Second Edition

Laser Therapy in Veterinary Medicine

Photobiomodulation

Edited by
Christopher J. Winkler
Lisa A. Miller

WILEY

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Published by John Wiley & Sons, Inc., Hoboken, New Jersey.
Published simultaneously in Canada.

Library of Congress Cataloging-in-Publication Data:
Names: Winkler, Christopher J., 1973– editor. | Miller, Lisa A. DVM, editor.
Title: Laser therapy in veterinary medicine : photobiomodulation / edited by Christopher J. Winkler and Lisa A. Miller.
Description: Second edition. | Hoboken, New Jersey : Wiley-Blackwell, [2025] | Includes bibliographical references and index.
Identifiers: LCCN 2024031882 (print) | LCCN 2024031883 (ebook) | ISBN 9781394205325 (hardback) | ISBN 9781394205332 (adobe pdf) | ISBN 9781394205349 (epub)
Subjects: MESH: Laser Therapy–veterinary | Low-Level Light Therapy–veterinary
Classification: LCC SF745 (print) | LCC SF745 (ebook) | NLM SF 745 | DDC 636.089/7058–dc23/eng/20240909
LC record available at https://lccn.loc.gov/2024031882
LC ebook record available at https://lccn.loc.gov/2024031883

Cover image: Courtesy of Kaitlan Hovis
Cover design: Wiley

Set in 9.5/12.5pt STIXTwoText by Straive, Pondicherry, India

Dedication and Acknowledgments

This book is dedicated with deep appreciation to Ronald J. Riegel and John C. Godbold Jr. for all their previous hard work and efforts, the groundwork they have laid, their contributions to this work and to the field of veterinary medicine, and especially for the inspiration they so willingly and freely share with others.

We would like to thank the extraordinary efforts of our authors, experts, and their staffs for their distinct contributions to the subject of veterinary photobiomodulation. This past year has been a wonderfully illuminating education in each of your fields, and we are very proud and grateful for the privilege of presenting your brilliant work to our readers. It has been the greatest of pleasures collaborating with you. A heartfelt Thank You to you all.

To our editors, Vallikkannu Narayanan, Erica Judish, and Susan Engelken, for all your advice and assistance.

To my co-editor, Lisa Miller. I could not have done this without you. Words cannot express how much I admire your talent, your dedication, or my great appreciation for how synergistically we were able to complete this work together. May it not be our last.

To my family, friends, and colleagues for their support, especially to my parents, Nancy and Joseph, who taught me the value of a well-written word, and taught compassion and love by example. To my children, John and Kevin, who will forever remain my greatest endeavor, and to Nicole, my beloved wife and companion in this our adventure together. I love you all very much.

For Jack.

—Christopher

To my family, friends, and colleagues, thank you for your support and understanding for all the weekends of turned-down plans and late nights of working on this book. To my co-editor, Chris Winkler who is one of the most knowledgeable and kindest human beings I have met, and who kept the train on the tracks. To Dr. Juanita Anders, for being a pioneer and queen in the photobiomodulation world and for mentoring and guiding many of us. Lastly, to my colleagues who continue to inspire me daily with their innovation, passion, and dedication to the field of veterinary medicine; I thank you all.

Ad Astra Per Aspera.

—Lisa

Contents

Biography

Christopher J. Winkler, DVM graduated from Ross University School of Veterinary Medicine in 2001, and worked on Long Island, New York, as an emergency room veterinarian and associate general practitioner before purchasing Suffolk Veterinary Group in 2006. Incorporating surgical and therapy lasers into his practice in 2010, he began formal training a short time later, earning certifications in Veterinary Laser Medicine and Surgery from the American Board of Laser Surgery (ABLS) in 2015, and Veterinary Medical Laser Safety Officer from the American Institute of Medical Laser Applications (AIMLA) in 2016.

Dr. Winkler has spoken on laser surgery and laser therapy and served as an associate laser surgery wet-lab instructor for a number of national veterinary conferences, including the NAVC, AVMA, the WVC, the Great Smokies Veterinary Conference, and the Colonial Veterinary Conference. He has also conducted webinars on laser therapy and laser safety for veterinary technicians and Ross University students, and published articles on laser surgery for Veterinary Practice News. He is a member of the American Society for Laser Medicine and Surgery (ASLMS), and is a Fellow and Faculty member of both the American Laser Medicine College and Board (ALMCB) and the American Laser Study Club (ALSC), for which he also sits on the editorial board of its journal. Dr. Winkler is editor and co-author of the textbook *Laser Surgery in Veterinary Medicine* (Wiley-Blackwell, 2019), and he is the recipient of the 2021 Kumar C. Patel prize for outstanding contributions to veterinary laser surgery education. He receives referrals from and trains veterinarians locally and nationally on laser surgery and laser therapy procedures, continues to advise educating bodies on veterinary laser curricula, and offers his services as a laser consultant to veterinarians and equipment manufacturers.

Dr. Lisa A. Miller is the vice president of Clinical Veterinary Medicine for Companion Animal Health and is a graduate of the University of Tennessee, College of Veterinary Medicine. After graduation, Dr. Miller completed an internship in internal medicine and then became certified in canine rehabilitation therapy. Working in a large referral hospital, she practiced rehabilitation, sports medicine, and acupuncture for several years before returning to general practice and later, joining the animal health industry.

