DO BREAST MICROCALCIFICATIONS IMMORTALISE TISSUE PATHOLOGY? - A PRELIMINARY STUDY

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Two types of breast calcification[1]

Type I
> Only in benign tissue
> Calcium oxalate

Type II
> Benign & malignant tissue
> Hydroxyapatite
> Highly substitutable

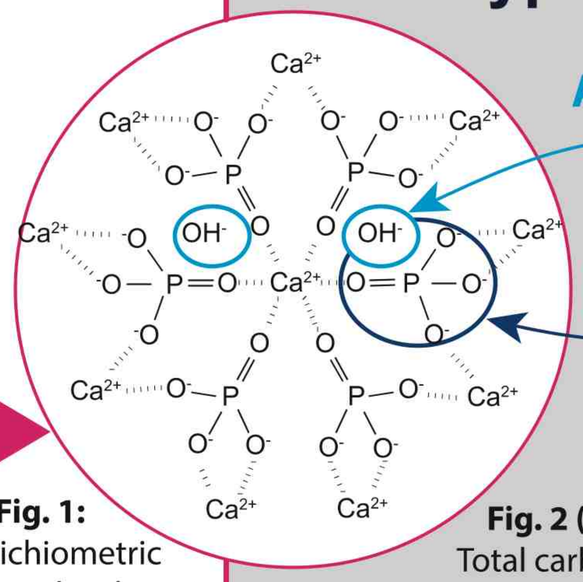
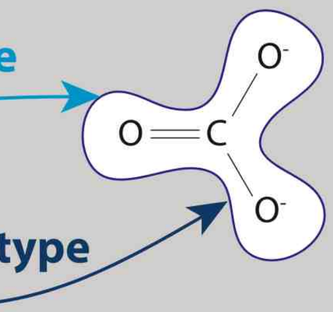


Fig. 1: Stoichiometric hydroxyapatite and carbonate substitutions

Two types of carbonate



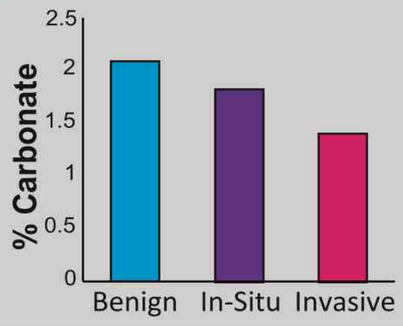


Fig. 2 (right): Total carbonate content of microcalcifications found by FTIR[2]

Formation mechanisms

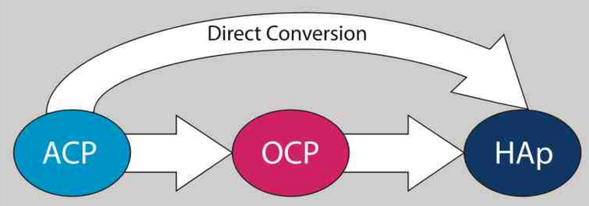


Fig. 3: Two possible formation mechanisms for hydroxyapatite (HAp) directly from amorphous calcium phosphate (ACP) or through an octacalcium phosphate (OCP) precursor phase, dependant on environmental conditions.

X-ray diffraction

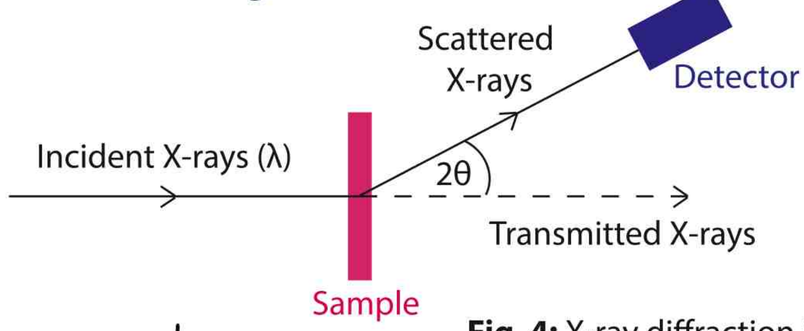


Fig. 4: X-ray diffraction in transmission.

