ACADEMIC PRESS
An imprint of Elsevier

OSTEOPOROSIS

THIRD EDITION • TWO-VOLUME SET

Edited by

Robert Marcus
Professor Emeritus, Stanford University, Palo Alto, California, U.S.A.

David Feldman
Stanford University School of Medicine, Palo Alto, California, U.S.A.

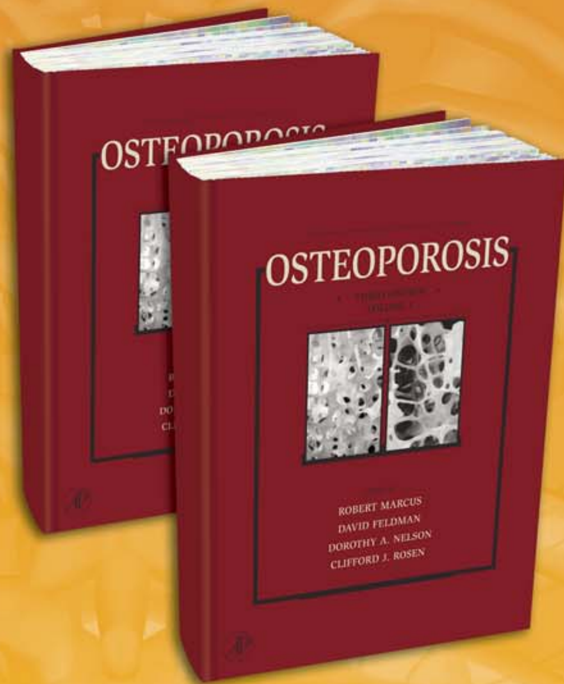
Dorothy A. Nelson
Wayne State University, Detroit, MI, U.S.A.

Clifford J. Rosen
St. Joseph Hospital, Bangor, Maine, U.S.A.

Now in its third edition, **Osteoporosis** is the most comprehensive, authoritative reference on this disease. Written by renowned experts in the field, this two-volume reference is a must-have for academic and medical libraries and physicians. Worldwide, 200 million women between 60-80 years of age suffer from osteoporosis and have a lifetime risk of fracture between 30 and 40 percent continuing to make osteoporosis a hot topic in medicine. This newest edition covers everything from basic anatomy and physiology to diagnosis, management and treatment in a field where direct care costs for osteoporitic fractures in the U.S. reach up to $18 billion each year. Academic and medical libraries, as well as professionals in bone biology, endocrinology, osteology, neuroendocrinology and drug companies developing osteoporosis medications will find all of their information needs met in this classic reference.

NEW TO THIS EDITION:

- Offers critical reviews of reproductive and hormonal risk factors, ethnicity, nutrition, therapeutics, management, and economics comprising a tremendous wealth of knowledge in a single source not found elsewhere
- Examines essential updates on estrogen prevention and treatment and the recent results from the Women's Health Initiative
- Recognizes the critical importance of the Wnt signaling pathway for bone health
- Incorporates new chapters on osteocytes, phosphatonins, mouse genetics, and CNS and bone
- Discusses the controversial topics of screening and clinical trial design for drug registration
- Includes essential updates on therapeutic uses of calcium, vitamin D, SERMS, bisphosphonates, and parathyroid hormone



September 2007, Hardback c. 1900 pp.
ISBN: 9780123705440

INTRODUCTORY PRINT PRICE*:
$320.00 / €270.00 / £185.00

List Print Price:
$400.00 / €335.00 / £230.00

**Introductory prices are valid for three months after publication.*

books.elsevier.com/osteo

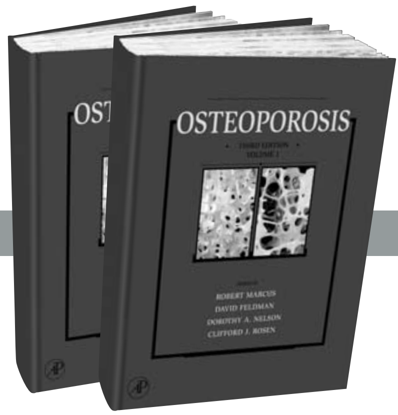
Let's Talk BOOKS
www.info.sciencedirect.com/books

Also available online via ScienceDirect™!

See inside flap for details!

