Morphological heterogeneity in ductal carcinoma in situ of the breast

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Background

Ductal carcinoma in situ (DCIS) of the breast is a heterogeneous disease in terms of morphology and genetics. Morphological classification of DCIS is challenging, as DCIS lesions often present with a heterogeneous morphology. Moreover, the histopathological evaluation of DCIS is characterized by substantial inter-observer variability among histopathologists.[1,2]

At present, there are four clinical trials ongoing that explore the possibility of active surveillance as a valid 'treatment' option for patients with a biopsy diagnosis of low risk DCIS. If so-called 'watchful waiting' will be introduced into clinical practice, it is of utmost importance that biopsies are representative for the DCIS lesion in the breast. The representativity of a biopsy might possibly be hampered by intra-tumour heterogeneity.

This retrospective study therefore explored the extent of heterogeneity of 6 histopathological features of DCIS. The histopathological features of pure DCIS in the initial biopsy were compared with the features of the pure DCIS lesion in the subsequent resection specimen.

Materials & Methods

Fifty-one DCIS biopsies were correlated with their subsequent resection specimen. The percentage of ducts containing a particular histopathological feature was assessed on the biopsy slide and three representative slides of the lumpectomy or mastectomy specimen.

A **histoscore** was determined for each feature to allow assessment of the degree of histopathological heterogeneity. For instance, the histoscore for nuclear grade was calculated as follows: (% grade 1 nuclei) + (% grade 2 nuclei)*2 + (% grade 3 nuclei)*3, with a score ranging from 100-300. Heterogeneity was arbitrarily defined as a mean histoscore with a standard deviation >10% of the maximum histoscore. Statistical analysis comprised Friedman tests, post hoc Wilcoxon tests (+Bonferroni correction), and Spearman's correlation.

Want to know more?

1. Van Bockstal et al, Histopathology 2018. PMID 30168167

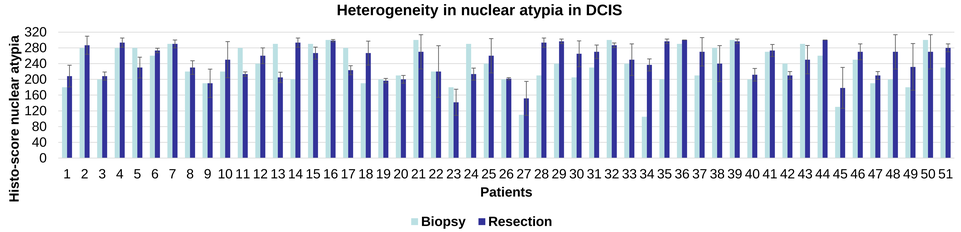
2. Dano et al. Modern Pathology 2020. PMID 31534203

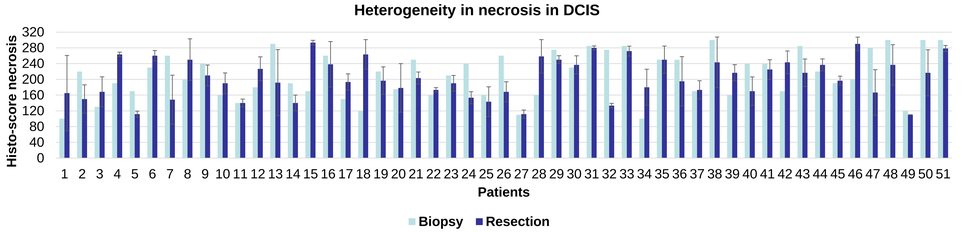
Conclusion

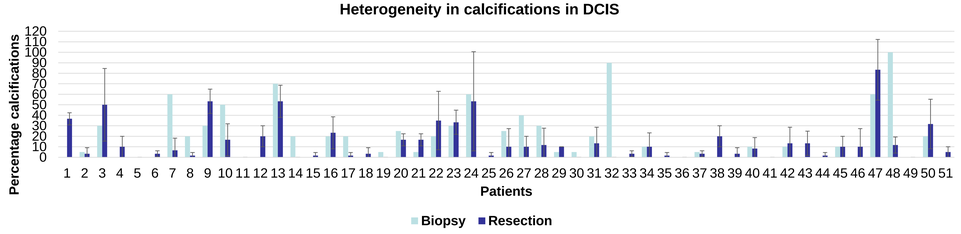
DCIS lesions present with a heterogeneous histoscore for each histopathological feature (41%-57%). All features determined in the biopsy correlated well with the surgical specimen, except for necrosis. We therefore conclude that overall heterogeneity in pure DCIS has only a limited impact, and that biopsies of pure DCIS are generally representative for the entire DCIS lesion.

