lamellar bone to that of Bio-Oss Collagen® devices throughout the post implantation period.

MATERIALS:

XenoGraft Bone Graft Materials:

SalvinOss® Collagen XenoGraft Bone Graft Material is a non-pyrogenic porous bone mineral and collagen matrix used in periodontal, oral, and maxillofacial surgery. It is a mixture of 90% SalvinOss® anorganic bone and 10% bovine collagen provided in a cylinder form. The SalvinOss® granules are produced by removing organic components from porcine bone utilizing a trade-secret multi-step chemical and thermal process that maintains the chemical and physical (i.e. - porosity) characteristics of native bone. SalvinOss® Collagen devices are sterilized by gamma-irradiation. Scanning Electron Microscope (SEM) imaging and Micro-Computed Tomography (MicroCT) analysis of the device presented an average pore size of 181.2 microns with an estimated overall porosity of 75.1% (Figure 1).

Bio-Oss Collagen® devices consisted of 90% Bio-Oss® granules with the addition of 10% porcine collagen. Bio-Oss® granules are a porous anorganic bovine bone mineral matrix physically and chemically comparable to the mineralized matrix of human bone. Combining Bio-Oss® granules with collagen enhances its handling characteristics. Bio-Oss Collagen® devices are sterilized by gamma-irradiation. SEM imaging and MicroCT analysis of Bio-Oss Collagen® presented an average pore size of 146.6 microns with an estimated overall porosity of 56.3% (Figure 2).

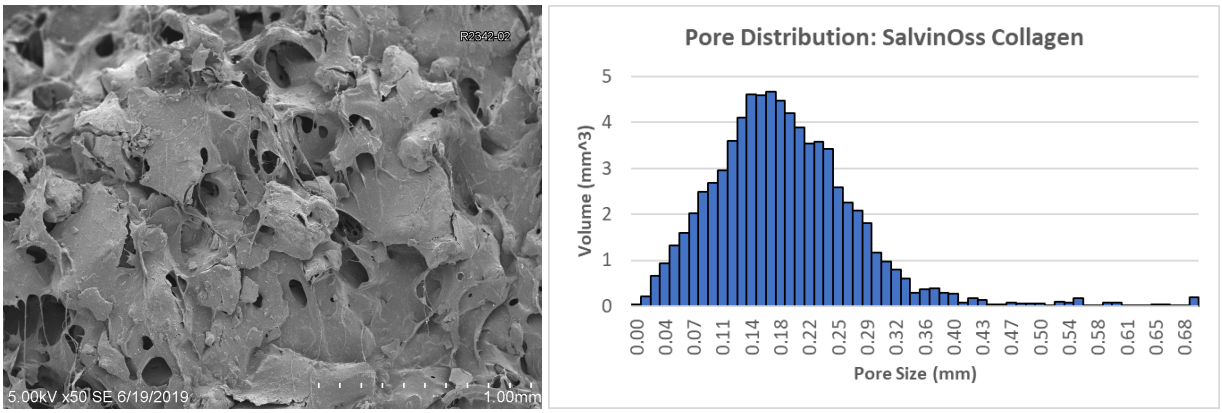


Figure 1: SEM Image of SalvinOss® Collagen device at 50x magnification & MicroCT Graph showing Pore Size Distribution

