

# Biophysical Methods for Diagnosing Human Tissue Anomalies



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Edited by

Nathan Blaunstein and Ben-Zion Dekel

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## PREFACE

The book is intended to appeal to any practicing radio and optical scientist and engineer, as well as to any expert from bio-medicine and bio-technology, who is concerned with the design, operation, and service of the corresponding systems and devices for resolving the problems of detection, imaging and identification of any inner and outer physiopathology and anomaly – cancerous and non-cancerous, of human tissue and body, for earlier diagnosis of such kinds of pathologies.

It will be also interesting and useful for any medical doctor who deals with practical testing of patient on subject of detection and diagnosis of human's tissue pathologies and anomalies, inner and outer. It also can be useful for postgraduate students of disciplines regarding bio-technology, bio-medicine, and applications of various techniques and technologies for human tissue earlier diagnosis by use optical and electromagnetic non-invasive methods of testing of patients.

For these objectives, cutting-edge technologies, accompanying theoretical models, and innovative instrumentation have been developed. These technologies encompass thermo-imaging, which operates in the integral regime, and optical infrared spectroscopy, functioning within the spectral domain. Leveraging both the visual and infrared (IR) segments of the optical spectrum, these techniques are well presented for diagnosing external and internal human tissue anomalies.

For early breast cancer diagnosis using radio mammography, an advanced radio tomographic synthesis technology was introduced, accompanied by innovative radio systems and devices. These have been effectively adapted for the non-invasive early diagnosis of breast tissue and the human brain. This approach relies on gigahertz (GHz) band radiation, enabling the detection and visualization of pathologies or anomalies within the breast. This line of investigation emerged as a distinct approach after it was established that infrared (IR) band rays have limited penetration into the human body, reaching tissue depths of only a few millimeters.

The initial set of challenges was effectively addressed from the early seventies of the last century through to the present, as documented in the works listed in the bibliography below. In recent years, the authors of this book have published several articles comprehensively detailing the evolution of external and internal human tissue pathologies, ranging from

minor skin anomalies or pressure injuries to aggressive cancerous physio-pathologies.

Over just a short span of years, the methods of radio tomography originally developed to address direct and inverse problems in radiolocation—especially for detecting foreign objects concealed within clutter, as detailed in publications such as (Shipilov et al. 2020; Blaunstein and Yakubov 2019; Yakubov 2017) —were successfully examined for early, non-invasive diagnosis of pathologies in breast radiology and the human brain.

It is important to note that there are two distinct sets of problems within the fields of classical and applied electrodynamics and electromagnetism. The first set, known as direct problems, concerns determining the wave field given a known distribution of sources. The second, the inverse problems, focuses on identifying the distribution of irradiated sources.

Given the similarities between optical and radio waves, which are distinct portions of the wave frequency spectrum, their application and the associated mathematical descriptions largely depend on the relationship between respective wavelengths (optical and radio) and the specific human tissue anomalies and pathologies being studied. This relationship is important in choosing the appropriate technology, methodology, techniques, and equipment for evaluating human tissue.

It is thus evident that the initial descriptions of both radio and optical wave propagation through diverse environments are inherently part of applied electrodynamics and electromagnetism. The foundational laws of these disciplines were established in the early parts of the last century, building upon the rigorous foundations of advanced mathematics and vector algebra, which have their origins dating back 200-250 years ago.

While preparing the manuscript for the proposed book, the authors integrated various facets of optical and radio engineering that had previously been introduced through separate courses offered to students globally.

Thus, Prof. Nathan Blaunstein over a span of more than 25 years, provided students with foundational knowledge in high-level mathematics, classical and applied electrodynamics, and electro-optics. He emphasized the main aspects of classical electrodynamics, the propagation of radio and optical waves in various media and structures, and subsequently explained on the applications of different radars and LIDARs.

Prof. Sergey Shipilov over a period of more than 20 years, along with his PhD colleagues, introduced students to several themes within 'radiophysics'. These themes emphasized the fundamentals required to address both direct problems (pertaining to radio communication) and

inverse problems (related to radiolocation) in reconstructing and identifying foreign objects embedded in cluttered environments.

