

## INTRODUCTION

Haematological malignancies: leukaemia, lymphoma and myeloma, are relatively common globally (Keykhaei *et al.*, 2021) however breast manifestations of such malignancies are very rare (0.04-0.5%) (Wienbeck *et al.*, 2017).

Acute lymphoblastic leukaemia (ALL) is an aggressive malignancy of B or T lymphoblasts (Puckett, 2022). ALL has a high level of relapse usually within the CNS or with osseous involvement (Gogia *et al.*, 2014). Mammary involvement while rare is more commonly seen in cases of acute myeloid leukaemia or non-Hodgkin’s Lymphoma (Kulkarni *et al.*, 2016). It is highly uncommon in ALL usually occurring in the setting of relapse (Glazebrook *et al.*, 2014) and in young patients (Kulkarni *et al.*, 2016).

Patient presentation is usually as a solitary breast lump or diffuse breast enlargement with associated lymphadenopathy but on clinical investigation bilateral involvement is common (Masood, Sayeed and Aslam, 2021). It is often confused with primary breast cancer clinically, highlighting the need for thorough patient history and radiological investigation.

Mammography is of limited utility due to the typically young presentation and associated increased breast density thus lowering mammographic sensitivity (Karbasian-Esfahani *et al.*, 2008). While US findings are non-specific and variable, in mammographically occult cases and young presentations US is invaluable in lesion assessment with a high degree of sensitivity and specificity (95.7% and 82.4% respectively) (American College Of Radiology, 2016). However multiple studies have found varied sonographic appearances ranging from hypo- to hyperechogenicity for example (Shin, 2016). Ultimately imaging findings need to be consolidated by tissue biopsy and sampling (Kulkarni *et al.*, 2016).

In this case we discuss the varied appearances of leukemic mammary deposits and demonstrate the value of ultrasound as a safe, cheap and accessible modality that facilitates the consolidation of its image findings via US-guided biopsy.

