

Exploring dose-response relationships in vertebral bone loss after pelvic radiotherapy: The prospective RadBone trial

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1. Background

- Pelvic radiotherapy is associated with insufficiency fractures and long-term skeletal morbidity.
- Relationship of dose and bone mineral density (BMD) loss remains poorly defined.
- Prospective dual energy absorptiometry (DXA)-based studies are rare, limiting **evidence-based bone health guidance**.

RadBone is the first prospective randomised pilot study to:

1. Quantify vertebral dose-response in women receiving curative pelvic radiotherapy.
2. Assess feasibility and effect of a musculoskeletal health package (MHP) intervention.

2. Methods

Study design

- Pilot study of 26 women recruited prior to pelvic radiotherapy (cervical n=9, endometrial n=13, anorectal n=4).
- Participants randomised to MHP (n=11; prehabilitation exercise, calcium and vitamin D supplementation) or observation (n=15)
- L1–L4 BMD measured by DXA at baseline and 18 months; %ΔBMD calculated per vertebra.

Analysis

- 1
 - L1-L4 autosegmented from radiotherapy planning computed tomography (CT)
- 2
 - 104 vertebrae analysed with median dose received by vertebra volume (D50) extracted; out-of-field D50 imputed with random forest multiple imputation
- 3
 - **Full cohort analysis:** Linear mixed effects model adjusted for age, menopause, baseline BMD, vertebra location
- 4
 - **Subgroup analysis:** vertebra receiving dose D50 > 5Gy (n=27 vertebrae; 15 patients), adjusted for age and menopause
- 5
 - Secondary analysis: effect of MHP

