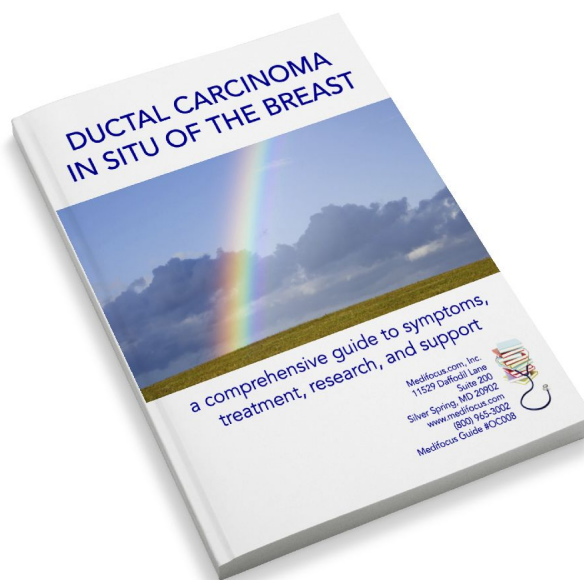


## Preview of the Medifocus Guidebook on: Ductal Carcinoma in Situ of the Breast

Updated January 3, 2022



This document is only a SHORT PREVIEW of the **Medifocus Guidebook on Ductal Carcinoma in Situ of the Breast**. It is intended primarily to give you a general overview of the **format and structure** of the Guidebook as well as select pages from each major Guidebook section listed in the Table of Contents.

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# Table of Contents

<b>Background Information</b> .....	8
Introduction .....	8
About Your Medifocus Guidebook .....	10
<b>The Intelligent Patient Overview</b> .....	13
<b>Guide to the Medical Literature</b> .....	48
Introduction .....	48
Recent Literature: What Your Doctor Reads .....	49
Review Articles .....	49
General Interest Articles .....	58
Surgical Therapy Articles .....	84
Clinical Trials Articles .....	97
Radiation Therapy Articles .....	106
<b>Centers of Research</b> .....	109
United States .....	111
Other Countries .....	123
<b>Tips on Finding and Choosing a Doctor</b> .....	142
<b>Directory of Organizations</b> .....	148

# 1 - Background Information

## Introduction

Chronic or life-threatening illnesses can have a devastating impact on both the patient and the family. In today's new world of medicine, many consumers have come to realize that they are the ones who are primarily responsible for their own health care as well as for the health care of their loved ones.

When facing a chronic or life-threatening illness, you need to become an educated consumer in order to make an informed health care decision. Essentially that means finding out everything about the illness - the treatment options, the doctors, and the hospitals - so that you can become an educated health care consumer and make the tough decisions. In the past, consumers would go to a library and read everything available about a particular illness or medical condition. In today's world, many turn to the Internet for their medical information needs.

The first sites visited are usually the well known health "portals" or disease organizations and support groups which contain a general overview of the condition for the layperson. That's a good start but soon all of the basic information is exhausted and the need for more advanced information still exists. What are the latest "cutting-edge" treatment options? What are the results of the most up-to-date clinical trials? Who are the most notable experts? Where are the top-ranked medical institutions and hospitals?

The best source for authoritative medical information in the United States is the National Library of Medicine's medical database called PubMed®, that indexes citations and abstracts (brief summaries) of over 7 million articles from more than 3,800 medical journals published worldwide. PubMed® was developed for medical professionals and is the primary source utilized by health care providers for keeping up with the latest advances in clinical medicine.

A typical PubMed® search for a specific disease or condition, however, usually retrieves hundreds or even thousands of "hits" of journal article citations. That's an avalanche of information that needs to be evaluated and transformed into truly useful knowledge. What are the most relevant journal articles? Which ones apply to your specific situation? Which articles are considered to be the most authoritative - the ones your physician would rely on in making clinical decisions? This is where *Medifocus.com* provides an effective solution.

*Medifocus.com* has developed an extensive library of *MediFocus Guidebooks* covering a wide spectrum of chronic and life threatening diseases. Each *MediFocus Guidebook* is a

high quality, up- to-date digest of "professional-level" medical information consisting of the most relevant citations and abstracts of journal articles published in authoritative, trustworthy medical journals. This information represents the latest advances known to modern medicine for the treatment and management of the condition, including published results from clinical trials. Each *Guidebook* also includes a valuable index of leading authors and medical institutions as well as a directory of disease organizations and support groups. *MediFocus Guidebooks* are reviewed, revised and updated every 4-months to ensure that you receive the latest and most up-to-date information about the specific condition.

