Non-Invasive Breast Cancer: Ductal Carcinoma In Situ (DCIS) — Diagnosis and Treatment

Non-invasive breast cancer can be either ductal carcinoma in situ or less commonly lobular carcinoma in situ. Ductal carcinoma in situ is of epithelial type, and there is usually no basement membrane invasiveness. Because of the lack of invasiveness, these tumors are unlikely to metastasize by the lymphatics or blood vessels. Ductal carcinoma in situ is usually diagnosed by a mammography and not by physical examination. Microcalcifications on mammography are the most common presenting feature. Local excision of the lesion is recommended to obtain histopathologic data and guide treatment. Total mastectomy or breast conservation therapy are the two options for the treatment of ductal carcinoma in situ.

Definition of Non-Invasive Breast Cancer

A non-invasive carcinoma, also known as an in-situ carcinoma, is a term used to describe the malignant transformation of epithelial cells that remain in their origin site without invading the basement membrane.
Two types of non-invasive breast cancer exist, namely ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS). DCIS represents 95% of the cases of non-invasive breast cancer and is a truly premalignant lesion; hence this article will mainly discuss DCIS.

Epidemiology of Non-Invasive Breast Cancer

The incidence of non-invasive breast cancer is expected to be under-reported due to the lack of any specific symptoms or signs. DCIS, the clinically relevant form of non-invasive breast cancer, can be identified in approximately 15% of all cases of breast cancer. The introduction of routine mammography screening protocols made the early diagnosis of DCIS possible.

The majority of the cases nowadays have a tumor that is less than 10 mm in diameter. Such a small size is unlikely to be detected by palpation, but can be easily identified with mammography.

Most patients with DCIS are aged 45 to 65 years. This is the same age group for invasive breast cancer, and these patients also share several similar risk factors to invasive breast cancer, such as family history of breast cancer, early menarche and late menopause.

Pathophysiology of Non-Invasive Breast Cancer

Ductal carcinoma in situ arises from the ductal epithelium. Due to poorly understood reasons, ductal epithelium can undergo hyperplasia. At a certain point, ductal hyperplasia starts showing dysplastic features and atypical ductal hyperplasia ensues.

These atypical epithelial cells eventually undergo malignant transformation and ductal carcinoma in situ occurs. If left untreated, uncontrolled cellular proliferation will eventually obliterate the whole ductal space and, at this point, basement membrane invasion can occur.

Ductal carcinoma in situ does not invade the basement membrane. Accordingly, DCIS does not have access to lymphatics and/or blood vessels and lymphatic spread or distant
metastasis is not usually a problem with non-invasive breast cancer.

Clinical Presentation of Non-Invasive Breast Cancer

The introduction of routine mammography and clear screening guidelines for breast cancer made the diagnosis of non-invasive breast cancer easier and earlier. Accordingly, nowadays, most patients with ductal carcinoma in situ of the breast present to the clinic for their routine mammogram only to find a small, less than 10 mm tumor in the breast.

Patients who do not undergo routine mammography, for some reason, might present with a palpable mass, nipple discharge or Paget’s disease of the nipple. These presentations are unlikely to happen when the tumor is less than 1 cm in diameter.

Diagnostic Work-up for Non-Invasive Breast Cancer

Mammography

The most common finding in DCIS is microcalcification on a mammogram. Most of the malignant lesions with microcalcification on mammography are DCIS. Additionally, the pattern of microcalcification can help identify the nuclear grade of DCIS.

High-grade DCIS, which also has comedo necrosis, presents with linear-branching microcalcifications. On the other hand, low-grade DCIS usually presents with fine granular microcalcifications.

Bilateral mammography is indicated.

Histologic examination

An image-guided biopsy is indicated to establish the diagnosis of DCIS and guide treatment. A mammography-guided local excision of the small tumor is indicated.
This procedure is adequate as it removes all the abnormal tissue, while preserving the normal breast tissue.

After the removal of the tumor, several features need to be noted to determine prognosis. The tumor size, if more than 1 cm, might predispose the patient to possible microinvasion.

Additionally, the nuclear grade and presence or absence of comedo-type necrosis is also important prognostic factors in DCIS.

### Treatment of Non-Invasive Breast Cancer

Treatment of non-invasive breast cancer or DCIS involves **total mastectomy**, **breast conservation therapy** and/or **breast irradiation**.

**Total mastectomy**, with or without **axillary lymph node clearance**, provides effective and curative treatment of DCIS, but can be easily judged as an over-treatment for a relatively non-invasive disease. Additionally, up to 15% of patients with breast cancer are diagnosed in this early stage, and providing a total mastectomy to this large number of patients is indeed challenging.

Finally, patients who are diagnosed with DCIS by mammography are usually younger than your typical patient with invasive breast cancer, and they can prefer a more conservative approach.

Because of these reasons, more research has been done to evaluate the role of either breast conservation therapy or **local excision of the tumor alone** as possible treatments for DCIS.

**Breast conservation therapy** includes local excision of the tumor plus **radiotherapy**. Local excision should be mammographically guided and care should be taken to achieve a safe negative margin of the resection. A repeat mammogram after excision should be negative for microcalcifications before initiating radiotherapy.

Approximately four weeks after the local excision of the non-invasive breast cancer lesion, radiotherapy is usually started. Current approaches utilize **whole breast**
**irradiation therapy.** Current protocols for adjuvant radiotherapy do not include lymph node irradiation.

Patients with very small tumors and without any occult invasive breast cancer can benefit from local excision alone without adjuvant radiotherapy. Local recurrence after local excision alone is estimated to be about 33% for patients with high-grade DCIS and 2% for low-grade DCIS. This interesting finding can help the patient choose a more appropriate approach, such as conservative breast therapy instead of local excision alone when they have high-grade DCIS.

Patients with high-grade DCIS, or a tumor that is large in size with evidence for occult invasive breast cancer disease, might not be possible candidates for breast conservation therapy due to other comorbidities and contraindications to radiotherapy, such as pregnancy, collagen vascular diseases, or a previous history of chest irradiation therapy. In this case, total mastectomy remains the most effective method to prevent local recurrence.

Low to intermediate grade DCIS was found to express estrogen and progesterone receptors. Accordingly, tamoxifen was used for primary and secondary prevention of DCIS. It was found that primary prevention of breast cancer is possible with the use of tamoxifen, but there is still debate on who should receive tamoxifen for primary prevention of breast cancer.

**Tamoxifen** was used for secondary prevention of breast cancer in the contralateral breast with very good results and is currently recommended. Currently, tamoxifen is used for secondary prevention of DCIS only in clinical trials.

**References**


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