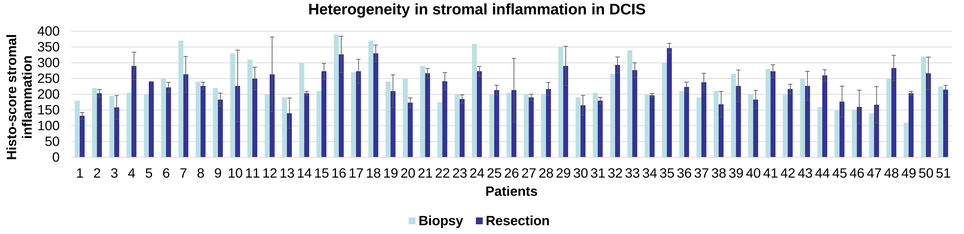
Results

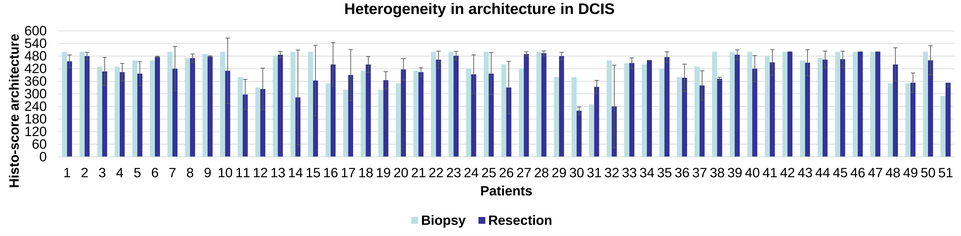
Barcharts illustrating the heterogeneity of histopathological features in DCIS : histo-score per feature for each biopsy and the subsequent resection specimen (three tissue blocks evaluated per specimen)

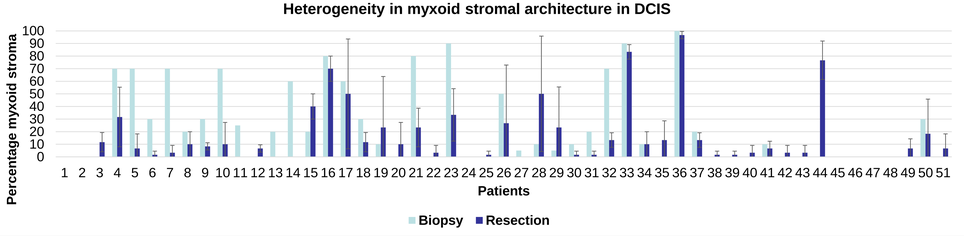


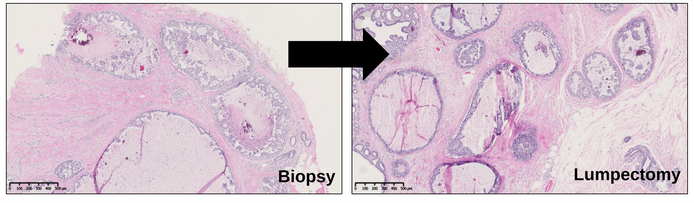












A biopsy is representative for the subsequent resection specimen

- Twenty-four cases of 51 (47%) showed heterogeneity for nuclear atypia, 25 of 51 (49%) for DCIS architecture, 23 of 51 (45%) for calcifications, 29 of 51 (57%) for necrosis, 22 of 51 (43%) for myxoid stromal architecture, and 21 of 51 (41%) for stromal inflammation.
- The presence of heterogeneity was not associated with patient age, DCIS size or type of surgery except for one weak association (p=0,048) between heterogeneity in stromal inflammation and DCIS size : DCIS with heterogeneous inflammation tended to be of smaller.
- No relationship between heterogeneity in nuclear atypia and heterogeneity in other histopathological features was observed.
- Spearman's correlation tests showed that histopathological features in the biopsy correlated significantly with the resection specimen except for necrosis.

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