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Editorial

Celebrating 50-years: the history and future of the International Society of Bone Morphometry

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Abstract

The International Society of Bone Morphometry (ISBM) is dedicated to advancing research, education, and clinical practice for osteoporosis and other bone disorders by developing and improving tools for the quantitative imaging and analysis of bone. Its initial core mission was to promote the proper use of morphometric techniques in bone research and to educate and train clinicians and basic scientists in bone morphometry. This article chronicles the evolution of the ISBM and the history and development of bone morphometric techniques for the past 50-years, starting with workshops on bone morphometry in 1973, to the formal incorporation of the ISBM in 1996, to today. We also provide a framework and vision for the coming decades. This effort was led by ISBM presidents Dr Erica L. Scheller (2022-2024) and Dr Thomas J. Wronski (2009-2012) in collaboration with all other living ISBM presidents. Though the underlying techniques and questions have changed over time, the need for standardization of established tools and discovery of novel approaches for bone morphometry remains a constant. The ISBM fulfills this need by providing a forum for the exchange of ideas, with a philosophy that encourages the open discussion of pitfalls and challenges among clinicians, scientists, and industry partners. This facilitates the rapid development and adaptation of tools to meet emerging demands within the field of bone health at a high level.

Keywords: bone histomorphometry, analysis/quantitation of bone, analysis/quantitation of bone, bone qct/microct, analysis/quantitation of bone, bone modeling and remodeling

History and evolution of bone morphometry

The word "morphometry" is defined as the quantitative analysis of form, with an emphasis on assigning meaningful, numerical outputs to diverse 2D and 3D representations (Figure 1). The term "bone morphometry" has traditionally encompassed both the size and the shape of the bone but has evolved to include bone quality, cell-level metrics such as number and surface, dynamic indices of bone formation, aspects of cell movement and reconfiguration in real time, and, more recently, the precise distributions of genes, proteins, and metabolites in skeletal tissues with spatial-omics techniques (Figure 1).

Hundreds of years of discovery across imaging disciplines have contributed to our understanding of skeletal biology using bone morphometric techniques (Figure 2). This includes the invention of the microscope in the 1500s and the discovery of X-rays and autoradiography in the late 1800s, followed by the advent of the first fluorescence and electron microscopes and the discovery of immunolabeling all in the mid-1900s. Throughout these early years, the skeleton was recognized as an indispensable structural component of the living body and further respected as an important record of life after death. However, beyond this, our understanding of bone as an organ was very limited. This was due at least in part to the challenges

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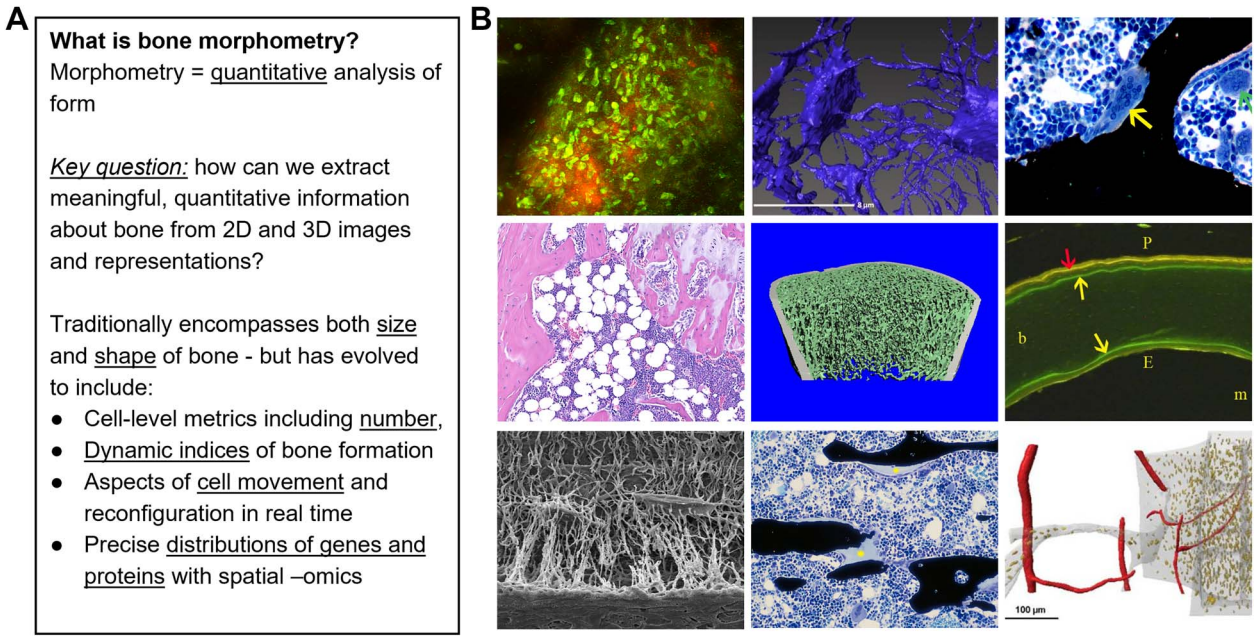

Figure 1. Bone morphometry definition and examples. (A) Bone morphometry is the quantitative analysis of form using diverse 2D and 3D representations. (B) Example images of bone tissues that can be used to analyze diverse aspects of morphometry. Microscopic and tomographic images and representations provided by members of the ISBM.

associated with cutting thin histologic sections from hard, mineralized tissues.