ELSEVIER
MARKETING DEPARTMENT **DM89535**
525 B Street, Suite 1900
San Diego, CA 92101-4495, USA

Presorted Standard
U.S. Postage
PAID
Elsevier



ALSO AVAILABLE ONLINE VIA

ScienceDirect™

www.info.sciencedirect.com

OSTEOPOROSIS

THIRD EDITION, TWO-VOLUME SET

November 2007, Hardback c. 1900 pp,
ISBN: 9780123705440

INTRODUCTORY PRINT PRICE*:
$320.00 / €270.00 / £185.00

List Print Price: $400.00 / €335.00 / £230.00

Prices are in US Dollar, Euro, and British Pound Sterling and are subject to change without notice.
Introductory price valid for three months after publication date

Order from your favorite bookseller or directly from:

In the Americas, Asia & Australia:
ELSEVIER
Order Fulfillment Department
11830 Westline Industrial Drive
St. Louis, MO 63146-9938, USA
Tel: 1 800 545 2522
Fax: 1 800 535 9935
E-mail: usbkinfo@elsevier.com

In Europe, Middle East & Africa:
ELSEVIER
Books Customer Service
Linacre House
Jordan Hill, Oxford, OX2 8DP, UK
Tel: +44 1865 474110
Fax: +44 1865 474111
E-mail: eurobkinfo@elsevier.com

FAX OR MAIL THIS FORM • **DM89535**

ISBN: 9780123705440, Osteoporosis, Third Edition, 2-Volume Set

Qty	Prices	Amount
_____	**Introductory Print Price: $320.00/€270.00/£185.00** List Print Price: $400.00/€335.00/£230.00	$/€/£__________
	Shipping*	$/€/£__________
	Local Sales Tax*	$/€/£__________
	Total	$/€/£__________

☐ Please find my check enclosed*
☐ Please charge my credit card*
☐ Bill my company (purchase order attached)*
☐ Bill me directly

*Local sales tax, VAT or GST taxes and shipping will be added where applicable.
For shipping and sales tax rates based on your mailing address, please contact us.

Name *(Please Print)*______________________________

Tel. (____) ______________ Fax (____) ______________

Address______________________________

City______________State_____Zip/Postcode________Country____________

E-mail ______________________________

Charge Card#______________________Exp. *(Mo/Yr)*__________

Signature______________________________

❏ Please remove my details from your mailing list.

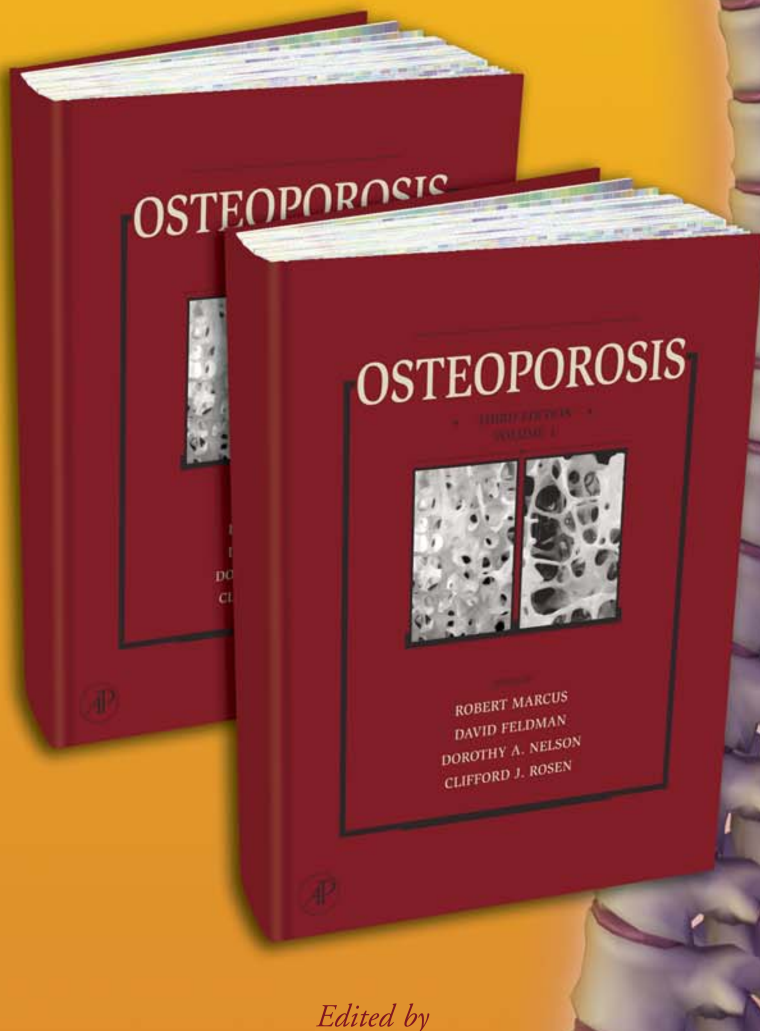
For more information, please visit: **books.elsevier.com/osteo**

Prices are in US Dollar, Euro, and British Pound Sterling and are subject to change without notice. Prices are valid for individual customers only.

