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117.1 Author

Jowsey J, Phil D, Kelly PJ, Riggs BL, Bianco AJ, Jr, Scholz DA, Gershon-Cohen J.

117.2 Reference

J Bone Joint Surg Am. 1965;47:785–806.

117.3 Institution

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117.4 Abstract

Quantitative microradiography has been promoted for studying bone turnover and has been applied to a study of normal and osteoporotic human bone. Proof is presented that this method is reproducible and provides an accurate measure of bone formation and resorption. It was demonstrated that bone from the majority of osteoporotic patients differs from normal bone by increased amounts of resorption. Bone formation is generally normal. However, in Cushing's syndrome, after steroid therapy and after immobilization, bone formation decreases.

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117.5 Summary

Jowsey et al. used the technique of microradiographs to study the mineral content of sections of harvested bone from cadavers, and live patients undergoing spinal fusion procedures.

In the first part of the paper, the method and process of obtaining the bone sample, obtaining the microradiograph, and interpreting the results are discussed. In the second part of the paper, the authors compare the appearances of normal and osteoporotic bone in human samples using microradiographic studies.

Firstly, the use of microradiographs to quantitatively analyze bone had not previously been extensively studied. It was hypothesized that this was a superior method of analyzing bone formation and resorption than previous methods, namely use of radioisotopes and histological analysis.

Secondly, the comparison of normal and osteoporotic bone showed that osteoporotic bone has a negative net resorption, and that bone formation is not different to that of normal bone. Normal bone demonstrated an increase in resorption with advancing years, but this was not as marked as in those patients with osteoporosis. In addition, younger patients with osteoporosis resorb bone at a faster rate than patients over 70. Increased resorption does not seem to continue unabated. There is a point where it decreases to a level where equilibrium is maintained between formation and resorption.

117.6 Citation Count

425

117.7 Related References

1. Boivin G, Meunier PJ. The degree of mineralization of bone tissue measured by computerized quantitative contact microradiography. *Calcif Tissue Int.* 2002;70(6): 503–11.

2. Sissons HA. Microradiography of bone. *Br J Radiol.* 1950;23(265):2–7.
3. Chappard D, Baslé MF, Legrand E, Audran M. New laboratory tools in the assessment of bone quality. *Osteoporos Int.* 2011;22(8):2225–40.

117.8 Key Message

Quantitative microradiographic studies, by Jowsey of bone biopsy samples from osteoporotic patients demonstrated that bone-forming surfaces generally are normal, and that bone-resorbing surfaces are increased by a factor of two to four. Osteoporosis is a disease of bone resorption not formation.

117.9 Why It's Important

Jones provided a detailed description of the technique of microradiography and largely established the criteria for the interpretation of microradiographs.

This was one of the earliest studies on uncoupling of bone formation and resorption leading to osteoporosis. This knowledge has been subsequently applied to new therapeutic strategies to control bone resorption i.e. bisphosphonates.

117.10 Strengths

An accurate measure of bone formation and resorption was described. This is a reproducible method. Human samples were studied using a standardized method.

117.11 Weaknesses

Although briefly discussed, the causes of excess bone resorption in osteoporotic patients were not explored in detail. At this time however, there were only theories and no firm evidence regarding this. The number of samples used is not representative of a population and obtaining samples in live patients is a painful procedure that limits the number of samples that can be obtained.

The method depends on the analysis of biopsy material, the relationship between the part of the skeleton examined and the whole of the skeleton must be established.

In addition quantitative microradiography measures the amounts and not the rates of formation and resorption in terms of lengths of bone surface. In order to determine the rate of bone formation or resorption, the width of tissue laid down or removed over a defined interval has to be measured.

117.12 Relevance

The technique of producing a microradiograph of a section of mineralized bone involves placing a thin section of undecalcified bone on a high-resolution emulsion and exposing it to a fine beam of X-rays, which are differentially absorbed by the mineralized bone. The emulsion is developed and the image is viewed through a microscope, the variations in greyness corresponding directly to variations in the mineral density of bone.

The process permits recognition of different densities of mineral and also quantitation of bone turnover by measurement of the lengths of bone surfaces where formation or resorption is taking place in a defined area of a bone sample.

The method of quantitation depends on the surface limited nature of formation and resorption of bone. A standard area of bone is prepared and the total surface in that area is measured on an enlarged photograph of the microradiograph. Any surface that is in the process of active resorption or formation is marked on the photograph and also measured. The values that are expressed in the results represent the amount of formation and resorption of bone occurring in this unit area of bone as a percentage of the total available surface in that same area.

Microradiography has been used for the study of the structure, distribution and composition of bone tissue. The uneven distribution of bone mineral was revealed by this technique and quantitative information obtained on the mineral content of different areas of bone.

Since the pioneering research of Jowsey et al., numerous microradiographic studies have been performed on diseased bone states [1]. This paper provided a very early description of the osteoporotic process and provided key information regarding the development and treatment of osteoporosis and other metabolic bone diseases. This gain in understanding led to the development of bisphosphonate as a treatment for osteoporosis.

Microradiography of bone has now been progressively abandoned in favor of the non invasive dual energy x-ray absorptiometry (DEXA) scanning for quantifying calcified bone mass.

A large number of other more sophisticated techniques now exist to explore bone quality on bone samples. These include dynamic histomorphometry on undecalcified bone after tetracycline labeling, backscattered electron imaging and synchrotron radiation micro-computed tomography [2].

Dynamic bone histomorphometry has developed as a method for evaluating alterations in bone remodeling at the level of the basic multicellular unit [3]. This technique allows bone microarchitecture to be explored in 2D on histological sections and in 3D by micro CT or synchrotron.

It allows measurement of parameters such as the mineral apposition rate, bone formation rate, bone activation frequency, bone volume fraction and percent eroded surface.

In summary, in the mid 1960's, before the days of DEXA scanning, Jones et al. refined the criteria for the interpretation of microradiographs. This allowed more detailed studies of diseased bone quality.

References

1. Brown DM, Jowsey J, Bradford DS. Osteoporosis in ovarian dysgenesis. *J Pediatr.* 1974;84(6):816–20.
2. Boivin G, Meunier PJ. The degree of mineralization of bone tissue measured by computerized quantitative contact microradiography. *Calcif Tissue Int.* 2002;70(6):503–11.
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