The field of bone morphometry changed in 1948 when Dr James Arnold and his team used plastic embedding to reliably produce thin ~5-8 μm sections of non-decalcified bone[1,2] (Figure 2). The quality of these sections exceeded that of both decalcified paraffin sections and ground undecalcified specimens.[2] In addition, this method allowed for the autoradiographic study of bone-seeking radionuclides. Autoradiography is a method by which a mirror image on a slide coated with a photographic emulsion can be created from the tissue section after binding of a radioactive substance.[3] This is achieved by placing both slides in contact long enough for the emulsion to be properly exposed, prior to the development of the film. Darker spots within the mirror image on the emulsion are proportional to the emissions from the radionuclide in the tissue. Radioactive tracers can be administered systemically in vivo or by direct application to the section after isolation. Initial work in bone focused primarily on characterizing the skeletal incorporation of plutonium, uranium, and radium in toxicity studies.[4,5] This was often prominent on endosteal surfaces and at other sites of new bone formation. These foundational observations were later leveraged to quantify the skeletal tissue distribution and, starting in 1957, the rate of uptake of radiolabeled ligands such as calcium.[3,6,7] For the first time, this allowed the temporal visualization of distinct phases of bone turnover including appositional growth, resorption, and remodeling,[6] the foundation of the basic multicellular unit (BMU) theory of bone homeostasis.

Also in 1957, Drs Milch, Rall, and Tobie provided the first opportunity to move beyond radiolabeled ligands when they discovered that tetracycline antibiotics also incorporated at sites of new bone formation in vivo and that this could be visualized in non-decalcified sections.[8] Early advances in sectioning and staining of undecalcified bone, primarily human rib samples, and measurements of tetracycline-based bone formation indices were made by Dr Harold M. Frost and colleagues at Henry Ford Hospital in Detroit, MI, USA.[9,10] These colleagues included future ISBM presidents such as Dr Z.F.G. Jaworski, Dr Pierre Meunier, and Dr Hideaki Takahashi in addition to laboratory technician Dr Anthony R. Villaneuva (creator of the Villaneuva bone stain) and several students of the Wayne State University Medical School and Detroit Dental School.[11-13] These studies performed by Dr Takahashi as an orthopaedic surgical resident with Dr Frost also demonstrated that bone resorption preceded bone formation, establishing the sequence of events in bone remodeling.[14,15] By 1969, methods to transform the resulting microscopic findings into quantitative, physiologically meaningful information pertaining to bone formation and turnover were established for human cortical bone.[16] These technical developments coupled with emerging clinical demand prompted the First Workshop on Bone Morphometry (a precursor to the ISBM) in 1973. It was also at this point that the Upjohn Company called for a clinical study to analyze dynamic histomorphometry in sequential transiliac biopsies to study the effects of vitamin D treatment in renal dialysis patients.[17] To meet this need, Dr Frost spent several years adapting and standardizing the tetracycline labeling technique for use in cancellous bone, introducing it for the first time at the Second Workshop on Bone Morphometry in 1976 with later publication in 1977 as part of the conference proceedings.[18]

Techniques for quantitative microradiography of bone also evolved throughout the 1950s and 1960s alongside histologic methods.[3,19] A microradiograph is an X-ray of a thin section of bone tissue that facilitates the 2D visualization of patterns of mineral distribution. With training, microradiographs could also be used to quantify surfaces of bone formation and resorption based on mineral density and appearance.[3] This provided another method, in addition to histology, tetracycline labeling, and autoradiography, that could be used to study the physiology of bone tissues. The next big advance

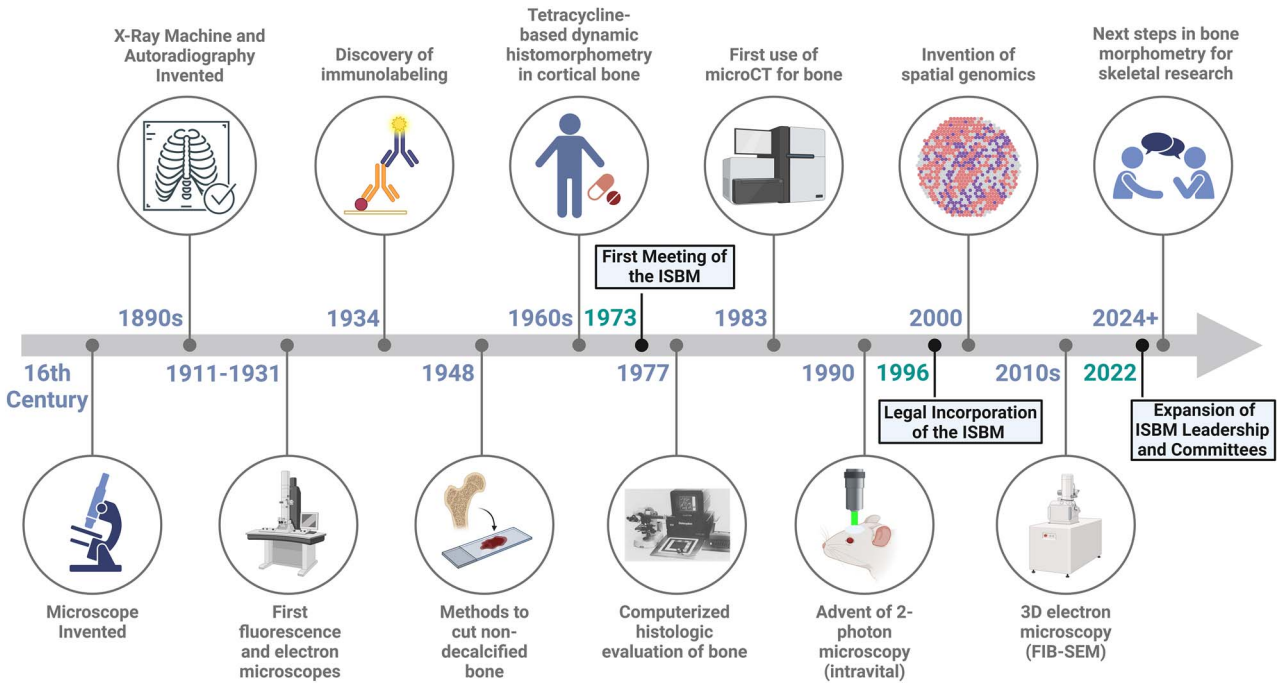

Figure 2. Twelve milestones in bone morphometry. Twelve scientific and technical milestones in the history of bone morphometry are highlighted in this timeline ranging from the 16th century to modern day. Key dates in the initiation, incorporation, and evolution of the ISBM are also noted. Graphic created in BioRender, Xray icon by Anton Kalashnyk.

