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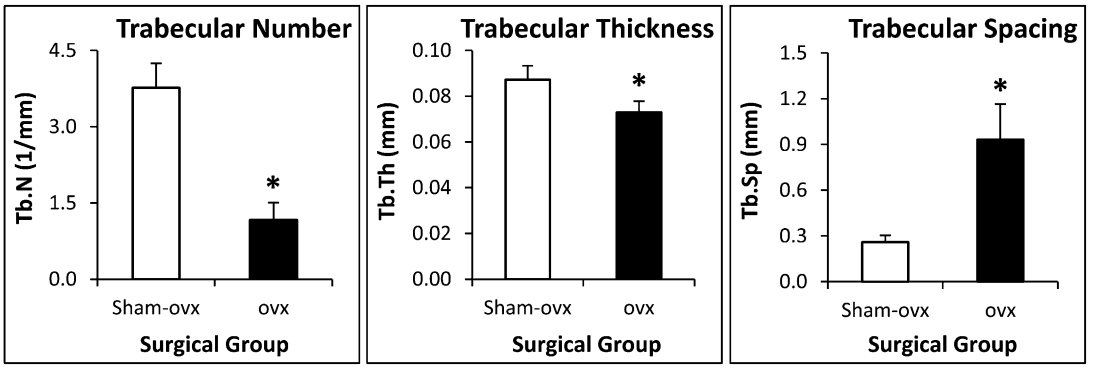

Fig. E-1

Bar graphs showing baseline trabecular architecture values: mean trabecular number (Tb.N), trabecular thickness (Tb.Th), and trabecular spacing (Tb.Sp) (and standard deviation) by surgical group. These results indicate that the ovariectomy-induced decrease in bone volume per total volume shown in Figure 2 was due to lower trabecular number and thickness combined with increased trabecular spacing (* = different from sham-ovx control; $p < 0.001$ for all comparisons).