For more than 20 years, Dr. Ben-Zion Dekel has granted knowledge to students through practical exercises and a series of courses. His teachings emphasized the integration of electro-optics, both wireless and fiber-optic, into biomedicine and biotechnologies. This included exploration into human tissue pathologies and anomalies, both malignant and benign, with the aim of early diagnosis using mainly FTIR spectroscopy.

Arkadii Zilberman, as an expert in optical physics and electro-optics, introduce a great impact in skin anomalies detection and identification – cancerous and non-cancerous, by use different types of image devices and spectroscopes. His experience till nowadays is used by students in practice of detection, visualization, and identification of other kinds of human tissue anomalies.

Yaniv Cohen in his PhD dissertation obtained in 2022, presented wide spectra of applications of IR non-invasive radiation in detection, imaging and identification of human tissue outer and inner anomalies, some elements of which were taken for the corresponding lectures for postgraduate students from bio-medicine and biotechnology.

In the course of their collaborative scientific discussions about the subject matter for the proposed book, the authors established the foundational concepts for its content. Firstly, every practicing physician should be familiar with the subject of study, namely human tissue — both internal and external. This includes an understanding of anatomy, physiology, pathologies, and the temporal and spatial evolution of tissue anomalies. Concurrently, any radio or optical engineer, as well as physicists, should possess a solid grounding in advanced mathematics and the core principles of classical electrodynamics and electromagnetism. Equipped with this knowledge, readers will be better positioned to explore various challenges related to the propagation of radio and optical waves, especially those related to the detection, imaging, and identification of human tissue anomalies.

At the same time the current book presented for the reader a description of different techniques and models of machine learning based on strict statistical analysis of obtained clinical testing results for human tissue cancerous and non-cancerous structures identification. The theoretical of machine learning is presented with a short description of neurone analysis.

In our assessment, this book stands out as one of the few texts, alongside works published between 15 to 25 years ago (Murphy 1997; Freedberg et al. 1999; James, Berger, and Elston 2006; Bansal 2006; Wolff et al. 2008; Pieper 2013), that goes deeply into cutting-edge optical and radio

technologies for detecting, imaging, and identifying human tissues—both internal and external. It integrates a multidisciplinary approach, merging mathematical and physical characterizations of natural processes within the human body. This unique methodology underscores the similarities in diagnosing human tissues across both optical and radio wave spectra. This comprehensive view is further enriched by recent publications which analyze for example human tissue diagnostics using optical and radio tomography (B. Dekel et al. 2016; Cohen et al. 2020; Shipilov et al. 2020) or infrared spectroscopy analyzing liquid biopsy (Zlotogorski-Hurvitz et al. 2019).

The proposed book is organized into four parts, including a total of 11 chapters.

Part I encompasses Chapters 1 and 2, offering an overview of predominant human tissue anomalies and the contemporary diagnostic techniques and equipment employed for their detection.

Part II, spanning Chapters 3 to 6, goes deeply into the foundational theories and concepts surrounding electromagnetic waves—both optical and radio—and their application in the early diagnosis of internal and external human tissue anomalies and pathologies. Chapter 3 describes the similarities between optical and radio waves as distinct segments of the electromagnetic spectrum, emphasizing their synergistic propagation characteristics in free space, at media interfaces, and within diverse materials and media. Chapter 4 provides a clear and detailed exposition of the theoretical foundations of radio tomography, considering a range of object locations within different media. Chapter 5 deals with different methods and models describing radio tomographic synthesis based on different techniques of rays focusing and defocusing for various location of the embedded and hidden object. In Chapter 6, theoretical background of IR thermography and spectrography is described based on corresponding theoretical framework performed by the authors of this chapter.

