News Release

Title

Low energy irradiation of narrow-range UV-LED prevents osteosarcopenia: development of a novel device for safe and low-cost supplementation of vitamin D

Key Points

・We determined the minimal irradiance and dose of UV-LED needed to produce sufficient 25(OH)D in mice.

・ Low energy irradiation of narrow-range UV-LED was effective in improving osteoporotic and sarcopenic changes in the presence of vitamin D deficiency in a senescence-accelerated mouse model.

・ Low energy irradiation of narrow-range UV-LED did not induce severe skin damages.

Summary

Prof. Yoshihiro Nishida at Department of Rehabilitation, Dr. Kazuya Makida at Department of Orthopaedic Surgery, Nagoya University Hospital, revealed low energy irradiation of narrow-range UV-LED supplied vitamin D efficiently, and prevented osteosarcopenia associated with vitamin D deficiency in senescence-accelerated mouse prone 6.

Osteosarcopenia is a novel concept denoting the co-existence of decreased density/volume of both bone and muscle, namely osteoporosis and sarcopenia. This condition promotes falls and insufficiency fractures that impede the activities of daily living (ADL) of elderly persons. Vitamin D is one of the most important molecules associated with osteosarcopenia. However, it has been reported that the elderly were consistently deficient in vitamin D. The purpose of this study is to determine the minimal irradiance intensity and dose of short-range UV-LED that would be effective in supplying sufficient levels of serum Vitamin D, and to examine the effects of UV-LED with a determined irradiance and dose on osteosarcopenia in animal models of senescence-accelerated mouse prone 6 (SAMP6).

First, they conducted a preliminary experiment to determine the minimum irradiance and dose of UV irradiation that adequately supplies vitamin D for mice. Next, SAMP6 were irradiated the UV-LED with the irradiance intensity and dose determined by the preliminary experiment. Serum levels of vitamin D, trabecular bone mineral density on micro-CT, grip strength and muscle mass were higher in the group with UV irradiation than in the group without UV irradiation. Signs of severe damage induced by UV irradiation was not found in skin by histological analyses.

UV irradiation with this UV-LED device could be clinically useful for patients with osteosarcopenia with few side effects.

Research Background

Osteosarcopenia is a novel concept denoting the co-existence of decreased density of both bone and muscle, namely osteoporosis and sarcopenia. This condition promotes falls and insufficiency fractures that impede the activities of daily living (ADL) of elderly persons. This impairment of ADL is becoming an increasingly serious social problem, associated particularly with the aging of society seen in developed countries.

Vitamin D is one of the most important molecules associated with osteosarcopenia. However, it has been reported that the elderly are consistently deficient in vitamin D. Adequate supplementation of vitamin D for elderly persons with low cost and high safety is an urgent issue for all rapidly aging societies.

They previously reported that narrow-range UV irradiation using LED was effective for elevation of serum vitamin D levels and prevention of bone brittleness in an animal model of vitamin D deficiency. In that study, the protocol of UV irradiation was considered to be a high risk of harm to the human body, particularly to skin. The purpose of this study is to determine the minimal irradiance intensity and dose of short-range UV-LED that would be effective in supplying sufficient levels of serum Vitamin D, and to examine the therapeutic effects of UV-LED with a determined irradiance and dose on osteosarcopenia in animal models of senescence-accelerated mouse prone 6 (SAMP6).

Research Results

1. Determination of the minimum irradiance and dose of UV irradiation

First, they conducted an experiment to determine the minimum irradiance of UV irradiation that adequately supplies vitamin D. Second, they conducted an experiment to determine the minimum dose of UV irradiation that adequately supplies vitamin D. Based on the results of the two experiments, they considered 0.16 mW/cm^2 as the minimal UV irradiance and 1000 J/m^2 as the minimal dose needed to produce sufficient 25(OH)D in our subsequent main experiments.

