DCIS: a critical review from the pathologist

Farid Moinfar
Department of Pathology, Hospital of the Sisters of Charity, Linz
Department of Pathology, Medical University of Graz

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Presentation outline

• Traditional classification of intraductal proliferative lesions of the breast

• Major problems and limitations of the traditional classification

Is there an alternative approach?

• Future works on controversial issues
Traditional classification of intraductal proliferations of the breast

• Intraductal hyperplasia or usual ductal hyperplasia (UDH)

• Atypical ductal hyperplasia (ADH)

• Ductal carcinoma in situ (DCIS)
Relative risks (RR) of intraductal proliferative lesions

• Intraductal hyperplasia without atypia: 1.5-2 x

• Atypical intraductal hyperplasia: 4-5 x

• DCIS: 8-10 x
Traditional Classification:
IDH (UDH), AIDH (ADH), DCIS

- Lesions are considered as Cancer or Noncancer
Problems with the traditional classification (ADH/DCIS terminology)
Current classification of UDH, ADH, and DCIS

• Implies a linear progression from UDH to DCIS: A very simplistic model not supported by recent molecular-genetic findings!
Disadvantages of ADH/DCIS terminology

2) Considers ADH and DCIS as two separable entities. The criteria for such separation, however, are arbitrary. There is no scientific basis for such proposed criteria: High interobserver and intraobserver variability.
Disadvantages of DCIS terminology

3) Relative risk (RR) of DCIS for subsequent invasive carcinoma: 8-10x (classic study by Page et al)

Problem:

No separation between low, intermediate, and high grade DCIS with regard to the relative risks.

What is the RR of low grade DCIS compared to that of ADH?
Disadvantages of ADH/DCIS terminology

4) Implies different treatment approaches for ADH versus low grade DCIS.
Lesion A
Pathologist 1: ADH
Pathologist 2: Low grade DCIS

Therapy

- ADH (pathologist 1): follow-up, currently no re-excision is required. No radiation therapy. No hormonal treatment.

- DCIS (pathologist 2): in many centers radiation therapy. Re-excision if at the margin. Adjuvant hormonal treatments in some centers.
Fig. 4.27. Borderline or markedly atypical ductal hyperplasia. A micropapillary or cribriform proliferation of cells across the lumen forms a regular architecture without fibrovascular support, but there is a partial prominent myoepithelial layer, overlapping of the nuclei, and marked variation in the size and configuration of the extracellular lumina.
Disadvantages of DCIS terminology

5) Uses the word „CANCER“ for a precancerous, non invasive tumor. There is a big difference between a malignant tumor (cancer) which is always invasive and a tumor with malignant potential!!! Many patients with DCIS do believe that they have a true „CANCER“.
“One problem is in the very name of these things as cancer. It is a problem for intraductal carcinoma (DCIS) and a much bigger problem for LCIS, which we don’t regard as cancer at all. But once patients hear the word “cancer”, what they envision is metastatic disease, and it’s difficult to get beyond that to the idea that you are talking about risk and future cancer.”
Ductal Carcinoma in Situ of the Breast

Editor

MELVIN J. SILVERSTEIN
Insanity of Ductal Carcinoma in Situ

MELVIN J. SILVERSTEIN

A perfectly healthy woman has been told that she has breast cancer, albeit a very favorable form called ductal carcinoma in situ (DCIS). Confusing and contradictory data are presented. A range of expert opinions is obtained. Then she is asked to make a decision. She has the final word, the decision is hers.

In 1972, I was an assistant professor of surgery in the division of surgical oncology at UCLA. Cancer was my life. It was all I cared about. I worked from 7 am until 10 pm almost every day and made rounds every weekend; yet, I had never seen a case of DCIS. To be honest, if I had, it would not have made much difference. I would have treated the patient like any other patient with breast cancer. The scenario for most women with breast cancer in 1972, regardless of the type of cancer, was relatively "simple." The patient felt a lump and was admitted to the hospital rather quickly the night before surgery. For some physicians, even the remote possibility of breast cancer was a relative emergency at that time. She was operated upon the next morning using general anesthesia. When she awoke, she had had a mastectomy—"the one-stage procedure. It was quick, it was straightforward, it was easy, and it was sad. The one thing it was not was "crazy-making" because of indecision, multiple opposing opinions, and the patient's freedom of choice. At that time, the patient generally played no role in the decision-making process. Everything happened fast, without much discussion, and without choice. Everything was relatively urgent as an attempt to remove the cancer before it had time to "spread."

