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Active Surveillance of Ductal Carcinoma In-Situ

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Abstract

Purpose of Review Tailoring treatment strategies to the biological features of invasive disease and the individual needs and preference of each patient has transformed the way we manage breast cancer. This article calls for a similar shift in the management paradigm of ductal carcinoma in situ (DCIS) from a uniform treatment model toward a risk-stratified stepwise approach that aligns with the heterogeneous nature of the disease to avoid overtreatment.

Recent Findings Most DCIS lesions are hormone receptor positive, and only a subset have a risk for progression to invasive cancer. Early results from observational and clinical studies indicate that active surveillance is a safe and feasible alternative to upfront surgical treatment for low-risk DCIS. Ongoing clinical trials like RECAST will further inform and refine strategies for optimal management of this condition.

Summary The integration of risk-adapted management strategies, endocrine risk-reducing interventions, and advanced imaging modalities into active surveillance protocols hold significant potential to reduce overtreatment and personalize care for patients with DCIS. Early data from clinical trials support the notion that providing a period of active surveillance is safe and offers a critical assessment window during which DCIS treatment can be individualized. Strengthening the evidence base to support the adoption of active surveillance as an initial approach in the management of DCIS is an important clinical priority.

Keywords Ductal carcinoma in-situ · DCIS · Active surveillance · Endocrine therapy · De-escalation · Overtreatment

Introduction

Before the widespread adoption of screening mammograms in the 1980s, ductal carcinoma in-situ (DCIS) was uncommon and accounted for less than 1% of breast cancer diagnoses. With the increased utilization of mammography and biopsies of non-palpable radiographic abnormalities, the incidence of DCIS has risen markedly. This number varies by country and is dependent on screening protocols. In the United States where annual screening mammography is recommended for women beginning at age 40, the American Cancer Society estimates that approximately 56,500 new cases of DCIS were diagnosed in the United States in

2024, representing over 25% of all breast cancer diagnoses. By comparison, in the United Kingdom where women aged 50–65 years are screened every 3 years and recall rates are about half of that in the US, 8,500 new DCIS cases were diagnosed annually between 2017 and 2019, which accounted for about 13% of all diagnoses [1–3]. Although screening plays an important role in reducing breast cancer mortality, there are concerns about overdiagnosis and overtreatment, particularly of women with pre-neoplastic lesions that would not have become clinically apparent in the woman’s lifetime. The primary concern however, is not the diagnosis itself but the risk of unnecessary treatment, highlighting the need to refine treatment algorithms rather than reduce screening efforts. Optimal management of DCIS continues to be a debated topic in breast cancer literature due to its variable malignant potential and lack of long-term studies that track its natural history as most lesions are resected upon diagnosis.

Views about DCIS are polarized, with some calling for a change in nomenclature and others insisting that DCIS should be treated like a cancer [4–6]. Referring to this

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disease as “carcinoma” instills fear and urgency and can lead physicians to recommend and patients to choose more aggressive treatment (such as bilateral mastectomy) even for small low-grade lesions. Most surgeons today favor urgent surgical intervention for patients diagnosed with DCIS. Our understanding of the biology of this disease has evolved and we know that some DCIS may never progress or lead to invasive cancer. Perhaps then, a better way to think about this diagnosis is to consider it more like a high-risk lesion with its identification presenting a window of opportunity for prevention. This would remove the urgency for intervention and enable a graduated approach to management that is more in line with how low-grade prostate cancer is now managed. In this review, we will discuss the biology of DCIS, current management, and emerging approaches in trials for de-escalation of therapy.