2. The effect for serum vitamin D, bone mineral density, grip strength and muscular mass

SAMP6 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+). Serum levels of vitamin D were increased in Vit.D−UV+ group as compared with Vit.D−UV− group (Fig. 1). Trabecular bone mineral density on micro-CT was higher in Vit.D−UV+ group than in Vit.D−UV− group (Fig. 2). In the histological assay, the amount of osteoid tissues, representing incomplete calcification of the bone matrix, was greater in Vit.D−UV− group than in Vit.D−UV+ group (Fig. 3). Grip strength and muscle mass were higher in Vit.D−UV+ group than in Vit.D−UV− group (Fig. 4).

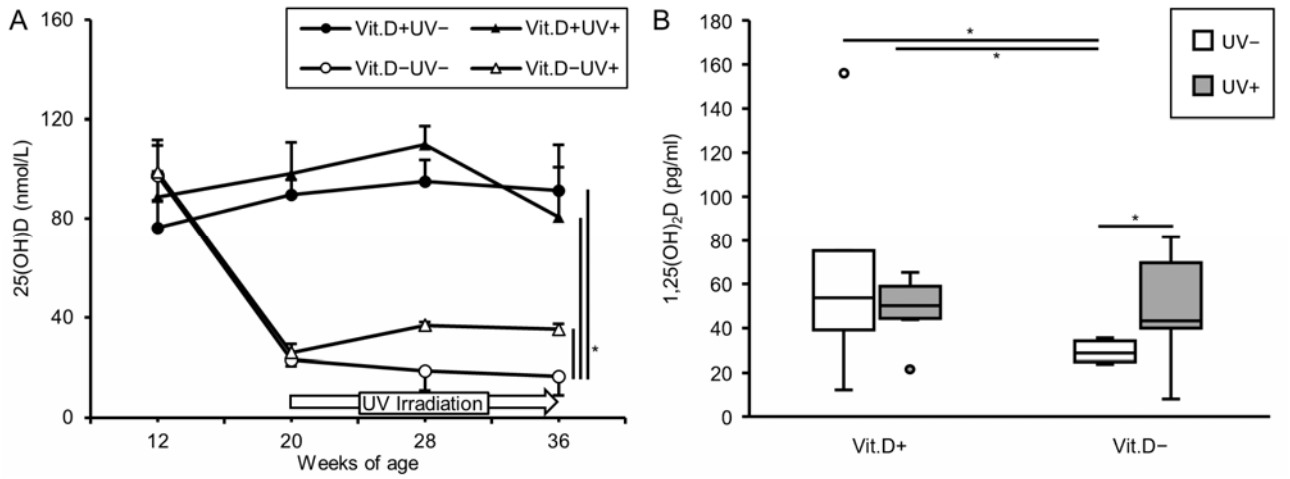

Fig. 1: Serum levels of 25(OH)D and $1,25(OH)_2D$ in main study. Serum for 25(OH)D examination was obtained at 12 weeks of age (initiation of vitamin D–deficient diet or vitamin D–containing diet), 20 weeks (initiation of UV irradiation), 28 weeks (8-weeks of UV irradiation), 36 weeks (16-weeks of UV irradiation). Serum for $1,25(OH)_2D$ examination was obtained at 36 weeks (16-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.