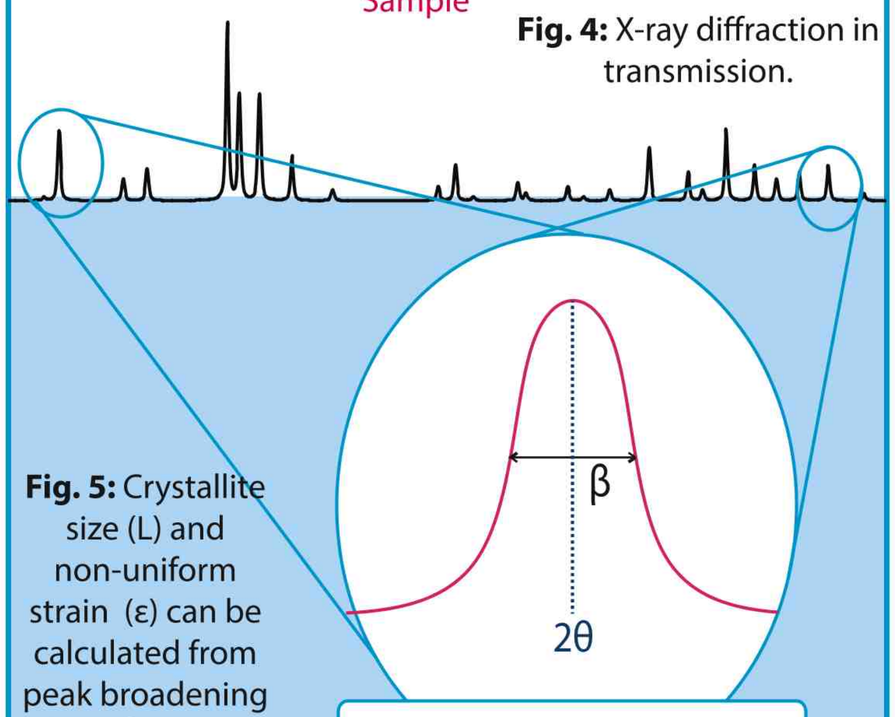


Fig. 5: Crystallite size (L) and non-uniform strain (ε) can be calculated from peak broadening (β) and position (θ) using the Williamson-Hall equation

