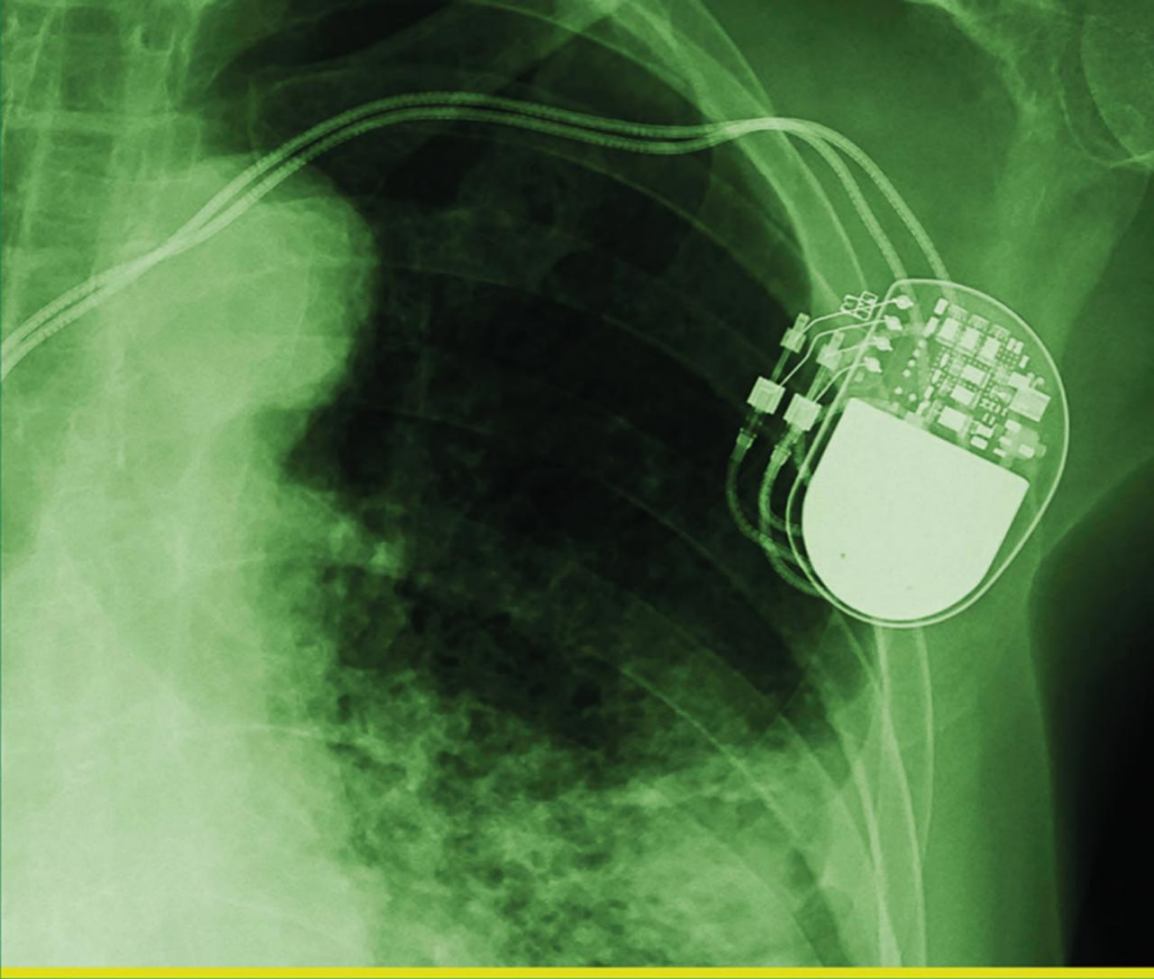

Toxicological Aspects of Medical Device Implants

Edited by
Prakash Srinivasan Timiri Shanmugam
Logesh Chokkalingam
Pramila Bakthavachalam

Toxicological Aspects of Medical Device Implants

Toxicological Aspects of Medical Device Implants

Edited by

PRAKASH SRINIVASAN TIMIRI SHANMUGAM
HCL America Inc., Sunnyvale, CA, United States

LOGESH CHOKKALINGAM
HCL America Inc., Sunnyvale, CA, United States

PRAMILA BAKTHAVACHALAM
HCL, ELCOT-Sez Park, Chennai, India

ACADEMIC PRESS
An imprint of Elsevier

Academic Press is an imprint of Elsevier
125 London Wall, London EC2Y 5AS, United Kingdom
525 B Street, Suite 1650, San Diego, CA 92101, United States
50 Hampshire Street, 5th Floor, Cambridge, MA 02139, United States
The Boulevard, Langford Lane, Kidlington, Oxford OX5 1GB, United Kingdom

Notices
Knowledge and best practice in this field are constantly changing. As new research and experience broaden our understanding, changes in research methods, professional practices, or medical treatment may become necessary.

