Facts Views Vis Obgyn, 2014, 6 (4): 210-218

Review

Current view on ductal carcinoma in situ and importance of the margin thresholds: A review

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Abstract

Ductal carcinoma in situ (DCIS) is a heterogeneous group of diseases that differ in biology and clinical behaviour. Until 1980, DCIS represented less than 1% of all breast cancer cases. With the increased utilization of mammography, DCIS now accounts for 15% to 25% of newly diagnosed breast cancer cases.
The Van Nuys Prognostic Index (VPNI) is a commonly used tool for ductal carcinoma in situ (DCIS) treatment approach. Patient age, tumour size, tumour margins and pathological grade are used in order to stratify patients into three groups pertaining to risk of local recurrence: low-, intermediate- and high risk.
Patients in the low-risk subgroup will always be treated with excision alone, while in the highest subgroup mastectomy is the safest option. Just like invasive breast cancer (IBC) there might be a curative dilemma in the intermediate-risk group.
Many trials confirm that tumour margins are the most important prognostic factor of local recurrence for DCIS patients treated with breast conserving surgery alone or with breast conserving surgery plus radiotherapy. In this article we focused specifically on the literature concerning margin thresholds.

Key words: **Breast cancer, carcinoma in situ, DCIS, DCIS outcome, DCIS treatment, Van Nuys Prognostic Index, VNPI.**

Introduction

Definition DCIS

The term "carcinoma in situ" was first used in 1932 by Broder (Broder, 1932). Ductal carcinoma in situ (DCIS) forms a group of heterogeneous lesions with different clinical behaviour. DCIS is characterized by the development of cancerous cells in the milk ducts of the breast. In situ refers to the absence of basal membrane infiltration of the ducts (Wellings and Jensen, 1973). DCIS can evolve to an invasive breast cancer (IBC) when untreated.

Epidemiology

Until 1980, DCIS diagnosis was based on physical signs or symptoms representing 1% of all breast cancer cases. The widespread implementation of mammographic breast cancer screening increased the incidence of DCIS up to 20% of newly diagnosed breast carcinomas (Armed Forces Health Surveillance, 2013).

The risk to develop DCIS progressively increases, starting mostly at the age of 40 and reaches a plateau after the age of 60 (Allegra et al., 2009).

Breast lesions (benign and malignant) are relatively common. In several autopsy studies, in a series of women who died from causes, other than breast cancer, up to 18% had latent DCIS (Nielsen et al., 1984; Bhathal et al., 1985).

DCIS has a good prognosis, with an overall mortality of 1-2%.

Diagnosis

Clinical diagnosis

DCIS is not usually detectable by clinical examination. Nevertheless, clinical examination

remains useful, especially to exclude other clinical abnormalities. Overall, 13% of pure DCIS present symptomatically (palpable mass, nipple discharge or Paget's disease of the nipple) (Barnes et al., 2014). Palpable DCIS constitutes almost a tenth of new diagnosed cases and was associated with more aggressive biological features like high grade and comedonecrosis. (Sundara Rajan et al., 2013).

Imaging techniques for DCIS diagnosis

DCIS is commonly diagnosed by mammography screening. The mammographic features of DCIS are well known. Typically clustered microcalcifications are common in 85-90% of the cases (Evans et al., 1999). Potential findings include circumscribed masses, focal nodular patterns, asymmetry, dilated retroareolar ducts, ill-defined, rounded tumour, focal architectural distortion, subareolar mass and developing density, but they are less common (Ikeda and Andersson, 1989). Up to 20% of DCIS remain mammographically occult due to the lack of calcifications and/or small tumour dimensions. Breast MRI has a high sensitivity in the diagnosis of invasive breast cancer, varying from 90% to 100%; the sensitivity for the diagnosis of DCIS is 77-96% (Nadrljanski et al., 2013). The sensitivity of mammography decreases with increasing nuclear grade, whereas that of MRI is improved. In a prospective study mammography missed nearly half of the high-grade lesions (48%) (Kuhl et al., 2007). The fact that MRI detects many DCIS lesions that go unnoticed on mammography implies that some cancers can be prevented by timely intervention on the basis of MRI finding. The disadvantages of MRI are the limited availability and the high cost. For the time being, the primary role of MRI in DCIS is limited to the evaluation of lesion extension and thus the planning of breast-conserving surgery (BCS).