Natural History and Current Management of DCIS

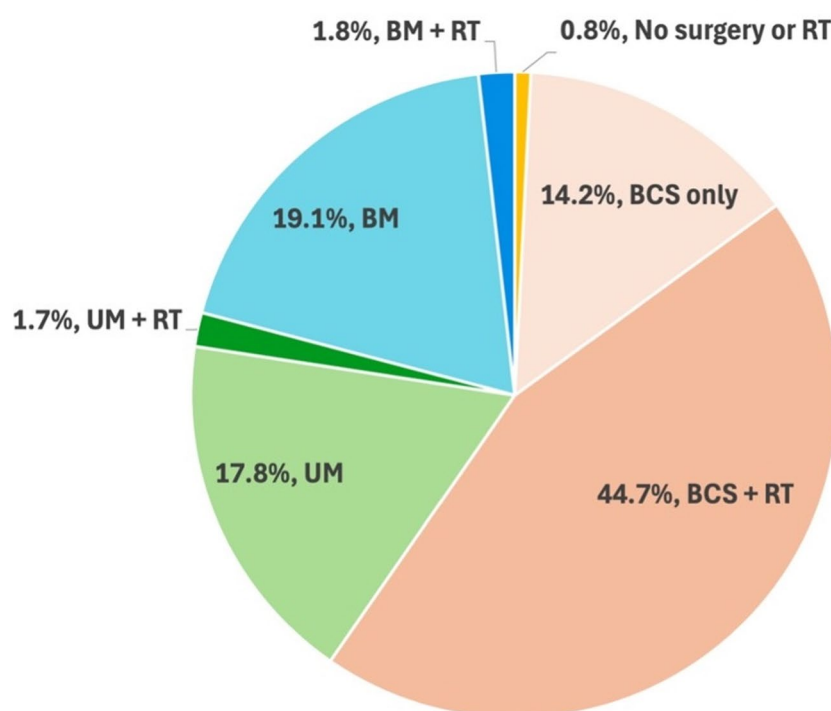
DCIS is considered a non-obligate precursor to invasive cancer. The estimated risk of developing invasive cancer following a diagnosis of DCIS ranges from 15 to 85% [7], depending on the biological characteristics of the DCIS. The underlying biology of DCIS lesions is a key factor in determining the type of invasive cancer that arises [8]. Of the lesions that harbor risk for invasive progression, most

(80%) are slow growing and hormonally driven, and only a subset develops into more aggressive disease. Despite this, DCIS has traditionally been managed like an early-stage breast cancer. Most women with DCIS undergo upfront local excision. A margin width of at least 2 mm is targeted. Many surgeons elect to take patients back for additional surgery if this target is not achieved. The majority of women (75%) are then recommended to have adjuvant radiation after excision. Endocrine therapy is often offered postoperatively to patients with hormone receptor positive disease, although this has traditionally not been considered as important as adjuvant radiation. Furthermore, national trends indicate rising mastectomy rates for DCIS, particularly among younger women, raising concerns about potential overtreatment in cases where less aggressive surgical management may be equally effective [9]. A review of surgical trends revealed that a significant proportion of young women opt for mastectomy over breast conserving surgery for DCIS despite its classification as a pre-invasive cancer (Fig. 1). Notably, among women diagnosed before age of 40, mastectomy was more frequently selected than breast conserving surgery (39% vs. 35%), with bilateral mastectomy more common than unilateral mastectomy, even though current evidence does not support a survival advantage [10].

To better understand how we should approach DCIS, it is worth looking at how our management strategy for invasive cancer has evolved. Over the past decade, there has been a significant de-escalation in the way we treat breast cancer

Fig. 1 Surgery type for DCIS in young women <50y, NCDB 2004–2016 (Byun et al. *Annals Surg Onc* 2021 [10]). BCS: Breast Conserving Surgery; RT: Radiation Therapy; UM: Unilateral Mastectomy; BM: Bilateral Mastectomy

Surgical Management of DCIS in Young Women



without compromise to the rates of locoregional recurrence, distant disease or breast cancer specific mortality. Multiple trials have found that the addition of radiation in early-stage hormone positive cancer in postmenopausal women does not impact mortality and only modestly reduces (2–10%) the risk of local recurrence [11–13]. Notably, treating a recurrence does not affect overall outcomes, emphasizing that for many cancers, beginning with less aggressive treatment is safe and can prevent most women from undergoing unnecessary therapy. Recently, it has been shown that women with small solitary invasive lesions do not benefit from radiation therapy (RT), as recurrence rates without RT are in the range of 2% [14]. Similarly, the surgical management of breast cancer has shifted from the aggressive and morbid Halsted radical mastectomy to a significantly less invasive and aesthetic lumpectomy, in some cases without a sentinel node biopsy. There have been many large randomized controlled trials that provide evidence for the safety of less surgery for breast cancer. The NSABP B-06 and Milan trials showed that lumpectomy and radiation was equivalent to mastectomy in terms of oncologic outcomes and led to the increasing adoption of breast conserving surgeries for the management of invasive breast cancer [15, 16]. NSABP B-18 demonstrated that neoadjuvant chemotherapy for invasive cancer allowed tumor downstaging and increased eligibility for breast conserving surgery and avoidance of axillary node dissection in good responders [17, 18]. Personalization of breast cancer treatment based on tumor biology and patient preference can allow for concerted therapeutic de-escalation, whether from surgery, radiation, or systemic therapy. Studies are being conducted where patients are randomized to no surgery after radiographic complete response with neoadjuvant therapy or omission of sentinel node biopsy following pathologic complete response after preoperative systemic treatment [19–21].