came in the early 1980s when physicist Dr Lee Feldkamp developed the first micro computed-tomography system to evaluate ceramic materials in 3D for the Ford Motor Company.[20,21] A meeting between Dr Feldkamp and Dr Michael Kleerekoper led to the first use of microCT for bone, the scan of an iliac crest biopsy that was reported at the 1983 meeting of the American Society for Bone and Mineral Research.[22] This new tool brought 3D bone microstructure to the forefront of many morphologic investigations, further evolving the capabilities of the field. A detailed review of the use of bone morphometry for clinical medicine and research can be found here.[23]

Since the 1980s, research in bone morphometry has focused on refining and adapting these foundational histologic and tomographic imaging methods to provide ever growing amounts of information (Figure 2). Efforts have also been made to define "normal" bone histomorphometry in both adult men and women as a clinical reference point.[24,25] Bone histomorphometric data were initially collected in histologic sections with an eyepiece reticle (i.e., Merz grid) with points and sinusoidal lines for measuring areas and perimeters of interest. This technique provided useful data but was tedious and time-consuming. In the early 1980s, Dr Hartmut H. Malluche developed a system consisting of computer, drawing tube, digitizing plate, and software for semi-automatic measurements and calculations of 2D and 3D bone histomorphometric parameters[26] (Figure 2). This system was marketed by Zeiss as Osteoplan according to Malluche. In the mid- to late 1980s, Bioquant and Osteometrics introduced similar software for computer-assisted, semi-automatic measurements of cell numbers, areas, and perimeters. These major technical advances made collection and calculation of bone histomorphometric data much more efficient with improved accuracy and expanded the use of histomorphometry as an essential bone research tool. Bioquant and Osteometrics have continued to improve their software over the years and served as consistent sponsors and exhibitors at most ISBM meetings to this day.

Throughout the evolution of these foundational histologic and CT-based tools for bone morphometry, exciting new technologies for the quantitative imaging and analysis of bone at the cellular and subcellular level also emerged (Figures 1 and 2). This includes the use of 2-photon microscopy for the imaging and analysis of live skeletal cells in vivo, applications of ultra-high-resolution techniques such as electron microscopy, X-ray microscopy, nanoCT, and FIB-SEM, advancement of spectroscopy tools to study skeletal composition, and synthesis of imaging and -omics techniques for precise localization of genes, proteins, and metabolites in bone (Figures 1 and 2). For the past 50 years, the ISBM has provided a forum for discussion, exhibition, and training that brings together both experts and those new to the field to advance all aspects of imaging-based tools for bone morphometry. Overall, the focus on improving bone health remains a common goal across disciplines and of the ISBM.

The first workshops on bone morphometry: Ottawa 1973 and Lyon 1976

The technological advances in the 1950s and 1960s led to a new paradigm of skeletal physiology and a sharp increase in the interest in bone morphometry, particularly by clinicians. In the 1960s, Dr Z.F.G. Jaworski and Dr Pierre J. Meunier took their sabbatical year at the Henry Ford Hospital with Harold Frost and at the University of Utah with Dr Webster S.S. Jee, another pioneer in bone morphometry and future ISBM President (Table 1). In response to his experiences, Dr Jaworski organized the "First Workshop on Bone Morphometry" in

Table 1. Congresses of the International Society of Bone Morphometry from 1973 to 2024.

Congress	City	Country	Organizer(s) and President
16th Congress – 2024	Toronto	Canada	Drs. Elizabeth Zimmerman, Joel Boerckel, Frank Ko (organizers) and Dr Erica. L. Scheller (President)[b]
15th Congress – 2022	Odense	Denmark	Dr Thomas L. Andersen
14th Congress – 2019	Orlando	Florida, USA	Dr D. Rick Sumner
13th Congress – 2015	Tokyo	Japan	Dr Masaki Noda
12th Congress – 2012	Minneapolis	Minnesota, USA	Dr Thomas J. Wronski
11th Congress – 2009	Zell am See	Austria	Dr Reinhold G. Erben
10th Congress – 2006	Philadelphia	Pennsylvania, USA	Dr Brendan F. Boyce
Ninth Congress – 2002	Edinburgh	Scotland, UK	Dr Juliet E. Compston
Eighth Congress – 1999	Scottsdale	Arizona, USA	Dr David W. Dempster
Seventh Congress – 1996[a]	Alghero	Sardinia, Italy	Dr Gastone Marotti
Sixth Congress – 1992	Lexington	Kentucky, USA	Dr Hartmut Malluche
Fifth Congress – 1988	Niigata	Japan	Dr Hideaki E. Takahashi
Fourth Congress – 1984	Aarhus	Denmark	Dr Fleming Melsen
Third Congress – 1980	Sun Valley	Idaho, USA	Dr Webster S. S. Jee and Dr A. Michael Parfitt
Second Congress – 1976	Lyon	France	Dr Pierre J. Meunier
First Congress – 1973	Ottawa	Canada	Dr Z.F.G. Jaworski

The role of meeting organizer and society President overlapped from 1973 to 2022. [a]The ISBM was formally incorporated as a non-profit organization in 1996. [b]The role of the meeting organizer(s) and the ISBM President were formally split after the 15th Congress in 2022 based on decisions by the ISBM Board, led by Drs T.L. Andersen, E.L. Scheller, and M. McDonald, to expand the activities of the society.