Tumourbiopsy

There are three non-surgical biopsy procedures used: fine-needle aspiration (FNA), core needle biopsy (CNB) and vacuum assisted needle biopsy (VANB). The diagnosis of DCIS implies accurate exclusion of stromal invasion, which is only possible for a histologically intact specimen, thus FNA cytology is unreliable for DCIS (Leifland et al., 2003); ultrasound/stereotactic CNB or VANB are mostly used for DCIS diagnosis. With ultrasound CNB there is real-time needle visualization and no need of ionizing radiation. For findings that are visible on a mammogram, but not palpable, stereotactic CNB may be useful. The directional vacuum-assisted biopsy is superior in case of calcifications. At this time, mammography and SCNB represent the gold standard for DCIS diagnosis (Lee et al., 2000).

Sentinel lymph node biopsy (SLNB)

SLNB is recommended for patients with invasive breast cancer to determine prognosis and treatment approach. In general, SLNB is not recommended for patients with a definitive diagnosis of DCIS.

For patients with pure DCIS, the overall risk of microinvasion or metastasis to ipsilateral axillary lymph nodes is less than 1%. Therefore, SLNB is not likely to affect the outcome of treatment. It can, however, be useful when the lesions demonstrate microinvasion, or in case of clinically palpable node, a large comedo-type DCIS and multicentric or extensive lesions (Silverstein et al., 1991). SLNB is also mandatory in cases of mastectomy because the risk in these cases is much higher (up to 48%) (Yen et al., 2005).

Natural history

The natural history of DCIS is poorly understood. The most direct evidence regarding the progression of DCIS to invasive cancer comes from studies where DCIS was initially misdiagnosed as benign and treated by biopsy alone; between 14-53% of DCIS treated with excision alone may progress to invasive cancer over a period of 10 or more years (Lippman 1993; Eusebi et al., 1994; Dickson and Lippman, 1995; Collins et al., 2005; Sanders et al., 2005).

Current thinking is that most IBCs evolve through a non-obligatory series of increasingly abnormal stages over long periods of time. These successive stages are generally referred to as hyperplasia, atypical hyperplasia, and in situ carcinoma. DCIS represents an advanced or late stage of premalignant tumour progression, and it is the direct precursor of most IBCs (Erbas et al., 2006; Allred, 2010).

Risk Factors

For developing DCIS

The risk factors for DCIS and IBC are mostly common and include age (unusual before age of 30, peaks at age 60-75 years), race (less common among African, American, Asian, and Hispanic women), positive family history and/or positive for BRCA 1/2 mutations), parity (increased risk among women with no children or one child and older age at first birth), chemoprevention (decreased DCIS risk with

tamoxifen relative to raloxifene), mammography (increased DCIS with screening) and a previous breast biopsy (increased risk if the patient had a biopsy) (Claus et al., 2003). The body mass index (BMI) and hormone replacement therapy (HRT) with oestrogen plus progestin are not related to an increased risk for DCIS in contrast to IBC (Virnig et al., 2010). There is no association between the use of oral contraceptives and an increased risk of DCIS (Claus et al., 2003).

For recurrence of DCIS

The risk factors for local recurrence of DCIS are well described. Patient-related risk factors include young age, a positive family history, BRCA 1/2 mutation, symptomatic detection race (slightly increased risk among African-American women) and radiation of the chest wall. Tumour-related factors include tumour-size, pattern of duct distribution (micropapillary), comedonecrosis/high grade, multifocality/multicentricity, positive surgical margins (less than 1 mm) and biological markers: ER-/PR-, Her-2/neu+, absence of Her-4, p53 mutation, High Ki-67 index, angiogenesis (Altintas et al., 2009; Wei et al., 2012; Collins et al., 2013; Kong et al., 2014).

Women with high-nuclear-grade DCIS or DCIS detected by palpation who are treated by lumpectomy alone are at relatively high risk of having an invasive breast cancer recurrence (Kerlikowske et al., 2003).

Treatment options

The main goal of treating DCIS is to prevent the development of IBC. DCIS is a heterogeneous disease, meaning that there is no optimal treatment strategy; treatment should rather be personalized and entail a multidisciplinary approach. We describe briefly the acceptable options:

Mastectomy

Mastectomy used to be the gold standard several years ago. The survival rate after mastectomy for DCIS is reported to be 98-99% (Silverstein et al., 1995). The major indications for mastectomy are multifocality, large and high grade DCIS lesions, failure to achieve adequate margins after lumpectomy, age less than 40, previous radiation of the breast and/or contra-indication for radiotherapy. The proportion of patients with DCIS who undergo mastectomy has strongly decreased over the last years; however, still one third are treated with mastectomy (Baxter et al., 2004; Kricker and Armstrong, 2004).