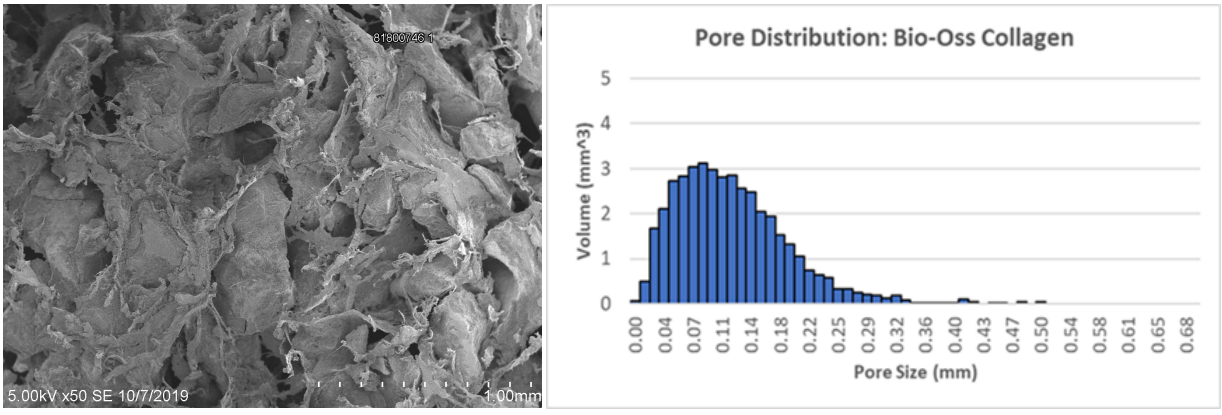


Figure 2: SEM Image of Bio-Oss® Collagen device at 50x magnification & MicroCT Graph showing Pore Size Distribution

Methods for In Vivo Study:

In Vivo Study Subjects and Surgical Procedure:

Thirteen (13) male beagle dogs at least one year of age (skeletally mature) had second and fourth premolars (P2 and P4) extracted from the mandible bilaterally. Radiographs were taken 8 weeks following extraction to assess adequate bone healing within the extracted root, with subsequent radiographs taken every two weeks until adequate bone healing was achieved, which was deemed to be at 12 weeks post-extraction. One-wall critical sized defects were then created at the healed extraction sites to yield four critical sized mandibular defect sites per dog. Reference notches were made into the root surface, at the base of the defects, of the adjacent P3 and M1 rostral roots. Treatment of the defects were randomly assigned to receive a SalvinOss® Collagen device or a Bio-Oss Collagen® device. Following implantation with bone graft material, the defects were covered with Bio-Gide® dental membranes (purchased on the open market) and the gingiva was closed. Four (4) animals per timepoint were euthanized at 10, 16, and 24 weeks post-implantation.

In Vivo Study Evaluation Methods:

Radiographic - Post-implantation radiographs were taken to evaluate new bone formation and any other radiographically visible changes immediately following implantation, and at 10 and 24 weeks post-op. All radiographic images were taken using a Progeny VetVision DC (digital capture) machine and viewed using the supplementary software Progeny Imaging.

MicroCT - Two (2) mandible specimens containing defect sites were harvested per animal. Quantitative analysis of MicroCT images was used to determine average ridge height, width, and regenerated area within the defect sites in mandible specimens. Region of interest subsections were isolated from the data sets, thresholded and analyzed. Starting volumes were calculated based on dimensions measured at the time of implantation and average regenerated area was calculated and compared to starting volumes.

Histology - Following MicroCT analysis, approximately 2 mm thick segment of each defect site was collected in a central plane along the axis of the tooth/jaw (mesial-distal vertical plane). This segment was placed into a cassette and allowed to fix in 10% neutral buffered formalin. Tissues were then decalcified using a buffered formic acid solution. After decalcification, tissues were processed for paraffin embedding. Sections approximately 5 microns thick were collected from the cut surface at the first full block face. Multiple step sections (at least 2 levels) were collected as necessary to capture/demonstrate the center of the tooth root canal and other landmarks (i.e. notch in tooth root, periodontal ligament, cementoenamel junction). Slides were stained with xylene-free hematoxylin and eosin (H&E). A board-certified veterinary pathologist performed the histologic examination using incandescent and polarized light microscopy. Woven bone regeneration was evaluated via H&E and Masson Trichrome staining. The amount of bone regeneration was scored on the following scale:

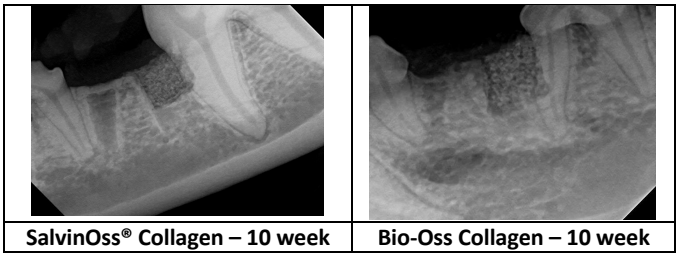
0 = regeneration not evident;
1 = some regeneration is evident;
2 = regeneration is evident, but not complete;
3 = regeneration appears complete

