News Release

Title

Short-range UV-LED irradiation in postmenopausal osteoporosis using ovariectomized mice

Key Points

- **Low energy irradiation of narrow-range UV-LED was effective in improving osteoporotic changes in the presence of vitamin D deficiency in an ovariectomized mouse model.**

Summary

Prof. Yoshihiro Nishida at Department of Rehabilitation, Dr. Satoshi Ochiai at Department of Orthopaedic Surgery, Nagoya University Hospital, revealed low energy irradiation of narrow-range UV-LED supplied vitamin D efficiently, and improved bone strength in ovariectomized mouse.

Postmenopausal osteoporosis, like age-related osteoporosis, is a condition that increases the risk of fractures and, as a result, can significantly reduce an individual's quality of life. Vitamin D is one of the most important molecules associated with osteoporosis and its sufficiency is important for both postmenopausal and age-related osteoporosis. However, it has been reported that vitamin D deficiency is present not only in the elderly but also in postmenopausal women. Previously, our research group found that low-energy UV-LED irradiation could be an effective source of vitamin D in aged mice. The purpose of this study is to investigate whether low-energy UV-LED irradiation leads to effective treatment for postmenopausal osteoporosis.

Previously, our research group determined UV-LED irradiation conditions that have the least adverse effects on the body and are effective in supplying vitamin D. This time, UV-LED was irradiated to the ovariectomized mice under the irradiation conditions. As a result, in the vitamin D deficient state, the mice irradiated with UV-LED had higher levels of vitamin D in the serum than the mice not irradiated with UV-LED, and both the cortical thickness and bone strength increased.

UV irradiation with this UV-LED device could be clinically useful for patients with not only age-related, but also postmenopausal osteoporosis with few side effects.

Research Background

Osteoporosis and associated fractures are associated with poor quality of life, increased risk of physical harm, and significant financial burden. If a novel device that was efficient, cheap, and minimally invasive to the body could be developed, the healthy life expectancy could be extended by preventing the bedridden state, and medical costs could be reduced by reducing the number of patients needing surgery.

Vitamin D is a molecule that plays a central role in bone metabolism, and 90% of the body's vitamin D is produced by the skin upon exposure to sunlight and ultraviolet rays. Despite this importance of vitamin D, the majority of older women with osteoporosis are reported to be deficient in vitamin D, possibly because of reduced opportunities to go out, and subsequent reduced sunbathing. There are also reports that vitamin D is deficient not only in the elderly but also in postmenopausal women.

Up to now, no medical device for treating osteoporosis has been developed. The development of a medical device that effectively produces vitamin D would be a revolutionary treatment for osteoporosis for not only elderly patients with osteoporosis, but also postmenopausal osteoporosis ones. For the purpose of prevention and treatment of osteoporosis, we aim to develop a therapeutic device that efficiently produces vitamin D in the body using the light emitting diode (LED) technology.

In this study, we investigated whether irradiation of short-range UV-LED supplies sufficient levels of serum Vitamin D, and improves osteoporosis in a mice model with postmenopausal osteoporosis.

Research Results

1. Determination of the timing of UV irradiation after ovariectomy

We wanted to evaluate whether ovariectomy (OVX) was appropriately performed to create a postmenopausal osteoporosis model. In addition, we examined how many weeks after OVX bone changes occur in C57BL/6 female mice, which provided important basic data for determining the irradiation timing of the main experiment. Based on the results of the experiment, we considered 8 weeks after OVX was appropriate timing of UV irradiance in our subsequent main experiments.

2. The effect for serum vitamin D, bone morphology and bone strength test

C57BL/6 female mice were divided into 4 groups: vitamin D-repletion without UV irradiation (Vit.D+UV−), vitamin D-repletion with UV irradiation (Vit.D+UV+), vitamin D-deficiency without UV irradiation, (Vit.D−UV−), and vitamin D-deficiency with UV irradiation (Vit.D−UV+). All mice were ovariectomized at 16 weeks of age. Serum levels of vitamin D were increased in Vit.D−UV+ group as compared with Vit.D−UV− group (Fig. 1). Cortical thickness of the metaphysis was significantly increased in Vit.D−UV+ group as compared with Vit.D−UV− group after 24 weeks of irradiation (Fig. 2). In the bone strength test of femur, the stiffness were increased in Vit.D−UV+ group as compared with Vit.D−UV−

group (Fig. 3). In the histological assay, cortical thickness was thicker in Vit.D-UV+ mice than in VitD-UV− ones, which correlated with the results of the CT examination (Fig. 4).