Dr. Miller has been working with laser therapy/photobiomodulation (PBM) since 2006. She has lectured worldwide and led workshops on laser therapy and rehabilitation-related topics, including lectures at Western Veterinary Conference, VMX, the London Vet Show, Southern European Veterinary Conference, American Society of Laser Medicine & Surgery Conference, and Laser Florence. She has authored numerous research papers, articles, and chapters on PBM in veterinary practice. Her publications have appeared in *Photobiomodulation, Photomedicine, and Laser Surgery*, *Journal of Nanotechnology*

Research, Frontiers in Veterinary Science, Clinician's Brief, *Integrative Veterinary Care*, *Today's Veterinary Practice*, and the first edition of the textbook *Laser Therapy in Veterinary* Medicine. In her current role, she coordinates all veterinary and advanced PBM research involving Companion Animal Health technologies and is a consultant and reviewer for PBM research worldwide. Dr. Miller is a member of the American Veterinary Medical Association (AVMA), the American Association of Rehabilitation Veterinarians (AARV), the American Society of Laser Medicine & Surgery (ASLMS), and the World Association of Laser Therapy (WALT).

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Foreword

In mid-2015, we took deep breaths and committed to coediting the pioneering textbook about the clinical use of photobiomodulation in veterinary medicine. Despite our prior experience in writing and publishing, neither of us had any idea of the scope of the task ahead. We did not realize the effort needed to gather 37 contributing authors from academia, clinical practice, and industry, nor did we anticipate the 18-month journey of editing 43 chapters covering nearly 500 pages. Regardless, the contributions of those chapter authors became the award-winning textbook *Laser Therapy in Veterinary Medicine: Photobiomodulation*.

The chapters on the history, theory, and science of photobiomodulation helped establish the credibility of therapeutic laser use. The chapters on clinical applications made the book a practical clinical reference across the full spectrum of veterinary practice. For the first time, a reliable, comprehensive, and evidence-based resource had been developed to provide practical insights into clinical veterinary photobiomodulation.

Even prior to the release of that first edition, we anticipated the rapid advancements in technology and the emergence of new research and clinical applications that would necessitate a second edition. Since its initial publication in 2017, the landscape of veterinary photobiomodulation therapy has evolved significantly, underscored by the publication of over 150 peer-reviewed articles. These developments have enriched our understanding of the conditions amenable to photobiomodulation therapy and refined our approach to its delivery.

With the aim of bringing new insight, energy, and perspective to *Laser Therapy in Veterinary Medicine: Photobiomodulation,* we engaged two gifted colleagues to coedit the second edition, Dr. Chris Winkler, and Dr. Lisa Miller. As coeditors, Chris and Lisa have again marshaled dozens of gifted contributing authors, authored chapters themselves, and overseen bringing veterinary medicine a new, up-to-date, and valuable resource for clinical photobiomodulation therapy.

Drs. Winkler and Miller have over 30 years of combined experience with therapeutic lasers. Both have general and specialty practice experience, as well as years of contributing to photobiomodulation therapy continuing education, research, and publication about the technology. Currently, Chris remains in general practice and Lisa is the vice president of Clinical Veterinary Medicine for Companion Animal Health. Their backgrounds and experiences, and their roles as leading experts on veterinary photobiomodulation, combine to bring the profession this valuable second edition.

While updating previous information in this book, Chris and Lisa continued to focus solely on photobiomodulation and the diagnostic technologies that support it. More complete and up-to-date information regarding dosing and treatment parameters is included. They make this edition usable by readers in a diversity of clinical settings since the information presented is not confined to specific techniques or equipment. Treatment procedures and protocols are provided in generic, noncommercially specific ways.

The editors include new chapters addressing urinary conditions, oncological applications, photobiomodulation in the critical care setting, and use for working dogs. Additionally, there is a new chapter on the use of thermal imaging to target photobiomodulation treatment areas and monitor response to therapy.

This second edition is now the definitive resource for veterinary students, general practitioners, specialists, and those involved in the continued development of new veterinary therapeutic laser devices. We thank the chapter authors, Chris and Lisa, for significantly improving our first edition. We are confident this text will prove to be an invaluable addition to readers' libraries, facilitating continued growth and excellence in the field of veterinary photobiomodulation therapy. It will be a well-used addition to our own libraries.

John C. Godbold, Jr., D.V.M.
Jackson, Tennessee

Ronald J. Riegel., D.V.M.
Marysville, Ohio

Preface

The United Nations fortuitously proclaimed 2015 as the International Year of Light and Light-Based Technologies. This seemed most apropos to me at the time, for it would also be the year I would begin to meet and work with many of the luminaries of veterinary laser medicine and surgery.

Having just finished a year of study and certification on the subject, I was then looking forward to my first conference of the American Society for Laser Medicine and Surgery. While there, I attended lectures on laser therapy delivered by Dr. Juanita Anders and Dr. Praveen Arany. It was at these that I first heard the word "photobiomodulation," and as I listened, I had the distinct sense of being present at an important milestone in science and medicine, the introduction of a new term and definition to our lexicon.