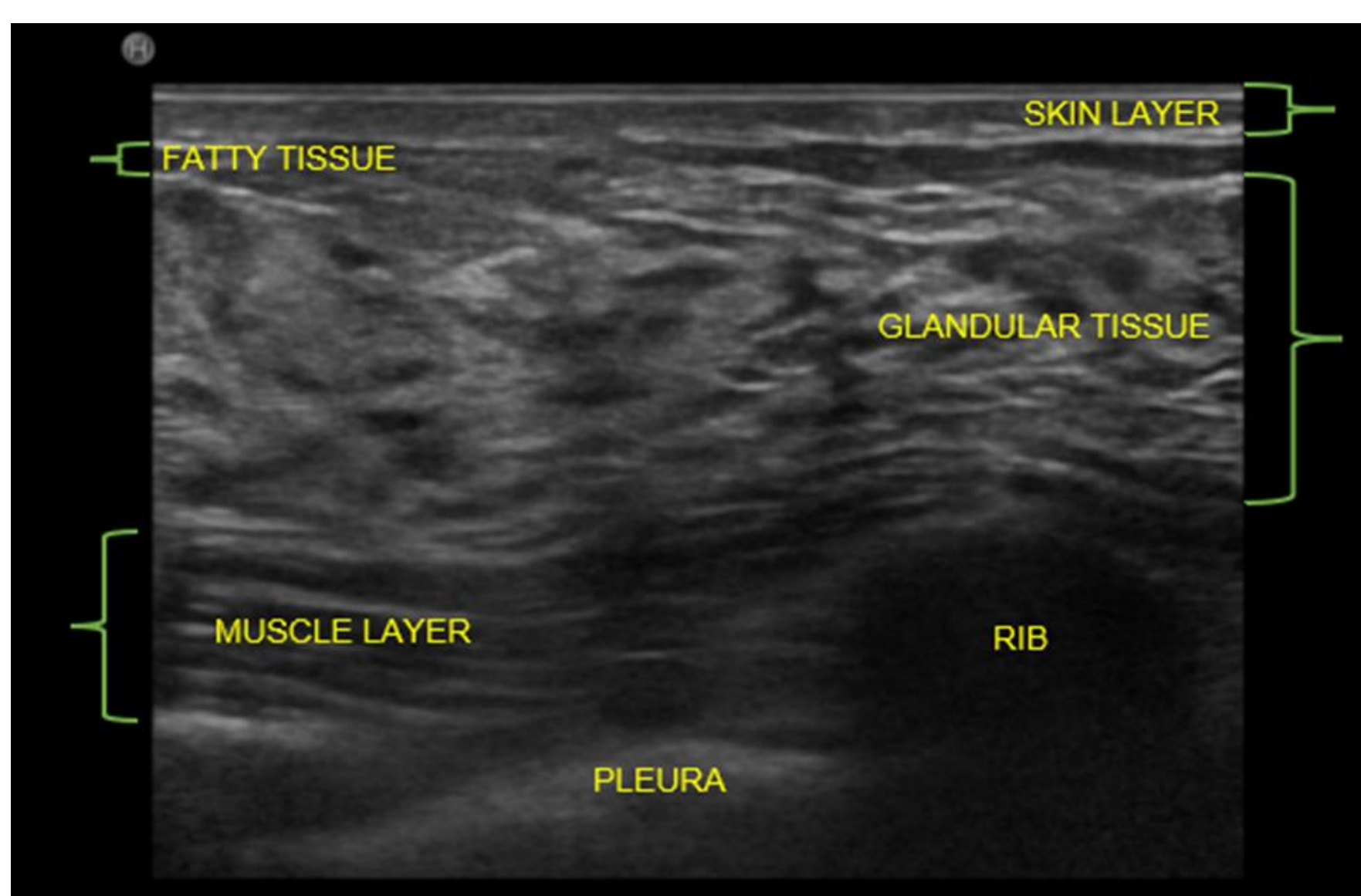
## PATIENT BACKGROUND

A 34-year-old female presented from the breast clinic with a right sided non-tender breast lump. She noticed it a week prior to presentation and upon consultation did not highlight any associated nipple or skin changes. She previously had US guided biopsy for a left sided lump which was found to be benign breast tissue. The patient had a significant history of acute lymphoblastic leukaemia (ALL) but had been in remission for 2 years.

On clinical examination clinicians found skin tethering in the upper outer quadrant of the right breast associated with a firm 2-3 cm lump findings typical of malignancy (American College Of Radiology, 2016). Bilateral involvement was also identified, with left-sided lesions also examined. Clinician concerns were immediately raised for disseminated metastatic breast deposits versus primary breast cancer.

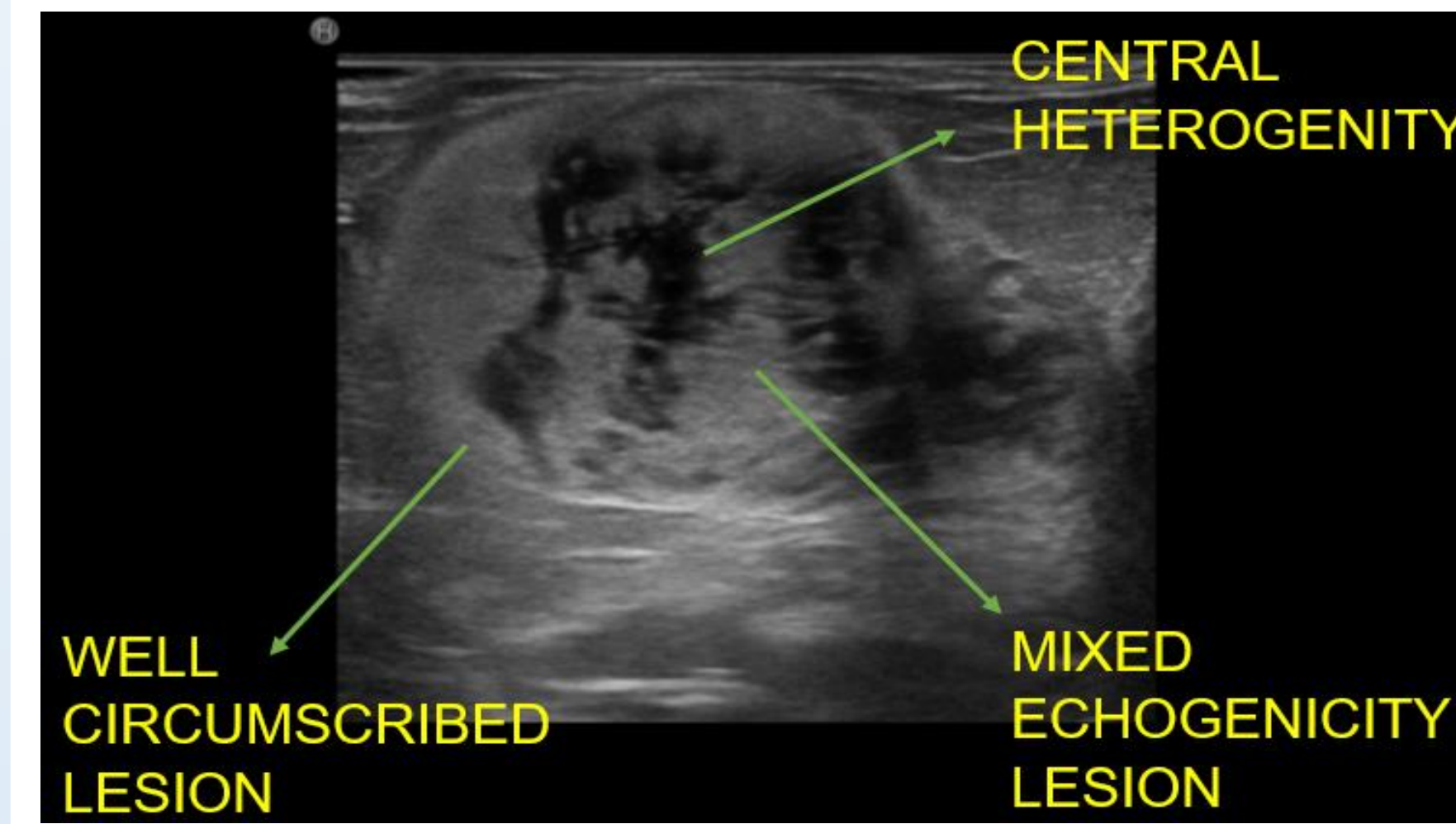
## ULTRASOUND EXAMINATION

Both breasts were scanned using a high frequency (7.5-12MHz) linear probe to ensure appropriate resolution of normal anatomy and any discernible pathology. Initial assessment was via B-Mode imaging.