Risk Stratification and Rethinking the Order of Therapy for DCIS

Despite these advances in the management and therapeutic personalization in invasive breast cancer, treatment strategies for DCIS have remained largely stagnant. Similar to invasive cancer, DCIS is a heterogeneous disease, necessitating risk stratification to guide management. This stratification can be performed using clinicopathologic features such as the presence of a mass, size of disease, grade and receptor statuses of the lesion.

Accurate and reliable risk stratification is essential for tailoring treatment and avoiding overtreatment or undertreatment. A retrospective study from the European Institute of Oncology in Milan examined patients with low- to

intermediate-grade DCIS smaller than 2 cm who met active surveillance trial criteria. It reported an overall upgrade rate of 23.6%, with 18.2% (64/351) upstaged to invasive cancer and 5.4% (19/351) to high-grade DCIS [22]. These findings suggest that current clinicopathologic criteria for defining low-risk DCIS may be insufficient, and that incorporating molecular or genomic markers could better identify patients suitable for surveillance. Molecular profiling of DCIS and its microenvironment through genomic assays can help refine the differentiation between low- and high-risk disease. Genomic assays have shown clinical value in radiation oncology; for instance, DCISionRT (a 7-gene biosignature) altered radiation therapy recommendations in 38% of patients, leading to a 20% reduction in its use [23], while OncotypeDCIS (a 12-gene assay) influenced decisions in approximately 30% of cases [24, 25]. Genomic signatures in DCIS are currently applied to guide decisions regarding radiation therapy and with further development, and may also have the potential utility in predicting the likelihood of response to endocrine therapy. However, an important opportunity to assess the value of endocrine therapy, and potentially offering greater insight than a genomic assay, is the initiation of neoadjuvant endocrine therapy for DCIS. This strategy provides a direct, real-time measure of response to anti-hormonal treatment, offers valuable information into disease biology, and helps refine risk stratification for the likelihood of developing invasive cancer within the next five years.

Genomic analyses of DCIS treated with surgery and subsequent invasive recurrences have shown that the majority (75%) of cancers were clonally related to the initial lesion, while 18% were clonally unrelated [26]. These findings suggest that residual tumor cells may persist after surgery, and that DCIS also serves as a marker of risk for future invasive disease. Given that endocrine therapy has demonstrated durable risk-reduction benefits in the adjuvant setting, particularly when taken for at least two years [27, 28], initiating a period of neoadjuvant endocrine therapy may be beneficial to patients with hormone receptor-positive DCIS. This approach will also help motivate patients to continue risk-reducing medication if a therapeutic benefit is observed. Results from ongoing trials described below will be critical in validating active surveillance approaches and ultimately shift the treatment paradigm away from upfront surgery.

Clinical Trials and Evidence for the Safety of Neoadjuvant Therapy for DCIS

Early data from recently completed and ongoing active surveillance trials support the safety of a sequential management approach for low-risk DCIS. This involves deferring

immediate surgical intervention in favor of observing the natural course of DCIS over time, either alone or in conjunction with endocrine therapy. Short term data from the COMET, LORIS, LORD and LORETTA trials suggest that it is not an emergency to operate on DCIS lesions, particularly if they have favorable biological features. Instead of initial surgery, a period of close monitoring and risk reduction with endocrine therapy offers a valuable opportunity to gain insight into disease behavior while reducing the risk of overtreatment. In the following section, we summarize key findings from these trials, which are likely to inform and reshape future approaches to DCIS management.