## About Your MediFocus Guidebook

### ***Introduction***

Your *MediFocus Guidebook* is a valuable resource that represents a comprehensive synthesis of the most up-to-date, advanced medical information published about the condition in well-respected, trustworthy medical journals. It is the same type of professional-level information used by physicians and other health-care professionals to keep abreast of the latest developments in biomedical research and clinical medicine. The *Guidebook* is intended for patients who have a need for more advanced, in-depth medical information than is generally available to consumers from a variety of other resources. The primary goal of a *MediFocus Guidebook* is to educate patients and their families about their treatment options so that they can make informed health-care decisions and become active participants in the medical decision making process.

The *Guidebook* production process involves a team of experienced medical research professionals with vast experience in researching the published medical literature. This team approach to the development and production of the *MediFocus Guidebooks* is designed to ensure the accuracy, completeness, and clinical relevance of the information. The *Guidebook* is intended to serve as a basis for a more meaningful discussion between patients and their health-care providers in a joint effort to seek the most appropriate course of treatment for the disease.

### ***Guidebook Organization and Content***

#### **Section 1 - Background Information**

This section provides detailed information about the organization and content of the *Guidebook* including tips and suggestions for conducting additional research about the condition.

#### **Section 2 - The Intelligent Patient Overview**

This section of your *MediFocus Guidebook* represents a detailed overview of the disease or condition specifically written from the patient's perspective. It is designed to satisfy the basic informational needs of consumers and their families who are confronted with the illness and are facing difficult choices. Important aspects which are addressed in "The Intelligent Patient" section include:

- The etiology or cause of the disease
- Signs and symptoms
- How the condition is diagnosed
- The current standard of care for the disease
- Treatment options

- New developments
- Important questions to ask your health care provider

### **Section 3 - Guide to the Medical Literature**

This is a roadmap to important and up-to-date medical literature published about the condition from authoritative, trustworthy medical journals. This is the same information that is used by physicians and researchers to keep up with the latest developments and breakthroughs in clinical medicine and biomedical research. A broad spectrum of articles is included in each *MediFocus Guidebook* to provide information about standard treatments, treatment options, new clinical developments, and advances in research. To facilitate your review and analysis of this information, the articles are grouped by specific categories. A typical *MediFocus Guidebook* usually contains one or more of the following article groupings:

- *Review Articles*: Articles included in this category are broad in scope and are intended to provide the reader with a detailed overview of the condition including such important aspects as its cause, diagnosis, treatment, and new advances.
- *General Interest Articles*: These articles are broad in scope and contain supplementary information about the condition that may be of interest to select groups of patients.
- *Drug Therapy*: Articles that provide information about the effectiveness of specific drugs or other biological agents for the treatment of the condition.
- *Surgical Therapy*: Articles that provide information about specific surgical treatments for the condition.
- *Clinical Trials*: Articles in this category summarize studies which compare the safety and efficacy of a new, experimental treatment modality to currently available standard treatments for the condition. In many cases, clinical trials represent the latest advances in the field and may be considered as being on the "cutting edge" of medicine. Some of these experimental treatments may have already been incorporated into clinical practice.

The following information is provided for each of the articles referenced in this section of your *MediFocus Guidebook*:

- Article title
- Author Name(s)
- Institution where the study was done
- Journal reference (Volume, page numbers, year of publication)

- Link to Abstract (brief summary of the actual article)

*Linking to Abstracts:* Most of the medical journal articles referenced in this section of your *MediFocus Guidebook* include an abstract (brief summary of the actual article) that can be accessed online via the National Library of Medicine's PubMed® database. You can easily access the individual abstracts online via PubMed® from the "electronic" format of your *MediFocus Guidebook* by clicking on the corresponding URL address that is provided for each cited article. If you purchased a printed copy of a *MediFocus Guidebook*, you can still access the article abstracts online by entering the individual URL address for a particular article into your web browser.

## **Section 4 - Centers of Research**

We've compiled a unique directory of doctors, researchers, medical centers, and research institutions with specialized research interest, and in many cases, clinical expertise in the management of the specific medical condition. The "Centers of Research" directory is a valuable resource for quickly identifying and locating leading medical authorities and medical institutions within the United States and other countries that are considered to be at the forefront in clinical research and treatment of the condition.