Results for *In Vivo* Study:

Radiographic Evaluation:

Defect Creation - Dental radiographs were taken following the creation of the one-wall critical sized periodontal defect and placement of the test articles. Both test articles were radiographically visible. The adjacent P3 and M1 roots associated with each defect appeared healthy, and the defect notch was visible within the rostral roots.

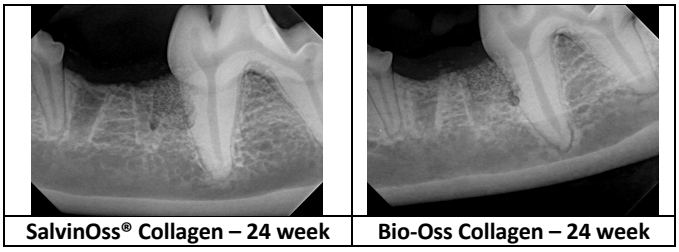
10 Week Interval - Both test articles were visible. Adjacent P3 and M1 roots were visible and showed no evidence of root resorption. The SalvinOss® Collagen and Bio-Oss Collagen® sites showed maintenance of ridge height and similar remodeling at this time point (Figure 3).



SalvinOss® Collagen – 10 week	Bio-Oss Collagen – 10 week

Figure 3: Radiographic Images of SalvinOss® Collagen & Bio-Oss Collagen® at 10 Weeks

24 Week Interval - Defect site boundaries had become somewhat difficult to distinguish radiographically from surrounding bone due to new bone formation within the defect with remodeling and associated article absorption. Adjacent P3 and M1 roots showed minimal evidence of root resorption that was not interpreted to be adverse (Figure 4).



SalvinOss® Collagen – 24 week	Bio-Oss Collagen – 24 week

Figure 4: Radiographic Images of SalvinOss® Collagen & Bio-Oss Collagen® at 24 Weeks

MicroCT Evaluation:

To accurately calculate total regenerated area, the measured bone volume and test article volume were combined from the MicroCT scans. The Bio-Oss Collagen® test group initially exhibited a high average regenerated volume of 37% at 10 weeks, which reduced to 25% at 16 weeks and to 26% at 24 weeks. This decrease in regenerated volume is likely due to the resorption of the Bio-Oss Collagen® material. The average regenerated volume for the SalvinOss® Collagen test group remained fairly consistent between 25-30% throughout the duration of the study. Average regenerated percentages for each time point were statistically equivalent between the two materials (Table 1).

Furthermore, the Bio-Oss Collagen® test group showed a reduced average ridge height and ridge width as compared to the SalvinOss® Collagen test group. This is attributed to the demonstrated elastic behavior of the SalvinOss® Collagen device, as it was shown to reestablish its shape following application of forces (DSM ETF-05410).

Table 1: Key MicroCT Results at 10 weeks, 16 weeks, and 24 weeks

SalvinOss® Collagen™	***Bone + Article Volume (mm^3)***	***Bone + Article Volume (%)***	***Ridge Height (mm)***	***Ridge Width (mm)***
10 Weeks	*57.5 ± 32.9*	*27.6 ± 11.5*	*4.9 ± 0.7*	*3.7 ± 0.6*
16 Weeks	*68.9 ± 38.3*	*29.9 ± 16.4*	*4.8 ± 1.0*	*2.9 ± 0.9*
24 Weeks	*45.5 ± 24.6*	*25.0 ± 10.8*	*3.6 ± 0.6*	*2.1 ± 1.2*
Bio-Oss Collagen®	***Bone + Article Volume (mm^3)***	***Bone + Article Volume (%)***	***Ridge Height (mm)***	***Ridge Width (mm)***
10 Weeks	*54.6 ± 27.9*	*37.4 ± 14.8*	*3.9 ± 0.9*	*3.3 ± 0.5*
16 Weeks	*41.1 ± 8.5*	*24.8 ± 4.1*	*2.6 ± 0.4*	*0.7 ± 0.5*
24 Weeks	*48.0 ± 26.4*	*26.3 ± 9.0*	*3.0 ± 0.7*	*0.8 ± 0.6*