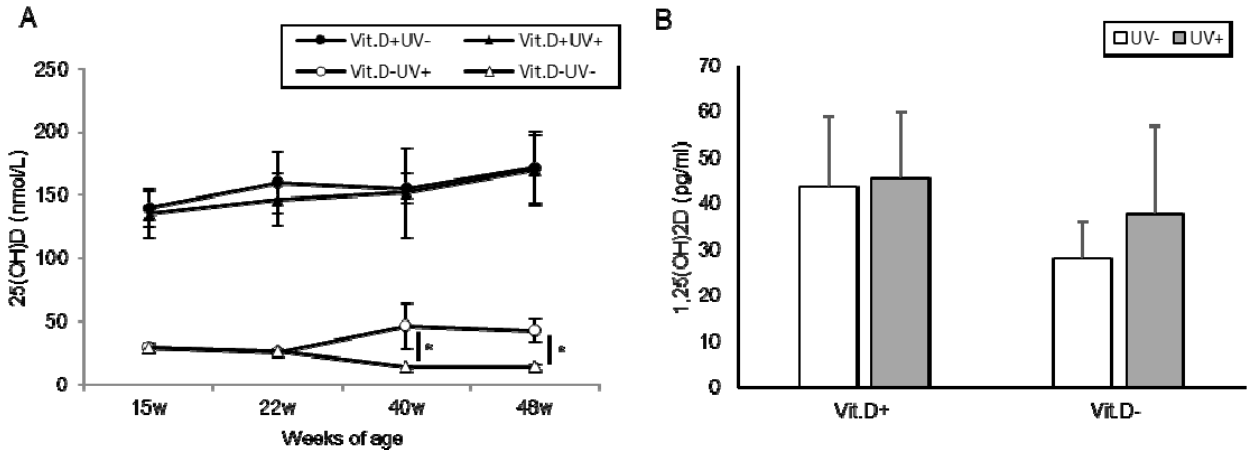

Fig. 1: Serum levels of 25(OH)D and 1,25(OH)2D in main study. Sera for 25(OH)D examination were collected at 15 weeks of age (ovariectomy), 22 weeks (start of UV irradiation), 40 weeks (16-weeks of UV irradiation), 48 weeks (24-weeks of UV irradiation). Sera for 1,25(OH)2D examination were collected at 48 weeks (24-weeks of UV irradiation). (**A**) Serum levels of 25(OH)D. (**B**) Serum levels of 1,25(OH)2D. *$p < 0.05$. *Vit.D*− vitamin D-deficient diet; *Vit.D*+ vitamin D-replete diet; *UV* ultraviolet irradiation.