Part III consists of chapters 7 to 9 which deals with practical aspects of human tissue diagnosis using optical and radio tools. In Chapter 7, the authors present both theoretical and experimental diagnostic approaches to breast cancer using radio mammography. The chapter explains the processes of signal pre-processing and post-processing in tomosynthesis. Moreover, it showcases detailed measurements conducted on breast phantoms with cancerous structures and on brain samples exhibiting anomalies. Chapter 8 goes deeply into the clinical evaluation of skin anomalies, encompassing both nevi and cancer, using the IR spectrum of radiation. The chapter highlights the benefits of IR radiation compared to visual optical radiation and provides pertinent statistics on skin cancer

diagnosis. Furthermore, this chapter provides an overview of different types of skin pressure injuries, including their anatomy and pathology. Discussion encompasses the methodologies employed in testing these injuries, complemented by the introduction of an emerging diagnostic device currently in development. Chapter 9 presents the use of mid-IR diagnostics for detecting internal human tissue abnormalities, including oral and gynecological cancers. Additionally, the chapter discusses the examination of incubation mediums to enhance the likelihood of successful pregnancy. These investigations employ FTIR spectroscopy with the assistance of machine learning techniques.

Part IV includes chapters 10 and 11 dealing with applications of machine learning techniques for diagnosing anomalies in human tissues and explores several innovative applications for future development. In Chapter 10, we go through the components of artificial intelligence, emphasizing neural analysis derived from clinical trial statistics and various machine learning models. The chapter briefly outlines the neural configuration of artificial intelligence. Building on this foundation, several machine learning techniques for the statistical pre-processing of experimental data are explored. Data is analyzed using the IROS system fabricated by the authors of this chapter. Chapter 11 presents a collaborative perspective from the authors on the future applications of innovative technological approaches for diagnosing human tissue anomalies. This vision includes the integration of optics, radio-waves with artificial intelligence and machine learning. Furthermore, the chapter explores the conceptualization of an optimal healthcare service network, encompassing clinics, medical practitioners' offices, and individual patients.

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## EDITORS

**Nathan Blaunstein**, PhD (1984), DSc (1991), Professor (1992) from Academy of Science of USSR, currently is a professor-emeritus in Ben-Gurion University (Beer Sheva) and an Invited Professor in Sami Shamoun Engineering College (Beer Sheva and Ashdod) in Israel.

He is an author of 15 books, 6 chapters in Handbooks, over 220 articles in scientific journals and in reports of worldwide pier conferences and a co-author of 7 patents in radiophysics and optics, and their applications in electromagnetic and IR tomography including bio-medicine regarding human tissue earlier non-invasive diagnosis by use wide spectra of sensors and devices.

His research interests include direct and inverse problems of radio and optical wave propagation in various media and materials for the purpose of radiolocation (Radar) and optical location (Lidar) by use theoretical frameworks of wave tomography and spectrography with applications in industry, geophysics, bio-technology, bio-medicine, defense, and security.

**Ben-Zion Dekel**, Ph.D. (2002), serves as a senior lecturer within the Faculty of Engineering at the Academic Center Ruppim, Israel. He received his doctorate by the Department of Electrical Engineering, specializing in Physical Electronics, at Tel Aviv University.

Prior to his tenure at Ruppim, Dr. Dekel was engaged with IAI - MLM, focusing on electro-optical applications. His work entailed the development of mathematical and physical models and simulations for the detection of flying objects. Moreover, he was working on a star tracker project tailored for small satellites and various projects emphasizing imaging in the mid-IR spectral range, specifically within the 3-5 $\mu\text{m}$  and 8-12 $\mu\text{m}$  wavelengths.

Dr. Dekel's research activities are primarily centered around FTIR spectroscopy, integrated with machine learning, aimed at biomedical applications. This includes malignancy detection across diverse tissue organs and projects exploring fertility in both men and women.

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Prof. Nathan Blaunstein is grateful for Prof. Yakubov, who passed away only three years ago, creating before a strong scientific group in radiophysics in Tomsk State University (former USSR), radio-physical faculty, and continued (from 1972) of mutual collaboration in the fields of radio-wave propagation in various media during a period after Prof Blaunstein left Tomsk (1976) and then, former USSR (1992).