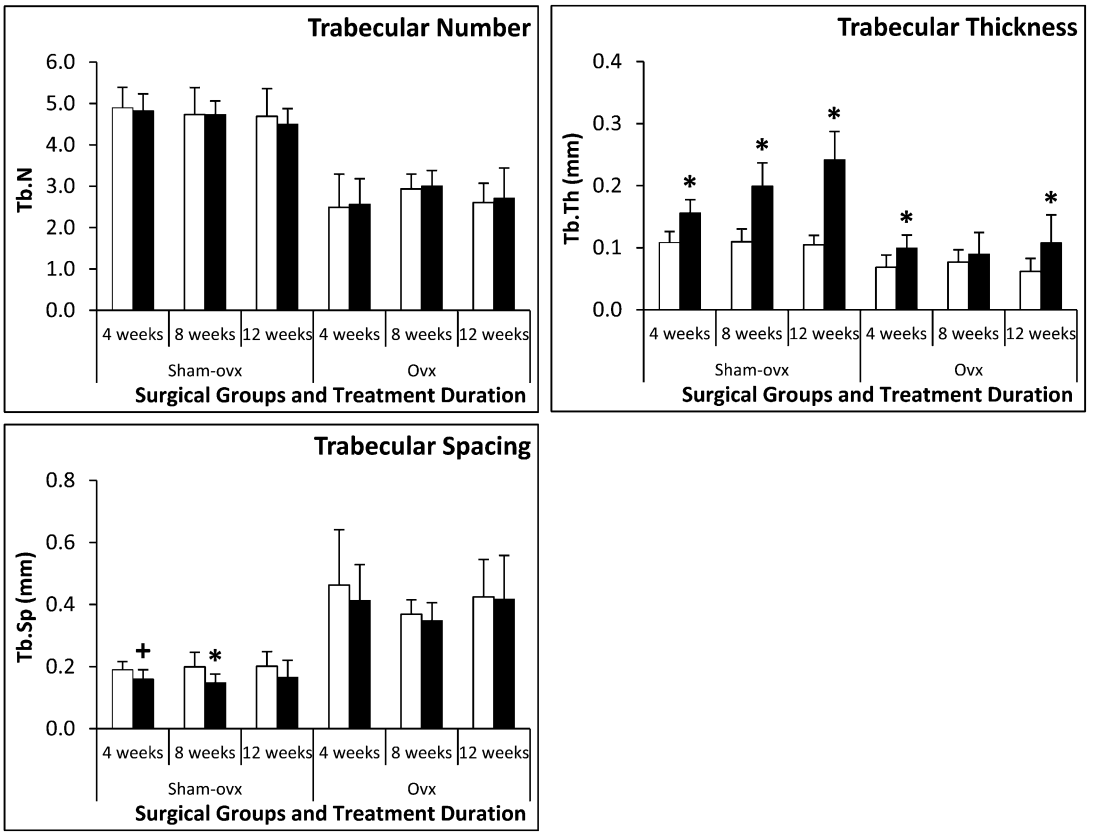

Fig. E-2

Bar graphs showing peri-implant trabecular architecture values: mean trabecular number (Tb.N, per mm), trabecular thickness (Tb.Th), and trabecular spacing (Tb.Sp) (and standard deviation) in rats treated with the vehicle (open bars) or with Scl-Ab (filled bars). Differences between control and treated rats at the same time point in the same surgical group are indicated by "*" if $p < 0.017$ (the adjusted level for significance, taking into account multiple comparisons) or "+" if $p < 0.05$ but > 0.017. Interactions between treatment (Scl-Ab or vehicle), time (four, eight, or twelve weeks), and surgery (sham-ovx or ovx) were determined using ANOVA. Tb.N showed significance for surgery; Tb.Sp was significant for treatment and surgery; and Tb.Th exhibited significance for treatment, time, surgery, treatment by time, treatment by surgery, time by surgery, and treatment by time by surgery ($p < 0.05$).

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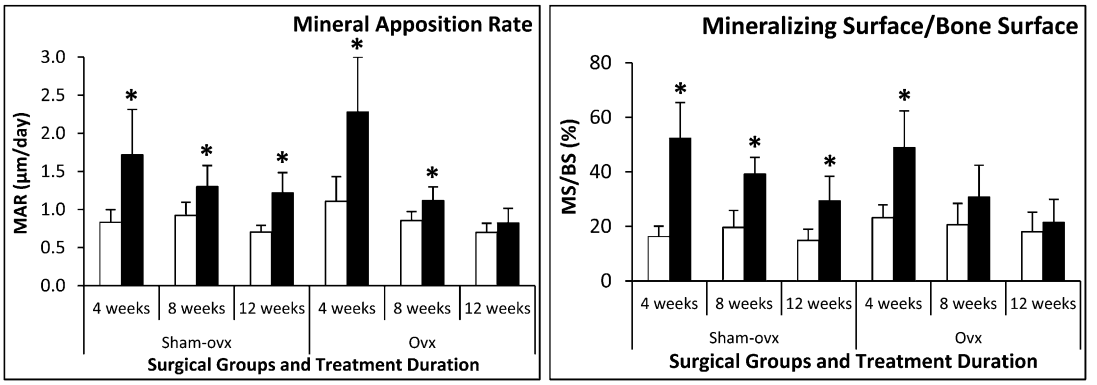

Fig. E-3

Bar graphs showing values from dynamic histomorphometry: mean mineral apposition rate (MAR) and mineralizing surface per bone surface (MS/BS) (and standard deviation) in rats treated with the vehicle (open bars) or with Scl- Ab (filled bars). Differences between control and treated rats at the same time point in the same surgical group are indicated by "*" if $p < 0.017$ (the adjusted level for significance, taking into account multiple comparisons) or "+" if $p < 0.05$ but > 0.017. Interaction analyses between treatment, time, and surgery revealed that treatment, time, and treatment by time were significant for MS/BS. For MAR, treatment and surgery were significant ($p < 0.05$).

TABLE E-1 Sample Sizes for Study Groups and Outcome Measures*

	Sham-Ovx						Ovx					
	Four Weeks		Eight Weeks		Twelve Weeks		Four Weeks		Eight Weeks		Twelve Weeks	
Variable	Veh.	Scl-Ab	Veh.	Scl-Ab	Veh.	Scl-Ab	Veh.	Scl-Ab	Veh.	Scl-Ab	Veh.	Scl-Ab
Animals completing study	12	12	12	12	12	11	12	12	11	12	12	12
Mechanical testing	12	12	12	12	12	11	9	8	10	12	11	12
BIC	7	7	7	7	8	7	7	6	6	8	6	6
BV/TV	12	12	12	12	12	11	12	12	11	12	12	12
Ct.Th	12	12	12	12	12	11	12	10	11	12	12	12
BFR/BS	9	10	7	9	8	8	8	7	7	9	7	7
ES/BS	7	7	7	7	8	7	7	7	6	8	7	6

*The number of rats that completed the implant arm of the study and the number of rats used in each assay are shown. Ovx = ovariectomized, veh. = vehicle, and Scl-Ab = sclerostin antibody. For the mechanical testing of implant fixation strength, interface stiffness, and energy to failure, the goal was to analyze all specimens available for analysis. For these variables, three specimens were eliminated because the implants were grossly loose at the time of sacrifice (one in the ovx four-week vehicle group, one in the ovx four-week Scl-Ab group, and one in the ovx twelve-week vehicle group), and six specimens were eliminated because of technical errors during testing (two in the ovx four-week vehicle group, three in the ovx four-week Scl-Ab group, and one in the ovx eight-week vehicle group). Chi-square tests examining the distribution of eliminated samples by treatment group were not significant. For the microCT variables of bone volume per total volume (BV/TV) and cortical thickness (Ct.Th), the targeted minimum sample size was ten per treatment group per time point. For the variables that depended on histologic preparation (bone-implant contact [BIC], bone-formation rate per bone surface [BFR/BS], and eroded surface per bone surface [ES/BS]), the targeted minimum sample size was six per treatment group per time point.