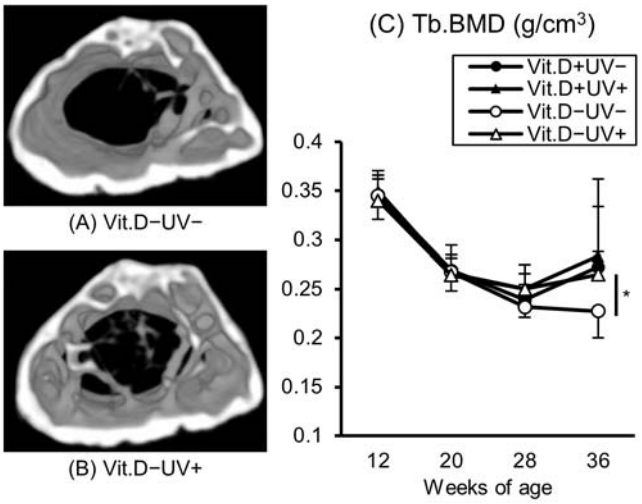

Fig. 2: Three–dimensional digital images and Tb.BMD of right femur. Three–dimensional images of right femur were reconstructed and Tb.BMD were calculated based on micro–CT data at 36 weeks of age. **A** Vit.D−UV− image from a distal viewpoint. **B** Vit.D−UV+ image from a distal viewpoint. **C** Tb.BMD of right femur. Vit.D−UV+ group showed higher density of trabecular bone than that in Vit.D−UV− group. * $p < 0.05$. Vit.D−, vitamin D-deficient diet; Vit.D+, vitamin D-replete diet; UV, ultraviolet irradiation; Tb.BMD, trabecular bone mineral density.

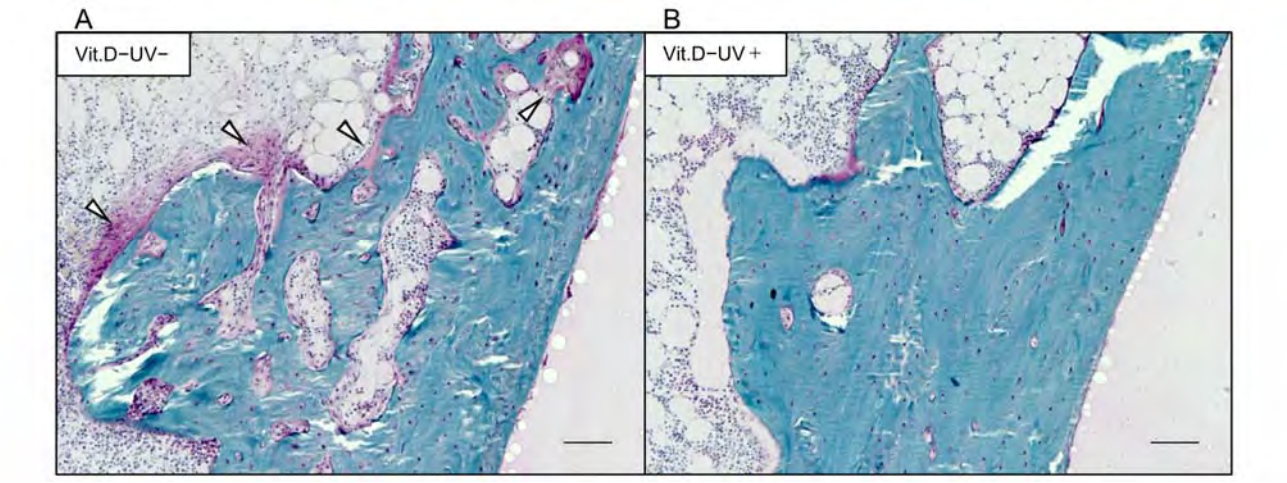

Fig. 3: Results of Villanueva Goldner staining. Coronal sections of the medial metaphysis of left femurs at 36 weeks of age were stained (original magnification ×200, bars indicate 100 μm). **A** Vit.D−UV− group. **B** Vit.D−UV+ group. A greater amount of red-colored osteoid tissues (white arrowheads) was observed in Vit.D−UV− group than in Vit.D−UV+ group. Vit.D−, vitamin D-deficient diet; Vit.D+, vitamin D-replete diet; UV, ultraviolet irradiation.