During the recent decade, Prof. Shipilov, contributor to four chapters within this book, have established a group of PhD researchers (Andrey Klokov, Dmitry Sukhanov, Rail Satarov, Alexander Erimeev, Ilya Tsiplyaev), converting together with Profs. Yakubov and Blaunstein their knowledge in solving the direct and inverse problems of radio communication and radio location to the problems regarding bio-medicine and bio-technology, with main impact in non-invasive radio methods of earlier diagnosis of human tissue, breast and brain, pathologies and anomalies. All of them are contributors of two chapters of this book.

After starting with Ben Gurion University (BGU, Israel) in 1993, Prof. Blausenstein created a group of students, which then, after obtaining their PhD degrees, were involved in fields of earlier diagnosis of skin (Boris Melnik and Arkadi Zilberman) and breast (Matwey Bereznitsky) anomalies by use visual and IR optical techniques. Another MSc student, Yaniv Cohen have been sent to finish his PhD in National Research University of High School of Economics (NRUHSE, Moscow), under supervision of Prof. Nathan Blaunstein and Prof. Eugeny Krouk, in frames of multidisciplinary collaboration and joint research in fields of artificial intellect and machine learning created between BGU and NRUHSE.

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**PART I:**  
**INTRODUCTION TO THE SUBJECT**

# CHAPTER 1

## OVERVIEW OF TYPES OF HUMAN TISSUE ANOMALIES

BEN-ZION DEKEL AND YANIV COHEN

### 1.1 Overview of the Subject

Tissue anomalies in the human body can be understood as deviations from the typical cellular or structural organization of specific tissues. These anomalies can arise due to genetic factors, environmental influences, or a combination of both.

As for the genetic factors, many anomalies are rooted in our DNA. Mutations, whether inherited or acquired, can result in a wide array of congenital conditions and diseases. Examples include Down syndrome, which results from an extra chromosome 21, and cystic fibrosis, caused by mutations in the CFTR gene. Environmental etiology relates to anomalies induced by external factors, particularly during crucial stages of fetal development. Teratogens, including certain medications, infections, and radiation, can disrupt normal embryonic growth. For example, a pregnant individual's exposure to the rubella virus might result in congenital rubella syndrome in the offspring, manifesting as heart defects, hearing impairments, and other abnormalities. Another source of anomalies is multifactorial inheritance, where a blend of genetic predispositions and environmental influences come into play. Numerous congenital heart and neural tube defects, such as spina bifida, are attributed to this combined etiological foundation.

Tissue abnormalities can be categorized into several types based on their manifestation and underlying causes. Physical or structural anomalies are visible defects in body structure, with cleft lip and palate, clubfoot, and congenital hip dysplasia being notable examples. Biochemical anomalies, such as metabolic disorders including phenylketonuria (PKU) and Tay-Sachs disease, arise from enzyme deficiencies that lead to detrimental accumulations of substances in the body. Functional anomalies relate to



irregularities in the operation of body systems, with arrhythmias exemplifying disruptions in the heart's electrical system. Lastly, behavioural or neurological anomalies encompass conditions like autism spectrum disorders, ADHD, and dyslexia, which signify deviations in behavior or neural function.

The origin of tissue anomalies often lies in specific biological disruptions. Firstly, anomalies may arise from interruptions in typical developmental or physiological events, such as cell growth and differentiation. During embryogenesis, cells undergo proliferation, migration, and specialization to forge organs and systems. Interferences in these actions, whether instigated by genetic alterations or external teratogens, can culminate in anomalies. For instance, Hirschsprung disease results from disturbances in the routine migration of neural crest cells. Secondly, anomalies can emerge from irregularities in gene expression, occurring when genes aren't manifested appropriately or timely. An illustration of this is Marfan syndrome, where a mutation in the fibrillin-1 gene compromises the integrity of connective tissue. Lastly, some anomalies are engendered by physiological imbalances; certain conditions stem from perturbations in homeostatic frameworks. Case in point, irregularities in calcium management can induce conditions like hyperparathyroidism or hypoparathyroidism.