Breast conserving surgery without radiotherapy

Breast conserving surgery aims to complete removal of DCIS and represents an acceptable treatment for selected patients. Low risk for recurrence disease may not require radiation therapy sparing patients from overtreatment. Retrospective studies of excision alone approach, reported 20%-44% local recurrence rates in 10 years (Solin, 2006). ECOG conducted a non-randomized prospective study for the efficacy of lumpectomy alone for low-risk DCIS. At a median follow-up of 6.7 years, the low-risk group had a 10.5% risk of local relapse (Hughes et al., 2009). Another prospective trial had to be stopped because of an unacceptable high rate of local recurrence (Wong et al., 2006). NCCN included excision alone as an acceptable approach for low-risk DCIS, but without defying the subset of patients where radiotherapy was appropriate.

Breast conserving surgery with radiotherapy

In a study from Motwani et al. (2011) patients with DCIS were treated with breast-conserving surgery plus radiotherapy, instead of complete local excision alone. The 5-year and 7-year ipsilateral breast tumour recurrence for the low to intermediate grade (size > 0.3 cm but < 2.5 cm and margins > 3 mm) cohort was 1.5% and 4.4% compared to 6.1% and 10.5% when treated with local excision alone as in the E5194 study. For the high grade (size < 1 cm and margins > 3 mm) cohort the corresponding 5 and 7-year rates were 2.0% and 2.0% vs 15.3% and 18%. This study suggests that adjuvant radiation therapy reduced the risk of local recurrence of the ipsilateral breast.

Five large randomized trials (the NSAPB B-17 US trial, the NSABP B-24 trial, the EORTC 10853 trial, the UK Coordinating Committee on Cancer Research (UKCCCR) DCIS trial and the SweDCIS trial (Fisher et al., 1999; Fisher et al., 1999; Houghton et al., 2003; Emdin et al., 2006; Group et al., 2006)) examined the effectiveness of radiotherapy in reducing local recurrence rates following breast-conserving surgery. In all these trials, radiotherapy reduced local recurrence rates by almost 50%. However, radiotherapy did not seem to influence overall survival, while follow-up in some trials was too short to assess long-term risks of radiotherapy, resulting in questionable benefit of radiotherapy in DCIS.

The role of hormonal treatment in DCIS

The randomized trial NSABP B-24 investigated the role of tamoxifen in women treated with breast-

conserving surgery and radiotherapy. In a median follow-up of 13.6 years, tamoxifen reduced the risk of local recurrence with 32% (Wapnir et al., 2011). Unfortunately tamoxifen did not influence overall mortality and was associated with an increase of endometrial cancer and thromboembolic events. The UK DCIS trial showed that tamoxifen reduced the recurrence of ipsilateral DCIS and contralateral tumours without any effect on ipsilateral invasive disease (Cuzick et al., 2011). These doubtful results question the role of adjuvant hormonal treatment in DCIS.

The role of Herceptin in DCIS

On-going trials validate the role of other agents, such as anastrazole and trastuzumab, in high-risk, HER2-positive DCIS (NSAPB B-43 study, Siziopikou et al., 2013).

Methods

We searched the electronic databases of PubMed and the references and citations of included studies until March 2014. Search terms included: "DCIS", "diagnosis", "epidemiology", "natural history", "treatment", "DCIS margins", "Van Nuys Prognostic Index" and "VPNI". 46 articles related to diagnosis, epidemiology and treatment; 11 articles related to margin status and 11 articles related to VNPI were included.

Tumour margins

Many trials confirm the prognostic role of tumour margins for local recurrence in DCIS patients treated with breast conserving surgery alone or combined with radiotherapy (Silverstein et al., 1999; Douglas-Jones et al., 2002). Inadequate margins may result in a high incidence of local recurrences, while excessively large resections may lead to poor cosmetic outcome without additional benefit.

According to Laleh et al. larger lesions and a smaller volume of resection are commonly related to positive margins. Age at diagnosis, histologic subtype, tumourgrade, and oestrogen and progesteronereceptor status are most unlikely to be related with the margin status (Melstrom et al., 2010).

The histological evaluation of excision margins is critical when a DCIS patient is considered for breast-conserving surgery. Various techniques (inking of specimen margins, two-dimensional radiography, cavity shavings and tumour bed biopsies) have been used to improve the accuracy. Holland et al. (1998) proved that cavity shavings are ineffective in ensuring complete excision.