Another of those luminaries lecturing that week was Dr. Ron Riegel, one of several veterinarians speaking about laser applications in veterinary medicine. It was the first of many such lectures I have since heard from Dr. Riegel, and after bearing witness numerous times to his extensive expertise, his infectious exuberance, and his appreciable passion for this field, it came as absolutely no surprise to me that he would later go on with my first and most notable laser teacher, Dr. John C. Godbold Jr., to create the first edition of *Laser Therapy in Veterinary Medicine*.

The surprise came later when they both asked me to create the second edition.

Seeking assistance, I welcomed Dr. Godbold's recommendation of Dr. Lisa Miller. I had heard Dr. Miller speak at an American Institute of Medical Laser Applications function on the use of laser therapy for osteoarthritis, and from Dr. Godbold's confident description of her expertise, I knew she would be exactly what this project needed.

Our ideas for a second edition text were congruent from the beginning. We wanted to see the first edition text respected while also being updated with as much new information as possible. Indeed, the reader will note hundreds of new references, the majority of which are dated after the first edition's publication. We sought in this update to focus solely on photobiomodulation and the diagnostic technology that supports it, make it approachable and clinically usable by readers globally without specifically being beholden to singular techniques or equipment, and continue to provide more complete dose and parameter recommendations than previously available.

We wished to continue to push the envelope and offer better patient care as well as encourage both laser researchers and laser manufacturers to move forward with studies that challenge previous thoughts and technology innovations. We also wanted to add new content (particularly regarding veterinary oncology) while prompting our veterinary colleagues to continue to think outside the box, to consider treating new patients or conditions they may not have previously considered treating, and to utilize that same "veterinary ingenuity" that first interested them in this modality to begin with – something that John C. Godbold Jr. would always value and emphasize in his lectures. Colloquially (for now, anyway), while the first edition might say, "Never shine it in their eyes," this second edition would now say, "Don't shine it in their eyes – not yet."

The history of photobiomodulation research and clinical application is rather unfortunately marked by a plethora of underdosed and poorly or incorrectly reported parameters. It is for this reason that we further wish to encourage those desiring to perform research within the veterinary community to reach out to colleagues in the photobiomodulation world and learn more about how to optimally execute and report parameters with this exciting and effective modality, so that we can all continue to improve our knowledge base and optimize outcomes for our patients without repeating research and reporting mistakes of the past.

We certainly look forward with anticipation to exploring and discussing tomorrow's discoveries, innovations, and collaborations in future editions to come. Until then, we sincerely hope this new edition serves you well.

April 29, 2024

Christopher J. Winkler, DVM
Lisa A. Miller, DVM

Disclaimer

Please read the statements and the therapeutic protocols within this text carefully before utilizing any of this information. The information and recommendations are based on previously published scientific information and years of practice, clinical, and research experience by the contributing authors.

Knowledge about photobiomodulation (PBMT) is constantly changing through ongoing research, clinical trials, and day-to-day clinical experience. The information within this text is presented for educational purposes only and is designed to be a reference to complement formal training about laser therapy.

This text contains neither complete nor comprehensive information about any of the conditions addressed, and each condition should be evaluated on an individual basis in each patient prior to surgery. This text is not a substitute for professional advice, care, diagnosis, or treatment. It is the sole responsibility of the veterinarian, veterinary technician, veterinary assistant, and veterinary therapist to gain the knowledge and comply with all federal, national, provincial, state, and local laws regarding the use of therapeutic and surgical lasers for any condition. Dr. Christopher Winkler, Dr. Lisa Miller, all of the contributing authors of this text, and anyone involved with the publication of this text expressly disclaim any and all responsibility and legal liability for any kind of loss or risk, personal or otherwise, which is the result of the direct or indirect use or application of any of the material within this text.

Part I

The History of Laser Therapy

1

A Brief History of Laser Therapy

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Treatment with Light

Heliotherapy. Phototherapy. Light therapy. Cultures around the world have attributed many names to this remedy as they have practiced it in various forms over the past several millennia. Healers in Egypt and India used sunlight to treat leucoderma 3500 years ago (Hönigsmann, 2013). Physicians in Ancient Greece and Rome – including renowned Greek historian Herodotus in the sixth century BCE, and Hippocrates, the father of medicine – also realized the benefits of such therapy (Ellinger, 1957). Likewise, the Inca and Assyrian cultures worshiped the sun with the belief that it would bring them health. There are records in the Buddhist literature from around 200 CE and Chinese documentation from the tenth century recording similar therapeutic effects from light.

Niels Ryberg Finsen, a Faroese physician and scientist of Icelandic descent, is widely regarded as the original proponent of phototherapy. In 1903, he was awarded the Nobel Prize in Medicine and Physiology for the successful treatment of diseases using phototherapy, specifically lupus vulgaris, a skin infection caused by *Mycobacterium tuberculosis* (Nobel Prize, 2014b). He also famously utilized ultraviolet light to treat smallpox lesions (Nobel Lectures, 1967).

A Closer Look

In the seventeenth century, Sir Isaac Newton discovered that prisms could disassemble or separate white light into seven different visible colors, a phenomenon he described in his book *Optick*s (Newton, 1704). Newton first used the word *spectrum* (Latin for "appearance" or "apparition") while describing refracted light in 1671. Today we also use another word to describe these and other colors of light: *wavelengths*.