Practitioners and researchers must always rely on their own experience and knowledge in evaluating and using any information, methods, compounds, or experiments described herein. In using such information or methods they should be mindful of their own safety and the safety of others, including parties for whom they have a professional responsibility.

To the fullest extent of the law, neither the Publisher nor the authors, contributors, or editors, assume any liability for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein.

British Library Cataloguing-in-Publication Data
A catalogue record for this book is available from the British Library

Library of Congress Cataloging-in-Publication Data
A catalog record for this book is available from the Library of Congress

ISBN: 978-0-12-820728-4

Publisher: Andre Gerhard Wolff
Acquisitions Editor: Kattie Washington
Editorial Project Manager: Anna Dubnow
Production Project Manager: Maria Bernard
Cover Designer: Mark Rogers

Typeset by MPS Limited, Chennai, India

Contents

List of contributors

Sadasivam Anbumani
Ecotoxicology Laboratory, Regulatory Toxicology Group, CSIR-Indian Institute of Toxicology Research, Lucknow, India; Academy of Scientific and Innovative Research (AcSIR), CSIR-Indian Institute of Toxicology Research, Lucknow, India

Pramila Bakthavachalam
HCL, Chennai, Tamil Nadu, India

Jesudas Balasubramanian
HCL, Chennai, Tamil Nadu, India

Nobel Bhasin
Department of Medicine, University of Chicago, Chicago, IL, United States

Logesh Chokkalingam
HCL America Inc., Sunnyvale, CA, United States

Bhagyashree Choudhari
Department of Pathology, PRADO, Preclinical Research and Development Organization, Private Limited, Pune, India

Shreya Dwivedi
Ecotoxicology Laboratory, Regulatory Toxicology Group, CSIR-Indian Institute of Toxicology Research, Lucknow, India

Krishna Gautam
Ecotoxicology Laboratory, Regulatory Toxicology Group, CSIR-Indian Institute of Toxicology Research, Lucknow, India; Academy of Scientific and Innovative Research (AcSIR), CSIR-Indian Institute of Toxicology Research, Lucknow, India

Mounika Gudeppu
HCL, Chennai, Tamil Nadu, India

Praveen Kumar Gupta
Department of Toxicology, PRADO, Preclinical Research and Development Organization, Private Limited, Pune, India

Shobana Navaneeethabalakrishnan
Department of Endocrinology, Dr. ALM Postgraduate Institute of Basic Medical Sciences, University of Madras, Chennai, India

Nandakumar Palani
HCL America Inc., Sunnyvale, CA, United States

Somnath Pandey
Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States

S. Priya
Department of Pharmacology, Sathyabama Dental College and Hospital, Chennai, India

T. Pugazhenthan
Department of Pharmacology, AIIMS Raipur, Chhattisgarh, India

Manish Ranjan
Department of Surgery, Northwestern University, Chicago, IL, United States

V. Sajitha
Department of Microbiology, AIIMS Raipur, Chhattisgarh, India

Thamizharasan Sampath
ACSMCH, DRMGR Educational & Research Institute, Chennai, Tamil Nadu, India

Monisha Saravanan
IQVIA, Bangalore, Karnataka, India

M. Sathish Babu
Department of Biochemistry, JIPMER Karaikal, Puducherry, India

Prakash Srinivasan Timiri Shanmugam
HCL America Inc., Sunnyvale, CA, United States

Rajeev Sharma
Department of Toxicology, PRADO, Preclinical Research and Development Organization, Private Limited, Pune, India

Dhirendra Singh
Pathology Laboratory, Regulatory Toxicology Group, CSIR-Indian Institute of Toxicology Research, Lucknow, India

Karnika Singh
OSU Comprehensive Cancer Center, Columbus, OH, United States

Sandhiya Thamizharasan
SDC, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India

Priya Gupta Vajrapu
Boston Medical Center, Boston, MA, United States

A.R. Vijayakumar
Department of Pharmacology, JIPMER Karaikal, Puducherry, India

Pralhad Wangikar
Director, PRADO, Preclinical Research and Development Organization, Private Limited, Pune, India

About the editors

Prakash Srinivasan Timiri Shanmugam, PhD is currently contracted as an SME—Biocompatibility at Baxter International, Inc. in Round Lake, IL, United States. He was previously contracted at Johnson & Johnson Medical Device Sector. He has an MSc and a PhD in the specialization of Pharmacology and Toxicology with Chemistry (interdisciplinary) from the University of Madras, Chennai, India and completed his postdoctoral research at Tulane University and LSUHSC-Shreveport, Louisiana. He has authored a book, contributed several book chapters, and published research articles in various peer-reviewed international journals and conference proceedings/abstracts.

