Spaceflight Bone Atrophy: Problem Solved?

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Statement of Problem: What do we know from the supporting data?

- **Bone loss:** ISS (Table 1, Fig. 1); Skylab (single photon absorptiometry, Ca balance); Mir (DXA)
- **Elevated bone resorption markers:** ISS (Fig. 2); Skylab; multiple bed rest studies
- **Elevated urinary Ca:** ISS (Fig. 4); Skylab; multiple bed rest studies
- **Uncoupled remodeling:** ISS (Figs. 2,3); multiple bed rest studies

Table 1. QCT vBMD and FE Strength Changes

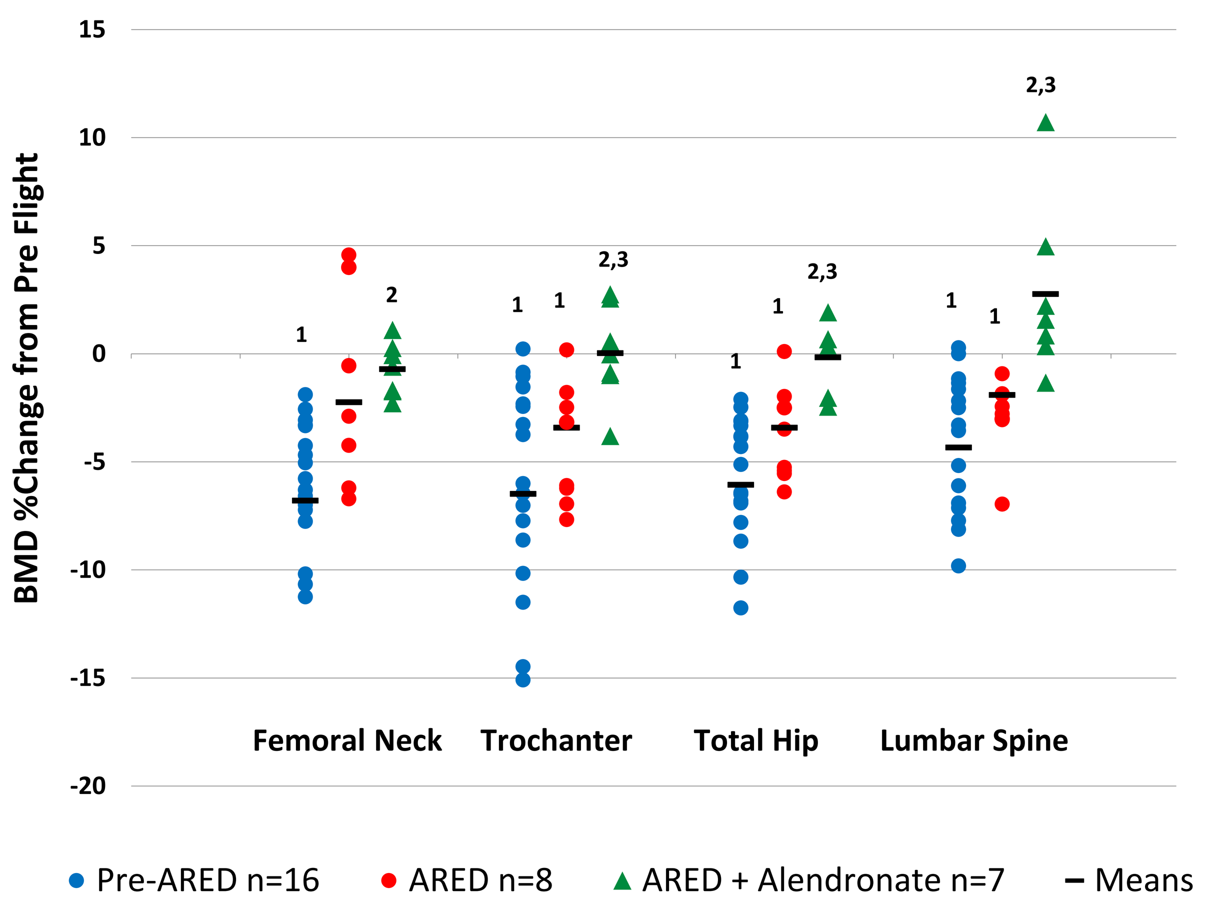
Pre-ARED (Low Resis Ex) vs ARED (High Resis Ex) vs ARED + Alendronate, R + < 2 weeks