COMET Trial [29] - The COMET (Comparison of Operative versus Monitoring and Endocrine Therapy for Low-Risk DCIS) trial was a multi-center, randomized non-inferiority trial conducted in the USA that evaluated outcomes of women with low-risk DCIS receiving active monitoring with breast imaging and physical exams every 6 months to those receiving guideline concordant care of surgery with or without radiation therapy. Both groups had the option to receive endocrine therapy. The trial enrolled 995 women aged 40 or older with screen detected, low or intermediate grade, hormone receptor positive DCIS. The primary outcome was 2-year cumulative risk of ipsilateral invasive cancer. The median age of women in each group was comparable at age 64. Women in the active surveillance arm were recommended surgery if they developed a new breast mass, nipple or skin changes, or imaging changes concerning for disease progression with subsequent biopsy confirming invasive disease. 264/473 (52%) of patients in the guideline concordant care group and 82/484 (16.9%) in the active monitoring group underwent surgery for DCIS. 46 women were diagnosed with invasive cancer, 27 in the guideline concordant care group and 19 in the active monitoring group. At 2 years, the cumulative incidence of ipsilateral invasive cancer was 4.2% in the active monitoring group vs. 5.9% in the guideline concordant care group with a difference of -1.7%, suggesting that active monitoring is not inferior to surgery in a select group of women with low-risk DCIS. It is important to note that these results are based on an intention-to-treat analysis, however there was a cross-over rate of about 20–30% from the active surveillance to surgery group due to patient anxiety, radiologic progression and/or upstaging to invasive cancer on repeat biopsy. Also of note, there was a crossover rate of about 40% from the surgery group to active monitoring due to patient's desire to potentially avoid unnecessary surgery. Analysis of this cohort is planned at 5, 7 and 10 years, and will help determine if active surveillance is indeed a safe option for low-risk DCIS.

LORIS Trial [30] - The LORIS (LOW RiSk DCIS) trial is a prospective Phase III multi-center trial conducted in

the United Kingdom that randomized women age 46 and above, with asymptomatic or screen detected low grade DCIS or intermediate grade disease with low grade features, to immediate surgery and standard adjuvant treatment or to a non-interventional approach of active monitoring with at least 10 years of annual mammograms. No anti-estrogen treatment was recommended in the treatment arm; however the trial will be stratified for intended endocrine treatment. The trial was closed early after enrolling 188 patients due to recruitment difficulties, and results from this cohort are pending.

LORD Trial [31] - The LORD (LOW RiSk DCIS) trial in the Netherlands was designed to evaluate whether active surveillance is a safe alternative to standard treatment for women aged 45 or older with screen-detected low-grade DCIS. Due to patient preferences for active surveillance or standard of care, the trial transitioned from a randomized controlled trial to a patient preference model in July 2020, and recruitment is anticipated to be completed in the next 1–2 years.

LORETTA Trial (JCOG 1505) - The LORETTA trial, conducted in Japan, is a surveillance study evaluating the safety and efficacy of tamoxifen alone, without surgery, for women aged 40 years and older with estrogen receptor positive, low-grade DCIS measuring less than 2.5 cm. The primary endpoint is the 5-year incidence of ipsilateral invasive breast cancer. This study completed its recruitment in January 2024 with a total of 360 participants.

Active Surveillance of DCIS as an Opportunity for Risk Reduction

Balanced decision-making during surveillance requires evaluation of outcomes such as progression to invasive cancer, cancer specific mortality, and overall mortality, alongside consideration of patient factors like age, comorbidities, quality of life, anxiety and personal preference. An observational study of patients with DCIS at the University of California San Francisco who chose not to pursue surgical resection provide support for a period of active surveillance to help risk stratify lesions and guide decision-making. The cohort comprised 71 patients and 73 lesions enrolled between 2002 and 2019 with a mean follow up of 8.5 years (range 2.1–21.5 years). All patients were monitored with physical exams and MRI every 3–6 months, and all patients with hormone receptor positive (HR+) disease were offered endocrine therapy (tamoxifen 20 mg daily or an aromatase inhibitor). Resection of the lesion was recommended if there was suspicion for invasive disease, such as patients with persistent or enlarging non-mass enhancement or development of a new mass. The average age of