In 1916, Albert Einstein made several hypotheses to support his theory of relativity. Einstein proposed that an excited atom in isolation can return to a lower energy state while emitting photons, a process he termed "spontaneous emission." Other atoms will absorb such photons of the correct wavelength; causing those atoms to enter a higher-energy state and setting the stage for further spontaneous emission.

Einstein then predicted that as light passes through a substance, it stimulates the emission of more light (Hilborn, 1982). Einstein's theory hypothesized that a large collection of atoms already containing a great deal of excess energy will be ready to emit photons – photons that prefer to travel together in the same state. If one such stray photon of the correct wavelength passes by an atom already in an excited state, its presence will stimulate that atom to release its own photons early. The new photons will then travel together in the same direction as the original stray photon, with identical frequency and phase. A cascading effect could thus ensue: As the identical photons move through other atoms, ever more identical photons are emitted (Pais, 1982). Einstein termed this phenomenon "stimulated emission," postulating the theory of laser light 43 years prior to its realization.

A Momentous Device

On May 16, 1960, Theodore Maiman produced the first laser device at the Hughes Aircraft Research Laboratory in Malibu, California, using a simple flashlamp to stimulate

Laser Therapy in Veterinary Medicine: Photobiomodulation, Second Edition. Edited by Christopher J. Winkler and Lisa A. Miller.

a solid medium (a ruby rod) to emit collimated photons of coherent light. At a press conference to announce his invention, he predicted that such a light would be useful in medicine and surgery (Hecht, 2005). Maiman based his invention on Albert Einstein's explanation of stimulated emission of radiation, coupled with Charles Townes's and Arthur Schawlow's work with optical masers (Schawlow and Townes, 1958; Itzkan and Drake, 1997). The acronym LASER (Light Amplification by Stimulated Emission of Radiation) itself was first coined and recorded by Townes's graduate student Gordon Gould. Gould's subsequent struggles for recognition for his work with lasers would result in one of the most lengthy, controversial, and important patent battles in US history (Taylor, 2000). Meanwhile, advancements in the development of laser media and devices within other industries would indeed lead to new applications of lasers in medicine and surgery over the following decades.

Subsequent studies revealed that particular wavelengths of laser light could be produced by stimulating particular laser mediums. The first diode laser, utilizing coherent light emission from a gallium arsenide (GaAs) semiconductor diode, was revealed in 1962 by two groups: Robert N. Hall at the General Electric Research Center (Hall *et al*., 1962) and Marshall Nathan at the IBM T.J. Watson Research Center (Nathan *et al*., 1962).

In 1962, other teams at the MIT Lincoln Laboratory, Texas Instruments, and RCA Laboratories also demonstrated the emission of light and lasing in semiconductor diodes. Early in 1963, a team led by Nikolay Basov in the Soviet Union utilized GaAs lasers to achieve emission of light (Nobel Prize, 2014a).

In 1970, the first laser diode to achieve continuous-wave (CW) emission was revealed simultaneously by Zhores Alferov and his collaborators in the Soviet Union, and by Morton Panish and Izuo Hayashi in the United States (Ghatak, 2009). However, it is widely accepted that Alferov and his team reached the milestone first, and they were consequently awarded the Nobel Prize in Physics in 2000.

While many types of therapeutic lasers were in use around the world, it was not until 2002 that Class IIIb lasers gained Food and Drug Administration (FDA) approval for therapeutic purposes in the United States. These lasers are colloquially referred to as "cold lasers" or "low-level laser therapy" (LLLT) devices. They are limited to 500 mW and are considered effective in the treatment of superficial conditions. The term "cold lasers" refers to the lack of a heating effect on tissue cultures in early experiments, while the term "LLLT" helped to differentiate low-power therapeutic lasers from surgical lasers.

Class IV therapy lasers, operating in excess of 500 mW, were approved by the FDA in 2006. This was the dawn of "high-power laser therapy" (HPLT). Delivery systems and precise dosage software have evolved (over the past several decades) to allow the safe and effective delivery of 500 mW–60 W to target tissues.

An Innovative Therapy

Just a few years after the invention of the laser, Dr. Endre Mester became the first to experimentally document its healing effects. Because he used mice as his experimental model, this is also the first documented use of lasers to accelerate healing in veterinary medicine (Mester *et al*., 1967). Considered the founding father of laser therapy for his pioneering work, Dr. Mester's experiments would also later prove that the acceleration of healing was actually a systemic event rather than merely a localized one (Perera, 1987). Mester observed a cascading effect of the healing process, motivating other researchers in Western and Eastern Europe to recognize the value of laser therapy and initiate studies of their own.

Early in the 1970s, the use of laser therapy was documented in Eastern Europe, China, and the Soviet Union; much of the early research emanates from these geographical regions. Over the next decade, the use of laser therapy spread to Western Europe and became accepted as an effective physical therapy modality (Goodson and Hunt, 1979).

Yo Cheng Zhou, an oral surgeon in China, was the first to stimulate an acupuncture point with a laser. He used laser stimulation instead of standard local anesthetic protocols during routine dental extractions. A beam from a 2.8–6.0 mW helium-neon laser apparatus (Model CW-12, Chengdu Thermometer Factory) was applied for 5 minutes before the removal of a tooth (Zhou, 1984).