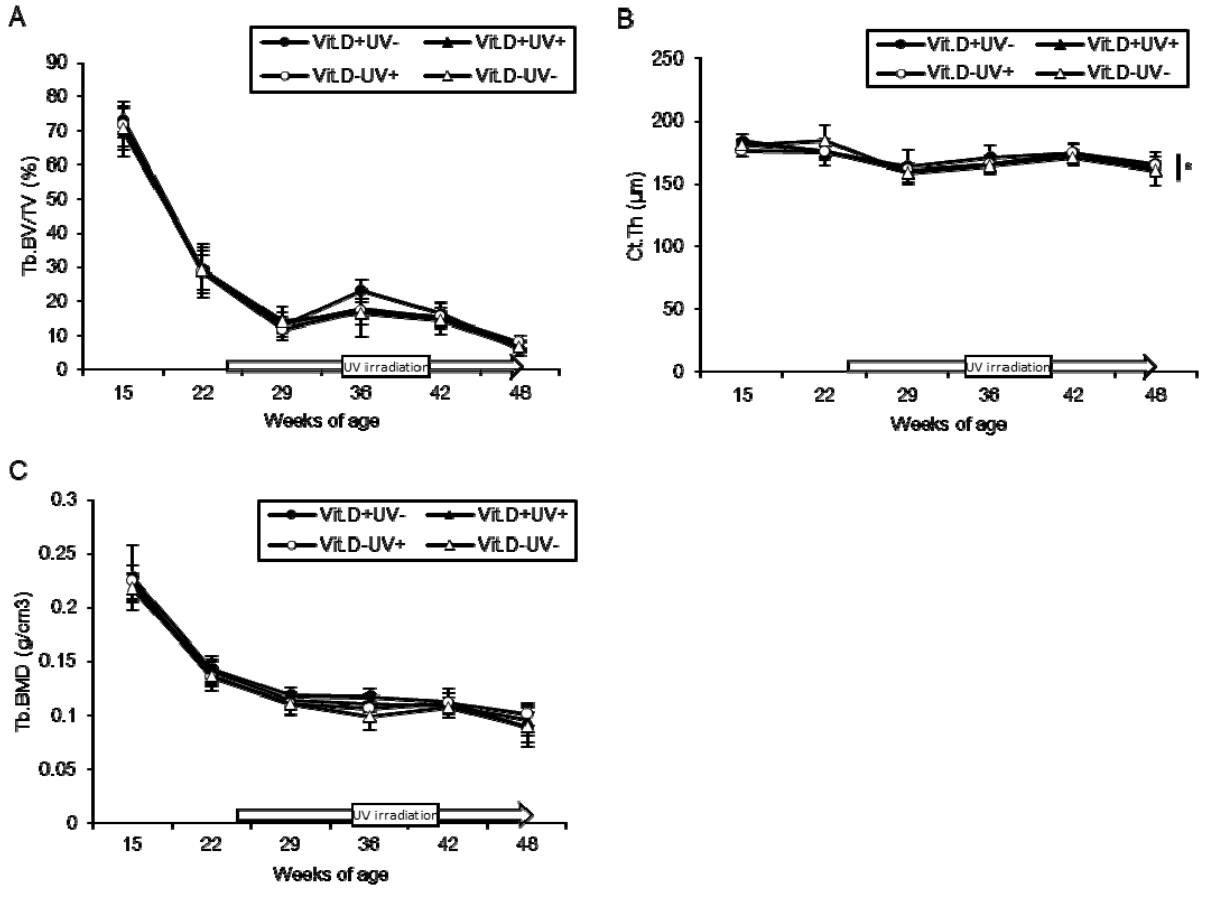

Fig. 2: Bone morphological parameters with micro-CT analyses. Each parameter evaluated by micro-CT is compared at 15, 22, 29, 36, 42, 48 weeks of age. (**A**) Trabecular percent bone volume [Tb.BV/TV] (**B**) Cortical thickness [Ct.Th] (**C**) Trabecular bone mineral density [Tb.BMD] $*p < 0.05$. *CT* computed tomography; *Vit.D–*, vitamin D-deficient diet; *Vit.D+* , vitamin D-replete diet; *UV* ultraviolet irradiation.