these patients at time of diagnosis was 53.8 years (range 29.8–78.8 years), 34 (46.6%) of the lesions occurred in premenopausal patients, 60 of the lesions were intermediate or high grade (82.1%), 68 lesions (93.2%) were hormone receptor positive, and 63 patients (88.7%) opted for endocrine therapy [32]. 34 lesions were surgically excised and of these 19 (55.6%) had IDC and 15 (44.1%) had DCIS. One patient was lost to follow up and subsequently presented with metastatic disease, resulting in 20 total cases with IDC. Despite the higher risk cohort, over half (52.1%) remained on active surveillance without evidence of invasive disease with a mean duration of 7.4 years.

Importantly, we were able to use all the data we collected on frequent MRI imaging surveillance to create an artificial intelligence based recursive partitioning model to identify patterns of response that predicted lesions at low, intermediate and high risk of developing an invasive cancer over the next 5 years, reflecting a 10–15%, 20–25% and 60% risk, respectively. The key features that emerged were the conspicuity of the lesion in relation to the background parenchymal enhancement of the tissue on MRI, and the change in these lesions over time. We were then able to develop a semiquantitative algorithm to support a confirmatory trial [33]. Taken together, this observational study provided support for the safety of changing the order of treatment for DCIS, starting with neoadjuvant endocrine therapy instead of surgical excision, and provided support for using a 6-month read out on MRI changes that predicted risk at 5 years.

Active Surveillance Protocols and the RECAST Trial

The shift in paradigm toward active surveillance for DCIS places increased emphasis on imaging to monitor for disease progression. Implementing an effective surveillance protocol requires careful consideration of imaging modalities, follow-up intervals, physical exam frequency and triggers for biopsy. DCIS is commonly detected as microcalcifications on mammogram; however, mammography is limited in detecting non-calcified non-mass forming lesions and often under-estimates the true extent of disease. In contrast, breast MRI offers greater sensitivity for assessing the full extent of DCIS and provides information about the total landscape of both breasts, including background enhancement and distribution of mass and non-mass enhancement. These imaging characteristics reflect important clinical information regarding the behavior and risk posed by the DCIS.

MRI offers two key insights for surveillance. First, the presence or absence of a distinct focal lesion can influence management decisions. Low grade DCIS often presents as scattered foci, which may contribute to high rates of positive

margins upon resection. Furthermore, low grade DCIS can be histologically similar and difficult to distinguish from atypical ductal hyperplasia [34, 35], a known risk factor for future invasive cancer anywhere in the breast. As such, in cases where no clear focal enhancement is detected and the lesion is indistinct from background enhancement, the lesion may behave more like ADH. Given that endocrine therapy for ADH reduces the risk of developing invasive cancer by 75–80% [36], such lesions may be more appropriately managed with endocrine therapy rather than surgery. Second, significant background parenchymal enhancement on MRI that diminishes with endocrine therapy to reveal a more defined focal lesion may suggest an endocrine sensitive breast environment and an endocrine insensitive lesion. In these cases, surgical excision may be more appropriate choice for optimal management. Observing changes in background enhancement and changes in conspicuity of a lesion following endocrine therapy provides a non-invasive means to evaluate the safety of continued active surveillance [33]. These principles served as the basis for the design of our prospective randomized trial, RECAST DCIS (see below).

RECAST (ClinicalTrials.gov identifier NCT06075953) - The RECAST DCIS Study (Re-Evaluating Conditions for Active Surveillance Suitability as Treatment for DCIS) is a multi-institutional Phase 2 study in the USA which compares several different endocrine therapies, including new investigational agents that may be better tolerated and potentially more effective than traditional anti-estrogen therapies, in the management of patients with hormone receptor positive DCIS [37]. MRI imaging obtained at baseline, 3 months and 6 months, as well as molecular based biomarker analyses are used to monitor for response to hormone therapy. The aim of the study is to lower the risk of an invasive cancer using endocrine agents and to use the 6-month assessment period to determine how suitable each person is for active surveillance. With this information, surgeons can better identify those who are good candidates for avoiding surgical intervention and those who are much less likely to successfully avoid resection. This allows for a stepwise evaluation, giving all women who participate in the trial the opportunity to use information gleaned during the 6-month window to assess their risk for development of breast cancer and guide next steps in their care.