Inclusion of the names of specific doctors, researchers, hospitals, medical centers, or research institutions in this *Guidebook* does not imply endorsement by Medifocus.com, Inc. or any of its affiliates. Consumers are encouraged to conduct additional research to identify health-care professionals, hospitals, and medical institutions with expertise in providing specific medical advice, guidance, and treatment for this condition.

## **Section 5 - Tips on Finding and Choosing a Doctor**

One of the most important decisions confronting patients who have been diagnosed with a serious medical condition is finding and choosing a qualified physician who will deliver high-level, quality medical care in accordance with currently accepted guidelines and standards of care. Finding the "best" doctor to manage your condition, however, can be a frustrating and time-consuming experience unless you know what you are looking for and how to go about finding it. This section of your *Guidebook* offers important tips for how to find physicians as well as suggestions for how to make informed choices about choosing a doctor who is right for you.

## **Section 6 - Directory of Organizations**

This section of your *Guidebook* is a directory of select disease organizations and support groups that are in the business of helping patients and their families by providing access to information, resources, and services. Many of these organizations can answer your questions, enable you to network with other patients, and help you find a doctor in your geographical area who specializes in managing your condition.

## 2 - The Intelligent Patient Overview

# DUCTAL CARCINOMA IN SITU OF THE BREAST

### Introduction to Ductal Carcinoma in Situ

The female breast is made up of glands that produce and release milk after childbirth. The glands that make the milk are called *lobules* and the tubes that connect them to the nipple are called *ducts*. The breast itself is made up of lobules, ducts, and fatty, connective, and lymphatic tissue.

*Lymph* is a clear fluid that contains immune system cells. The fluid is carried in *lymphatic vessels* that lead to small, pea-sized collections of tissue called *lymph nodes*. Most lymphatic vessels of the breast lead to lymph nodes under the arm called *axillary lymph nodes*.

There are several types of tumors that can occur in the breasts. Most are benign (non-cancerous) and are related to fibrocystic changes. Cysts are fluid-filled sacs and fibrosis refers to the forming of connective tissue or scar tissue. Benign breast tumors are abnormal growths, but they do not appear outside of the breast and they are not life threatening.

Breast cancer is the most common cancer among women, other than skin cancer. It is the second leading cause of cancer death in women after lung cancer. Fortunately, deaths from breast cancer have declined significantly, which is thought to be due to better detection and improved treatment.

*Ductal carcinoma in situ* (DCIS) of the breast is an early, localized cluster of cancer cells that start in the milk passages (ducts) but have not penetrated the duct walls into the surrounding tissue. The term "in situ" refers to a tumor that has not spread beyond the place where it originally developed. By definition, DCIS is a non-invasive form of breast cancer because the cancer cells are confined to the milk ducts of the breast.

Ductal carcinoma in situ is sometimes described as "pre-cancerous", "pre-invasive", "non-invasive", or "intraductal carcinoma". Although, by definition, DCIS is a non-invasive form of breast cancer, if left untreated, it may progress to 'true' breast cancer by spreading into and invading the surrounding healthy breast tissue. Because doctors cannot predict with any degree of certainty whether DCIS will develop into invasive breast cancer, early diagnosis and treatment is crucial. With appropriate treatment, the prognosis (outlook) for women with DCIS is excellent.

Fortunately, DCIS can often be detected on screening mammography before any symptoms develop. Ductal carcinoma in situ usually appears on mammography as an area of *microcalcification* (groups of small calcifications clustered together within the breast). With the increased availability of mammography, breast cancers are being detected earlier.

The incidence of DCIS has increased dramatically since the introduction of widespread screening



mammography. In 1983, approximately 5,000 cases of DCIS were reported, however, due to the widespread use of screening mammography, the number of women being diagnosed with DCIS has increased about 10-fold. According to the American Cancer Society, approximately 54,000 cases of DCIS were diagnosed in the United States in 2010.

According to a study published in January 2010 in the *Journal of the National Cancer Institute*, the incidence of DCIS in the United States has increased from 1.87 per 100,000 during 1973 - 1975 to 32.5 per 100,000 in 2004. Although an increase in the incidence of DCIS was found across all age groups, the greatest increase in incidence of DCIS was found in women over age 50. According to this study, approximately 15% of women diagnosed with DCIS and treated with either lumpectomy or mastectomy later went on to develop invasive breast cancer.