From the mid-1970s to the early 1980s, laser therapy became an accepted physical therapy modality throughout Western European and several Asian countries. It finally appeared in the United States around 1977, but there were only a small number of therapists who understood its potential. Laser equipment in the United States during this time frame was limited to the 1–5 mW range, and acceptance by the medical and veterinary professions was very limited due to inconsistent clinical results. Extensive *in vitro* studies of the effects of various wavelengths of light on cell cultures was conducted throughout the 1980s and 1990s by researchers such as Dr. Tiina Karu, leading to a closer study of photoacceptors and the mechanisms of action of laser therapy (Karu, 1987). Laser therapy's association with cytochrome c oxidase and nitric oxide continues to be studied in innovative ways (Wong-Riley *et al*., 2005).

The first Independent Institutional Review Board for Laser Acupuncture Research was established in 1993, based on research compiled by Margaret Naeser, Ph.D.,

Lic.Ac. through the Robert Wood Johnson Foundation of Princeton, New Jersey. This initiated the effort and motivation of several colleagues to compile enough current information and research to be in compliance with US FDA regulations. Dr. Naeser has since published papers on utilizing laser therapy in stroke cases (Naeser and Hamblin, 2011).

A New Name

The history of laser therapy and the development of laser therapy devices have produced confusing terminology. Multiple terms initially and rapidly sprang up to describe both this technology and its utilization, each of them often lacking adequate scope of the therapy they attempted to relate. Many such terms were more representative of the devices being used than of the therapy itself being provided.

Several associations have formed over the years to encourage scientists and practitioners to exchange knowledge and information on laser therapy. The American Society for Laser Medicine and Surgery (ASLMS), formed in 1981, was the first. It was the dream of its founders that this organization be unique and include physicians, clinicians, and outstanding researchers in the areas of biophysics, biochemistry, biomedical engineering, laser biology, and laser safety. In 1994, the World Association for Laser Therapy (WALT) was formed by combining the International Laser Therapy Association (ILTA) and the International Society for Medical Laser Applications (ISLA). The North American Association for Laser Therapy (NAALT) was established in 1998. It included the regions of Mexico, Canada, and the United States of America. In 2015, the association changed its name to the North American Association for Photobiomodulation Therapy, retaining the same acronym, NAALT. These organizations share the same common goals: improving the understanding of photobiological mechanisms, promoting research, establishing treatment and regulatory guidelines, and providing education, clinical applications, and new clinical techniques.

Recognizing that an accurate, clear, and unambiguous name was needed, 15 international participants joined in a nomenclature consensus meeting at the joint conference of NAALT and WALT in September 2014 (Anders *et al.*, 2015). Respected authorities Dr. Jan Bjordal and Dr. Juanita Anders co-chaired the meeting. The term "photobiomodulation therapy" (PBMT) was recognized as being most descriptive of a science that involves complex mechanisms, some that are stimulatory, some inhibitory. Since that meeting, the National Library of Medicine (United States) has added the term "photobiomodulation therapy" to the MeSH database (MeSH, 2016).

The committee defined the term photobiomodulation therapy as

> *"A form of light therapy that utilizes non-ionizing forms of light sources, including lasers, LEDs, and broadband light, in the visible and infrared spectrum. It is a nonthermal process involving endogenous chromophores eliciting photophysical (i.e., linear and nonlinear) and photochemical events at various biological scales. This process results in beneficial therapeutic outcomes including but not limited to the alleviation of pain or inflammation, immunomodulation, and promotion of wound healing and tissue regeneration."* (Anders et al., 2015)

Older terminology continues to be used even as photobiomodulation therapy becomes more commonplace in publications and practical applications. In this text, the terms "laser therapy" and "photobiomodulation therapy" (or simply "photobiomodulation," PBM) will be used interchangeably.

A Better Tomorrow

As thousands of veterinary practitioners around the world continue to adopt laser therapy into their practices and a wealth of evidence regarding the use and efficacy of laser therapy continues to be published, we as veterinarians should continue to be at the forefront of this scientifically and clinically proven modality. Continued collaboration and sharing of information between us is essential to the future development of this advanced medical technology. We invite you to be a part of both this distinguished history of laser therapy and the new developments within this burgeoning field, which tomorrow's veterinarians will continue to quote in the future.

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Part II

The Theory and Science of Laser Therapy

2

Laser Physics in Veterinary Medicine

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Introduction

Crucial to you getting the most out of the rest of this book is your understanding of some very basic properties of light. The more you understand about the complete set of characteristics of the magic that comes out of your therapy laser, the better equipped you will be to tailor your treatment protocols and enhance the clinical efficacy of your therapy. You are going to read chapters that tell you about *in vitro* experiments that demonstrate the enhancement of cellular mechanisms, followed by even more real-world data that show a broad range of clinical usefulness based on these mechanisms. Within this stockpile of evidence, there will be some basic recommendations on dose prescriptions, power settings, pulse frequency characteristics, and treatment periodicity. These will be necessarily broad, to account for patient and condition variations, but also because the parameters used throughout both the anecdotal reports and the well-controlled experiments are quite mixed. My goal in this chapter is to have an informal conversation (rather than an encyclopedic lookup) that identifies what can be tweaked, explains its significance, and gives you a glimpse of its clinical implications.