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TABLE E-2 Animal Body-Weight Data*

Treatment Group	Length of Follow-up	Time of Weighing	Treatment	Descriptive Statistics			P Value†
				No.	Mean Weight *(g)*	Std. Dev. *(g)*	
Sham-ovx	Four weeks	Implantation	Vehicle	12	307	17	0.567
			Scl-Ab	12	313	30	
		Sacrifice	Vehicle	12	287	21	0.086
			Scl-Ab	12	303	24	
	Eight weeks	Implantation	Vehicle	12	293	31	0.858
			Scl-Ab	12	295	36	
		Sacrifice	Vehicle	12	297	26	0.824
			Scl-Ab	12	293	44	
	Twelve weeks	Implantation	Vehicle	12	310	31	1.000
			Scl-Ab	11	310	33	
		Sacrifice	Vehicle	12	293	26	0.097
			Scl-Ab	11	315	34	
Ovx	Four weeks	Implantation	Vehicle	12	356	30	0.266
			Scl-Ab	12	368	23	
		Sacrifice	Vehicle	12	344	29	0.481
			Scl-Ab	12	352	22	
	Eight weeks	Implantation	Vehicle	11	363	32	0.372
			Scl-Ab	12	351	31	
		Sacrifice	Vehicle	11	347	33	0.625
			Scl-Ab	12	341	29	
	Twelve weeks	Implantation	Vehicle	12	349	45	0.891
			Scl-Ab	12	347	44	
		Sacrifice	Vehicle	12	359	44	0.623
			Scl-Ab	12	352	28	

*Body-weight data at the times of implantation and sacrifice are presented. Ovx = ovariectomized, and Scl-Ab = sclerostin antibody. The data were evaluated through a repeated-measures ANOVA, with weight at time of implantation and weight at sacrifice as the within-subjects factors and group (sham-ovx versus ovx), time point (four weeks versus eight weeks versus twelve weeks), and treatment (vehicle versus Scl-Ab) as the between-subjects factors. Weight was significant as a main effect ($p = 0.004$) because all groups showed a weight change from the time of implantation to sacrifice. Group was a significant main effect ($p < 0.001$) because the ovx rats were heavier than the sham-ovx rats. A weight-by-time-point interaction ($p = 0.016$) was present because the groups kept for longer times had more weight gain. There was a significant weight-by-group-by-treatment interaction ($p = 0.041$), implying a differential effect of treatment on weight gain in the sham-ovx and ovx groups, but none of the post-hoc t tests comparing the two treatment groups were significant. None of the other terms in the analysis were significant. †T test.

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TABLE E-3 Results of the Three-Way ANOVAs*

Variable	No.	Treatment-by-Time-by-Surgery	Treatment-by-Time	Treatment-by-Surgery	Time-by-Surgery	Treatment	Time	Surgery
Fixation strength	133	0.038	0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Interface stiffness	133	0.684	0.224	0.091	0.857	0.011	0.004	<0.001
Energy to failure	133	0.061	0.001	<0.001	<0.001	<0.001	<0.001	<0.001
BIC	82	0.580	0.947	0.246	0.204	<0.001	<0.001	0.009
BV/TV	142	0.075	0.031	<0.001	0.062	<0.001	0.314	<0.001
Ct.Th	140	0.582	0.522	0.327	0.147	<0.001	<0.001	0.004
BFR/BS	96	0.305	<0.001	0.532	0.041	<0.001	<0.001	0.351
ES/BS	84	0.724	0.770	0.136	0.071	<0.001	0.740	0.042

*Summaries of the ANOVAs for each assay; p values for the three-way and two-way interaction terms and for the main effects are presented. Treatment refers to use of Scl-Ab or vehicle, time refers to length of follow-up (four, eight, or twelve weeks), and surgery refers to the performance of a sham-ovariectomy or an ovariectomy. BIC = bone-implant contact, BV/TV = bone volume per total volume, Ct.Th = cortical thickness, BFR/BS = bone-formation rate per bone surface, and ES/BS = eroded surface per bone surface.

TABLE E-4 Calculation of Cumulative Fold Increase in Bone-Formation Rate*

	Fold Increase			
	Ovariectomy-Induced	Implant-Induced	Sclerostin-Antibody-Induced	Cumulative
Sham-ovx	1	2	7.0	14
Ovx	2	2	4.6	18.4

*The ovariectomy-induced fold increase and the Scl-Ab-induced fold increase in bone-formation rate were estimated from the findings in the present study. The implant-induced fold increase was estimated from our findings in a previous study[29]. The cumulative fold increase was calculated by multiplying the previous three values.