The risk of ipsilateral recurrence is lower for patients with DCIS treated with breast conserving surgery, upon negative margins. However, there is no consensus for minimal margin width. In a meta-analysis by Wang et al. twenty-one studies that examined the relationship between risk of ipsilateral recurrence and margin status, in women treated with breast conserving surgery with and without radiotherapy, were evaluated; in a total of 7564 patients, 1066 ipsilateral breast tumour recurrence events occurred; 565 ipsilateral recurrence events were reported in 3098 women treated with breast conserving surgery alone and 501 events in 4466 women treated with operation plus radiotherapy.

The risk of ipsilateral breast tumour recurrence in women with positive margins and treated with breast conserving surgery alone is 35% (95% CI = 29-41, n = 423) and 20% (95% CI = 16-24, n = 698) for those treated with breast conserving surgery plus radiation therapy. With margins of 0 mm the risk of recurrence was 20% (95% CI = 16-23, n = 1262) and 10% (95% CI = 8-13, n = 2057) respectively. The relative risks were 17% (95% CI = 12-22%, n= 163) and 9% (95% CI = 6-11, n = 742) respectively, for those who have margins of 2 mm while for margins of 5 mm the respective risks were 20% (95% CI = 3-36, n = 10) and 11% (95% CI = 1-20, n = 23). Remark the low number of patients in this subgroup. For patients with a margin threshold of 10 mm and treated with breast conserving surgery and radiation therapy, only 4% had an ipsilateral breast tumour recurrence compared to 9% (95% CI = 5-12, n = 421) of them who were treated with excision alone.

The results of this study indicate that wider margins minimize the risk of ipsilateral breast tumour recurrence and should be a priority for surgical planning independent of radiotherapy status. Compared to a negative margin of less than 2 mm, a negative margin of at least 10 mm was associated with a lower risk of ipsilateral recurrence. More studies are needed to understand whether margin thresholds greater than 10 mm are warranted. Breast conserving surgery strives for a balance between cosmetic outcomes and negative margins. The statement that free margins of at least 10 mm decrease the risk of ipsilateral recurrence suggested that a more radical excision is recommended, which may lead to poor cosmetic results (Wang et al., 2012).

The meta-analysis of Dunne et al. (2009) also examined the role of margin status on local recurrence. Unlike the meta-analysis of Wang et al.

(2012) only patients treated with breast conserving surgery and radiation therapy were included. Within 4660 patients from 22 trials examining breast conserving surgery and radiation therapy for DCIS, there was a significant difference in the rate of ipsilateral recurrence between patients with negative or positive margins (odds ratio [OR] = 0.36; 95% CI = 0.27-0.47). Patients with margins less than 2 mm had higher rates of ipsilateral recurrence compared to those with larger negative margins. However, a further decrease in local recurrence rates was not observed when margins of 2 mm or more were compared with margins of 5 mm or greater (OR = 1.51; 95% CI = 0.51-5.0; p > .05) (Dunne et al., 2009). This last finding is not in accordance with that of Wang et al. (2012).

Although margin width remains a clinical dilemma, in the NSABP B17 and B24 trials that required ink-free margins, only 72 (2.8%) of 2612 participants treated with breast conserving surgery with and without radiation therapy died of breast cancer after 15 years of follow-up (Wapnir et al., 2011). Thus, any net benefit of more widely free margins on the overall survival of women with DCIS would be extremely small or negligible (Morrow and Katz, 2012).

The effect of re-excision vs radiation therapy on margin width and thus local recurrence

Grade cannot be lowered, size cannot be reduced and age is not amendable. From the four predictors of the VNPI only the margin width is a variable under surgical control. When margins are positive or narrow, a re-excision that results in wider margins can theoretically decrease VNPI by 1 or 2 points and thus the risk of ipsilateral recurrence. Monteau et al. (2009) investigated whether re-excision could be replaced by an additional radiation dose. 208 Women with DCIS treated with breast conserving therapy were selected. 89 Of them had close margins (less than 2 mm), the remaining 119 patients had minimally (1-15 mm) involved margins. Involved margins were less frequent in the non-re-excision group than in the re-excision group (50% vs 74%); 55 patients (26%) underwent re-excision followed by whole-breast irradiation and 6 patients underwent mastectomy for persistent margin involvement. The rest 147 (71%) patients received breast irradiation with an additional dose to the tumour bed without re-excision. The 7-year loco-regional failure rates were 9.3% without, and 9.6% with re-excision. In carefully selected patients with close or focally-involved margins, re-excision could be avoided by delivering a proper additional dose to the surgical bed of the first excision. This could lead to a significant change in the management of patients with DCIS by omitting a second surgical procedure; because of the small population of patients in this study, these results require confirmation in independent series. Anyway, if there are contra-indications for re-excision, radiotherapy can be considered. However, from a critical point of view inadequate surgery cannot be replaced by radio-therapy.