Why Use Light?

Simply put, we use light because it can penetrate into the body and then cause a physiological change once it gets inside. An eighth-grader may not agree with that, since he cannot see through his own hand, and when he shines a flashlight on his arm he does not start to grow another. However, you are not so naïve. You have seen x-rays that have allowed you to peer inside the body. And you can read these pages, so you accept the idea (however unconsciously) that light gets absorbed by the cones in your eyes, which causes chemical reactions that lead to electrical signals that affect your chemistry and even your mood, your behavior, and your health.

Yes, ducking when you see a baseball coming toward your head is a health-altering effect of light's interaction with your biological self. However, visible light does not penetrate very well into our bodies, and your eyes cannot see x-rays. So what is the difference between these and the other flavors of light you are here to read about?

Flavors of Light

Despite the wide range of interactions and applications of light, there is literally only one fundamental difference between any two types: wavelength. To understand what this means, we first need to know what light *is* – an oscillating electric and magnetic field that travels in a straight line and at a constant speed (the speed of light). This is why the technical term for light is "electromagnetic radiation." That is all that light is; what it *does* is much more complex, and we will dive into some of that in this chapter. So, since light always travels at the same speed, the structure of its oscillation can be described equivalently either by the distance between its peaks and valleys, or by how many peaks or valleys it has in a given time. We call these values the "wavelength" and "frequency," respectively. This is not to be confused with pulse frequency or repetition rate. That has to do with turning light on and off periodically. We will get to that later.

Going forward, I will refer to the different types of light by either of these characteristics, but you will know that they refer to the same thing, and that is this one-dimensional scale of the oscillating electromagnetic wave we call light.

Laser Therapy in Veterinary Medicine: Photobiomodulation, Second Edition. Edited by Christopher J. Winkler and Lisa A. Miller.

Growing up, my favorite A.M. sports radio station broadcasted using light at a frequency of 660 kHz; I heated up my tea in the microwave this morning with light at a frequency of 2.45 GHz, but my favorite color is 450 nm (the wavelength of blue light). Indeed, these are all just different colors of light; the human eye only evolved to contain cones that can detect wavelengths from about 390 to 700 nm, which is what we call the visible part of the spectrum. The near-infrared spectrum spans from about 700 to 1100 nm.

If you were clever, you would have hesitated when I said "one-dimensional scale," since you know we experience three dimensions. In one classical way to visualize light, it is made up of oscillating electric and magnetic fields; each of these fields oscillate in a plane perpendicular (90°) to each other, both of which are perpendicular (90°) from direction of propagation (see the top of Figure 2.1). So there are the other dimensions for you, three in total. This brings us to two characteristics of light you may have heard referenced: polarization, which simply means the alignment of the electric (or magnetic) fields of light, and coherence, which means that the peaks and valleys of two different pieces of light are lined up. However, these values (and these other two dimensions) only matter when whatever you are shining the light on is structured enough to make a difference. Biological matter generally is not; but we are jumping ahead a little. First, we have to define the interactions, and then things will clear up a bit.

One more fundamental property of light: It turns out that the energy of light is directly proportional to its frequency (and therefore inversely proportional to its wavelength). The amount of energy any "piece" of light carries is discrete or "quantized." Therefore, in a sense, light is made up of individual packets of light, called "photons." No reason to explore the wave–particle duality of light here, but it was important to mention, since it will affect how we talk about light a little later. Figure 2.1 illustrates the fundamental structure of an electromagnetic wave and the relationship between wavelength, frequency, and energy.

So, how does this one fundamental property of light (frequency or wavelength or energy, however you want to refer to it) lead to such different effects in the different regions of the spectrum? In other words, why do different colors of light interact differently with matter?