Ductal carcinoma in situ represents 10-15% of all new breast cancers diagnosed in the United States and accounts for 30-50% of cancers detected by screening mammography in women less than age 50 and 15-25% in women over age 50. It also comprises approximately 7-10% of all breast biopsies.

Fortunately, DCIS is a highly curable disease with a 10-year cancer-specific survival of about 97%. Because DCIS is a "forerunner" of invasive breast cancer, early diagnosis and treatment are crucial for reducing the risk of developing invasive breast cancer.

## ***Most Common Types of Breast Cancer***

The most common types of breast cancers are *adenocarcinomas* that originate in the ducts or lobules of the breast. There are two main types of breast adenocarcinomas known as *ductal carcinomas* and *lobular carcinomas*. These can further be divided into the following subtypes:

- Ductal carcinoma in situ (DCIS)
  - represents the most common form of noninvasive breast cancer
  - may contain areas of necrotic (dead) cancer cells
  - pathologists use the term *comedocarcinoma* or *comedo DCIS* to describe DCIS if necrotic cancer cells are observed under a microscope
  - comedo DCIS is considered to be a more aggressive type of disease than non-comedo DCIS
- Lobular carcinoma in situ (LCIS)
  - LCIS is also considered to represent a noninvasive form of breast cancer
  - LCIS starts in the milk-producing lobules of the breast but does not penetrate the walls of the lobules.
  - the term "in situ" in the term "lobular carcinoma in situ" indicates that this is an early stage of breast cancer that is confined locally to area where the cancer started
  - some doctors believe that LCIS is a risk factor for developing invasive breast cancer and women with LCIS should undergo a physical exam at least twice each year as well as a yearly mammogram.

- Infiltrating (invasive) ductal carcinoma (IDC)
  - IDC is the most common type of breast cancer and represents about 80% of all invasive breast cancers.
  - IDC starts in the ducts of the breast but spreads to invade the surrounding normal breast tissue.
- Infiltrating (invasive) lobular carcinoma (ILC)
  - ILC is also considered as an invasive form of breast cancer but is much less common than IDC.
  - ILC starts in the lobules of the breast but can spread (metastasize) to other parts of the body.
  - ILC may be more difficult to detect with screening mammography than IDC.

## ***Stages of Breast Cancer***

Staging is the process of assessing how far the cancer has spread and is important in making treatment decisions and determining prognosis.

- Stage 0 - Noninvasive, Carcinoma in situ (DCIS)
- Stage I - Cancer cells have not spread beyond the breast and the tumor is no more than about an inch (2.5 cm or less) across
- Stage II - The tumor in the breast is less than 1 inch across and the cancer has spread to the lymph nodes under the arm, OR
  - the tumor is between 1 and 2 inches (less than 5.0 cm) with or without spread to the lymph nodes under the arm, OR
  - the tumor is larger than 2 inches (more than 5.0 cm) but has not spread to the lymph nodes under the arm
- Stage III - "Locally advanced cancer" - The tumor in the breast is large (more than 2 inches across) and the cancer is extensive in the underarm lymph nodes or It has spread to other lymph nodes or tissues near the breast. This stage includes inflammatory breast cancer.
- Stage IV - The cancer is metastatic, meaning it has spread from the breast to other parts of body.

*Recurrent breast cancer* means the disease has recurred despite initial treatment. Most recurrences appear within the first 2 or 3 years but can occur many years later.

---

## ***Classification of Ductal Carcinoma in Situ***

Ductal carcinoma in situ (DCIS) of the breast is not a single disease but rather a diversified group of breast lesions. Various types of DCIS can be distinguished on the basis of histological features, genetic characteristics, clinical symptoms, and radiographic appearance on mammography. Consequently, the biological behavior of different types of DCIS is also highly diversified. Although DCIS has the potential to develop into invasive breast cancer, the risk of malignant potential varies widely among the different types of DCIS. Clearly, most types of DCIS do not progress to invasive breast cancer, however, the fact that some evolve into malignant breast cancer indicates that they are more "aggressive" from a biological perspective. Unfortunately, at the present time, doctors cannot predict with absolute certainty which types of DCIS will eventually progress to invasive breast cancer.

In order to better estimate the malignant potential of DCIS, several different classification systems have been developed. It is important to note, however, that most of these classification systems more accurately predict the likelihood of recurrence of DCIS after surgical excision of the initial tumor rather than the likelihood for DCIS to progress to invasive breast cancer.