QCT BMD (g/cm3)	Pre-ARED Control (n=18) % Change	ARED Control (n=8) %Change	Alendronate + ARED (n=7) %Change
Total Hip			
Trabecular	-13.6 ± 6.4[1]	-7.6 ± 6.0[1]	-1.1 ± 9.8[2]
Cortical	-3.2 ± 3.5	-2.6 ± 1.8	-0.6 ± 4.7
Trochanter			
Trabecular	-13.5 ± 6.5[1]	-7.2 ± 6.6[1]	-1.9 ± 9.9[2]
Cortical	-3.2 ± 3.3[1]	-3.3 ± 2.7[1]	-0.5 ± 5.0
Femoral Neck			
Trabecular	-15.0 ± 9.8[1]	-15.7 ± 17.8[1]	6.5 ± 14.8[2,3]
Cortical	-4.0 ± 5.5	-1.8 ± 2.8	-1.0 ± 4.8
Finite Element Strength (N)			
Non-Linear Stance	-9.5 ± 5.6[1]	1.7 ± 7.9	1.9 ± 9.7[2]
Non-Linear Fall	-14.1 ± 8.1[1]	-2.7 ± 5.8	0.8 ± 10.1[2]

[1]Pre vs. Post, $P < 0.05$
[2]ARED + Alendronate vs. Pre-ARED, $P < 0.05$
[3]ARED + Alendronate vs. ARED, $P < 0.05$

Fig. 1 DXA BMD Changes

Pre-ARED (Low Resis Ex) vs ARED (High Resis Ex) vs ARED+Alendronate, R<2 Weeks

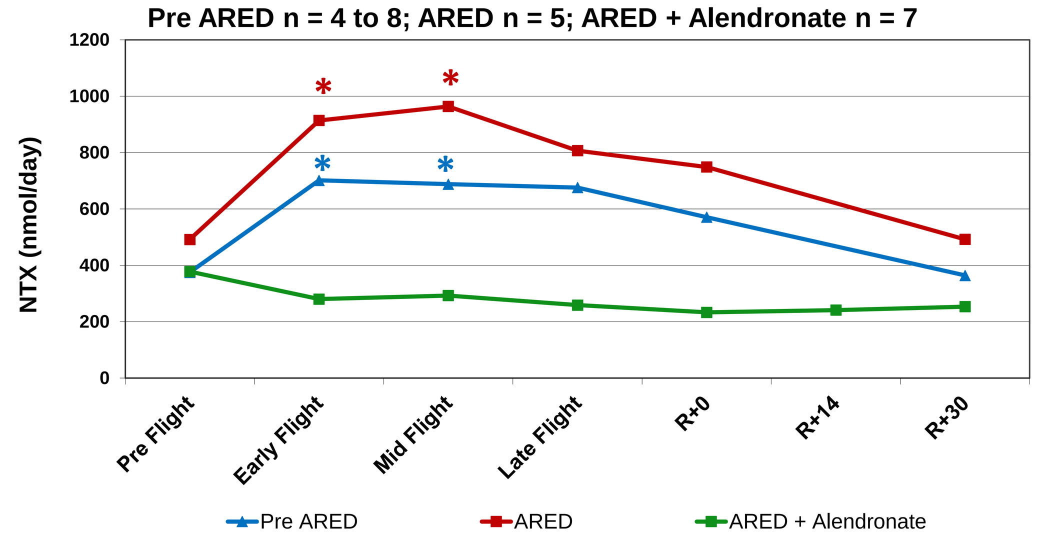


1 Pre vs. Post, $P < 0.05$
2 ARED + Alendronate vs. Pre-ARED, $P < 0.05$
3 ARED + Alendronate vs. ARED, $P < 0.05$

Bone Biomarker Changes

Fig. 2 NTX Changes

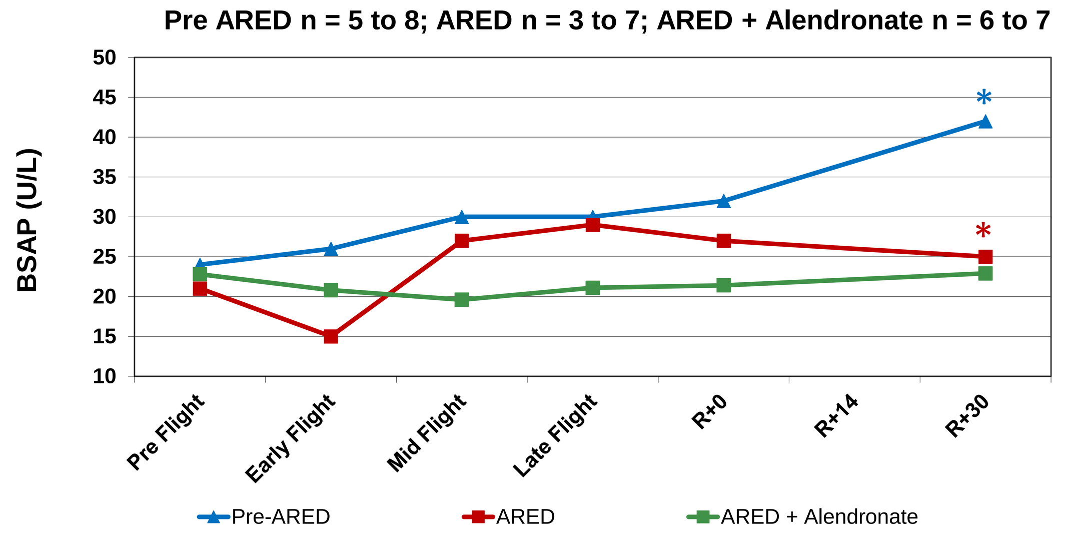
Pre-ARED (Low Resis Ex) vs ARED (High Resis Ex) vs ARED+Alendronate