Ottawa, Canada in 1973 in partnership with the University of Ottawa (Figure 3). Dr Jaworski was a nephrologist and Medical Research Council scientist that led many of the early studies on dynamic histomorphometry in clinical settings of hyperparathyroidism and renal failure.[27-29] The main motivation for this new workshop and focus on morphometric methods to quantify bone turnover was the emerging need to investigate the effects of hormones and pharmacotherapies on bone, and to characterize bone changes with age and in various syndromic and metabolic disorders.[3] This was aided by technical developments including the Bordier trephine, a tool and method developed by histomorphometry pioneer Philippe Bordier to sample iliac crest bone.[30] The first workshop gave the emerging investigators in the field a chance to meet in person and covered both the radiologic and histologic aspects of bone morphometry.

The interest in the topic and success of the first meeting prompted Dr Meunier to lead the organization of the "Second International Workshop on Bone Morphometry" in Lyon, France in 1976 sponsored by the University of Claude Bernard (Table 1, Figure 3A). Though still prior to the formulation of the ISBM, it was at this point that the term "international" became integral to the name. As a physician scientist, Dr Meunier was among the first to introduce histomorphometry to the field and contributed to pivotal advances in the development of new therapeutics for osteoporosis.[31] This second workshop focused mainly on histology, the dynamic aspects of histomorphometry, and quantitative approaches to electron microscopy. As written by Dr Meunier, "The aim of this workshop was to point out the problems of methodology and the significance of the measured data in order to give our clinical and biochemical colleagues a more precise tool to work with, but also to avoid dynamical misinterpretations of morphometric changes."[32] This launched the themes of standardization and quality control that have persisted throughout the ISBM meetings to this day. The 1976 meeting is notable for its celebration of the "activation, resorption, formation" or "ARF" model of the BMU and attendees such as Dr Frost were photographed wearing "ARF" ribbons or sashes (Figure 4B). It also showcased the first report of dynamic

Figure 3. Attendees of the first Workshop on Bone Morphometry. Attendee key: 1 Witmer, 2 Owen, 3 S Meema, 4 NA, 5 Bogorogh, 6 Liskova, 7 Weinberg, 8 Harrison, 9 Duncan, 10 Jaworski, 11 Norimatsu, 12 E Meema, 13 Ritz, 14 Van Eeck, 15 NA, 16 Doyle, 17 Fornasier, 18 Meunier, 19 Marotti, 20 Olah, 21 Shim, 22 Black, 23 Shulz, 24 Takahashi, 25 Villanoeva, 26 Baud, 27 Ubthoff, 28 NA, 29 NA, 30 NA, 31 Arnold, 32 Jee, 33 Lok, 34 Klosevyeh, 35 Bordier, 36 Del Pozo, 37 NA, 38 Myhal, 39 Cameron, 40 NA, 41 Coupron, 42 Kaye, 43 Hollins, 44 Jette, 45 Singh, 46 Jande, 47 Roberts, 48 Sturtridge, 49 NA, 50 Schock, 51 Edouard, 52 NA, 53 Dequeker, 54 Belanger, 55 Anderson, 56 Genant, 57 Parfitt, 58 Frame, 59 Roelfsema, 60 Copp, 61 NA, 62 Morgan, 63 Epker, 64 NA, 65 Guay, 66 Digabel, 67 NA, 68 NA, 69 Janigan, 70 NA, 71, Heaney, 72 Schenk, 73 NA, 74 NA, 75 Kimmel, 76 NA, 77 NA. NA = data not available.

histomorphometry of cancellous bone by Dr Frost and the introduction of the concept of the "reversal phase" of bone remodeling by then junior fellow Dr Roland Baron.[33,34] The full set of publications from the 1976 meeting is currently

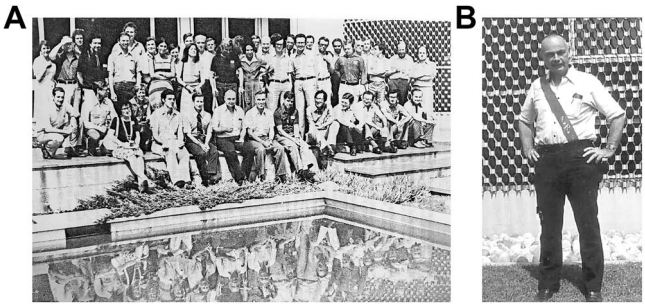

Figure 4. Second bone morphometry workshop in Lyon, France. (A) Group photo of the attendees of the second ISBM meeting. Participants (alphabetical): C. Alexandre, S.Y. Ali, M. Arlot, R. Baron, C.A. Baud, D.H. Birkenhager, H.E. Black, E. Bonucci, P.J. Bordier, A. Boyde, W.M. Bremer, F. Caulin, P. Courpron, G. Delling, J. Dequeker, A. Dhem, A. Dryll, H. Duncan, J. Duriez, C. Edouard, L. Flora, R.J. Francois, H.M. Frost, M.E. Holtrop, Z.G.F. Jaworski, W.S.S. Jee, M.R.A. Khairi, B. Krempien, A.M. Laponche, G. Lunel, C.R. Manegold, P. Marie, G. Marotti, J.L. Mattherw, F. Meersseman, F. Melsen, P.J. Munier, B. Mills, B. Moyen, R.W. Norrdin, A.J. Olah, A.M. Parfitt, N. Piret, A. Rebel, R.R. Recker, W.E. Roberts, B. Rosemeyer, J.L. Sebert, S. Teitelbaum, W. Van Eek, E. Vignon, G. Vignon, A.R. Villaneuva, W.J. Visser, and C.G. Woods. (B) Dr Harold Frost pictured wearing an "ARF ribbon" to celebrate the activation, resorption, formation paradigm of bone turnover at the second meeting of the ISBM in Lyon, France, in 1976.