ACADEMIC PRESS
An imprint of Elsevier

OSTEOPOROSIS

THIRD EDITION • TWO-VOLUME SET



Edited by

Robert Marcus
David Feldman
Dorothy A. Nelson
Clifford J. Rosen

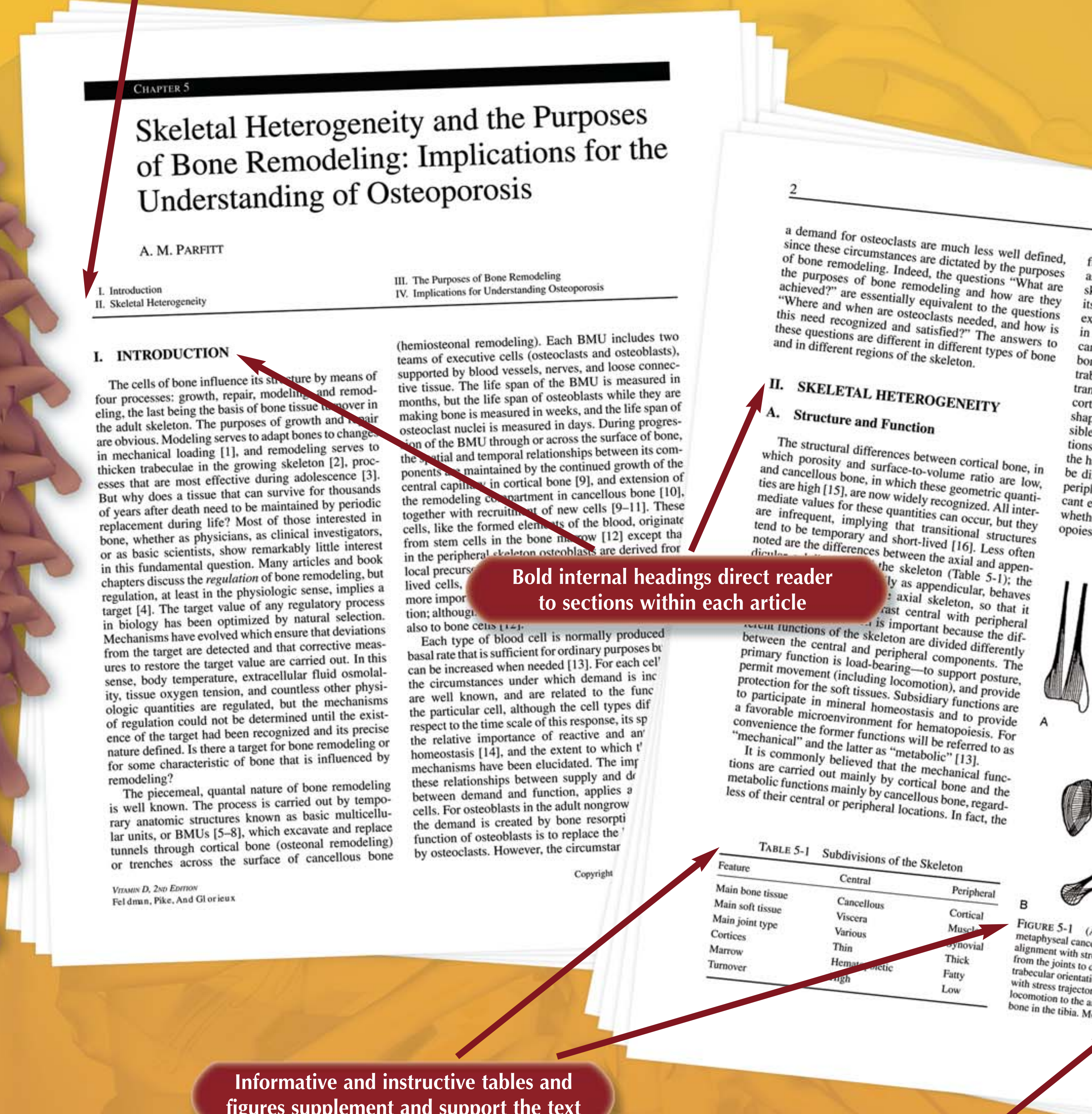
books.elsevier.com/osteo

Table of Contents

OSTEOPORO

THIRD EDITION • TWO-VOL

Opening Table of Contents outlines each chapter



CHAPTER 5

Skeletal Heterogeneity and the Purposes of Bone Remodeling: Implications for the Understanding of Osteoporosis