Microscopic Evaluation:

Both SalvinOss® Collagen devices and Bio-Oss Collagen® devices supported formation of new lamellar and woven bone within the treatment site, with the final volumes of bone between the two treatment modalities being similar. (See Figures 6 & 7)

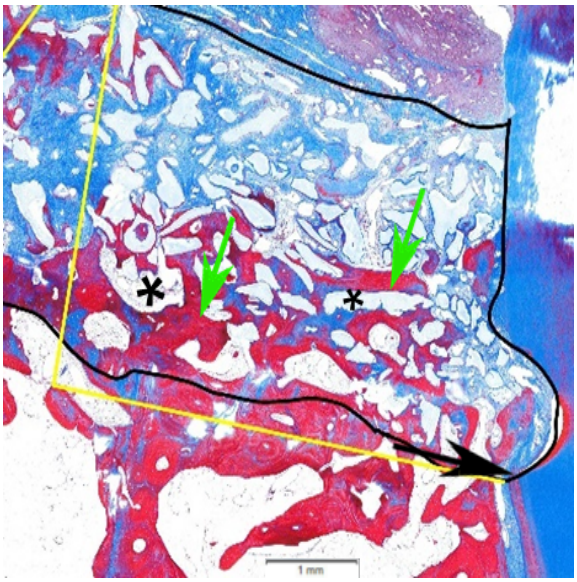


Figure 6: SalvinOss® Collagen – (T1) – 24 Weeks Post-Op

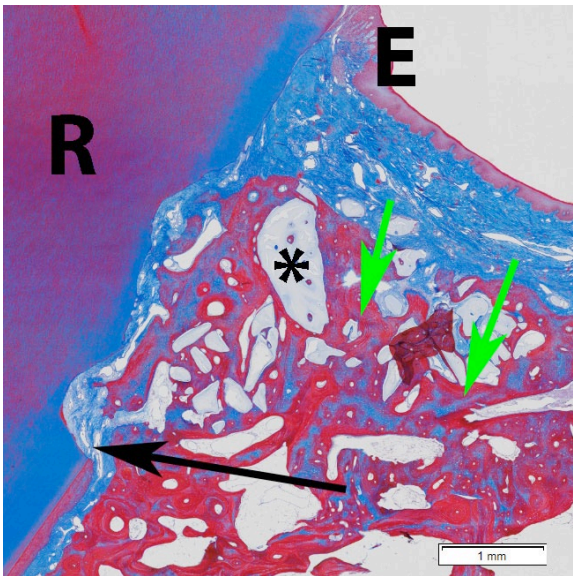


Figure 7: Bio-Oss Collagen® – (CC) – 24 Weeks Post-Op

Masson's Trichrome Stains. Note that the asterisks represent the implant material, the black arrows indicate the reference notch on the tooth root, and the green arrows show lamellar and woven bone regeneration. E = Epithelium; R = Tooth Root

DISCUSSION:

Both SalvinOss® Collagen and Bio-Oss Collagen® were effective in regenerating bone in a canine defect model. Radiographic evaluations demonstrated similar radio density post implantation between the two devices. SalvinOss® Collagen devices allowed for the defect site to remodel with similar volumes of lamellar and woven bone to that of Bio-Oss Collagen® devices throughout the 24 weeks post implantation.

Microscopic as well as MicroCT evaluations showed that SalvinOss® Collagen devices demonstrated greater ridge height and ridge width compared to Bio-Oss Collagen® devices throughout the study. Maintenance of ridge height and ridge width over time are both important in preserving the aesthetic appearance of the healed area.

In conclusion, SalvinOss® Collagen XenoGraft Bone Graft Material exhibited increased porosity and performed at least as well as Bio-Oss® Collagen Xenograft Bone Void Filler based on performance in a canine dental bone defect model.