maintained in the archives of the University of Claude Bernard in Lyon.[32]

Workshops on bone morphometry from 1980 to 1988: clinical trials, controversies, and new partnerships with the Japanese Society of Bone Morphometrics

Once established, Workshops on Bone Morphometry from 1980 to 1988 were held once every 4-years alternately in North America, Europe, and Asia (Table 1). During this period, the field was driven by a boom of clinical studies and trials for skeletal therapeutics with a primary focus on bone histomorphometry in iliac crest biopsy specimens of osteoporotic patients treated with emerging drugs such as bisphosphonates, selective estrogen receptor modulators, and parathyroid hormone. This prompted the first efforts toward global standardization of methodology and nomenclature for bone morphometry, which featured prominently at the ISBM meetings.[35] Specifically, Dr A. Michael Parfitt led efforts by the Histomorphometry Nomenclature Committee in partnership with the American Society for Bone and Mineral Research (ASBMR), resulting in the publication of the first set of standards for bone morphometry in 1987.[35] Dr Parfitt also organized the third workshop on bone morphometry with Dr Jee in Sun Valley, Idaho in 1980. One notable event at this meeting was the bringing together of Dr Flemming Melsen and Dr Hans Joergen Gundersen. Though they worked at the same university in the same city, they had never met. From this meeting, a long-term collaboration between the two arose that contributed greatly to the advancement of the stereological aspects of histomorphometric variables and important analyses of metabolic bone disease.[36] Dr Melsen had only recently obtained his doctorate in 1979 followed by a specialty in Pathology in 1982 but led the way to organize the forth bone morphometry workshop in Aarhus, Denmark in 1984.

The expansion of microCT-based techniques presented at these early meetings was notable, as was the substantial increase in the number of preclinical studies of bone morphometry using new rodent models of skeletal disease. Clinical researchers at early ISBM meetings were often vocal about their skepticism of the rodent as an animal model for adult human bone due to a perceived lack of bone remodeling (i.e., coupled bone resorption and formation) and continual growth of the rodent skeleton throughout life. However, this negative attitude gradually changed with histomorphometric evidence that bone remodeling does indeed occur in cancellous bone of adult rats, and findings that the ovariectomized rat proved to be highly predictive of the skeletal effects of potential osteoporosis treatments in postmenopausal women.[37] Notably, this shift in attitude led to a written apology from clinician Dr Harold Frost in 1992, published with a pioneer of rat models for osteoporosis and ISBM president Dr Webster S.S. Jee, regarding his prior outspoken advocacy against the utility of animal models of skeletal disease.[38] Subsequently, the interactions between bone clinical researchers and basic scientists using animal models of bone disorders became one of the strengths of the ISBM meetings.

This period also brought about the forging of new long-term partnerships with the Japanese Society of Bone Morphometrics (JSBM) led by Dr Hideaki E. Takahashi. Dr Takahashi attended the first Workshop on Bone Morphometry in 1973 (Figure 2) and subsequently founded the JSBM in 1979. This collaboration and international relationship led him to organize the fifth congress in 1988 as a joint meeting between JSBM and the pre-ISBM Workshops on Bone Morphometry in partnership with the University of Niigata (Figure 5A). The catchphrase for the fifth congress was the "interphase between morphology and cellular and molecular biology," reflecting the enhanced emphasis on basic science compared with past meetings (proceedings available in[39]). An exciting banquet also included folk music, dancing, and a conference song that was sung by several of the participants as a surprise. The comical lyrics, sung to the tune of "Oh My Darlin' Clementine," included the names of several participating researchers and were written by Dr D.C. Anderson and others once they arrived in Niigata (Figure 5A, Supplemental Figure 1). Most recently, Dr Takahashi and his colleagues Drs Iimura, Sakai, and Yamamoto welcomed current ISBM president Dr E.L. Scheller as a keynote speaker at the 2023 JSBM meeting in Sapporo, Japan (Figure 5C).

Congresses from 1992 to 1999: increased participation, incorporation of the ISBM as a nonprofit organization, and the first basic/translational ISBM president

The 1992 meeting in Lexington, Kentucky, organized by Dr Hartmut H. Malluche, was the largest congress to date with 330 attendees from 28 different countries. Growth in attendance had been matched by increasingly new and exciting research directions reflective of new approaches in the field of bone histomorphometry. The success of this meeting was made possible by generous support from 15 sponsoring companies. This brought many innovative exhibits on display including a newly developed electric powered biopsy drill developed by Dr Malluche and Straumann Company, "Osteoplan according to Malluche" produced by Kontron and Roche Image Analysis, and competitive systems from R&M Biometrics and Osteometrics. The broad spectrum of instruments and technologies was an impressive example

Figure 5. Fifth ISBM congress in Niigata, Japan, and long-term collaborations between ISBM and JSBM. (A) Group photo of the attendees of the fifth ISBM meeting in Niigata, Japan. (B) Singing of the conference song by led by D.C. Anderson to the tune of "Oh My Darlin' Clementine". Lyrics can be found in Supplemental Figure 1. (C) Image of Dr Hideaki E. Takahashi (right, organizer of the fifth ISBM congress; also attended the first workshop in 1973) and colleague Dr Noriaki Yamamoto (left) with current ISBM President Dr E.L. Scheller at the 2023 meeting of the JSBM.

of the importance of bone research to serve medical and clinical needs. The congress also featured 14 sessions with over 84 papers covering topics ranging from new perspectives in bone structure to quantitative assessment of the effects of bisphosphonate and calcitonin on bone. A session titled, "The use of transgenic mice" also introduced a novel molecular approach, opening a great number of research avenues to study foundational aspects of bone physiology. Workshops included discussions on quality control in bone morphometry and interlaboratory collaboration and highlighted, in many respects, new approaches to the overall field of bone morphometry. Full published abstracts and proceedings of the sixth congress are available.[40,41]