Human tissue anomalies, which encompass a broad spectrum of structural, biochemical, functional, and neurological deviations, have piqued considerable interest in the medical and scientific, and technological communities due to their profound impact on health. The emergence of advanced diagnostic technologies has revolutionized our ability to detect and understand these anomalies at an early stage. Techniques such as high-resolution imaging modalities, genomic sequencing, and metabolic profiling enable precise identification and characterization of abnormalities. Moreover, with the advent of targeted therapies, nanomedicine, and regenerative medicine, there's now an expanding repertoire of treatments tailored to address the root causes of these anomalies, rather than just managing their symptoms. The confluence of insights into the biology of tissue anomalies with technological advancements holds promise for improved patient outcomes and a deeper comprehension of human health.

In subsequent chapters of this book, our emphasis will shift toward the intricate interplay of biological, physical, and technological methodologies that facilitate the precise identification and characterization of tissue anomalies, specifically tumors. We will go deeply into the use of optical and radio technologies, examining their potential in diagnosing tissue anomalies, especially malignant tissues.

## **1.2 Types of Tissue Anomalies**

### **1.2.1 Tumor tissue anomalies**

#### **1.2.1.1 Overview**

Tissue anomalies, particularly those associated with tumors, represent some of the most pressing challenges in medical science. Among these, malignant tumors evoke the most concern and trepidation. Tumors, irrespective of their nature, arise from a common underpinning: the unregulated proliferation of cells. However, what differentiates a benign tumor from its malignant counterpart is the latter's aggressive tendency to invade neighboring tissues and metastasize to remote body sites. These malignant tumors, commonly referred to as cancers, can disrupt the body's physiological balance, often leading to severe complications. As we go deeply into tissue anomalies in the ensuing sections, our focus will be on understanding the underlying biology, progression, and potential interventions for these malignant growths.

Tumors represent a unique anomaly in human tissue dynamics, characterized by an uncontrolled proliferation of cells. While they can appear anywhere in the body, their genesis and subsequent behavior are often a consequence of a complex interplay of genetic, environmental, and physiological factors.

Detection and identification of these anomalies is crucial, particularly through optical means, a topic that will be elaborated upon in the subsequent paragraphs, and forms the primary focus of this book.

#### **1.2.1.2 Etiology of tumors**

At the genetic front, the appearance of tumors is predominantly linked to mutations in a cell's DNA. Some of these mutations are inherited, manifesting in patterns observed in familial cancer syndromes. However, others are acquired throughout an individual's life due to exposure to mutagens or random cellular errors. Key players in this genetic “dance” are oncogenes, which are the mutated versions of proto-oncogenes. When activated, oncogenes drive aggressive cell growth. An illustrative example is the HER2 gene, whose aberration is implicated in specific breast cancer types.

In proximity to oncogenes are the tumor suppressor genes, like P53 and BRCA. Their primary role in cellular biology is to maintain order by regulating cell division, ensuring it occurs in a controlled manner. However,

mutations in these genes can be likened to uncontrolled cellular proliferation.

Beyond genetics, environmental and lifestyle elements influence over tumor development. For instance, carcinogens, substances capable of causing cancer, are found in tobacco smoke and asbestos. These agents can directly interact with and damage DNA, increasing the mutation risk. Lifestyle choices, such as adopting a poor diet, leading a sedentary lifestyle, or frequently exposing oneself to harmful ultraviolet radiation, can also without noticing lay the groundwork for tumor formation.

Infectious agents, particularly certain viruses, have also been spotlighted in the oncology world. Viruses like HPV or Hepatitis B and C have dual mechanisms of promoting tumors: they can introduce foreign genetic material into host cells, triggering mutations, or they can cause prolonged inflammation, making tissues more susceptible to cancerous changes.

The immune system, our body's defense mechanism, when functioning optimally, acts as a vigilant guard, identifying and destroying aberrant cells. However, when this system is compromised or suppressed, as seen in individuals with diseases like HIV/AIDS or those on immunosuppressive drugs, its ability to repeal tumors diminishes.

