The NOSTRA-Feasibility MRI Sub-Study:

Use of breast MRI to predict pathological complete response (pCR) in HER2+/ER- breast cancer patients receiving neoadjuvant dual-targeted anti-HER2 treatment

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1. BACKGROUND

- Participants in **NOSTRA-Feasibility** had HER2+/ER- breast cancers treated with neoadjuvant chemotherapy with dual-targeted anti-HER2 treatment and surgery [1].
- Protocol-specified biopsies across the original tumour bed were taken pre-surgery, aiming to identify participants with residual disease.
- Magnetic Resonance Imaging (MRI) scans of the breasts (pre- and post-neoadjuvant treatment) were taken as part of standard care and collected from 16 participants.
- We hypothesised MRI could accurately evaluate Pathological Complete Response (pCR), defined here as no residual invasive tumour or DCIS.

2. OBJECTIVES

- To assess if parameters derived from baseline MRI scans can differentiate between ''responders'' (those with complete or partial response to neoadjuvant treatment at surgery) and "non-responders" (those with stable disease)
- To evaluate if MRI-derived parameters from post treatment scans correlate with the multiple ultrasound-guided tumour bed core biopsies and final pathology.

3. METHODOLOGY

- Appropriate ethical approval and informed consent were received.
- MRIs were collated and assembled into a mini PACS database at Cobalt Medical Charity.
- The MRI protocol consisted of:
  - 3T imaging with a dedicated breast coil
  - axial T2 -weighted imaging
  - diffusion-weighted imaging with two respective b factors (50, 850)
  - post gadolinium contrast enhanced dynamic axial T1-weighted imaging with fat suppression
  - delayed high resolution axial T1-weighted imaging with fat suppression.
- See Figure 1 for MRI sequence examples.

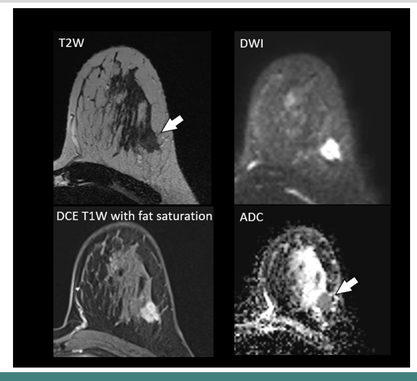


Figure 1: MRI sequences utilised

4. METHODOLOGY: IMAGE REVIEW

- MRIs were reviewed on dedicated breast MRI software (Philips IntelliSpace®):
  - independently and then in consensus
  - by two experienced radiologists
  - interpreted using American College of Radiology Breast Imaging- Reporting and Data System (BI-RADS®) lexicon 6th edition.
- The radiologists were blinded to:
  - clinical features
  - other imaging information
  - pathology results from final excision specimens.
- Pre- and post-treatment images of suitable quality from paired studies were reviewed including:
  - Background parenchymal enhancement
  - Mass or non-mass enhancement size (maximum diameter and perpendicular diameter)
  - shape and margins
  - Enhancement patterns; early and late phase curves
  - Restriction diffusion with Apparent Diffusion Coefficient (ADC) values
  - T2 signal intensity
  - The presence of peritumoral, pre-pectoral and diffuse oedema; and skin thickening
  - Axillary nodal involvement.
- The criterion for response assessment was **absence of any enhancement above background.**

5. RESULTS

- 15/16 participants' scans were suitable for review
- 12/15 of those reviewed had pCR at surgery (without DCIS) (ypT0).

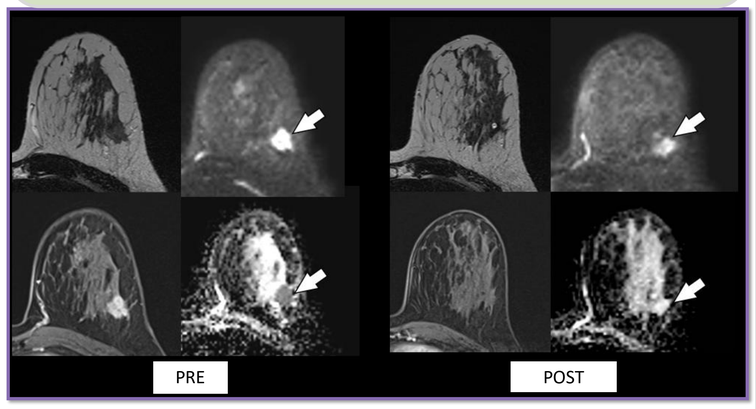


Figure 2:
Pre- and Post- treatment example MRIs of Complete Response
No residual enhancement in the tumour bed
and reduction in restriction of diffusion

MRI findings:

Breast:

- **7 Complete Response**:
  - 6 (85.7%) ypT0
  - Residual DCIS (ypTis) missed in 1 case.
  - See Figure 2 for example images.
- **7 Partial Response**:
  - 2 with residual invasive disease
  - 2 with DCIS (ypTis, RCB 0)
  - 3 (42.9%) with pCR.
- **1 Stable Disease**:
  - 1 Concordant with pathology.

Axilla:

- **5 Complete Response**:
  - 5 (100%) pCR.
- See Figure 3 for Pathology results by MRI summary group.

- **Overall correlation of MRI with final pathology for pCR**:
  - Sensitivity 66.67%
  - Specificity 83.33%
  - Positive Predictive Value: 85.71%
  - Negative Predictive Value: 62.50%
  - Overall accuracy 73.33%
- MRI had **100% sensitivity** for residual invasive disease.

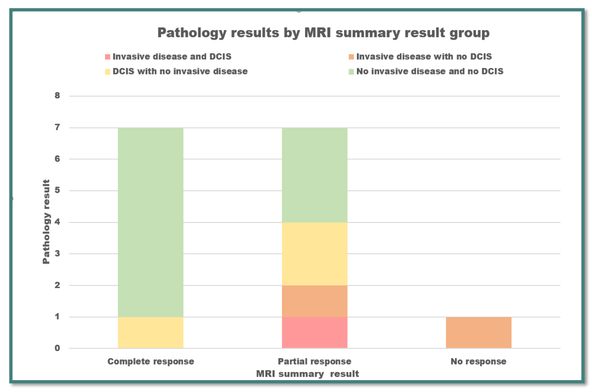


Figure 3: Pathology results by MRI result groups

6. CONCLUSIONS AND RECOMMENDATIONS

- This small tightly controlled series supports a potential future role of MRI in management algorithms to predict pCR in this breast cancer subtype
- It is reassuring that complete response on MRI correlated to pCR in 6/7 cases and that **no residual invasive** breast cancer was missed
- As with previous studies [2], MRI may not differentiate between residual disease and post treatment inflammation/fibrosis.

7. ACKNOWLEDGEMENTS

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8. REFERENCES

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