The traditional classification method for DCIS is based upon the appearance of the cells when examined under a microscope (histological features). Several histological parameters can be used to distinguish and classify the different types of DCIS. One classification scheme is based upon the presence or absence of necrotic (dead) cells at the center of the breast ducts. According to this classification system, DCIS may be grouped as follows:

- *Comedo DCIS* - characterized by the presence of necrotic (dead) cells at the center of the breast ducts (comedonecrosis). The comedo type of DCIS is usually a more aggressive than the non-comedo type of DCIS (absence of necrotic cells).
- *Non-comedo* types of DCIS include:
  - Micropapillary DCIS
  - Cribiform DCIS
  - Solid DCIS
  - Papillary DCIS

Another important histological parameter that can be used to classify DCIS is *nuclear grade* - an evaluation of the size and shape of the nucleus in the tumor cells and the percentage of tumor cells that are in the process of dividing and growing. On the basis of nuclear grade, DCIS can be classified into one of the following three groups:

- Low-nuclear-grade DCIS
- Intermediate-nuclear-grade DCIS
- High-nuclear-grade DCIS

Nuclear grade has been found to be an important feature that helps doctors predict the likelihood

of recurrence of DCIS after surgery. In an article published in 2003 in the *Journal of the National Cancer Institute*, researchers from the San Francisco Veterans Affairs Medical Center conducted a study of 1,036 women age 40 or older who were diagnosed with DCIS and treated with *lumpectomy* (surgical removal of a tumor and a small amount of surrounding tissue). The researchers reported that women with high-nuclear-grade DCIS had a 5-year risk of an invasive recurrence of 11.8% compared to only 4.8% for women with low-nuclear-grade DCIS. The finding that women with high-nuclear-grade DCIS are about 2.5 times more likely to develop an invasive recurrence than women with low-nuclear-grade DCIS, indicates that they should undergo additional treatment, such as postoperative radiation therapy, in order to reduce the risk of invasive recurrence. As mentioned previously, comedonecrosis (the presence of dead cells at the center of the breast ducts) is another histological feature that carries a high risk of invasive recurrence because comedo DCIS is usually associated with a high-nuclear grade.

In 1996, another classification system called the Van Nuys prognostic index (VNPI) was introduced to help doctors more accurately predict the risk of local recurrence after surgical excision of DCIS. The VNPI is a tool that uses the following four variables (prognostic indicators) to predict the likelihood of recurrence of DCIS in women following breast-conserving surgery:

- Tumor size
- Margin width
- Nuclear grade
- Comedonecrosis (present or absent)

In 2003, the VNPI was modified to include a woman's age as an additional prognostic indicator since younger age has been found to be associated with a higher risk of recurrence of DCIS.

A newer classification system for DCIS was proposed in 2006 that takes into account both histological features as well as molecular features in order to better predict the malignant potential of DCIS. Researchers have found that certain molecular abnormalities are associated with a more aggressive type of DCIS that increases its likelihood for developing into invasive breast cancer. Examples of some molecular features that are associated with more aggressive tumors include:

- Mutation of a gene called p53 (located on chromosome #17) that produces a protein called the p53 tumor suppressive protein. A tumor suppressive protein helps to prevent the uncontrolled proliferation and growth of cells. Mutation of the p53 gene leads to the production of a defective p53 tumor suppressive protein which cannot act to suppress the proliferation and growth of cells, thereby leading to cancer.
- Overexpression (amplification) of a human growth factor receptor called C-erbB2.
- Overexpression of a cellular molecular marker of proliferation called Ki-67.

In this classification system, DCIS is classified as either "highly aggressive"; "moderately aggressive"; or "low aggressive" using a combination of histological features (e.g., comedonecrosis, nuclear grade) and molecular abnormalities (e.g., p53; C-erbB2; Ki-67).

Doctors can use this classification system to make better treatment decisions for women with DCIS. For example, since "highly aggressive" DCIS has the greatest potential for local recurrence within 2 years after surgical excision and for progression to invasive breast cancer within 5 to 10 years, women with "highly aggressive" DCIS should be treated either by mastectomy or by local excision plus radiation therapy and, possibly, hormonal therapy. Women with "low aggressive" DCIS, on the other hand, can theoretically be treated with simple local excision alone since the risk of local recurrence and progression to invasive breast cancer is much lower.