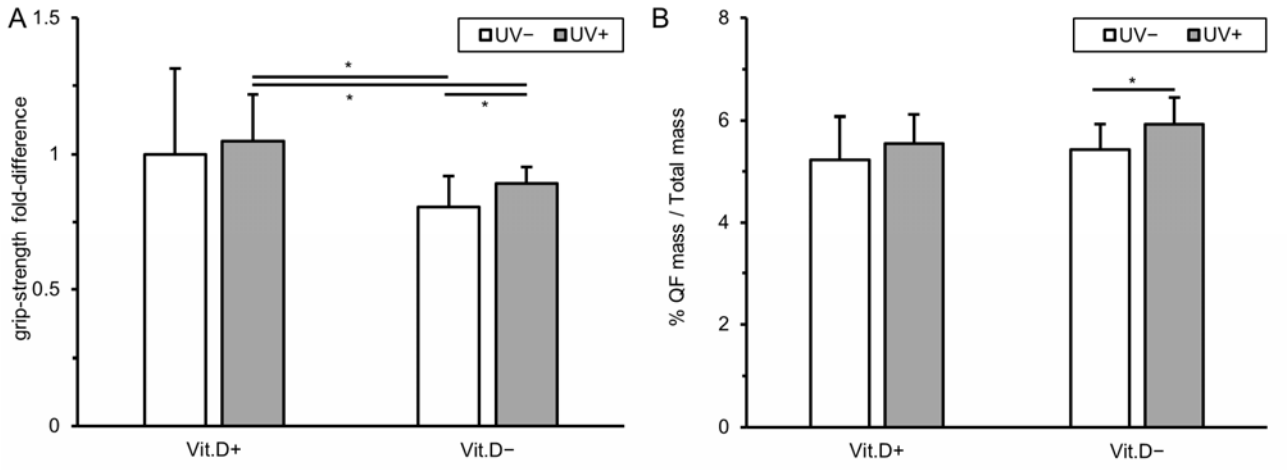

Fig. 4: Results of muscle strength and muscle mass evaluation. **A** Grip strength at 36 weeks of age was expressed with reference to that in Vit.D+UV− group as 1.0. measured in 15 trials per mouse. The values were corrected for body weight. B Muscle weight at 36 weeks of age corrected by body weight. * $p < 0.05$. Vit.D−, vitamin D-deficient diet; Vit.D+, vitamin D-replete diet; UV, ultraviolet irradiation; QF, quadriceps femoris.

3. Analysis of skin histology

In quantitative analysis, there were no differences in the skin epidermal or dermal thicknesses among the groups. Signs of severe damage induced by UV irradiation was not found in skin histology (Fig 5).