*Significant Diff. vs. Pre-Flight, *P* <0.05, with Bonferroni correction
Pre ARED data calculated from Smith paper 2012 JBMR

Fig. 3 BSAP Changes

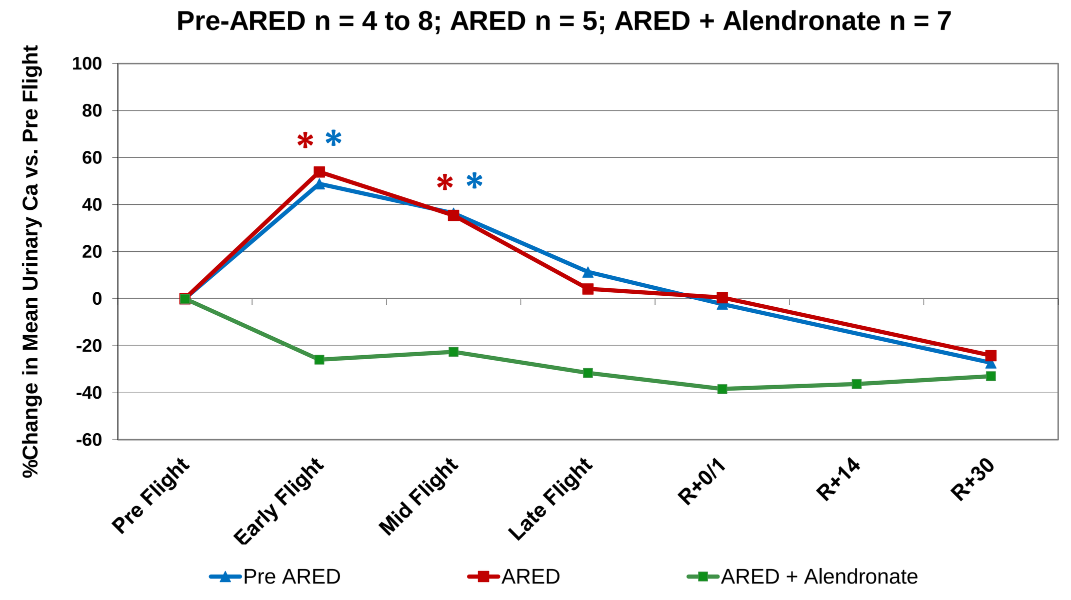
Pre-ARED (Low Resis Ex) vs ARED (High Resis Ex) vs ARED+Alendronate



*Significant Diff. vs. Pre-Flight, *P* < 0.05, with Bonferroni correction (based on absolute data)
Pre ARED and ARED data calculated from Smith paper 2012 JBMR

Fig. 4 Urinary Ca Changes

Pre-ARED (Low Resis Ex) vs ARED (High Resis Ex) vs ARED+Alendronate



*Significant Diff. vs. Pre-Flight, *P* < 0.05, with Bonferroni correction
Pre ARED data calculated from Smith Paper 2012 JBMR

Conclusions

1) From a flight risk standpoint, the problem is considered manageable
2) Data show that exercise plus an anti-resorptive will be effective, reducing bone loss, bone resorption and urinary Ca excretion (lowering renal stone risk)
3) Targeted high resistive exercise alone can significantly attenuate bone loss but not necessarily completely

Potential Research Areas

General

1) What are the molecular biology details for bone loss in space?
2) Related to the above, what is the explanation for the large variability in response between individuals and bone sites?

Topics Related to Resistive Exercise Use in Space

Why do resorption markers remain elevated while improving bone homeostasis?

1) Why do formation and resorption markers appear to remain essentially uncoupled? Do bone markers represent regional metabolic conditions?
2) Is there a compartmental redistribution of bone with targeted high resistive exercise?
3) How can in-flight resistive exercise be made more efficient/efficacious?
4) Does resistive exercise impact frequency and severity of inflight injuries and ways to prevent?

Topics Related to Pharmaceutical Use in Space

1) Drug stability for long missions
2) Operational plan needed, e.g., in cases of equipment failure or crew injury where exercise may not be possible
3) Suitability of other anti-resorptives (e.g., cathepsin K, Rank-L inhibitors)
4) Suitability of anabolic drugs