Close margins after mastectomy

Close margins occur in a minority of patients undergoing mastectomy for DCIS. Sullivan et al. sought to determine the incidence and consequences of close margins in patients with DCIS treated with mastectomy. In a study of 810 patients with DCIS treated with mastectomy, 94 (11.7%) of them had close margins (5 had positive margins, 54 negative but less than 1 mm and 35 had margins between 1.1-2.9 mm); seven patients received post-mastectomy radiation therapy, none of them relapsed. The 10-years local recurrence rate was 1%. (5% in the group of women with margins less than 1 mm, 3.6% for margins 1.1-2.9 mm, and 0.7% when margins are ≥ 3 mm). The incidence of local recurrence in patients with close margins is clearly elevated (Fitzsullivan et al., 2013). Interestingly, the risk of local recurrence for patients with close margins was lower than the risk of the development of a contralateral breast cancer (about 6.5%) (Meijnen et al., 2008). Excision and radiotherapy is successful in 90% of the patients developing local recurrence after being treated with mastectomy for DCIS (Kim et al., 2006). Based on this result, post-mastectomy radiotherapy is not systematically recommended in patients with close margins after mastectomy.

The Van Nuys Prognostic Index

There is controversy in optimal treatment strategy design for DCIS. The Van Nuys Prognostic Index (VNPI) was developed in 1996 by Silverstein as a guide for treatment decisions in DCIS patients. The original VNPI was based on tumour size, margin width, and pathologic classification (nuclear grade and comedonecrosis). Scores of 1 (most favourable) to 3 (most unfavourable) were assigned for each of the 3 predictors, as shown in Table I. The total VNPI score is the sum of the score of the three predictors and varies from 3 to 9. Depending on the final VNPI score a specific treatment is recommended (Table II). Excision only for patients with VNPI scores of 3 or 4 is defendable due to the low risk of recurrence. Patients with intermediate scores (5, 6

Table I. — Updated Van Nuys Prognostic Index score 1997, University of California.

Score	1	2	3
Tumour size (mm)	≤ 15	16-40	≥ 41
Margins[a] (mm)	≥ 10	1-9	< 1
Pathological Classification	Non-high grade[b] No necrosis[c]	Non-high grade[b] Necrosis[c]	High grade[b] With/without necrosis[c]

a: distance from tumour biopsy margin
b: nuclear grade
c: comedonecrosis.

Table II. — Treatment of Choice Based on VNPI 1997.

Score	Treatment
3-4	Tumourectomy
5-7	Tumourectomy + radiotherapy
8-9	Mastectomy

or 7) have a 17% decrease in local recurrence rates with radiation therapy. Mastectomy should be considered in patients with a VNPI score of 8 or 9 because they have extremely high local recurrence rates (Silverstein et al., 1996).

Different studies include the age at diagnosis as an important independent predictor of local recurrence (Goldstein et al., 2000; Szelei-Stevens et al., 2000; Vicini et al., 2000). In 2003 the VNPI was updated by adding age at diagnosis, as is demonstrated in table III (Silverstein 2003). The various treatments are adapted to the new VNPI scores (Table IV).

Since the VNPI is validated by a relatively small retrospective series of studies, its use is not worldwide accepted; prospective conformation with large number studies is needed.

Management of DCIS according to the VNPI

The VNPI is often used by clinicians to determine the management of ductal carcinoma. Patterns of management in Australia and New Zealand according to the VNPI were determined by Whitfield et al. For this study the National Breast Cancer Audit was used for the period 2004-2009 and 4578 cases were identified; during the duration of the study, more than three-quarters of DCIS management reports demonstrated good concordance with the Van Nuys recommendations. The National Breast and Ovarian Cancer Centre clinical practice guidelines for DCIS support the VNPI to determine management for DCIS patients (Whitfield et al., 2012). Other studies confirmed that the VNPI can be a useful tool in the treatment of DCIS but they also remark that its validity must be prospectively confirmed with large numbers of DCIS patients (Asjoe et al., 2007).