Novel Options for Endocrine Therapy

Endocrine therapy plays a key role in risk reduction in patients with hormone receptor positive DCIS and has been demonstrated in the NSABP B-24, UK/ANZ DCIS and IBIS-II trials to decrease both incidence of ipsilateral recurrence and contralateral breast cancer by 30–40%[38–40].

However, many of the drugs prescribed today (20 mg daily tamoxifen, aromatase Inhibitors) are not well tolerated by a substantial proportion of patients due to side effects such as hot flashes, arthralgias, bone loss, and increased risks of thromboembolic disease, endometrial cancer and cardiovascular events [28]. Many patients are hesitant to attempt endocrine therapy, much less remain compliant over several years. Due to its low likelihood and potentially slow transformation into invasive disease, it becomes more important to recommend not only an effective but tolerable anti-estrogen drug in the setting of risk reduction in women with low-risk DCIS. A lower dose and duration of tamoxifen, 5 mg daily for 3 years, has been shown to be effective in reducing the risk of breast cancer in women with high-risk pre-invasive lesions including DCIS by 52% compared to placebo, importantly with fewer side effects [41]. There are many novel endocrine agents such as selective endocrine receptor degraders (SERDs), androgen agonists and antagonists that may be as, if not more, effective than traditional tamoxifen or AI in risk reduction following DCIS. The RECAST study seeks to evaluate the efficacy and tolerability of novel anti-estrogen therapies such as testosterone, Elacestrant and Endoxifen in the management of DCIS, which can then be extrapolated for use in the invasive setting. As new options for anti-hormonal therapy that are better tolerated become available, there is potential for it to become a risk-reducing drug for breast cancer, not unlike taking a statin for prevention of cardiovascular disease.

Non-Surgical Management of High-Risk DCIS

At present, surgical excision remains the primary treatment for high-risk DCIS, particularly those that are characterized by hormone receptor negativity, mass lesions, or extensive disease. In patients presenting with segmental or widespread suspicious calcifications, representative biopsies should be obtained to define extent of disease. If these biopsies confirm DCIS alone, consideration may be given to an initial period of neoadjuvant endocrine therapy with close surveillance as an alternative to immediate mastectomy as it provides an opportunity to better characterize disease risk. In this setting, an MRI can aid in detecting invasive disease, with the presence of a mass suggesting a higher likelihood of malignancy. Neoadjuvant endocrine therapy has been shown to be safe and effective in stage 2–3 invasive breast cancer, supporting its safety in the DCIS setting, even if occult invasion is present.

A subset of DCIS, in particular high-grade lesions that are ER- and/or Her2+, display substantial immune cell infiltration. Endocrine therapy has not been a strategy that

appears to control these high-risk DCIS in women seeking to avoid surgical intervention. We and others have shown that tumor infiltrating lymphocytes (TILs) in DCIS may be a marker for better outcomes. Emerging evidence suggest that distinct immune cell subsets may influence either progression or regression of the disease [42]. Studies have shown that high density of TILs in invasive cancers is associated with decreased risk of local recurrence and improved overall survival. Additionally, cancers with prominent immune infiltrates are more likely to respond favorably to immunotherapy. In line with this, a Phase 1 open-label trial conducted at the University of California San Francisco demonstrated promising results using intra-tumoral immunotherapy in DCIS with high baseline levels of tumor infiltrating T-cells. The treatment involved direct injections of pembrolizumab combined with a nanoparticle encapsulated mRNA encoding immunomodulatory proteins into the tumor, which elicited a strong immune response and induced rapid regression of some of the high-risk DCIS lesions [43]. While additional research and better interventions are necessary, these findings offer proof of concept that intra-tumoral immunotherapy can induce regression of high-risk DCIS. Future trials investigating local immunotherapy or vaccine-based approaches may offer effective non-surgical approaches to prevent both local and distant recurrence from these higher risk lesions.