Logesh Chokkalingam is a Group Project Manager at HCL Technologies in Raynham, MA, United States. He has a bachelor's degree in Mechanical Engineering from Vellore Institute of Technology and earned a Diploma in Tool and Die Making from NTTF for passing a specialized course in the design and manufacturing of press tools, injection molds, jigs, and fixtures. He is a Mechanical Engineer with specialized knowledge on design development, program management, medical device regulations, supply chain integration, portfolio optimization, asset transfer, verification testing and validation, and value engineering.

Pramila Bakthavachalam, PhD, FASC (AW), MRQA is a Technical Manager for Medical Devices, Toxicology, and Biocompatibility at HCL Technologies PVT Ltd in Chennai, India. She has a Doctorate in Environmental Toxicology/Biotechnology and MPhil in Microbiology. She has experience in regulatory toxicology as a scientist and in quality assurance. She was instrumental in establishing a preclinical testing facility and GLP certification at Sri Ramachandra University. She has worked with pharmaceuticals, cosmetics, medical devices, agrochemicals, industrial chemicals, and veterinary drugs. She has numerous publications in both national and international journals in various disciplines such as environmental toxicology, toxicology, and pharmacology.

CHAPTER ONE

Introduction to medical implants

Nandakumar Palani*
HCL America Inc., Sunnyvale, CA, United States
*Corresponding author

Abstract

This chapter mainly focuses on the history and evolution of the medical implants, materials used in biomedical implantable devices, and consideration for medical implant materials that discuss the ease of fabrication, biocompatibility, and flexibility. It also discusses their characteristics such as electrical, chemical, thermal, and mechanical behaviors with a combination of different materials/alloys/prosthetics as composites. Implantable devices reside in the human body/biological medium either temporarily or permanently, for the purpose of diagnostics, monitoring, or therapeutic purposes. With the unique responsiveness and design in terms of clinical needs, responsive polymers have been used to facilitate the deployment or removal of the devices with minimum damage to the host tissue, support function of current devices to treat ailments, deliver drugs, control infection, or monitor physiological factors or biomolecules. This chapter also reviews the use of responsive polymers as various implants and devices, starting with addressing the biocompatibility issue of responsive polymers. Application of responsive polymers is based on the areas on which it is applied, including ophthalmic devices, surgical devices, cardiovascular devices, orthopedic dental, breast, respiratory devices, urogenital devices, and implantable biosensors. The biocompatible implants used for medical implants still have some chronic effects on the human body.

Keywords: Medical implants; generation/evolution of medical implants; silicone gel; inflammation; capsular contracture; rupture and deflation; implant materials; biological medium; tissues; alloys; polymers; temporary and permanent implants; biocompatibility; biosensors; chronic effects; implantable devices; standards

1.1 Introduction to medical implants

1.1.1 What is a medical implant?

Medical implants are planted into a human body by surgery or naturally formed cavity and are planned to retain over a short or long period

Toxicological Aspects of Medical Device Implants.
DOI: https://doi.org/10.1016/B978-0-12-820728-4.00001-0

depending upon the type of surgery. FDA came up with the standards to classify the devices that are placed in the human body regardless of the location and period also called as medical implants.

Implantable devices are partly human-made implants or natural implants that are fully introduced into the subject and planned to retain after the surgery for a period of time depending on the need.

It has been observed that around 10% of the people in the United States and around 6% of the people in industrial revolutionized countries have gone through the surgically medical implants for reconstructing the human body functions and attaining a better standard of life or increasing life span.

1.1.2 History of medical implants

In the olden days (in the late 1880s), body anatomy was improved by changing the size and shape of the breast. The materials used to fill in the breast were different forms made of synthetic materials, oil, rubber, ivory, and glass. Then, silicone and even injections were used to augment the breast.

Injecting liquid substances are the most used technique to augment the breast shape and size by using substances such as paraffin wax or oil and petroleum jelly. Later, silicone fluid was injected into the breast by some illegal practitioners. These methods caused severe damage to the human body including pain, skin color changing, infection to other parts of the body, breast disfigurement and breast loss, respiratory issues and pulmonary issues, liver damage, and even unconsciousness or death.