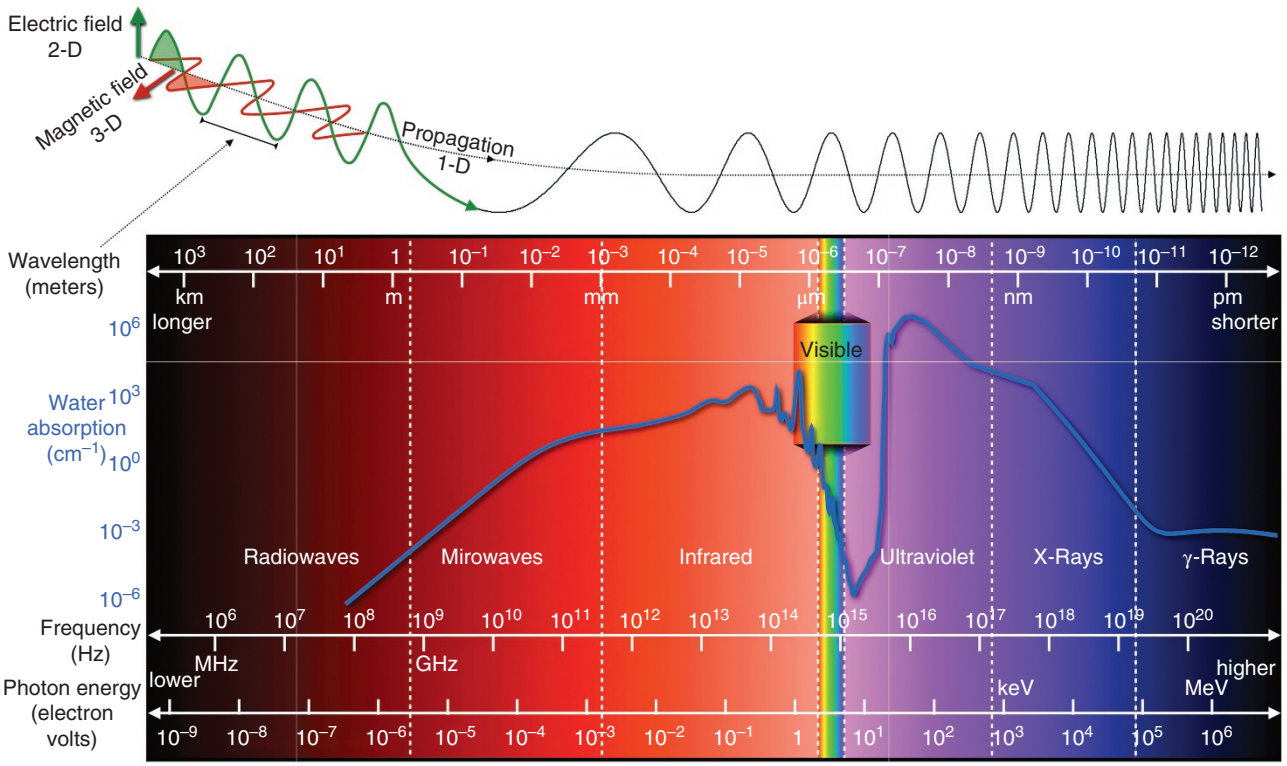

Figure 2.1 Electromagnetic structure and spectrum. The electric and magnetic fields of light are perpendicular to each other and to the direction of propagation. The name and effect of the radiation vary by wavelength (top axis), and equivalently by frequency and energy (bottom axes). The blue curve represents the absorption of water throughout the spectrum (Hale and Querry, 1973; Segelstein, 1981; Zolotarev *et al.*, 1969).

Interactions

In the region of the electromagnetic spectrum that concerns this book (the visible and near-infrared), there are two basic interactions: absorption and scatter. But before we get to these, we have to understand what we are shining the light on: biological matter. The body seems rigid enough, and it is at the scale of a baseball. However, when you are using light, you must see things at the scale of light, which we see is on the order of hundreds of nanometers (Figure 2.1). When you zoom in that closely, you will see that we are made up of molecules. If you zoomed in further, you would see atoms, but that would fall in the realm of x-rays (with wavelengths below 10 nm); visible and near-infrared light do not interact very strongly with objects that small.

Intra- and intermolecular bonds, however, are just the right size, and so they interact very well in this region. These bonds are nothing more than shared electron clouds (moving, charged particles), but they effectively act as springs between the constituent atoms. When charged particles are subject to an electric and magnetic field (like when you shine light on them), they experience forces, and since the field is oscillating, so do the bonds; and like strings on a guitar, they each have their own natural frequency.

Absorption

Absorption happens when the frequency of light is close to this natural frequency. Just like pushing someone on a swing or a mass on a spring, if you push in rhythm with the natural rhythm, you can transfer the most energy of your push to the system. In the visible and near-infrared region of the spectrum, photons of light either impart all their energy to the biological tissue they strike, or they bounce off; they are either completely absorbed or they scatter. So, in effect, light is absorbed by bonds that have just the right frequency, which makes it clear to see why absorption is wavelength- and tissue-dependent. Different tissues have different constituents, made up of bonds with different frequencies.

When these bonds absorb the light, they do what any excited spring does: bend, twist, expand, contract, and any combination of these. What this does, in effect, is change the shape of the molecule or chain of molecules. This is chemistry at its very core. You have to understand, the main way chemistry works (i.e., the way that two molecules combine) is a very sensitive, physical lock-and-key mechanism. Things that fit together nicely (both spatially and electrically) tend to bond together. If they do not fit, they do not bond. By changing the shape of one part of a molecule, even slightly and even on a very short time scale, you can cause the molecule to shed parts of itself or grab on to new things. What fascinating biochemical effects come from these absorption events is the topic of later chapters.

For those of you who have experience with surgical lasers (or kitchen microwaves, for that matter), you will realize that if you use enough light in a wavelength (or frequency) range that coincides with bonds that are prevalent in the tissue, these vibrations will reinforce themselves, create a lot of heat, and eventually shake molecules apart. Most of the time, the target molecules are water, and this boiling of water in the tissue either heats your food in a general way (if diffuse) or ablates the tissue in a very efficient, localized way (if focused).

In either case, absorption allows the targeting of molecules by light with the "right" frequency. However, statistically speaking, the majority of light bounces off something before it is absorbed.

