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Short Communication

# Radiation-Therapy Effects On Bone Hydroxyapatite Structure

**Ivan L. Quevedo[1*], Juan C.I. Ormeno[1], Max B. Shorwer[2]**

*[1] Department of Endocrinology, Medical School, University of Concepción, Chile; [2] Department of Oncology, Hospital Clínico Regional of Concepción, Chile*

## ABSTRACT

Radiotherapy is associated with radiographically detected osteoporosis. The precise pathophysiology is not completely known yet.

Hydroxyapatite (Hap, $Ca_{10}(PO_4)_6(OH)_2$) is the mineral component of the bone, and it can form chemical and mechanical bonds directly with living tissues, and with bone-implant interfaces as well.

The aim of this research was to study the influence of external radiotherapy in the Hap ultrastructure. The experimental study was carried out on a section of bone from a human humerus, extracted from a male donor (50 years old). The bone tissue sample was irradiated with a telecobalt therapy equipment (Phoenix 2000), applying 35 fractions of 2 Gray each from Monday to Friday, until completing 70 Gray.

The energy of the radiation and time of exposure used in this work was the same that it is used in common radiotherapy sessions.

The calculations to determine the radiation dose were performed using the three-dimensional planner Eclipse 8.0 software. To evaluate the changes in the crystal structure of the Hydroxyapatite after each irradiation, an X-ray diffractogram was carried out on the bone sample using an X-ray diffractometer (Bruker D8) equipped with the copper anode (K-alpha=1.5406 A) and a detection scan of 5-80°.

There are no differences between the diffractograms; thus, with the radiation-gamma, the same that it is used in common radiotherapy sessions, there are no appreciable changes in the crystal structure (ultrastructure) of Hap present in the bone.

We concluded that there are no differences between the diffractograms for different exposure times.

**Keywords:** Radiotherapy; Osteoporosis; Bone; Hydroxyapatite; Human

## INTRODUCTION

Radiotherapy is associated with radiographically detected osteoporosis and investigations have shown reduced bone mineral density and increased fragility after irradiation; however, the precise pathophysiology is not completely known yet [1].

A significant part of stereotactic radiotherapy (for peripheral non-small cell lung cancer) with tumors near the thoracic wall shows fractures of ribs in the follow-up, even in the areas of the thoracic wall that received a lower dose [2,3].

The primary effect of radiation on bone is atrophy, which involves a reduction in the number of functional structural components without a reduction in size [4]. There are several primary factors to be considered in the pathogenesis of radiation-induced alterations in bone: vascular changes, cellular changes and changes in the bone matrix collagen [5]; nonetheless, few researches have focused on changes in the bone's mineral component, and the few that have done so have not focused on the effects at the ultrastructural level.

**Correspondence to:** Quevedo IL, Department of Endocrinology, Medical School, University of Concepción, Chile, E-mail: equevedo@udec.cl

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Hydroxyapatite (Hap, $Ca_{10}(PO_4)_6(OH)_2$) is the mineral component of the bone, and it can form chemical and mechanical bonds directly with living tissues, and with bone-implant interfaces as well [6,7].

Irradiated bone has demonstrated the decreased capacity to heal. These effects are largely associated with the impact of radiotherapy on the existing vascular microarchitecture and the physiological processes of angiogenesis. Radiation directly impacts the existing microvasculature causing structural disruptions, decreased overall vascular density and obliteration of small blood vessels; however, it takes time for these changes to happen [1].

The almost instantaneous decline in bone architecture after radiation exposure cannot be attributed only to cellular processes (resorption) because the cellular population of the bone is heavily low the early days post-radiation; thus, the quick bone loss caused by irradiation must be a product of increased osteoclast activity and also physicochemical erosion by damage to the Hap [5,8].

The aim of this research was to study the influence of external radiotherapy in the Hap ultrastructure.

## MATERIALS AND METHODS

The experimental study was carried out on a section of bone from a human humerus, extracted from a male donor (50 years old).

The bone tissue sample was irradiated with a telecobalt therapy equipment (Phoenix 2000), applying 35 fractions of 2 Gray each from Monday to Friday, until completing 70 Gray.

The energy of the radiation and time of exposure used in this work was the same that it is used in common radiotherapy sessions.

To ensure the homogeneity of the radiation dose, and simulate the conditions of the bone in the human body, the bone samples were immersed in an acrylic cuvette (20 × 20 cm) filled with distilled water, submerging the bone to a depth of 5cm with a locking system.

The calculations to determine the radiation dose were performed using the three-dimensional planner Eclipse 8.0 software.