When the first silicone gel breast implant was introduced, it became popular even though there were many disadvantages; the silica gel is a gum with amorphous silica, which has a high modulus. These olden day implants are made of gel and thick outer shell, whereas the modern-day silicone rubber shell has a smooth surface and inside fluid with a sturdy silicone gel. The burst rates were low compared to other breast implants because of the strong shell. However, when the capsule shrinks, tightens, and compresses the breast implant, seepage complications occur.

To avoid the seepage and leaks, the implant is manufactured with inside partitions; this keeps the implant to hold the gel from sagging, and the holes/slits and layers are sealed with patches, holes, or slits to avoid leaks during manufacturing.

With the advancement of technology, thin implant shells with no gaps between one part and another are manufactured. When the first saline-filled implants emerged, they were heavy and easy to break, with

splashing noise that was audible, and the deflation rate was very high; the manufacturing process involves volcanization to strengthen the product.

Around the 1980s, the thick shell implants were replaced with thin shells, but this caused high burst rates and seepages that led to deflation. The next-generation implants were made with soft shells and different gel fluids that caused the burst rates and seepages to be high. Later, polyurethane foam, which was introduced in the market, reduced the burst rates and was increasingly popular among most women who underwent implant with this polyurethane foam shell. This foam shell implant was discontinued around the 1990s owing to inflammation, fluid buildup, swelling, pain, and infection side effects.

Breast implant types during these years evolved with different substances and shells; some of them were temporary or permanent. The burst rates or seepage frequencies for the implants vary in percentage based on the manufacturers with different generations.

The new-generation implants have improved silicone-gel implants and saline implants with less deflate rates with the help of stronger shells, partition layers, and textures. This type of implants comes with deflation and rupture rates and less gel diffusion or seepage. As there were no proper standards for breast implant manufacturing in America, more than 200 types of breast implant models were manufactured by different manufacturers with a difference in materials, shapes, sizes, and gels. It is also estimated that over 8000 types of breast implants are manufactured by different manufacturers with different materials over the years.

The major implant manufacturers today use single-lumen implants that are filled with silicone gel. The cover or shell is made of silicon rubber, which is a kind of elastic material called elastomer, and the inside partition is coated with fluorosilicone to prevent silicone gel seepage or bleeding from inside. The outer shell has a textured surface that allows the tissue to grow on its surface, causing an inflammatory reaction. The growth of fibrous scar tissue which is made of collagen that forms around the medical implant, tightens the capsule and squeezes the implant material leading to capsular contraction.

The modern-generation implants are not sure to be continued to use; the analysis and study results from the FDA will lead to a new generation of implants. The history of use and information is very less about the saline implants which was quickly evolved to silicone-gel implants. The saline implants history and usage information is very less which was quickly evolved to silicone-gel based implants.

1.1.3 Medical implant types and materials for implants

Natural as well as artificial medical implants are placed inside the body. Some of the artificial implants are made from prosthetics metal, ceramic, and plastic, which are placed inside the body for soft and hard missing body parts. The natural implants that are made from tissues, bone, and skin are used to support the human body to live a normal life. The implants are mostly used for medication, monitoring, and providing support to organs.

Implants can be temporary or permanent based on their use; some can be removed when the purpose is solved, or it can be placed permanently to provide life support to the human patient. For example, some of the tissues, skin, hip implants, and knee implants are intended to be permanent to support the human patient. In contrast, screws that are used to repair broken bones or metal plates are temporary, and they can be removed when no longer needed by the human patient.

Most surgical procedures have very less recovery time and very less risks, and the risks involved in medical implants are mostly related to the placement, infection, and implant failure; if the implant is not working as intended, then there is a high risk of operating again. Some implants are allergic and infectious to certain human patients and cause infections. The materials used to manufacture the implants can cause bruises, swelling, pain, and redness at the surgical site or even after recovering from surgery. Some of the implants are expected to have some common effects on the human patient like infections and bruises that will be reduced once the human patient's body adapts the implant, but some are very high risks that damage other parts of the body.

The implant life span is considered that, over time, they could break or are not working as expected. This could result in additional surgeries to repair or replace the implant in the human patient body.

1.1.4 Implant materials and purpose

Materials used for implants

- Alloys
- Biosensor
- Titanium
- Prosthetics
- Polymer
- Biocompatibility
- Biomaterials