In Situ Disease DCIS and LCIS

Summary

Up to 80-85% of DCIS is non-palpable and therefore presents on imaging, usually as microcalcifications on mammogram (Lakhani, 2006). Tricky as doesn't always correspond with pathology findings (Holland, 2000).

Traditionally, Van Nuys used to stratify risk of recurrence in DCIS. Bad prognostic indicators are: Margins<1mm, G3, comedo necrosis, poorly differentiated, Age <50 (particularly <40), ER-, HER2+. Tumour size has not been shown to be predictive.

LCIS – distinguish classical from pleomorphic. Classical – yearly mammogram for 5 years (though consider FH). Pleomorphic is treated as a variant of DCIS though some would argue there is not a good evidence base for this (Dutch guidance quotes that 33% have concurrent invasive components with pLCIS). Overall LCIS occurs younger than DCIS (late 40s and 70% pre-menopausal vs late 50s and 70% post-menopausal in DCIS) and also has no clinical or mammographic signs like DCIS. Risk of subsequent cancer is overall lower than for DCIS (25-30% vs 30-50%) but higher in the contralateral breast (50% rx in each breast versus 99% and 1% in ipsi/contra in DCIS). Given this, it is more of a predictor of overall breast disease.

Guidance

Dutch Guidance on DCIS

Highlights that predictors of presence of invasive disease are:

- Age >55
- Solid component on mammo i.e. mass forming
- Suspicious histology – moderate or poorly differentiated
- Palpable disease

From meta-analysis predictors of invasion are:

- High vs Low grade
- Size <-20mm or >-20mm
- Mass vs microcalcs on mammo
- Perhaps the size of biopsy 11 vs 14G

Hence why we do a SLNB in palpable or mass forming DCIS.

NICE

Very vague on treatment in DCIS and just state that you can consider Radiotherapy and endocrine therapy.

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Originally collated by Miss Amy Robinson. Last updated: May 2023

Emerging Evidence

Low RISk in DCIS – LORIS (UK)/LORD (Europe)/COMMET (Japan) trials – Needed to answer de-escalation.

These trials all look at low grade DCIS surgery versus active monitoring. US/Japan give optional and mandatory endocrine respectively.

In the UK based LoRIS is aged 46+ and can be grade 1 or 2, but not grade 3 or comedo necrosis. They get annual mammography.

Closed 2020. Precision = steering group but also using these trials to develop better biomarkers in DCIS. Unfortunately, LORIS closed with poor accrual.
Low dose tamoxifen aka "Baby Tam". The role of "Baby Tam", which is a 5mg dose in the context of ADH, DCIS, or LCIS has been explored. In a RCT of 500 (346 whom had DCIS), there were 14 neoplastic events with tamoxifen 5mg for 3 years and 28 with placebo. There was a 75% reduction in contralateral breast cancer. In the DCIS arm, recurrences occurred in 11 versus 20 (HR, 0.53; 95% CI, 0.25 to 1.11). There was a significant difference in hot flushes but no other adverse events. In our centres, we don't routinely use this, however may consider for example in a young patient with a family history and LCIS/ADH/DCIS excised. For further info see the papers section for "BabyTam for DCIS/ADH/LCIS JCO 2019".

Historical trials on DCIS

Radiotherapy?

SweDCIS, NSABP-17, EORTC 10853, UK/ANZ

- Meta-analysis of all 4 trials show that the HR 0.46 ie more than halved the rate of an ipsilateral breast event per year. 10-year cumulative risk 28.1% to 12.9% when RadioTx given. No effect on the OS.

Hormonal adjuvant therapy in DCIS?

NSABP-B24 (RCT 1.8k BCS for DCIS)

- Non-significant reduction in Ipsilateral DCIS recurrence but significant reduction in ipsilateral invasive recurrence (4.2% vs 2.1%, OR 0.56) and all breast cancer events highly sig (13.4% vs 8.2%, OR 0.63, p0.0009). Of note there was a 40% reduction in women under 50 with only a 20% non-significant reduction in women over 50yrs.
- UK/ANZ reported 30% reduction in invasive recurrence.
- Meta-analysis of NSABP-B24 and UK/ANZ trails OR 0.72 all events.
- But we know that endocrine does just act to reduce your risks – IBIS 1 and 2 trials and chemoprevention. Therefore, we do not tend to give endocrine therapy in DCIS.

Overview of Practice

Sloane 2018

AUDIT prospective cohort with standardised pathology and radiology reporting. Looked at records from 13k women complete data on 10k. Good coverage - 78 of 95 UK Screening units contributed.

- Under 60s 70% had BCS. Mx in high grade or large disease
- 7k BCS - 62% received RadioTx
- ET in 14% BCS and 8% Mx. Declined use over the 9 years
- At 64 months (5.3 yrs) breast event was 6.8%: 4.5% ipsilateral Regional/Distant recurrence in 2.3%
- Contralateral breast event rate 2.2%

For BCS:

- Radiotx for any ipsilateral event HR 0.59 (or HR 0.4 on multivariate analysis)
- RadioTx reduced ipsilateral risk of INVASIVE recurrence significantly 3.8% to 1.9% approx 4% to 2%, HR 0.51 i.e. halves. BUT not of DCIS recurrence.
- Endocrine HR 0.7 for any ipsiateral event or (HR 0.56 on multivariate analysis)
- High grade (HR1.5) and Comedo necrosis (HR 1.3) significantly increased the risk of a ipsilateral breast event.
- Margin <2mm ASSOCIATED with recurrence when did not receive RadioTx

Survival:

- Overall mortality in low approx 3% and very low for breast cancer mortality (46 of 9938 women died from breast cancer ie 0.5%)
- RadioTx did significantly reduce risk of all deaths HR 0.65 p<0.001 (even when adjusted for age) but not for breast cancer deaths HR 0.73 but p=0.4. (This is pretty predictable given how few events there are)
- Endocrine has no effect on either all cause or breast mortality.

Adjuvant radiotherapy (RT) after BCS is associated with a reduced risk of ipsilateral recurrence but not mortality

- Survival after treatment of DCIS is excellent, with few subsequent deaths from breast cancer.
- Further DCIS or invasive breast cancer is not uncommon (6.8% at 5 years)
- 5-year mortality was not impacted by the use of RT or endocrine therapy