Discussion

With the success in personalization of treatment strategies for invasive breast cancer, management of DCIS will also benefit from tailored approaches based on its risk of progression. A summary of a risk-adapted approach to the management of DCIS is presented in Fig. 2. Although clinical trials suggest that Her2+DCIS represents a higher-risk subtype, routine Her2 testing is not currently standard practice, as it does not influence treatment decisions. Incorporating Her2 testing into clinical trials, however, remains important to clarify its potential role as a marker that could impact treatment. As our understanding of Her2+DCIS evolves, testing may ultimately become part of routine care.

Active surveillance or watchful waiting is a viable option in many early-stage cancers, including prostate cancer, papillary thyroid cancer, renal cancer, and some leukemias and should become standard of care for DCIS. The UK-based ProtecT trial (Prostate Testing for Cancer and Treatment) showed that close monitoring of men with localized prostate cancer and switching to curative treatment only when there was evidence of disease progression did not increase the risk of death compared to immediate radical prostatectomy and radiotherapy which carries with it a non-trivial

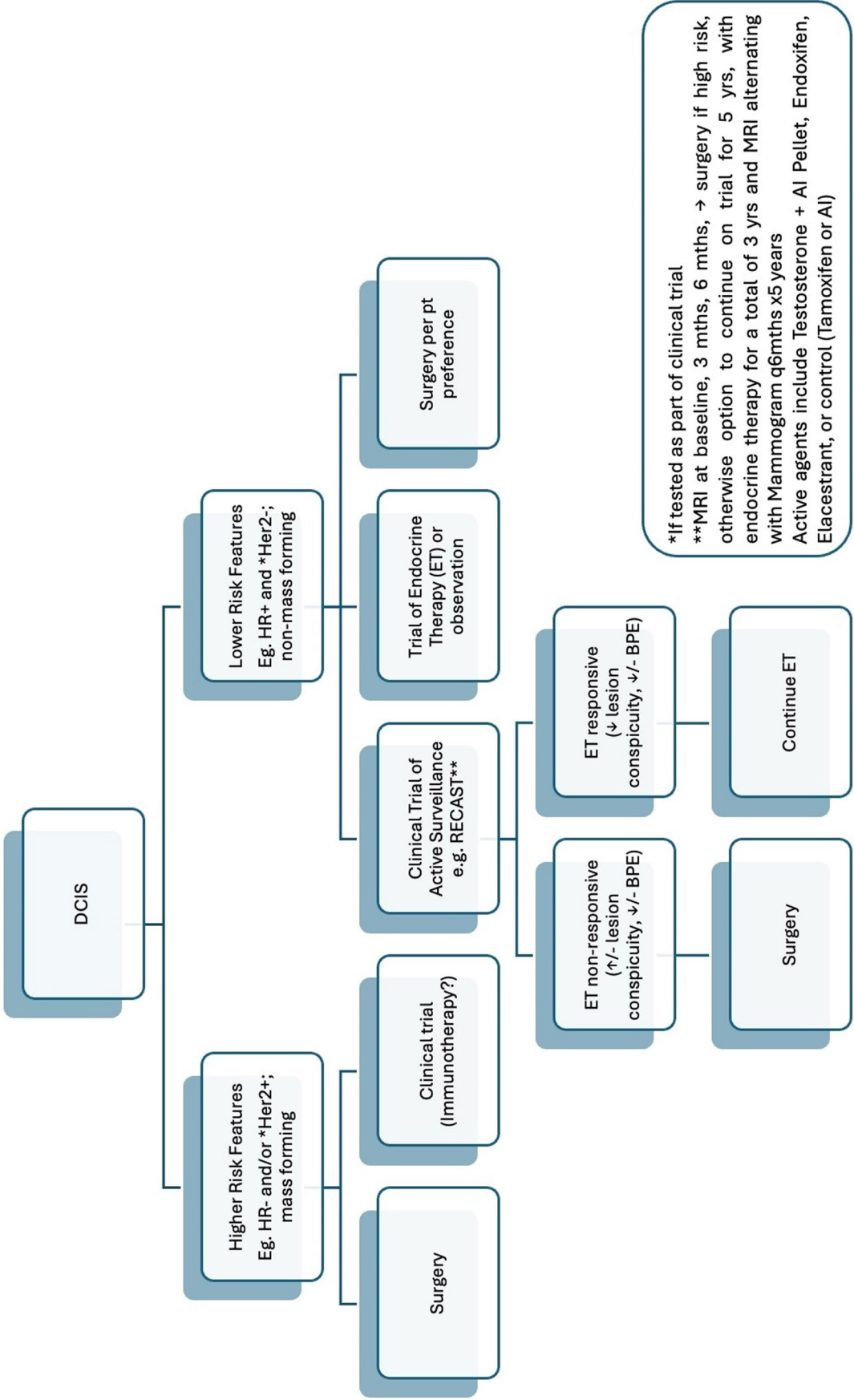


Fig. 2 Risk adapted approach to the management of DCIS (HR: hormone receptor; ↑/-/↓: increase/no change/decrease)

level of morbidity [44]. For DCIS lesions not at immediate risk of harboring occult invasive cancer, it would be prudent to consider changing the order of treatment. Patients seeking an alternative to surgery should ideally be referred to a clinical trial such as RECAST. However, where this is not feasible, a neoadjuvant course of endocrine therapy may be initiated for HR + DCIS. MRI is valuable in excluding invasive disease in this setting, with the absence of a discrete mass being reassuring. This approach is most applicable to screen-detected, small (≤ 2 cm) and of low to intermediate grade DCIS lesions. Surgical intervention may then be offered or deferred based on treatment response. Starting with neoadjuvant endocrine therapy would allow for a period of safe observation. The advantages are manifold, including affording us a valuable opportunity to monitor the natural progression of the heterogeneous group of disease and personalize treatment according to the biology of DCIS, allow for better approximation of disease extent and increase the number of patients eligible for breast conserving surgery, even no surgery or radiation for this pre-cancerous condition. In addition, clinicians can get a sense of the patient's tolerance for endocrine therapy which can then be integrated into the decision-making process when considering the type of surgery offered and adjuvant radiation therapy following breast conserving surgery as well as shift the focus from local control to risk reduction. Certainly, if it is safe to manage stage 2 and 3 breast cancer with neoadjuvant endocrine therapy for 6 months, it is safe to do so in the setting of DCIS.