To evaluate the changes in the crystal structure of the Hydroxyapatite after each irradiation, an X-ray diffractogram was carried out on the bone sample using an X-ray diffractometer (Bruker D8) equipped with the copper anode (K-alpha=1.5406 A) and a detection scan of 5-80°.

The objective of this work was to observe and quantify the effect of radiation on the ultrastructure of the hydroxyapatite.

## RESULTS

First, we examined the crystal structure of our bone sample before radiation through X-Ray Diffraction (XRD) (Figure 1). Our XRD pattern is in agreement with a standard XRD pattern of Hap (based on ICDD standard 9-432) because all diffraction peaks from standard Hap matched the pattern of our bone; therefore, it is concluded that there is indeed hydroxyapatite in our bone tissue sample.

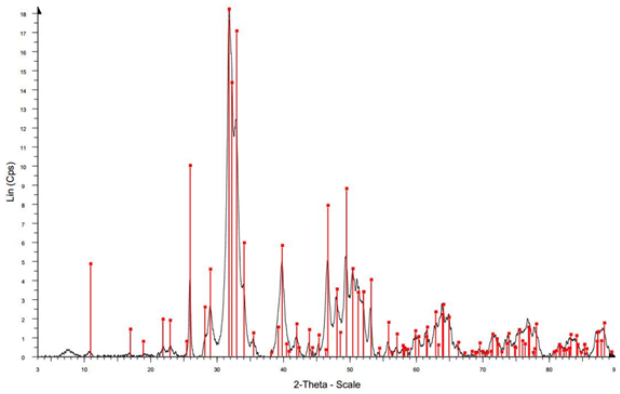


**Figure 1:** The standard XRD peaks of hydroxyapatite (based on ICDD 9-432) are shown in red, while the XRD pattern of our bone sample is shown in black.

The XRD patterns of our bone sample at different exposure time to radiation. The black XRD pattern (lower pattern) represents the bone before radiation (Figure 2).

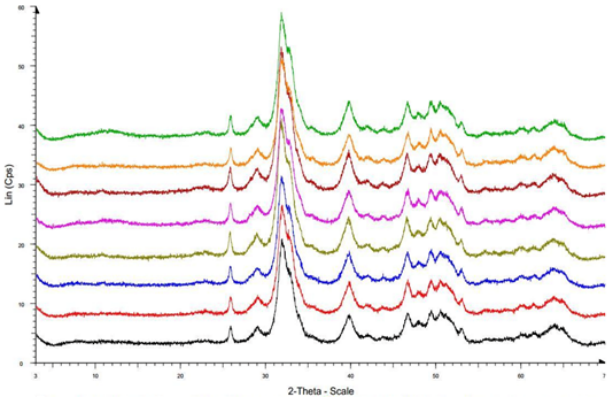


**Figure 2:** The XRD patterns of our bone sample at different exposure time to radiation. The black XRD pattern (lower pattern) represents the bone before radiation. Each XRD pattern above the black one had more accumulated exposure time to radiation. The red XRD pattern was measured the first week, while the upper XRD pattern (green one) was measured the last week of exposure to radiation. Every XRD pattern has the same peaks, but some are shown higher to compare them.

## DISCUSSION

The interaction of the organic matrix with Hap is mainly from the electrostatic binding of collagen side chain carboxylate and surface mineral phosphate groups via calcium ions. Studies have shown that there are changes on a molecular level in the bone matrix, because the side chain carboxylate groups of the collagen matrix that are involved in coordination with apatite bound calcium ions are partially removed by decarboxylation upon radiation and there are loss of acidic phosphate groups due to a formation of ion bridged phosphate groups in the apatite [9].

3D agent-based models in systems biology have been designed to simulate the interactions between bone marrow stromal cells and tumor cells. These models integrate events at different

spatial and temporal scales, and allows to virtually visualize in 3D the dynamics of the bone marrow stiffness; nevertheless, these models were designed to study the effects of tumors in the bone marrow rather than the effects of radiation [10].

Studies such as those mentioned above and a literature review revealed that the radiation effects on bone structure had been focused on the effects on the chemical structure of Hap, mechanical properties of bone, vascular architecture, collagen structure or osteoclast activity [5,9], however, none of them studied the effects on the ultrastructure of the Hap.

After evaluating the changes in Hap after each irradiation through diffractograms, we concluded that there are no differences between the diffractograms for different exposure times; therefore, with this gamma radiation, there are no appreciable changes in the ultrastructure of hydroxyapatite present in the bone.

The changes induced in the Hap after radiation have been shown on the molecular level, however, at a higher level, we found that there were no significant changes in the ultrastructure through this investigation.

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