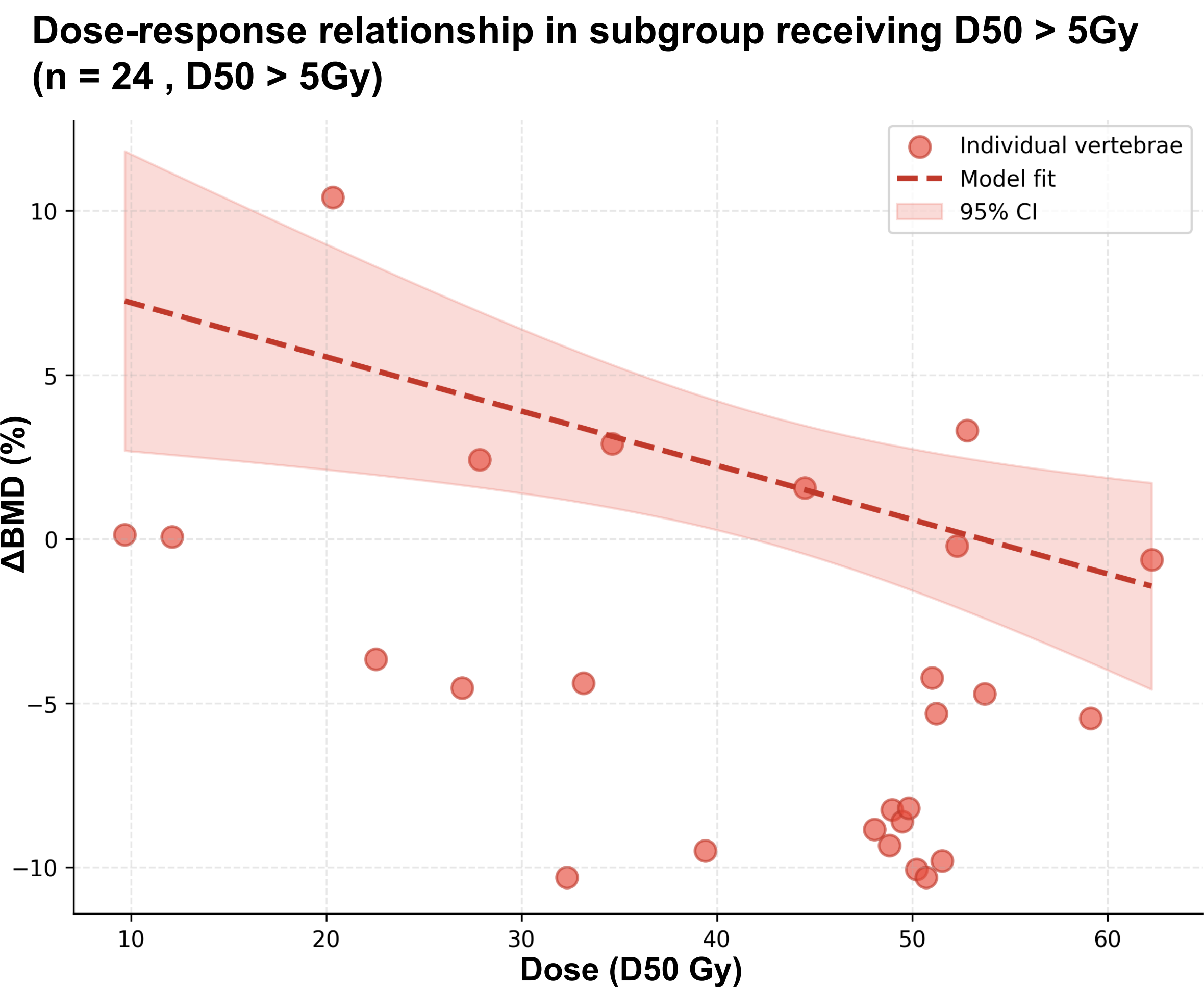


Figure 1: Linear mixed-effects model of %ΔBMD in the subgroup receiving D50 > 5Gy. Model fit with 95% confidence intervals. Vertebral dose was significantly associated with a 0.2% decrease in bone mineral density per Gy.