Therapeutic choices were not offered because there really weren't any. An occasional "radical" surgeon (a contradictory term) promoted a lesser surgical procedure; but those physicians were considered to be on the fringe of medicine. Halsted's legacy taught us that there was only one "right" way to treat breast cancer. We had an 80-year history by 1972. Informed consent was a concept in the minds of a few progressive and liberated individuals; it was not a reality for most patients. Breast conservation was European, not American, and certainly not Halstedian.

The only real textbook devoted to breast disease at that time was Diseases of the Breast (1) by Cushman Haagensen. In it, he classified tumors as intraductal "when at least 50% of the carcinoma grew within ducts," meaning that as much as 49% of the tumor could be invasive. That of course, is not the way DCIS is defined today. Thirty-eight percent of Haagensen's cases had metastases to axillary nodes with a 10-year survival rate of 68%. As far as Haagensen was concerned, intraductal carcinoma (the term he liked to use) was a fully malignant disease and all cases of intraductal carcinoma had infiltration even though it had not been seen microscopically. The prognosis, however, was somewhat better than for infiltrating ductal carcinoma of no special type.

Haagensen had an enormous effect on surgical practice in the United States and his recommendation that all cases of intraductal carcinoma be treated with radical mastectomy was followed religiously by many surgeons. Additionally, most surgeons did not read the pathology literature and most had little knowledge of the wholly noninvasive lesion that had been described since the turn of the century (Chapter 3).
National Institutes of Health
State-Of-The-Science Conference Statement

• Diagnosis and Management of Ductal Carcinoma in Situ (DCIS)
• September 22-24, 2009
• J Natl Cancer Inst 2010;102:161-169
• "It is also important for the medical community to consider eliminating the inclusion of the term "carcinoma" in this disease, as DCIS is by definition not invasive- a classic hallmark of cancer."
Conclusions

- “Clearly, the diagnosis and management of DCIS is highly complex with many unanswered questions including the fundamental natural history of untreated disease. Because of the noninvasive nature of DCIS, coupled with its favorable prognosis, strong consideration should be given to elimination of the use of the anxiety-producing term “carcinoma“ from the description of DCIS.“
Why shouldn’t we use an alternative and appropriate terminology?

- **Intraepithelial Neoplasia**
  - Ductal type = DIN
  - Lobular type = LIN
Concept of Mammary intraepithelial Neoplasia

• 1978–Haagensen- Lobular Neoplasia (ALH & LCIS). In 2003, WHO accepted LN as the optimal designation – 35 years and many unnecessary mastectomies post introduction of the term LN by Haagensen.

1991- Rosai- Mammary Intraepithelial Neoplasia proposed when significant interobserver variability was noted.

• 1996- Tavassoli- DIN, LIN
1) Does not use the term „CANCER“ for a pre-malignant (pre-invasive) neoplastic proliferation. The term carcinoma is reserved for invasive epithelial neoplasia with clinical malignant behaviour.
DIN
Advantages

2) does not distinguish between „ADH“ and low grade „DCIS“ as two separate entities. These are regarded as closely related, if not identical neoplastic proliferations with low risk of malignancy (low malignant potential).
DIN
Advantages

3) It includes the category of flat-lesions with low and high grade nuclear atypia („clinging DCIS“) in addition to more conventional types such as cribriform, micropapillary, solid, etc.