The hormonal environment within an individual can also impact tumor genesis. Hormones are crucial for cell growth and reproduction. Any imbalance, such as extended exposure to estrogen without opposition, has been epidemiologically linked to increased risks of certain cancers, notably breast cancer.

Lastly, physiological conditions, specifically chronic inflammation, can indirectly promote tumor growth. For example, individuals with inflammatory bowel disease, a condition marked by prolonged intestinal inflammation, have a notably increased risk of developing colon cancer. This is because chronic inflammation can lead to an environment rich in agents that cause mutations, thereby increasing the likelihood of tumor development.

### **1.2.1.3 Tumor types**

At the foundational level, tumors can be broadly classified into benign and malignant categories.

Benign tumors are non-cancerous growths that remain localized and do not invade surrounding tissues or metastasize to distant sites. While they can grow to a significant size and sometimes exert pressure on neighboring structures, they generally have a well-defined border and lack the aggressive

characteristics of malignancies. Examples include adenomas, lipomas, and fibromas.

Malignant tumors (cancers) have the ability to invade adjacent tissues and spread to other parts of the body, a process known as metastasis. Their cells often exhibit genetic mutations, varied morphology, and a high rate of proliferation. Depending on the cell type from which they originate, malignant tumors can be categorized into:

**Carcinoma:** At its essence, the term "carcinoma" refers to a category of cancer that originates from the epithelial cells. Epithelial cells are those that form the lining of the skin, blood vessels, internal organs, and various glands. These cells have a crucial role in providing a barrier between the internal and external environments, secretion, and absorption.

At the cellular level, carcinomas arise when epithelial cells begin to proliferate uncontrollably, often due to mutations in their DNA that either promote cell division (oncogenes) or prevent the natural apoptosis process (tumor suppressor genes). Carcinomas, epithelial origin, can be broadly classified into two main subtypes based on the cell appearance and characteristics.

The first is adenocarcinoma which originates in an epithelial cell that secretes mucus and other substances. They possess glandular properties and can be found in various body parts. Common examples include the prostate, breast, lung, and colon.

The second is Squamous Cell Carcinoma (SCC) which originates from the flat cells that form the surface of the skin and some internal organs, SCC is most commonly associated with areas exposed to UV radiation, like the skin. However, it can also be found in the lungs, esophagus, and cervix.

The progression of carcinoma is influenced by its microenvironment, which includes the surrounding immune cells, blood vessels, signaling molecules, and the extracellular matrix. This environment can either support or inhibit tumor growth. Additionally, the biological behavior of carcinomas is characterized by their ability to invade neighboring tissues and metastasize to distant organs, a feature that makes them particularly dangerous.

Examples of carcinoma cancer types include renal cell carcinoma which is a kidney cancer that originates in the lining of the proximal convoluted tubule, which is a part of the very small tubes in the kidney that transport waste molecules from the blood to the urine. In addition the hepatocellular carcinoma which originates in the liver and arises from hepatocytes that is the primary cell type in the liver (Llovet et al. 2021). Also, the Ductal Carcinoma In Situ (DCIS), as shown in Figure 1.1, and Invasive Ductal

Carcinoma (IDC) are both types of breast cancers, with DCIS remaining localized and IDC having the potential to invade surrounding tissues.

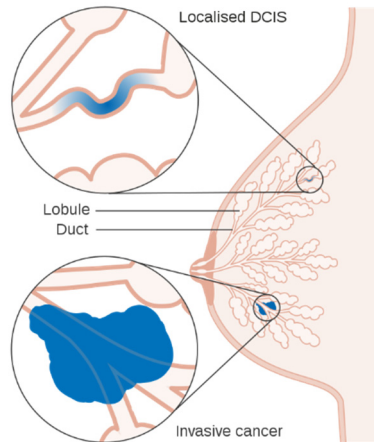


Figure 1.1: Diagram showing ductal carcinoma in situ (DCIS).

