Human Bone Matrix Changes During Deep Saturation Dives

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Background: From 1997 to 1999, the Naval Submarine Medical Research Laboratory (NSMRL) studied the effects of saturation diving on two markers of human bone metabolism: cross-linked N-telopeptide (Ntx), a marker for bone resorption and osteocalcin (OC), a bone formation/turnover marker. We present the results of the third saturation dive study (1999), as well as a meta-analysis of data from all three years.

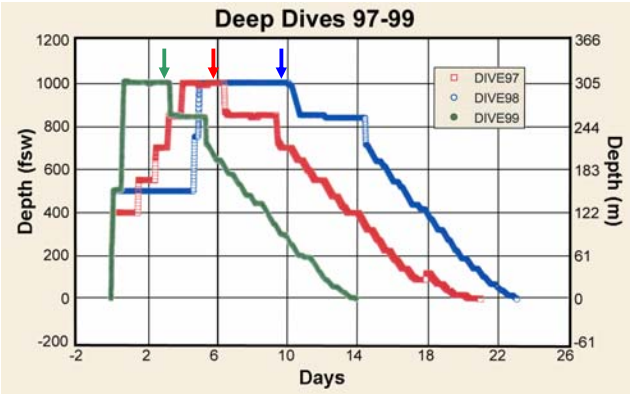

Figure 1: Depth-Time Profiles for Deep Dives 1997-99 (Arrows indicate timing of blood and urine samples at depth)

Methods: Eight U.S Navy divers underwent a dry hyperbaric chamber dive to 305 meters of seawater (msw). Measurements of serum osteocalcin (a bone formation and turnover marker) and urine crosslinked N-telopeptide (Ntx, a bone resorption marker) were made at baseline, 305 msw, and immediately after surfacing. To isolate the effects of medical lock transport on our results, additional Ntx and osteocalcin samples were taken from four control subjects at the surface. Half of these control samples were put on ice and compressed to 305 msw, returned to the surface under the same conditions as regular samples, and the results compared to those kept at the surface.

Analysis: The overall effect of the dive on mean osteocalcin and Ntx levels was compared using repeated-measures analysis of variance (ANOVA). If the ANOVA resulted in a significant F-statistic, planned comparisons were performed on compression and decompression effects. Data from similar points along each profile were pooled for dives conducted under similar circumstances from 1997-1998, using the same analysis strategy.

Results: The validation study showed no effects associated with compression or decompression on Ntx/osteocalcin levels for the samples drawn at surface, compared to samples that were never pressurized (Fig.2, Table 1). The data for the 1999 dive revealed a significant decrease in urine Ntx, with no change in serum osteocalcin (Fig. 3, Table 2). Data from the 1999 dive were combined in a meta-analysis with corresponding measurements taken during the 1997 and 1998 dives. The meta-analysis revealed a reduction in serum osteocalcin following saturation at 305 msw but no significant change in Ntx at depth. (Figs. 4 and 5, Table 3).

Table 1: Ntx and Osteocalcin results from method validation.

Marker	Mean (s.d.)	Range
Ntx† (nmol BCE/mmol Cr)		
-Baseline	30.3 (3.9)	28-36
-Immediately Frozen	35.3 (8.3)	25-45
-Compressed to 305	35.8 (8.30)	25-45
-Iced during compression	34.0 (8.41)	23-43
Osteocalcin‡ (ng/ml)		
-Baseline	15.2 (2.2)	12.8-18.1
-Immediately Frozen	17.0 (2.3)	14.1-20.1
-Compressed to 305	17.8 (1.4)	16.1-19.5
-Iced during compression	19.8 (4.3)	13.6-22.9
† Between groups F=1.36, df 3, 9 (p=0.3169)		
‡ Between groups F=2.12, df 3, 9 (p= 0.1672)		

Table 2: Ntx and Osteocalcin results from 1999 Deep Dive.

Marker	Mean (s.d.)	Range
Ntx†(nmol BCE/mmol Cr)		
-Baseline	43.1 (15.4)	24-75
-At 305 msw	33.1 (8.7)	21-46
-Surface	46.9 (19.5)	26-89
Osteocalcin‡(ng/ml)		
-Baseline	18.3 (4.4)	12.2-24.7
-At 305 msw	19.2 (3.3)	14.9-25.1
-Surface	15.3 (3.0)	11.8-18.9
† Between depths F= 5.41, df 2, 14 (p=0.0182)		
‡ Between depths F=3.41, df 2, 14 (p= 0.0622)		

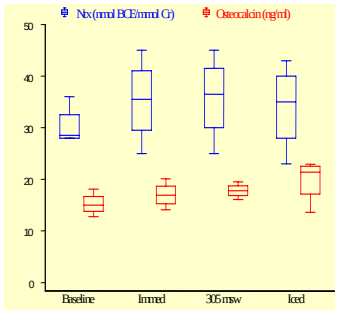

Figure 2: Ntx and Osteocalcin results from method validation (For all plots: line=median, box=25-75% CI, whiskers=95% CI)

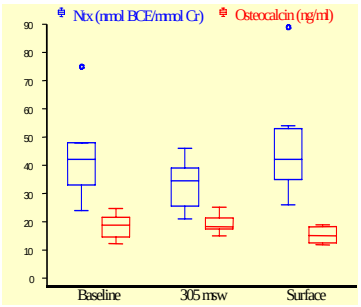

Figure 3: Ntx and Osteocalcin results from 1999 Deep Dive

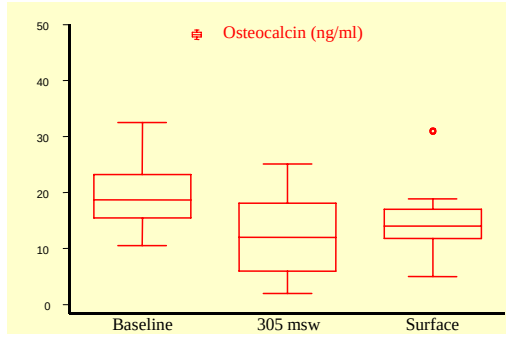

Figure 4: Osteocalcin results from 1997-1999 data

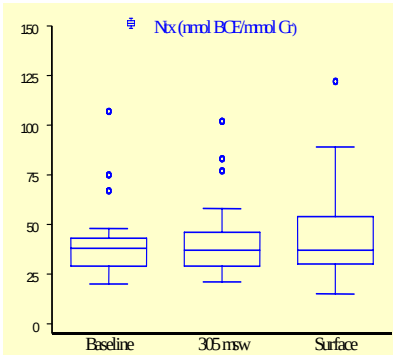

Figure 5: Ntx results from 1997-1999 data.

Table 3: Combined 1997-1999 results.

Marker	Mean (s.d.)	Range
Ntx†(nmol BCE/mmol Cr)		
-Baseline	40.5 (18.9)	20-107
-At 305 msw	41.8 (19.9)	21-102
-Surface	44.2 (23.4)	15-122
Osteocalcin‡(ng/ml)		
-Baseline	19.6 (5.8)	10.5-32.5
-At 305 msw	12.1 (7.6)	2.0-25.1
-Surface	14.9 (5.5)	5.0-31
† Combined data 97-99 (n=25),Between depths F= 0.63, df 2,48 (p=0.5381)	‡ Combined data 98-99 (n=17),Between depths F=6.62, df 2,32 (p= 0.0039)	

Conclusions: Taken together these studies may have identified a response of bone metabolism to changes in ambient pressure, however questions still remain as to whether blood sample handling/decompression procedures during these dives affected the meta-analysis results for osteocalcin.