Kelley et al. used the VNPI for analysing the risk of recurrence after mastectomy for DCIS. No recurrence was observed in a group of 250 patients with a score of 4 till 9 according to the VNPI treated with mastectomy. Mastectomy patients who scored 10-12 were significantly more likely to develop recurrence after mastectomy; 10% will recur at 12 years and 2-3 patients will develop metastatic

Table III. — Updated Van Nuys Prognostic Index score 2003, University of California.

Score	1	2	3
Tumour size (mm)	≤ 15	16-40	≥ 41
Margins[a] (mm)	≥ 10	1-9	< 1
Pathological Classification	Non-high grade[b] No necrosis[c]	Non-high grade[b] Necrosis[c]	High grade[b] With/without necrosis[c]
Ages (yrs)	> 60	40-60	< 40

a: distance from tumour biopsy margin
b: nuclear grade
c: comedonecrosis, not individual cells.

Table IV. — Treatment of Choice Based on VPNI 2003.

Score	Treatment
4, 5, 6	Tumourectomy
7, 8, 9	Tumourectomy + radiotherapy
10, 11, 12	Mastectomy

disease. Patients scoring 10-12 points are mostly young, have large, high-grade, multifocal or multicentric tumours. The latter group of patients are at risk of developing recurrence after mastectomy and post-mastectomy surveillance should be considered here (Kelley et al., 2011). Although the novel use of a validated tool is intriguing, it should be noticed that a number of factors, such as tumour biology, family history, tumour detected by palpation, multifocality and the adequacy of surgical therapy, are not included (Ballehaninna and Chamberlain, 2011).

Margins status and the VNPI

The margin status is the most important factor to predict ipsilateral breast tumour recurrence in women with DCIS treated with breast conserving surgery with or without radiation therapy as previous mentioned. Excision margin width has three times more power than grade in predicting local recurrence (Boland et al., 2003).

In the updated VNPI, margins were subdivided in less than 1 mm, 1 to 9 mm and greater than 10 mm. As a result of the importance of margin status in local recurrence, the VNPI is refined by Silverstein et al. More specific score of the tumour margins (less or more than 3 mm and less or more than 5 mm) were used to update treatment recommendations. This study included 949 patients treated with breast conservation. The local recurrence may not be more than 20% at 12 years. Nothing changed for the low-risk group; those with score 4-6 and the high-risk group, scoring 10-12. Excision alone for low-risk group is still the best option for treatment. Mastectomy in the high-risk group is required to keep local recurrence less than 20% after 12 years. There has been a shift in treatment in the intermediate group. Excision alone for patients who scored 7 but have margin widths ≥ 3 mm is recommended. Excision plus RT achieves the less than 20% local recurrence requirement at 12 years for patients who score 7 and have margins < 3 mm, patients who score 8 and have margins ≥ 3 mm, and for patients who score 9 and have margins ≥ 5 mm. Mastectomy is the best treatment for patients who score 8 and have margins < 3 mm and who score 9 and have margins < 5 mm (Silverstein and Lagios, 2010).

Discussion

DCIS develops in the milk ducts without invading the surrounding connective tissue. It represents a heterogeneous group of lesions. Progression to invasive carcinoma is slow and infrequent and is thus difficult to predict. The incidence of DCIS has greatly increased since the introduction of mammographic screening. The high incidence of DCIS and variations in treatment approach led to the introduction of the VNPI. This index is an easy and useful tool for the management of DCIS. It is based on four prognostic factors: age, tumour margins, tumour size and pathological grade. It was thought to strongly decrease overtreatment. Many clinicians are still convinced that breast conserving surgery plus radiation therapy is the best treatment even in the most favourable subgroup. This attitude may lead to overtreatment of DCIS. In 2008, the National Comprehensive Cancer Network included excision alone as an acceptable treatment alternative for patients with low-risk DCIS. There is no doubt about the fact that positive margins should be avoided because they are related to a very high risk of ispilateral recurrence. The margin status seems to be the most important factor to predict ipsilateral recurrence. There is no consensus about the optimal surgical margin in patients receiving breast-conserving surgery with or without postoperative radiation therapy. It is not possible to accurately assess the margin status intra-operatively. Once the margin status is defined post-operatively, further management can be determined by VNPI. The VNPI is recently more finely tuned to aid in the treatment decision-making process, which evidently should also take into account the informed preference of the patient.

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