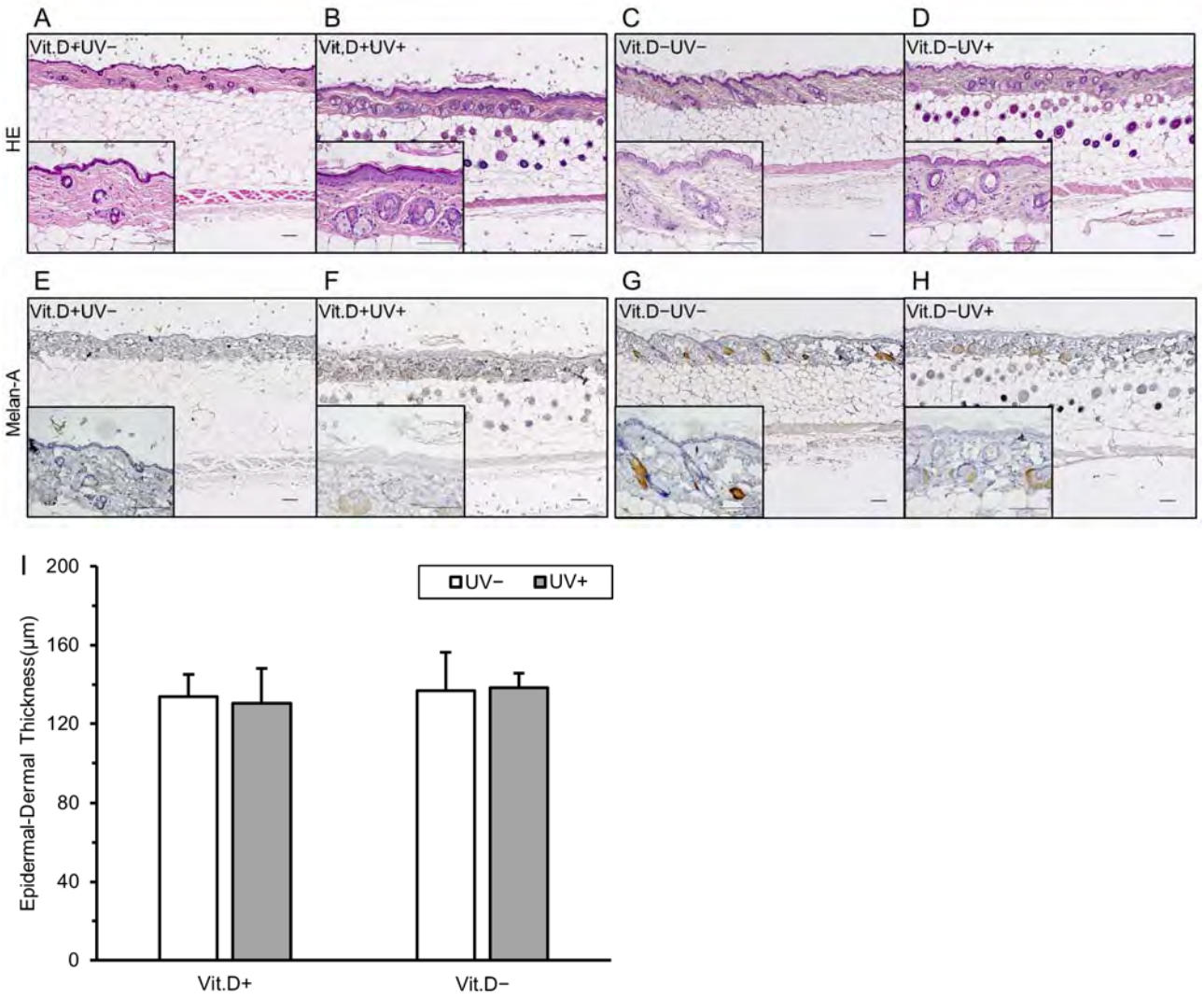

Fig. 5: Influence of UV irradiation on skin tissues. A–D Hematoxylin and eosin staining for epidermis and dermis, (original magnification ×10, bars indicate 100 μm). E–H Immunohistochemical staining with anti-Melan-A monoclonal antibody for epidermis and dermis (original magnification ×100, bars indicate 100 μm). I Quantification of epidermal and dermal thickness in 10 randomly selected area of low-power fields (×100). Vit.D−, vitamin D-deficient diet; Vit.D+, vitamin D-replete diet; UV, ultraviolet irradiation; HE, hematoxylin and eosin staining; Melan, immunohistochemical staining with anti-Melan-A monoclonal antibody.

Research Summary and Future Perspective

UV irradiation with this UV-LED device could be clinically useful for patients with osteosarcopenia with few side effects, particularly, patients with low mobility, and/or cannot sunbathe. 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. Considering that many developed countries face an increasingly aged population that is more susceptible to the burdens of osteosarcopenia associated with vitamin D deficiency, treatment by low energy UV irradiation with a narrow range UV-LED device may be a promising novel

therapeutic approach to this disease.

Publication

Kazuya Makida, Yoshihiro Nishida, Daigo Morita, Satoshi Ochiai, Yoshitoshi Higuchi, Taisuke Seki, Kunihiro Ikuta, Naoki Ishiguro. Low energy irradiation of narrow-range UV-LED prevents osteosarcopenia associated with vitamin D deficiency in senescence-accelerated mouse prone 6. *Scientific Reports,* published online on July 17, 2020.
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Japanese ver.
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