A. M. PARFITT

I. INTRODUCTION

The cells of bone influence its structure by means of four processes: growth, repair, modeling, and remodeling, the last being the basis of bone tissue turnover in the adult skeleton. The purposes of growth and repair are obvious. Modeling serves to adapt bones to changes in mechanical loading [1], and remodeling serves to thicken trabeculae in the growing skeleton [2], processes that are most effective during adolescence [3]. But why does a tissue that can survive for thousands of years after death need to be maintained by periodic replacement during life? Most of those interested in bone, whether as physicians, as clinical investigators, or as basic scientists, show remarkably little interest in this fundamental question. Many articles and book chapters discuss the *regulation* of bone remodeling, but regulation, at least in the physiologic sense, implies a target [4]. The target value of any regulatory process in biology has been optimized by natural selection. Mechanisms have evolved which ensure that deviations from the target are detected and that corrective measures to restore the target value are carried out. In this sense, body temperature, extracellular fluid osmolality, tissue oxygen tension, and countless other physiologic quantities are regulated, but the mechanisms of regulation could not be determined until the existence of the target had been recognized and its precise nature defined. Is there a target for bone remodeling or for some characteristic of bone that is influenced by remodeling?

The piecemeal, quantal nature of bone remodeling is well known. The process is carried out by temporary anatomic structures known as basic multicellular units, or BMUs [5–8], which excavate and replace tunnels through cortical bone (osteonal remodeling) or trenches across the surface of cancellous bone (hemiosteonal remodeling). Each BMU includes two teams of executive cells (osteoclasts and osteoblasts), supported by blood vessels, nerves, and loose connective tissue. The life span of the BMU is measured in months, but the life span of osteoblasts while they are making bone is measured in weeks, and the life span of osteoclast nuclei is measured in days. During progression of the BMU through or across the surface of bone, the spatial and temporal relationships between its components are maintained by the continued growth of the central capillary in cortical bone [9], and extension of the remodeling compartment in cancellous bone [10], together with recruitment of new cells [9–11]. These cells, like the formed elements of the blood, originate from stem cells in the bone marrow [12] except tha in the peripheral skeleton osteoblasts are derived fror local precurs lived cells, more impor tion; althoug also to bone cells [12].

Each type of blood cell is normally produced basal rate that is sufficient for ordinary purposes bu can be increased when needed [13]. For each cel the circumstances under which demand is inc are well known, and are related to the func the particular cell, although the cell types dif respect to the time scale of this response, its sp the relative importance of reactive and an homeostasis [14], and the extent to which t mechanisms have been elucidated. The im these relationships between supply and d between demand and function, applies a cells. For osteoblasts in the adult nongrow the demand is created by bone resorpti function of osteoblasts is to replace the by osteoclasts. However, the circumsta

a demand for osteoclasts are much less well defined, since these circumstances are dictated by the purposes of bone remodeling. Indeed, the questions "What are the purposes of bone remodeling and how are they achieved?" are essentially equivalent to the questions "Where and when are osteoclasts needed, and how is this need recognized and satisfied?" The answers to these questions are different in different types of bone and in different regions of the skeleton.

II. SKELETAL HETEROGENEITY

A. Structure and Function

The structural differences between cortical bone, in which porosity and surface-to-volume ratio are low, and cancellous bone, in which these geometric quantities are high [15], are now widely recognized. All intermediate values for these quantities can occur, but they are infrequent, implying that transitional structures tend to be temporary and short-lived [16]. Less often noted are the differences between the axial and appen- the skeleton (Table 5-1); the ly as appendicular, behaves axial skeleton, so that it rast central with peripheral is important because the different functions of the skeleton are divided differently between the central and peripheral components. The primary function is load-bearing—to support posture, permit movement (including locomotion), and provide protection for the soft tissues. Subsidiary functions are to participate in mineral homeostasis and to provide a favorable microenvironment for hematopoiesis. For convenience the former functions will be referred to as "mechanical" and the latter as "metabolic" [13].