Scatter

In the visible and near-infrared, virtually all of the scatter is elastic. In other words, photons retain their energy and simply bounce off particles in their path that do not have the "right" frequency to be absorbed (and even when they do, there is always a nonzero probability of each interaction). Which direction the photon travels after the bounce depends on what it bounced off of: mostly the size of the particle. Scattering of light by particles smaller than about 1/10th the wavelength of light is referred to as "Rayleigh scattering." Scattering by particles larger than that is referred to as "Mie scattering." The result of Rayleigh scattering is isotropic; the scattered light has equal intensity in all directions (except for at around 90°). Mie scattering, on the other hand, is very much forward-pointing, and the extent to which it points forward is represented by a number called the "anisotropy factor" (usually assigned the variable g) that can have values from +1 to −1. There are two ways to visualize this important concept: one with an individual photon in mind, and the other with a "beam" in mind. The technical way to define the anisotropy factor is the average cosine of the scattering angle of incoming light, which probably does not mean much to you as its written, but let us use some numbers. Anisotropy values for the near-infrared on biological tissue are in the 0.75–0.90 range, so let's take 0.85. This means that the average incoming photon is deflected by 31° ($\cos(31^\circ) = 0.85$). If the incoming light was headed north, then after scattering it would be headed somewhere in the NNW/NNE direction. The other way to interpret this is to say that it is the average percentage of the beam that remains going forward: A value of 1 means 100% keeps going (no scattering at all); a value of −1 means full back-scattering (like a super-efficient

mirror), and 0 means that the same amount of the beam goes forward and backward (and left and right and all around). So at $g = 0.85$, about 85% of the beam remains going in the same direction after scattering. You can see why I said that near-infrared scattering within the body is predominantly "forward-pointing."

How Much of Each

We do not talk about absorption and scattering on an individual basis, simply because there are more of these events in the first millimeter of skin than all of humanity could count in a lifetime. Instead, we talk about macroscopic quantities like absorption coefficients, μ_a, and reduced-scattering coefficients, μ_s', both of which have units of 1/length. These give you the average amount of absorption or scattering along the path of light and yield the shape of an exponential decay curve that describes the attenuation of light intensity (the percentage of the original beam) with depth. Inversely (i.e., if you take one divided by these quantities), you are left with what is called the "mean free path," which tells you the average distance between absorption and scattering events. Each of these quantities depends on both wavelength and tissue: for absorption, it is all about matching the frequency of light with the frequency of bonds, and for scatter, the story is dictated by how the wavelength of light relates to the size and number of the scattering particles (i.e., tissue composition and density).

Absorption coefficients are easy to understand, because a photon is either absorbed or it is not. Therefore, we use absorption coefficients along with depth from the surface to understand total absorption (and therefore the total relative intensity that is left in the beam). The blue curve in the background of Figure 2.1 shows the absorption coefficient of water throughout nearly the entire spectrum for reference.

Scattering is a bit trickier, because the direction the light bounces depends on what it bounced off of, and particularly its size. In addition, the path length of the light is never the same as the depth (and is usually a lot more), because of all the little bounces in different directions. Still, we do not track each bounce, but rather treat this directionality on average. This is why I referred to the *reduced* scattering coefficient, which incorporates the anisotropy into its calculation. Basically, the reduced scattering coefficient gives you a directionally corrected scattering coefficient that makes calculations simpler and lets you use the depth (which you know, or at least want to know) rather than individual path length of every light ray (which you do not know nor care about). The inverse, or reduced mean free path, thus gives you the average depth between scattering events.

These two quantities combine to form an effective attenuation coefficient, which is a generalized way of describing the loss of original beam intensity. With this, we can now understand how much light gets to what depth relative to how much we started with. Figure 2.2 illustrates the idea of attenuation in each of its mechanisms. Again, intensity is an exponentially decaying quantity, meaning that the deeper you go, the less light remains than in the original beam. That sounds simple enough. Just give me μ_a and μ_s' of a tissue, and I will tell how much light gets to that joint in the patient you are trying to treat.

Not so fast! In any target treatment area, there are many different amounts and types of tissue, which are not sliced and stacked neatly on top of on one another like deli meat in its packaging. So tracking the amount of absorption, type of scattering, and direction of scattering along the wide variety of interactions as light bounces around inside the body becomes a complicated mess. We can make some generalizations to help, though.

First, once inside the body, scattering is by far the dominant interaction in biological tissue, with its effect being strongest at shorter wavelengths. As some perspective, this means that the average depth of a scattering event is at most every half-millimeter (and usually less). At the skin, absorption and scattering play about equal roles, and there are a lot of both. Though the skin is not the ironclad barrier to the outside world as it is for, say, water, it is an obstacle for light. But since the anisotropy factor of visible and near-infrared light incident on biological tissue is very close to 1, on average these scattering events point the light even deeper into the patient.

Second, even though absorption is smaller in magnitude inside the body (a factor of 200–5000 times smaller than scattering coefficients), with absorption events taking place along the windy path, the light ends up bouncing along inside the body, and virtually all of the light that gets in is absorbed somewhere inside (Jacques, 2013). You do not see the animal glowing with near-infrared light as you treat them, even with an infrared camera. If you had a very sensitive detector, you would definitely find some light coming out, but the majority is absorbed by the body. In addition, a small fraction of absorption of a lot of photons still gives a lot of total absorption. How much are we talking about?

Units of Which You Have (Hopefully) Heard

We measure the energy of an individual photon in a unit called an electron volt (eV), with the energy of a photon