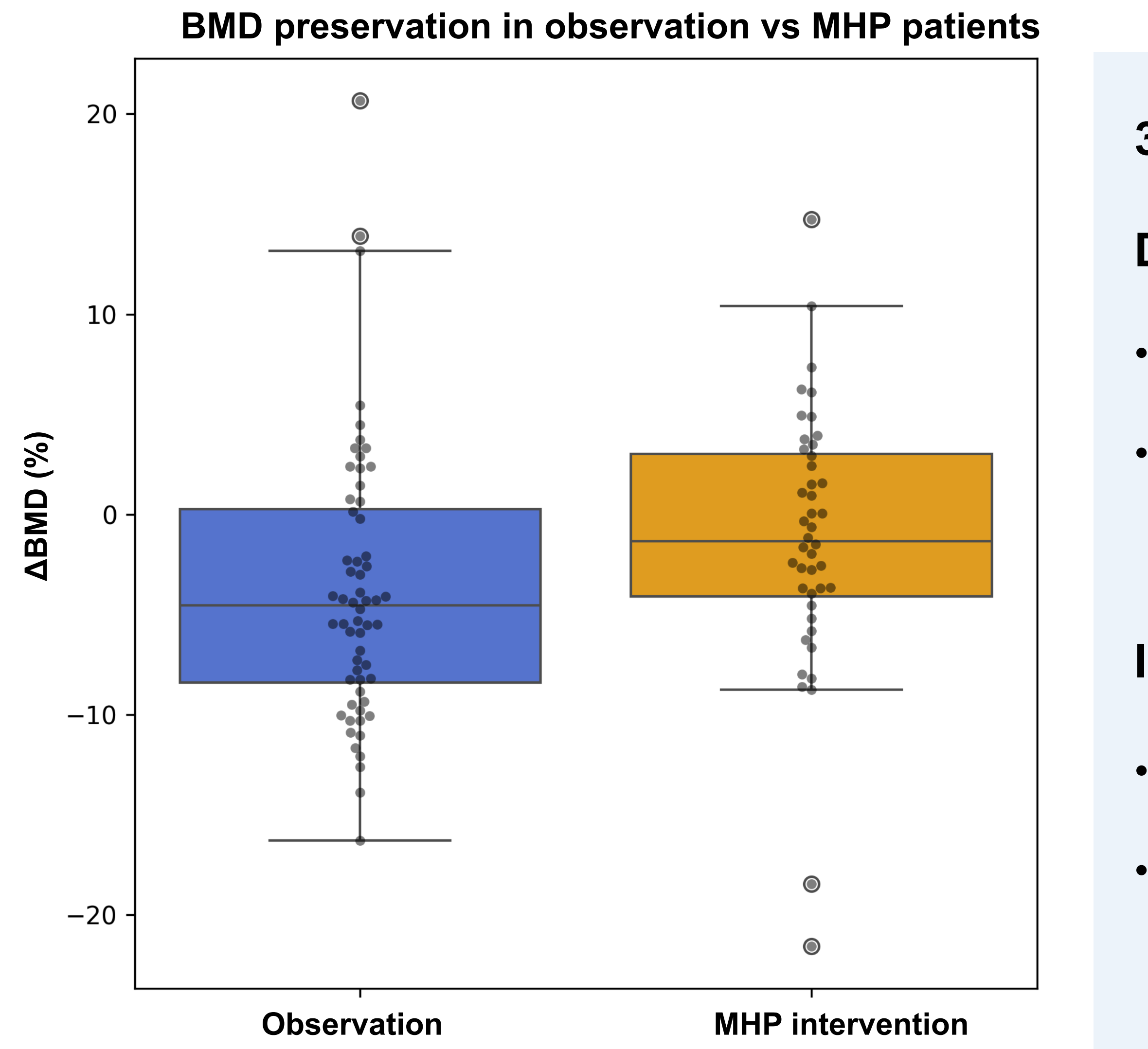


Figure 2. Boxplots showing the distribution of %ΔBMD by intervention group for the full cohort. Vertebrae from intervention patients (MHP, n = 44) showed significantly less BMD loss compared with the observation group (n = 60; mean = -1.25 vs -3.80 %, p = 0.0045).

Predictor	Estimate	SE	z	p-value	95% CI (Lower)	95% CI (Upper)
D50	-0.19	0.06	-3.35	0.001	-0.31	-0.08
Age	-0.36	0.20	-1.86	0.063	-0.74	0.02
Postmenopausal status	10.79	3.63	2.97	0.003	3.67	17.91
Between patient variance	0.18					

Table 1. Linear mixed effects model on subgroup receiving D50 > 5Gy, adjusted for age and menopausal status.

Predictor	Estimate	SE	z	p-value	95% CI (Lower)	95% CI (Upper)
D50	-0.25	0.05	-5.47	0.001	-0.34	-0.16
Age	-0.52	0.25	-2.06	0.039	-1.01	-0.03
Postmenopausal status	15.6	4.44	3.51	0.005	6.88	24.3
MHP	-1.27	2.89	-0.44	0.66	-6.93	4.4
Between patient variance	0.18					

Table 2. Linear mixed effects model on subgroup receiving D50 > 5Gy, **adjusted for intervention**. The addition of the MHP as a variable in the model did not alter the dose-response relationship.

3. Results

Dose-response

- No significant dose-response in full cohort
- Significant linear dose-response in subgroup with D50 > 5Gy: **-0.2% ΔBMD per Gy** (β = -0.19, p < 0.001; Figure 1, Table 1)

Intervention effect

- Median ΔBMD: **-3.3%** (IQR -7.3 to +1.5)
- MHP patients showed **significantly better BMD preservation** (-1.25% vs -3.80%, p = 0.0045, Figure 2)
- Adjusting for MHP did not alter dose-response relationship (Table 2)

4. Conclusions

- **Significant dose-response observed between vertebral dose and BMD decline, with threshold near 5Gy.**
- **MHP participants showed greater bone preservation than controls.**
- Multicentre studies are needed to validate results.
- Findings could inform future bone-sparing strategies in treatment planning.