It takes courage to implement a change, particularly one that goes against national and society guidelines. However, that is what clinical trials are designed for - to test new approaches and determine if a new surgical, medical or management strategy is better for patients and as good or better than current treatment. Our practices must evolve with our understanding of the disease process and alongside new evidence that has been generated not only for DCIS, but in a related condition such as prostate cancer. The use of early surrogates for success, such as MRI imaging, can accelerate the pace at which we learn, rather than waiting decades to accrue and analyze data to support the change and to avoid an unwarranted lag in our advancement of treatment strategies.

Conclusions

Active surveillance represents a promising and increasingly evidence-based approach for the management of DCIS, contributing to the movement toward personalized breast cancer care. By recognizing DCIS as an indicator of risk rather than an immediate precursor to invasive disease warranting

urgent intervention, clinicians can adopt a more nuanced, biology driven approach that avoids overtreatment. The integration of genomic profiling and advanced imaging techniques has enhanced our ability to identify patients with low-risk lesions. MR based imaging tools are being developed to identify for whom it may be safe to defer surgery in favor of endocrine therapy and careful monitoring. Early data support the safety and feasibility of this approach, and ongoing clinical trials will be critical in refining risk stratification tools and establishing evidence-based guidelines for surveillance. These developments have the potential to significantly reduce treatment-related morbidity while maintaining oncologic safety, ultimately improving quality of care for women with DCIS.

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This is the first published clinical trial to demonstrate that neoadjuvant endocrine therapy combined with close monitoring is as safe and effective as the standard approach of surgery, with or without adjuvant endocrine or radiation therapy, for patients diagnosed with low-risk DCIS.

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This retrospective analysis highlights the authors' observation of women who opt to forego initial surgery for DCIS and supports the idea that active surveillance can help risk-stratify DCIS lesions inform management decisions.

Author Contributions S.L. and L.E. wrote the main manuscript text and prepared figures 1-2. All authors reviewed the manuscript.

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Data Availability No datasets were generated or analyzed during the review.

Declarations

Human and Animal Rights and Informed Consent All reported studies / experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional / national research committee standards, and international / national / institutional guidelines).

Competing interests The authors declare no competing interests.

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