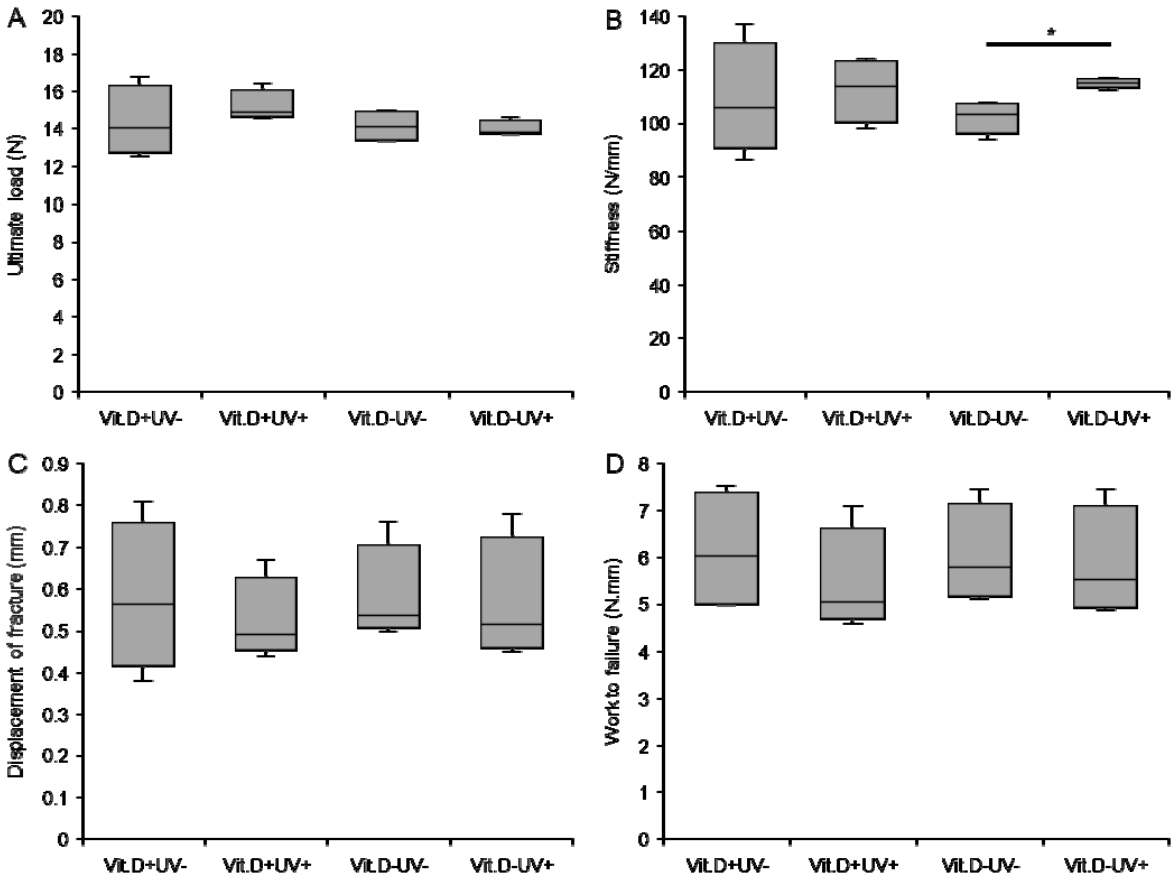

Fig. 3: Results of mechanical test. Three point bending test of femur was performed at 48 weeks of age, and plotted. (**A**) Ultimate load (**B**) Stiffness (**C**) Displacement of fracture (**D**) Work to failure $*p < 0.05$. *Vit.D–* vitamin D-deficient diet; *Vit.D+* vitamin D-replete diet; *UV* ultraviolet irradiation; *N* newton.

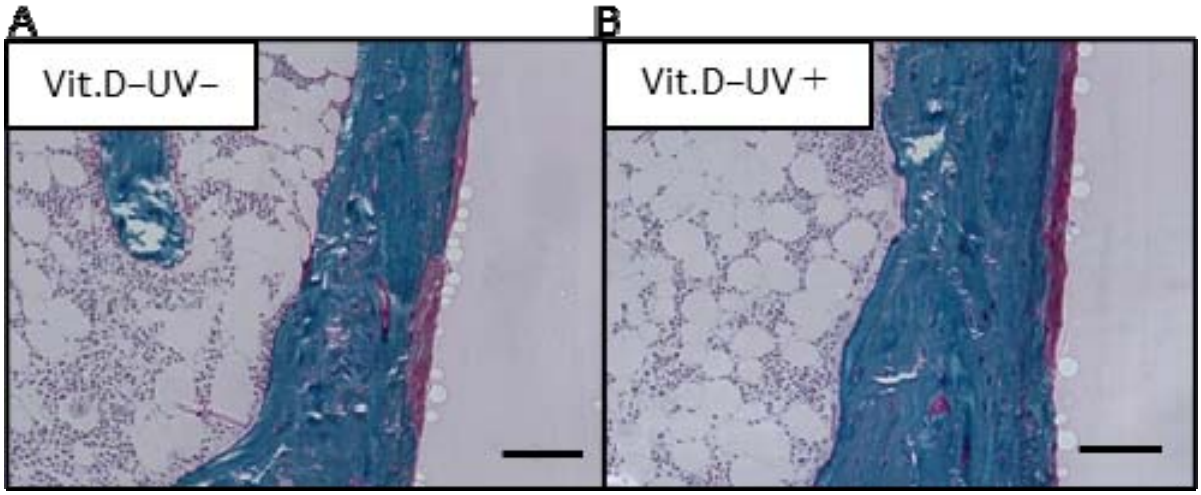

Fig. 4: Villanueva Goldner staining. Stained coronal sections were presented of the medial metaphysis of right femurs at 48 weeks of age (original magnification × 200, bars indicate 100 μm). (**A**) Vit.D− UV− group. (**B**) Vit.D− UV+ group. *Vit.D*− vitamin D-deficient diet; *UV* ultraviolet irradiation.

Research Summary and Future Perspective

UV-irradiation using a short-range LED device could increase serum levels of Vit. D, leading to increases of BMD and bone strength. Thus far, the therapeutic approach for osteoporosis is limited to exercise, sunbathing, and drug therapy. Use of a therapeutic device for osteoporosis is a modality with a novel concept for osteoporosis, and has the potential to reduce the associated medical costs. Since this device could be developed as a small and portable one, it could be easy to use in a variety of situations in the clinical setting from a general hospital to home-care. Treatment by low energy UV irradiation with a narrow range UV-LED device may be a promising novel therapeutic approach to osteoporosis, including postmenopausal one.

Publication

Satoshi Ochiai, Yoshihiro Nishida, Yoshitoshi Higuchi, Daigo Morita, Kazuya Makida, Taisuke Seki, Kunihiro Ikuta, Shiro Imagama. Short-range UV-LED irradiation in postmenopausal osteoporosis using ovariectomized mice. *Scientific Reports,* published online on April 12, 2021.
DOI : https://doi.org/10.1038/s41598-021-86730-0

Japanese ver.
https://www.med.nagoya-u.ac.jp/medical_J/research/pdf/Sci_Rep_210412.pdf