4) The malignant potential of intraductal proliferative lesions (risk of subsequent development of invasive carcinoma) is reflected by a grading system: DIN1 to 3 or low to high grade DIN.
DIN
Advantages

5) It uses the unifying concept of intraepithelial neoplasia as already used in other organs such as cervix (CIN), vagina (VAIN), vulva (VIN), prostate (PIN), gastrointestinal tract (pancreatic, colonic, or gastric intraepithelial neoplasia) or even in the breast (lobular neoplasia).
DCIS and LCIS are confusing and outdated terms. They should be abandoned in favor of ductal intraepithelial neoplasia (DIN) and lobular intraepithelial neoplasia (LIN)
Tradition
Tradition
Tradition
Tradition
Tradition
Tradition
Tradition
Tradition
Future works (unresolved issues!)

• 1) Changing of the current grading system into low versus high grade!

• 2) DIN ("DCIS") is a very heterogeneous breast disease. It cannot be treated in a "homogeneous" way!
Future works

• 3) Issue of minimal distance of DIN ("DCIS") from the resection margin(s)!
• 4) Issue of radiation therapy in low grade DIN ("DCIS")!
• 5) Issue of antihormonal therapy in patients with DIN ("DCIS")!
Conclusion

Insanity of “carcinoma in situ”

• It is time to admit that we are overdiagnosing the intraepithelial neoplasias of the breast as CANCER!

• we have to admit that the vast majority of patients are currently overtreated by doing postoperative radiation therapy and/or antihormonal treatment.
A simple question frequently asked by medical students!

• Why are there so many different and confusing names for non-invasive or precancerous neoplastic lesions in different organs?
• Atypical hyperplasia
• Atypical proliferating tumor
• Dysplasia (low and high)
• Carcinoma in situ
• Borderline tumor
• Intraepithelial carcinoma
• Intraepithelial lesions (LGSIL, HGSIL)
• Lesions with low malignant potential
• Non-invasive carcinoma
What exactly are we talking about?

• An intraepithelial neoplastic proliferation with low or high malignant potential:

• Intraepithelial Neoplasia!!!
Lesion B
Pathologist 1: Adenosis & FCC, „Columnar alteration“
Pathologist 2: „clinging carcinoma in situ“

Therapy ?!!!
301  HES × 64
302  HES × 160
Clinging carcinoma: epithelium with one cell layer. Note crowding of cells and apical protrusion of some nuclei thrown out in the lumen (hobnail appearance).

303  HES × 64
304  HES × 160
Clinging carcinoma: atypical nuclei, irregular luminal margin.

305  HES × 64
306  HES × 160
Clinging carcinoma: stratified epithelium with apical snouts, loss of nuclei polarity and one mitosis.
Figure 10–1  ‘Clinging carcinoma’. Loss of polarity and anaplasia of the lining epithelial cells is present but the bulk of the neoplastic tissue is much less than usually seen in comedo cancer and there is no obvious luminal necrotic debris. H and E. ×600.
Talking to patients with noninvasive breast cancer

• “Unfortunately, many patients are not aware of the difference between invasive and in situ disease, and report that when they heard their in situ diagnosis all that registered was the word “cancer“ with its attendant threat to their lives. In such situations, it is difficult to get beyond that to the idea that you are talking about risk and future cancer."

• Because the word cancer is used for both invasive and in situ disease, patients not surprisingly think of in situ disease as a real cancer. Actually, the use of the term „cancer“ for in situ disease is historic...

• „For many, the emotional impact of a cancer diagnosis is so great that they experience difficulty in thinking and sleeping for some weeks.“

Ductal carcinoma in situ of the breast, 1997
Melvin J Silverstein, p: 316
Figure 215
INTRADUCTAL HYPERPLASIA
The heterogeneity of the cellular proliferation is more apparent at higher magnification.
Figure 222
INTRADUCTAL HYPERPLASIA WITH ATYPISM
Secondary lumens are rounded and the cell population appears to be heterogeneous.
Figure 215
INTRADUCTAL HYPERPLASIA

The heterogeneity of the cellular proliferation is more apparent at higher magnification.

Figure 222
INTRADUCTAL HYPERPLASIA WITH ATYPISM

Secondary lumens are rounded and the cell population appears to be heterogeneous.