During the 1992 congress, Dr Malluche also received support for his idea to incorporate the meetings as a nonprofit society named the International Society of Bone Morphometry (ISBM, Figure 6A). This formalization of the ISBM as a research society in the United States had many advantages, such as legal representation, a transparent budget, and facilitation of tax-deductible donations from academia and industry in support of the ISBM meetings. This effort was completed in collaboration with the other seven appointed members of the ISBM Board of Directors and was finalized in 1996 (Supplemental Table 1). This was also the year in which the seventh ISBM congress was organized by Dr Gastone Marotti of the Istituto de Anatomia umana normale de l'Universita di Sassari, Italy.[42] Dr Marotti is acknowledged as the first elected President of the newly incorporated ISBM and commemorated Dr Malluche's role in the founding of the society by giving him a silver plate at the opening of the seventh congress (Figure 6B). Full abstracts from the seventh meeting are also available.[43]

It is important to point out that all members of the ISBM founding Board of Directors were MD-certified clinicians, reflecting the roots of the ISBM in clinical medicine. This changed with the appointment of Dr David Dempster, a PhD scientist, as the new ISBM President from 1996 to 1999. Dr Dempster and his wife Patti Dempster had spent part of their honeymoon at the seventh congress in Italy and it was at this time that they were recruited to organize the next meeting. The eighth congress was entitled "Bone Morphometry at the New Millenium" and was held in 1999 in Scottsdale, AZ, immediately after the ASBMR meeting, which was held in St. Louis, MO. There were ~200 attendees from 22 countries with 125 submitted abstracts, 10 plenary symposia, and 2 poster sessions. Ten young investigator awards were handed out, including one to Dr Ed Guo who went on to become chair of the Bioengineering Department at Columbia University. The social program for the meeting included a western-style theme party, a hike through Sedona & Oak Creek canyon, a tour of the Heard Museum, and a gala awards reception at which there was a memorable musical performance by Dr Dempster, a drummer, his wife Patricia, a singer, accompanied by Dr Rob Weinstein on harmonica. The program and abstracts for the meeting are maintained by the ISBM.

Congresses of the ISBM from 2002 to 2015: standardization efforts, new techniques, and the first woman president

There were five ISBM meetings during the period from 2000 to 2015 (Table 1). The 11th congress was organized in Edinburgh, Scotland in 2002 by Dr Juliet Compston. Dr Compston is an esteemed clinician scientist who has published over 280 articles on the pathophysiology and treatment of osteoporosis, including the effects of glucocorticoids and estrogens on bone remodeling. She is also notable for being the first woman to serve as ISBM President, reflecting increased recognition of the contributions of women to what had previously been a very male-dominated field. As had been done previously, ISBM meetings during this period typically had 100-300 attendees. This relatively small attendance and informal mingling at opening receptions, coffee breaks, and closing banquets was conducive to graduate students, postdocs, and junior investigators interacting with established senior investigators, resulting in job opportunities and initiation of research collaborations. The smaller number of attendees also allowed for some unique, memorable closing banquets such as a formal dinner at Lincoln Hall in Philadelphia (2006), a tram ride to a mountain-top chalet in Austria (2009), a dinner on Lake Minnetonka aboard the Queen of Excelsior in Minnesota (2012), and a harbor cruise in Tokyo Bay (2015).

The science at the meetings continued to evolve, grounded in a new tradition of including a keynote speaker in the Congress. The 10th congress in 2006 was organized by Dr Brendan Boyce in Philadelphia, Pennsylvania immediately after the 28th ASBMR annual meeting. Dr Robert Recker from Creighton University, Omaha, Nebraska, delivered the Keynote Lecture on "What Does the Future Hold for Bone Morphometry in Clinical Practice?". This and subsequent meetings began to highlight additional research areas that utilized bone morphometry. For example, the 11th congress

Figure 6. Incorporation and congresses of the ISBM from 1996 to 2022. (A) ISBM logo. (B) ISBM President Dr Gastone Marotti presents a commemorative plate to Dr Hartmut Malluche at the Seventh ISBM congress in recognition of his efforts to formally incorporate the ISBM as a non-profit society. (C) Dr Tom Wronski (ISBM President 2009-2012) and Dr Robert Recker (keynote speaker in 2006 and 2012) at the 12th ISBM congress in 2012. (D) Participants at the 12th congress aboard the Queen of Excelsior on Lake Minnetonka. Top: Karen Callon and Dr Natalie Sims (keynote speaker in 2022). Bottom: Dr Hua Zhou and Dr David Dempster (ISBM President 1996-1999). (E) Participants in Tokyo, Japan at the 13th congress in 2015, organized by Dr Masaki Noda. (F) Many travel award winners in Orlando, Florida at the 14th congress in 2019, organized by Dr D. Rick Sumner. (G) Participants gather at the Odense Zoo during the 15th congress in 2022, organized in Odense, Denmark by Dr Thomas Andersen.

in 2009, organized by Dr Reinhold Erben in Zell am See, Austria, included topics such as structure–function relationships in bone, disorders of mineral homeostasis, osteoimmunology, regenerative therapy of bone and cartilage diseases, and skeletal fragility, in addition to traditional sessions on morphometry and advancement of imaging technologies. The 2009 meeting also started with a full-day, hands-on practical training session. Dr Thomas Wronski continued this at the 12th congress in 2012, organized in Minneapolis, Minnesota, adding topical sessions on bone biomechanics and bone implants (Figure 6C and D). He and several other investigators and exhibitors brought microtomes to the meeting site and provided hands-on training in sectioning of undecalcified bone and identification of bone cells and structural features of bone in histologic sections. An introduction to the use of microCT for bone structural analyses was also made possible using analysis computers provided by manufacturers including Scanco and Skyscan.