The **Intelligent Patient Overview** in the complete **Medifocus Guidebook on Ductal Carcinoma in Situ of the Breast** also includes the following additional sections:

- **Diagnosis of Ductal Carcinoma in Situ**
- **Treatment Options for Ductal Carcinoma in Situ**
- **The Role of Complementary and Alternative Therapies in Cancer**
- **Quality of Life Issues in Cancer**
- **New Developments in Ductal Carcinoma in Situ**
- **Questions to Ask Your Health Care Provider About Ductal Carcinoma in Situ**

To Order the Complete **Guidebook on Ductal Carcinoma in Situ of the Breast** [Click Here](#)  
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## 3 - Guide to the Medical Literature

### Introduction

This section of your *MediFocus Guidebook* is a comprehensive bibliography of important recent medical literature published about the condition from authoritative, trustworthy medical journals. This is the same information that is used by physicians and researchers to keep up with the latest advances in clinical medicine and biomedical research. A broad spectrum of articles is included in each *MediFocus Guidebook* to provide information about standard treatments, treatment options, new developments, and advances in research.

To facilitate your review and analysis of this information, the articles in this *MediFocus Guidebook* are grouped in the following categories:

- Review Articles - 25 Articles
- General Interest Articles - 74 Articles
- Surgical Therapy Articles - 35 Articles
- Clinical Trials Articles - 22 Articles
- Radiation Therapy Articles - 8 Articles

The following information is provided for each of the articles referenced in this section of your *MediFocus Guidebook*:

- Title of the article
- Name of the authors
- Institution where the study was done
- Journal reference (Volume, page numbers, year of publication)
- Link to Abstract (brief summary of the actual article)

**Linking to Abstracts:** Most of the medical journal articles referenced in this section of your *MediFocus Guidebook* include an abstract (brief summary of the actual article) that can be accessed online via the National Library of Medicine's PubMed® database. You can easily access the individual abstracts online via PubMed® from the "electronic" format of your *MediFocus Guidebook* by clicking on the URI that is provided for each cited article. If you purchased a printed copy of the *MediFocus Guidebook*, you can still access the abstracts online by entering the individual URI for a particular abstract into your computer's web browser.

## 4 - Centers of Research

This section of your *MediFocus Guidebook* is a unique directory of doctors, researchers, medical centers, and research institutions with specialized research interest, and in many cases, clinical expertise in the management of this specific medical condition. The *Centers of Research* directory is a valuable resource for quickly identifying and locating leading medical authorities and medical institutions within the United States and other countries that are considered to be at the forefront in clinical research and treatment of this disorder.

Use the *Centers of Research* directory to contact, consult, or network with leading experts in the field and to locate a hospital or medical center that can help you.

The following information is provided in the *Centers of Research* directory:

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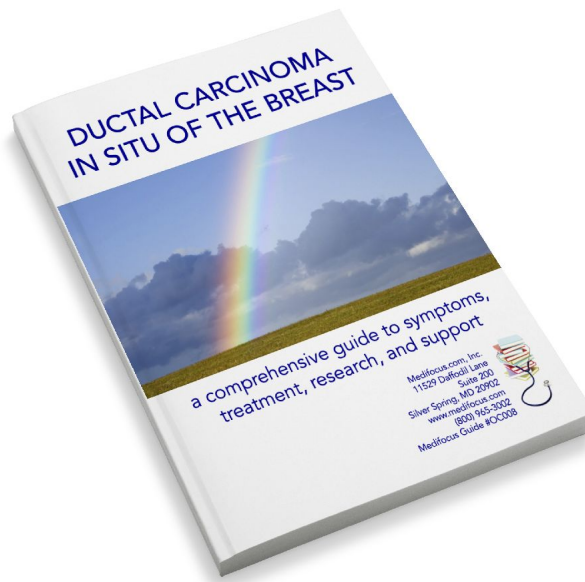
- United States: the information is divided by individual states listed in alphabetical order. Not all states may be included.
- Other Countries: information is presented for select countries worldwide listed in alphabetical order. Not all countries may be included.

- **Names of Authors**

- Select names of individual authors (doctors, researchers, or other health-care professionals) with specialized research interest, and in many cases, clinical expertise in the management of this specific medical condition, who have recently published articles in leading medical journals about the condition.
- E-mail addresses for individual authors, if listed on their specific publications, is also provided.

- **Institutional Affiliations**

- Next to each individual author's name is their **institutional affiliation** (hospital, medical center, or research institution) where the study was conducted as listed in their publication(s).
- In many cases, information about the specific **department** within the medical institution where the individual author was located at the time the study was conducted is also provided.



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