It is commonly believed that the mechanical functions are carried out mainly by cortical bone and the metabolic functions mainly by cancellous bone, regardless of their central or peripheral locations. In fact, the

TABLE 5-1 Subdivisions of the Skeleton

Feature	Central	Peripheral
Main bone tissue	Cancellous	Cortical
Main soft tissue	Viscera	Muscl
Main joint type	Various	ynovial
Cortices	Thin	Thick
Marrow	Hema oietic	Fatty
Turnover	igh	Low

A

B

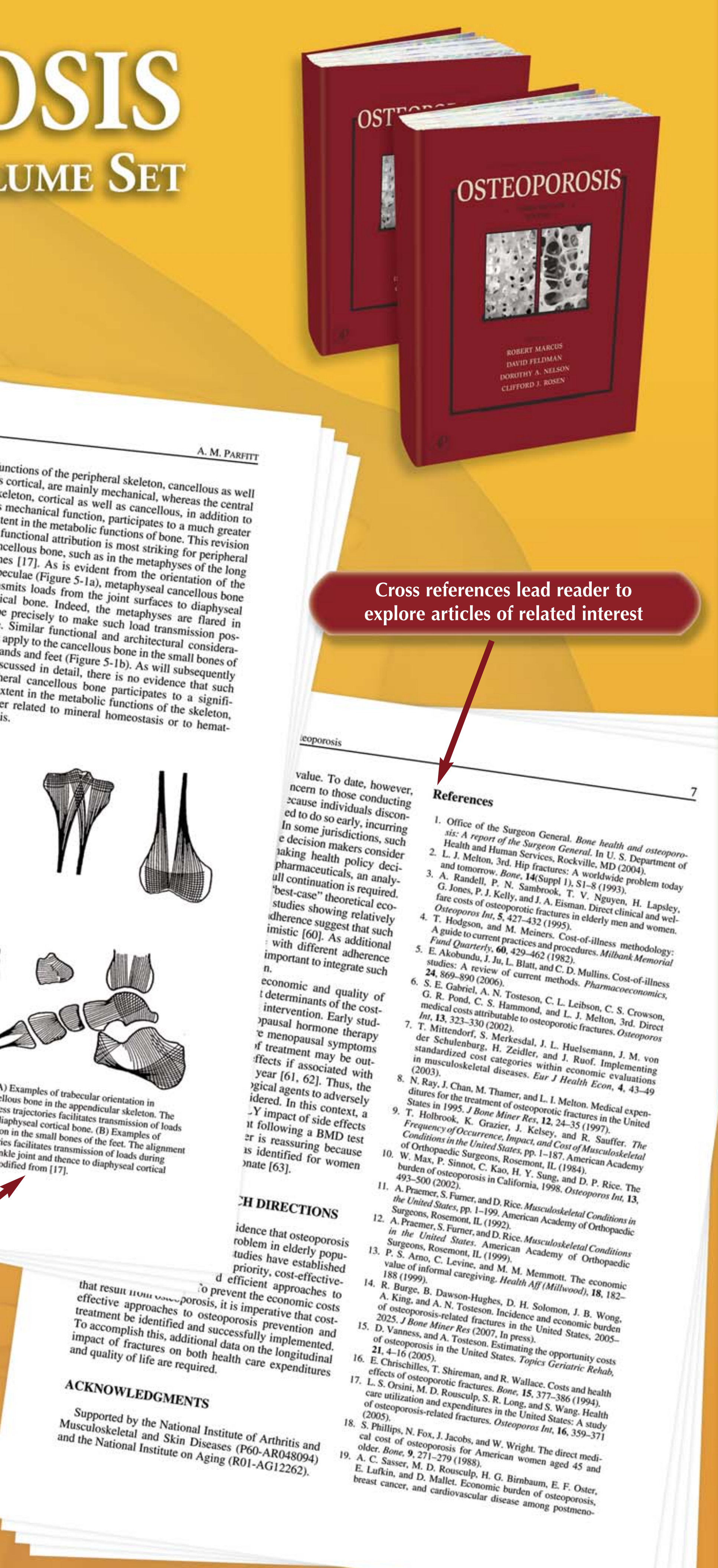
FIGURE 5-1 (A metaphyseal canc alignment with str from the joints to trabecular orientati with stress trajecto locomotion to the a bone in the tibia. M

Bold internal headings direct reader to sections within each article

Informative and instructive tables and figures supplement and support the text

In-depth captions provide additional information

books.elsevier.com/osteo



Books on ScienceDirect
www.info.sciencedirect.com/books

In addition to the reference works, handbooks and book series already available, ScienceDirect will launch approximately 4,000 books online in 2007, including ***Osteoporosis!***

Benefits of ScienceDirect

- Acquiring books on ScienceDirect enables librarians to best serve their user communities by providing simultaneous and remote user access, maximizing user productivity
- Helps researchers find and manage information easily and allows them to set up alerts to be updated on the latest developments
- Includes titles from high quality imprints such as Academic Press and Pergamon
- Flexible business models are available
- Pick and choose any book title or according to ScienceDirect subject collections

ScienceDirect™
makes sense.

For additional information, including pricing options, please visit

www.info.sciencedirect.com/books