The last congress during this period took place in Tokyo, Japan in 2015 and was organized by Dr Masaki Noda (Figure 6E). The keynote speaker was Dr Jack Martin from St Vincent Hospital in Melbourne, Australia. During this period, members of the ISBM also worked in partnership with ASBMR to create two working group publications. The first, led by ISBM past President Dr Dempster, updated the guidelines originally established by Dr Parfitt to provide standardized practices and nomenclature for bone histomorphometry.[44] These recommendations and standards have been

adopted by top journals in the field and remain in place to this day, having been cited in over 1100 NCBI-indexed manuscripts as of this writing. The second was led by Dr Ralph Muller, an active participant in the ISBM and future ISBM Board member, with a team of talented scientists to develop guidelines for the assessment of bone microstructure in rodents using micro-computed tomography.[45]

Congresses of the ISBM from 2019 to 2022: investment in the next generation and expansion of the ISBM mission

The meeting in 2019 unintentionally initiated a cascade of events that led to a unique period of change and evolution for the ISBM. The 14th congress in 2019 was organized by Dr D. Rick Sumner in Orlando, Florida. The keynote speaker was Dr Roland Baron from Harvard University, one of the original attendees and contributors to the 1976 ISBM workshop (Figure 3). As with previous conferences, there were topical scientific sessions, practical training workshops, and an exciting banquet that included dining surrounded by a floor to ceiling aquarium at SeaWorld in Orlando. In addition, there was an important, targeted effort to provide numerous travel awards to support junior scientist participation (Figure 6F) and to invite several young investigators to give plenary talks. This included three individuals that would go on to re-shape the society in the coming years: Dr Thomas Andersen, a histomorphometrist and spatial imaging expert from Denmark (ISBM President 2019-2022), Dr Erica Scheller, a professor in the United States with expertise in advanced imaging of marrow adiposity and nerves in bone (ISBM President 2022-2024), and Dr Michelle McDonald, a rising star in osteoclast and bone tumor biology making great strides in the area of real-time in vivo visualization of skeletal cells (current ISBM President elect, anticipated 2024-2026).

Historically, the President of the ISBM also served as the organizer of the congress. From 2019 to 2022, this role was held by Dr Thomas Andersen as he organized the 15th congress of the ISBM in Odense, Denmark in 2022. The program included a keynote lecture entitled "Shifting the focus from trabecular to cortical bone?" by Dr Natalie Sims, 8 oral sessions and 2 poster sessions with presentations of 16 invited speakers and 49 submitted abstracts, as well as 9 concurrent training workshops. Drs Jesper Thomsen and Christina Andreasen, and technicians Kaja Laursen and Malene Nielsen co-organized the congress. The 15th congress aimed to bring the ISBM into the era of spatial and molecular histology while highlighting key developments in bone imaging and morphometry. It also identified a pressing need for members of the society to communicate, collaborate, and share ideas in a more continuous fashion.

To achieve this, Dr Andersen in collaboration Drs Scheller and McDonald proposed to expand the mission and impact of ISBM as a society beyond the confines of the congresses. After much discussion with other members of the ISBM Board, the adopted solution was (1) to create a separation between the Presidency and the Meeting Organizers (Table 1) and (2) to establish committees and working groups that would allow the ISBM to develop and function more as a society during interim periods. This vision was fully implemented by the ISBM Board and subsequent ISBM President Dr Erica Scheller from 2022 to 2024 with the onboarding of 24 new members onto the ISBM leadership team, including 9 members of the new Scientific Leadership Committee and 15 members of the Early Career Investigator (ECI) Committee. Increased participation rapidly led to the emergence of new leaders and initiatives including the expansion of society-led communications (web, twitter/X @ISBM_society, and emailed newsletters),[46] in person meetups (Figure 7A and B), and organization of joint ISBM-led sessions at the annual meetings of the European Calcified Tissue Society, the Orthopaedic Research Society, and the ASBMR (Figure 7C). The ECI committee, led by Lejla Emini, Marta Diaz del Castillo, and Ahmed Al Saedi, embraced this era of virtual communication by developing a highly successful webinar series that engaged the growing ISBM membership with exciting content and showcased the broad scope that the ISBM encompasses. Sixteen webinars were scheduled from 2022 to 2024 with an average attendance of 50-90, inclusive of 500+ unique registered attendees. Recordings were also made available for members to revisit,[47] or view in their own time, creating an inclusive approach to facilitating knowledge gain within the ISBM community.

Looking toward the next 50-years: research focus areas, global connections, and a vision for the future

In 2024, we will hold the 16th congress in Toronto, Canada, directly after the 2024 ASBMR meeting. The 2024 program has been developed by Dr Joel Boerckel, an Associate Professor driving new discoveries in mechanobiology, Dr Elizabeth Zimmerman, an Assistant Professor focused on the preclinical and clinical imaging of mineralized tissues, and Dr Frank Ko, an Assistant Professor with expertise in light sheet microscopy and musculoskeletal repair (Table 1). Dr Boerckel and Dr Ko were also invited junior investigators at the 14th congress in 2019, and Dr Zimmerman gave a plenary talk at the 12th congress in 2012, launching their future leadership within the ISBM. To build on previous programs, the 2024 congress aims to showcase the diverse content within our field, encompassing quantitative measures (morphometry) of the skeleton from the macro whole tissue level to the molecular scale. A dedicated focus to open science and data sharing has also been initiated with support by grants from the Canadian Institutes of Health Research and the US National Institutes of Health. The 2024 program will highlight recent advances in clinical imaging, providing access to high-resolution 3D structural and bone quality parameters and excitingly, in vivo insight into the response of bone to implants and mechanical loads. Artificial intelligence has penetrated so many aspects of our world, including clinical imaging. Computational models, which utilize bone structural quantitative data, developed for improved fracture risk prediction and to model bone adaptations to changes in load response to disease will be discussed. We expect these themes to continue to evolve as a major aspect of the ISBM mission and research footprint over the coming decades.

