Atlas of
Mineralized
Bone
Histology
H.H. Malluche • M.-C. Faugere

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Atlas of mineralized bone histology / Hartmut H. Malluche, drug selection and dosage set forth in
this text are in accord with current
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time of publication. However, in
Bibliography: p. view of ongoing research, changes in government regulations, and the
includes
index. start flow of information relating to drug therapy and drug reactions, the
1. Bone and Bones - pathology - atlases 2. Bone Diseases, Metabolic - reader is urged to check
the package insert for each drug for any change in
pathology - atlases 3. Minerals - metabolism - atlases I. Title indications and dosage and for added
warnings and precautions. This is particularly important when the recommended agent is a new and/or infrequently employed drug.

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Foreword

Metabolic bone diseases are becoming an increasingly important part of medical practice because of improved diagnosis and the development of more effective therapy. These conditions cut across the usual specialty boundaries and involve many disciplines including internal medicine, family practice, endocrinology, nephrology, gastroenterology, rheumatology, gynecology, orthopedics, gerontology, radiology, nuclear medicine and pathology.

The value of bone histomorphometry in the management of patients with metabolic bone diseases is well established. First, it is an indispensable research procedure providing unique information that cannot be obtained by other methods. For example, only bone histology can assess the activity of bone cells and quantify bone turnover at the tissue and the cellular level. Second, bone histomorphometry is becoming an increasingly important procedure for the clinical assessment of these patients, particularly those with osteoporosis, osteomalacia and chronic renal failure. Third, information obtained by bone histomorphometry provides an indispensable conceptual framework for understanding the pathophysiology of the various metabolic bone diseases.

In their Atlas of Mineralized Bone Histology, Drs. Malluche and Faugere have provided an important book that will meet the needs of the researcher, the clinician and the student. This book includes extensive information on microanatomy and physiology of bone and a discussion of pathophysiological mechanisms by which alterations in bone cell activity lead to the various metabolic bone diseases. There is detailed information on the methodology of mineralized bone histology which
is required both for setting up this method and for evaluating the results obtained in individual patients. There is also a carefully selected bibliography that will allow a reader with little background information in this area to become familiar with the key articles which have shaped current concepts. Finally, the atlas is profusely illustrated with superb colored photomicrographs exemplifying the histologic appearance of bone in patients with many types of metabolic bone diseases.

The authors are eminently qualified to write this atlas because of their broad experience as clinicians, histomorphometrists and researchers. A book such as this has been needed for some time. It will surely become a major reference source for bone histomorphometry and a valuable guide for all those interested in patients with metabolic bone diseases.

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Preface

In recent years, an impressive body of knowledge has been accumulated in the understanding of metabolic bone diseases. Techniques such as bone cell culture, assays of calcitropic hormones, scanning techniques, photon absorptiometry and refinements in X-ray and histologic techniques were instrumental for these accomplishments. Several excellent textbooks have been published in which clinical presentation, pathogenesis and management of metabolic bone diseases are well described. A need exists to integrate bone histology into the variety of available information on clinical and basic features of metabolic bone diseases. It is the aim of this treatise to provide a combination of an atlas and a concise text which should help pathologists
and clinicians in the management of their patients. In addition, this text should help those who face the challenge of setting up a bone laboratory for mineralized bone histology. We tried to avoid complicating the field unnecessarily; the beauty and the usefulness of mineralized bone histology should be illustrated in this book to encourage more investigators and clinicians to become interested and to utilize this young and attractive tool for research and clinical management of metabolic bone diseases.

Many people have facilitated this book. The hundreds of patients who suffered from metabolic bone diseases and presented themselves for diagnostic bone biopsies allowed us to learn, gain experience and to present the variety of histologic abnormalities seen in metabolic bone diseases. We are particularly indebted to the patients who trusted us in the early years, when bone biopsies were considered an experimental procedure by many of our colleagues. Now, we appreciate the opportunity to expand our knowledge through many patient referrals from pathologists, nephrologists, orthopedic surgeons, pediatricians and other specialists throughout the country and the world. It is impossible to list the names of all persons who were of help along the long way of developing the bone biopsy technique, histologic techniques and eventually, in the collection of the presented material and data. Ms. Tomaschkowitz was instrumental during the first steps of setting up our method of mineralized bone histology. Later, Ms. Gisela Malluche contributed greatly to technical improvements and she deserves credit for many innovative ideas which enable us to present the quality of histologic sections shown in this book. The superb skills of Ms. Susan Barragan and Mr. Richard Wheaton were needed for the preparation, cutting and staining of thousands of bone samples. Ms. Kim Holtzclaw, Ms. Margaret Moon, Ms. Connie Prater, Ms. Mary Hood and, especially, Ms. Barbara Campbell have assumed the burden of typing,
retyping and editing the different versions of
the manuscript. We would like to thank them
deeply for their tireless efforts.
We owe respect and thanks to our mentors and
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and S.G. Massry. P. Meunier deserves credit for
kindling M.-C. Faugere’s interest in mineralized
bone histology.
Finally, no words can describe our feelings and
thanks to our families and our children, to whom
the book is dedicated. Their generous understanding,
sympathy and love provided the major force
for the accomplishment of the daily tasks throughout
the years, which allowed us to learn and to collect
what is presented in this book.

Introduction

Histologic evaluation of bone was hampered for
many years by formidable technical difficulties.
The major problem arose from the mineral content
of bone which made it impossible to cut thin sections
for histologic studies. Thus, for research or
diagnostic purposes, bone was studied after removal
of the mineral, that means decalcified, or by
alternate methods such as microradiography, autoradiography
or hand-ground sections. Decalcified
or demineralized bone sections retain the organic
matrix and bone cells if the decalcification process
is carried out carefully. Sections from decalcified
bone can be quite easily done; however, the drawbacks
of decalcified bone histology are obvious
since no information on mineralization status can
be obtained. Microradiography gives only indirect
information on cellular activities, and autoradiography
is useful mainly for research focusing on bone
cell kinetics. Hand-ground bone sections contain
bone mineral, but they are rather thick and bone
cells are usually not interpretable. The introduction
of celloidin [Bloom et al., 1941] and, subsequently,
other plastic monomers [Arnold and Jee, 1954;
Berlyne, 1963; Mollenhauer, 1964; Ruddell, 1967]
allowed the embedding of bone in plastic materials. Further refinements were needed such as additives to the plastic monomer which affect the hardening process, resulting in plastic blocks of nearly the same hardness as the embedded bone. ‘Sledge’ or ‘heavy duty’ microtomes equipped with diamond- or carbide-edged knives previously used for metallurgy or industrial purposes mainly were another necessary complementary step in the development of acceptable histologic techniques of bone without removal of the mineral, that is, mineralized bone histology. The introduction of tetracycline double labelling [Milch et al., 1958; Frost, 1963a, 1969] as a means to advance from static bone histology to dynamic evaluation of bone formation and resorption combined with manual [Merz and Schenk, 1970] or semiautomatic [Malluche et al., 1982a] quantitative histomorphometric methods provided the essentials to make mineralized bone histology a valuable tool for routine diagnosis, management and research of metabolic bone diseases.