(From: Wikimedia commons,

[https://commons.wikimedia.org/wiki/File:Diagram\\_showing\\_ductal\\_carcinoma\\_in\\_situ\\_%28DCIS%29\\_CRUK\\_115.svg](https://commons.wikimedia.org/wiki/File:Diagram_showing_ductal_carcinoma_in_situ_%28DCIS%29_CRUK_115.svg))

**Sarcoma:** Sarcomas are a relatively rare category of cancers that arise from transformed cells of mesenchymal origin. Mesenchymal cells are the precursors to connective tissue and other non-epithelial tissues. Thus, unlike carcinomas, which originate from epithelial cells, sarcomas develop from cells that form bone, cartilage, fat, muscle, vascular, and hematopoietic tissues.

Certain genetic mutations, and environmental exposures, including radiation, have been associated with their development. At a cellular level, sarcomas emerge when mesenchymal cells start proliferating uncontrollably due to mutations that either promote cell division or impede cell death processes. Sarcomas can be broadly classified into two primary subtypes based on their tissue of origin:

The first type is soft tissue sarcomas which appears mainly in the muscles, fat, blood vessels, tendons, nerves, and around joints. Angiosarcoma (originating from blood or lymph vessels), liposarcoma (from fat cells), and leiomyosarcoma (from smooth muscles) are examples.

The second type is bone sarcoma which is rare and emerges from bone tissues. Osteosarcoma, which arises from bone-producing osteoblast cells, and Ewing's sarcoma, which frequently appears in bones but can also appear in soft tissues, are some examples.

Sarcomas have the propensity to invade surrounding tissues and, in advanced stages, can metastasize, primarily to the lungs. Their progression is also influenced by the tumor microenvironment, which includes the surrounding immune cells, blood vessels, and signaling molecules.

Examples of sarcoma cancer types include Rhabdomyosarcoma (Margo, Johnson, and Mancera 2023) which is a type of sarcoma derived from cells that are related to skeletal muscle cells. Synovial Sarcoma is a soft tissue sarcoma found near joints, affecting the young adult population predominantly. The chondrosarcoma which arises from cartilage cells and is the second most common type of bone cancer and finally Gastrointestinal Stromal Tumor (GIST), as shown in Figure 1.2, which is found in the stomach (Venkataraman, George, and Cote 2023).

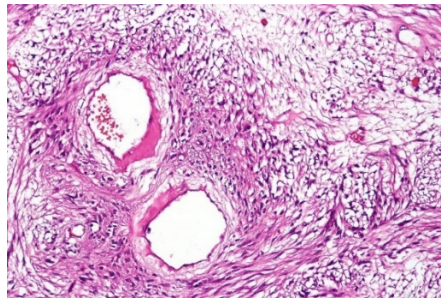


Figure 1.2: An intestinal gastrointestinal stromal tumor (GIST), spindle cell type, with areas of myxoid stromal change, prominent vasculature, hemorrhage and necrosis. H&E Stain. (From: Wikimedia commons, [https://commons.wikimedia.org/wiki/File:Gastrointestinal\\_stromal\\_tumor\\_%28GIST%29,\\_high\\_mag.1.jpg](https://commons.wikimedia.org/wiki/File:Gastrointestinal_stromal_tumor_%28GIST%29,_high_mag.1.jpg))

**Leukaemia:** Leukaemia is a hematologic malignancy characterized by the proliferation of abnormal blood cells, predominantly in the bone marrow, but also in the blood. Bone marrow is a soft tissue inside bones responsible for producing red blood cells, white blood cells, and platelets. In leukemia, the bone marrow produces a large number of abnormal white blood cells, damaging the marrow's ability to produce red blood cells and platelets effectively.

At the cellular level, leukemia arises when blood cell precursors experience DNA mutations, causing them to grow and divide uncontrollably. Several factors, including exposure to ionizing radiation, certain chemicals (e.g., benzene), some chemotherapy drugs, and specific genetic syndromes, can elevate the risk of developing leukemia. Chronic