Preclinical imaging modalities have also advanced, facilitating imaging of both bone matrix and cellular components. Multiscale analyses, which allow quantification of the relationship between bone matrix toughness and microstructures and localized bone structural changes to growth, have become commonplace. High-resolution static 3D and real-time dynamic imaging of cell types within intact bone have led to numerous recent discoveries. State-of-the-art imaging of bone vascular and lymphatic structures, skeletal progenitor

Figure 7. New leaders and evolution of the ISBM Mission from 2022 to 2024. (A) In person meetup of the ISBM leadership at ASBMR in 2023. From the left: Dr Michelle McDonald, Dr Marta Diaz del Castillo, Dr Ralph Muller, Dr Joel Boerckel, Dr Lilian Plotkin, Dr Ahmed Al Saedi, nd, Dr Sarah Dallas, Dr Pascale Chavassieux, Dr Thomas Andersen, Dr Aline Bozec, Dr Randee Hunter, Dr Erica Scheller, and Dr Frank Ko. (B) In person meetup of the ISBM leadership at ASBMR in 2022. From the left: Dr Julian Balanta Melo, Dr Frank Ko, Dr Michelle McDonald, Dr Marta Diaz del Castillo, Dr Thomas Andersen, Dr Ralph Muller, Dr Elizabeth Zimmerman, Dr Mohamed Hassan, Dr Sarah Dallas, Dr Joel Boerckel, Dr Lilian Plotkin, Dr Erica Scheller, Dr Ahmed Al Saedi, Dr Randee Hunter, and visiting colleague. (C) Dr Thomas Andersen presenting at the ISBM joint session at ASBMR in 2023 entitled "Meet the Experts: Histomorphometry and Quantitative Imaging of Bone."

cells, and bone marrow adipocytes further reveals novel insight into response of bone-associated cells and structures to injury or hormonal changes. In addition, light sheet imaging of embryonic bones provides new information into the mechanisms of bone development and growth. Our knowledge in osteocyte biology has also developed in recent years, by means of new-found ability to image osteocytes in vivo in high resolution. We will bring together experts in the field who will highlight advances in osteocyte biology including cell–cell communication and the complexities of osteocyte canalicular networks within bone matrix and osteocyte dynamics. The adaptation of spatial transcriptomics is also imminent in our field, with experts rapidly optimizing technical protocols to achieve high-quality data. Our ISBM members and experts will drive methodological developments and the biological insights these advanced spatial approaches in the coming decades.

In addition to a commitment to knowledge building, the ISBM will continue to embrace its educational mission by ending the 2024 congress with training workshops that have become integral to the ISBM meetings. These workshops aim to provide interactive opportunities for attendees from all levels to meet and discuss technical aspects of the multitude of morphometric approaches that our field now relies on. In 2024, this will include basic and advanced histomorphometry, basic and advanced microCT analysis, multiplex staining and spatial transcriptomics, and advanced imaging such as light sheet and intravital two-photon imaging. We envisage that these workshops will gain momentum with the continual growth of our society, leading to working group-initiated publications of updated and new protocol papers as a resource for the bone field. This includes the publication of methods and consensus articles in partner journals such as *JBMR Plus* that support the consistent application of methods advocated by ISBM. As always, rigorous application and standardization of techniques for skeletal imaging and analysis remains at the forefront of our mission and represents an ongoing area of growth.

As our society grows in both size and diversity of interest areas, so do our vital partners and sponsors. We are reaching more parts of the world and envisage that our global biennial meetings will initially rotate through North America, Europe/UK, and Asia/Oceana with potential for future expansion while building on our connections with sister societies across the globe through joint sessions and shared initiatives. The next generation of ISBM leaders is already knocking on our doors, and we are committed to providing opportunities for them through a supportive network of peers, mentors, and advisors and importantly, multiple opportunities to participate in our congresses, workshops, working groups, and webinars. We will continue to actively build a society and a leadership that reflects the diversity of race, gender, age, ethnicity, and national origin that exists in our field throughout the world. In 2024, we will also launch three inaugural named awards that exemplify the commitment of our past leadership to the future of the ISBM. Programs include the ASBMR Hartmut H. Malluche Early Career Investigator Awards (10 ECI travel awards funded jointly by ASBMR and Dr H.H. Malluche), the Juliet Compston Travel Award for Clinical Research in Bone Morphometry (funded by

Dr J.E. Compston), and the Patricia and David Dempster Rising Star Award for Excellence in Bone Metabolism Research (funded by Dr D.W. Dempster). ISBM truly is an international society. We have maintained numerous long-term partners and are now establishing multiple new relationships, with the goal of achieving the diverse team of leaders, members, and collaborators necessary to support the society as we embark on the next 50-years of bone morphometry.

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Author contributions

Erica Scheller (Conceptualization, Data curation, Project administration, Supervision, Visualization, Writing—original draft, Writing—review & editing), Michelle McDonald (Writing—original draft, Writing—review & editing), Thomas Andersen (Writing—original draft, Writing—review & editing), D. Rick Sumner (Writing—original draft, Writing—review & editing), Masaki Noda (Writing—original draft, Writing—review & editing), Reinhold Erben (Writing—original draft, Writing—review & editing), Brendan Boyce (Writing—original draft, Writing—review & editing), Juliet Compston (Writing—original draft, Writing—review & editing), David Dempster (Data curation, Visualization, Writing—original draft, Writing—review & editing), Hideaki Takahashi (Data curation, Visualization, Writing—original draft, Writing—review & editing), Hartmut Malluche (Data curation, Visualization, Writing—original draft, Writing—review & editing), and Thomas Wronski (Conceptualization, Data curation, Supervision, Visualization, Writing—original draft, Writing—review & editing)

Supplementary material

Supplementary material is available at *JBMR Plus* online.

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Conflicts of interest

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