$$\beta\cos\theta = 4\varepsilon\sin\theta + \frac{0.9\lambda}{L}$$

Crystallite size and strain increase

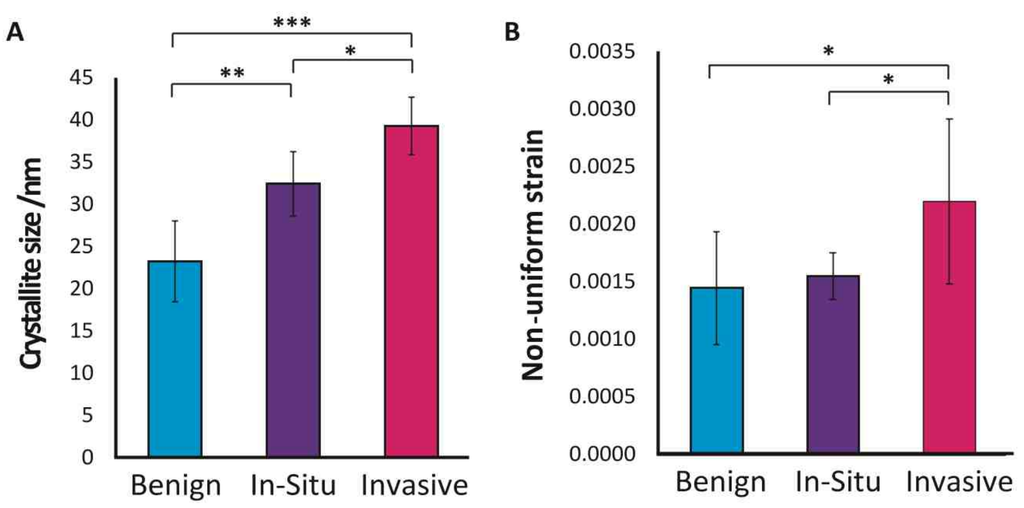
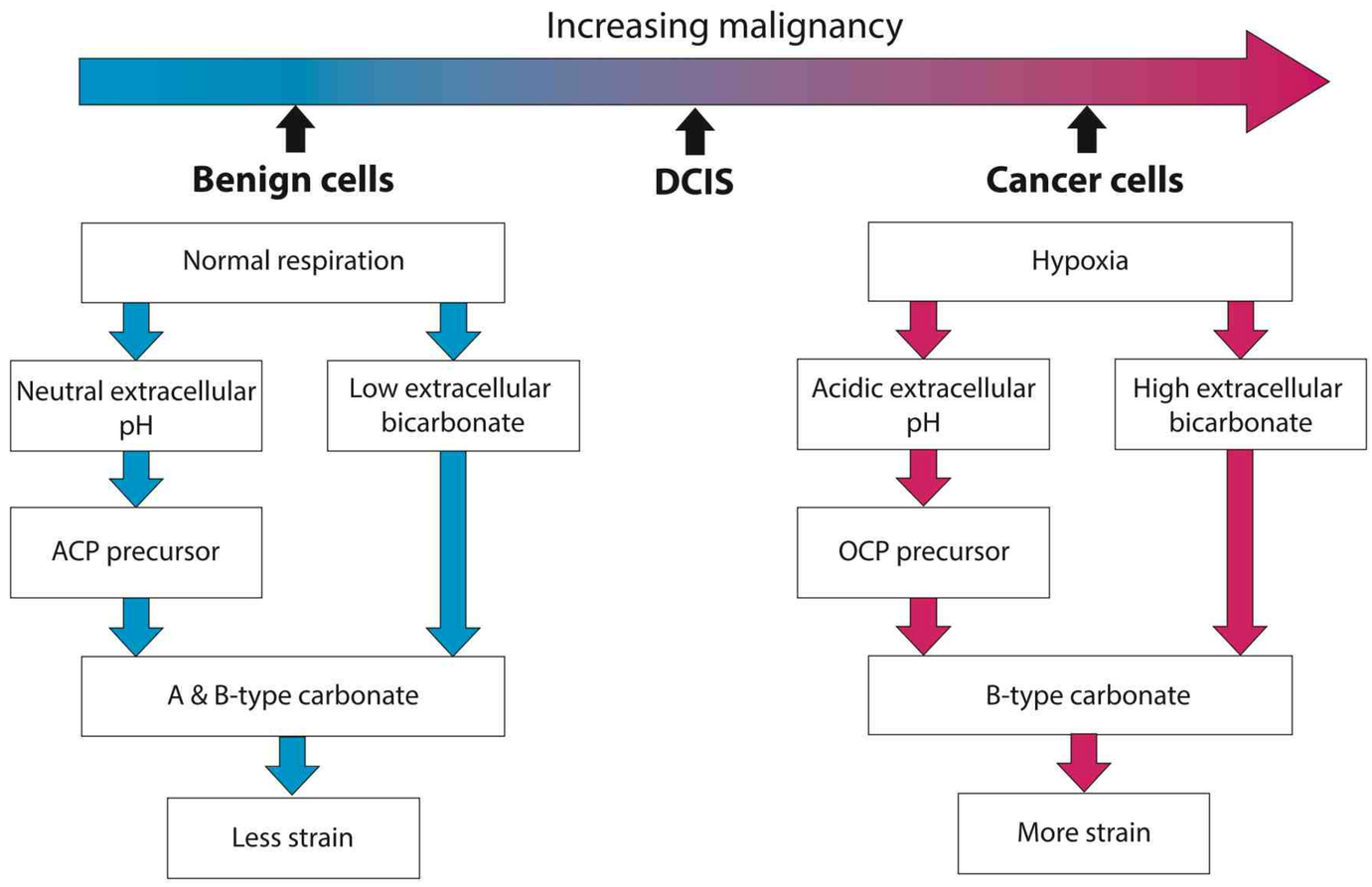


Fig. 6: Crystallite size (A) and non-uniform strain (B) of calcification crystallites increase with increasing tissue malignancy. Error bars are 95% CI. *P<0.05, **P<0.01, ***P<0.001, Mann-Whitney test. n=5, 4 and 6 respectively.

A new model for calcification formation



Conclusions

> Lower total carbonate leads to larger crystallite size with increasing malignancy[2]
> An increasing B/A type ratio with malignancy leads to an increased strain in invasive calcifications
> Tissue pathology governs calcification formation mechanisms

References

1. Wopenka B., Pasteris JD. Materials Science and Engineering: C. April 2005; 25(2): 131–143.
2. Baker R., Rogers KD., Shepherd N., Stone N. British Journal of Cancer. Nature Publishing Group; 2010; 103(7): 1034–1039.

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CRUK Grand Challenge DCIS PRECISION
An international conglomerate working to identify novel biomarkers for DCIS which will progress into or recur as invasive carcinoma
ref. C38317/A24043

MRC Immortalisation of Breast Pathology
An MRC funded project to identify crystallographic differences between calcifications found in a wide range of breast tissue pathologies