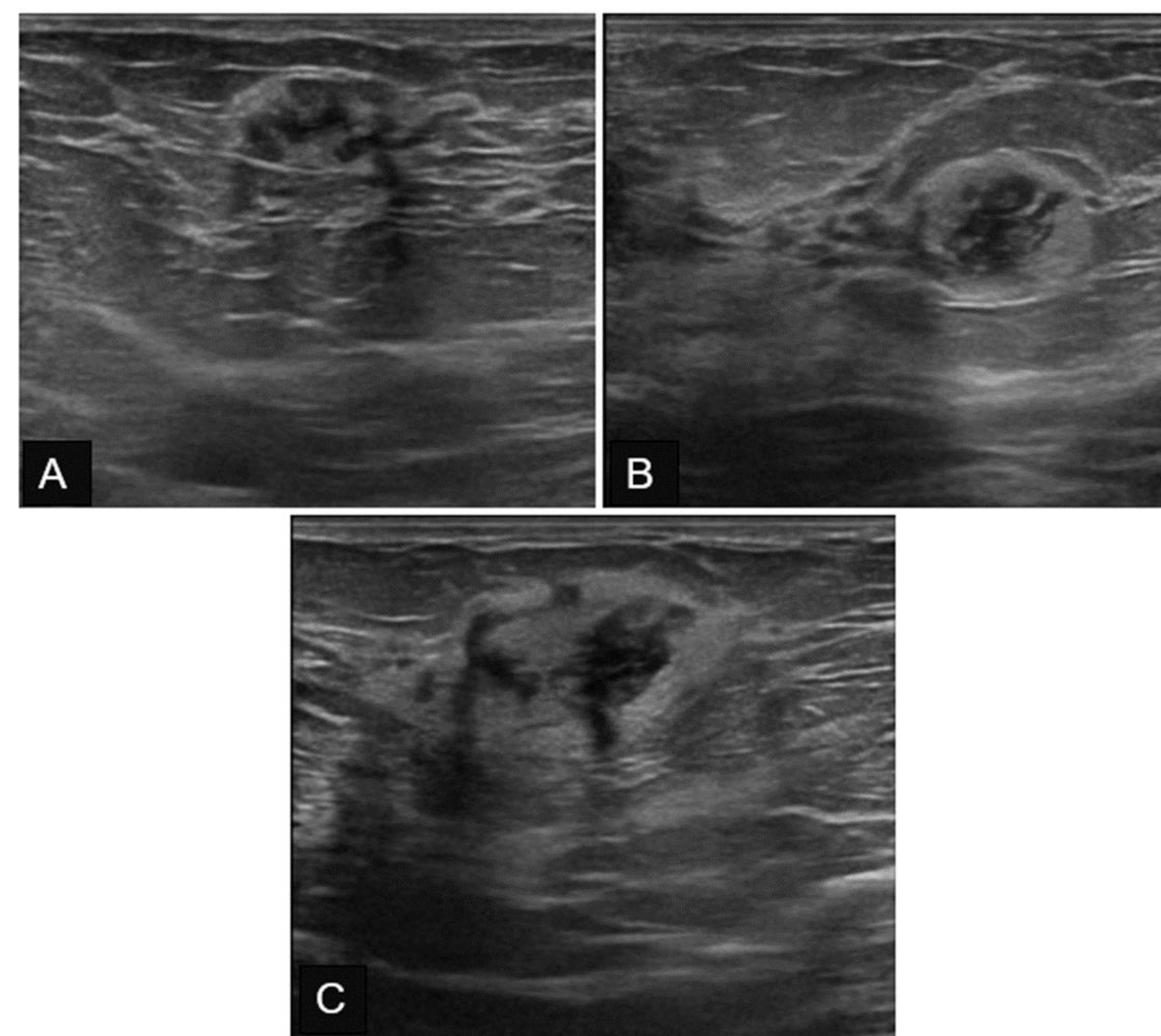


**Figure 1:** Normal Breast Appearances. A Homogenous echogenic skin layer with a thin hypoechoic adipose layer relative to the thick echogenic glandular tissue is demonstrated. Inferiorly a striated muscle layer with alternate echogenic and hypoechoic layering is demonstrated encapsulating a rib with a well delineated anterior border and pronounced posterior acoustic shadowing. A thin echogenic line inferior to rib represents the pleural margin.

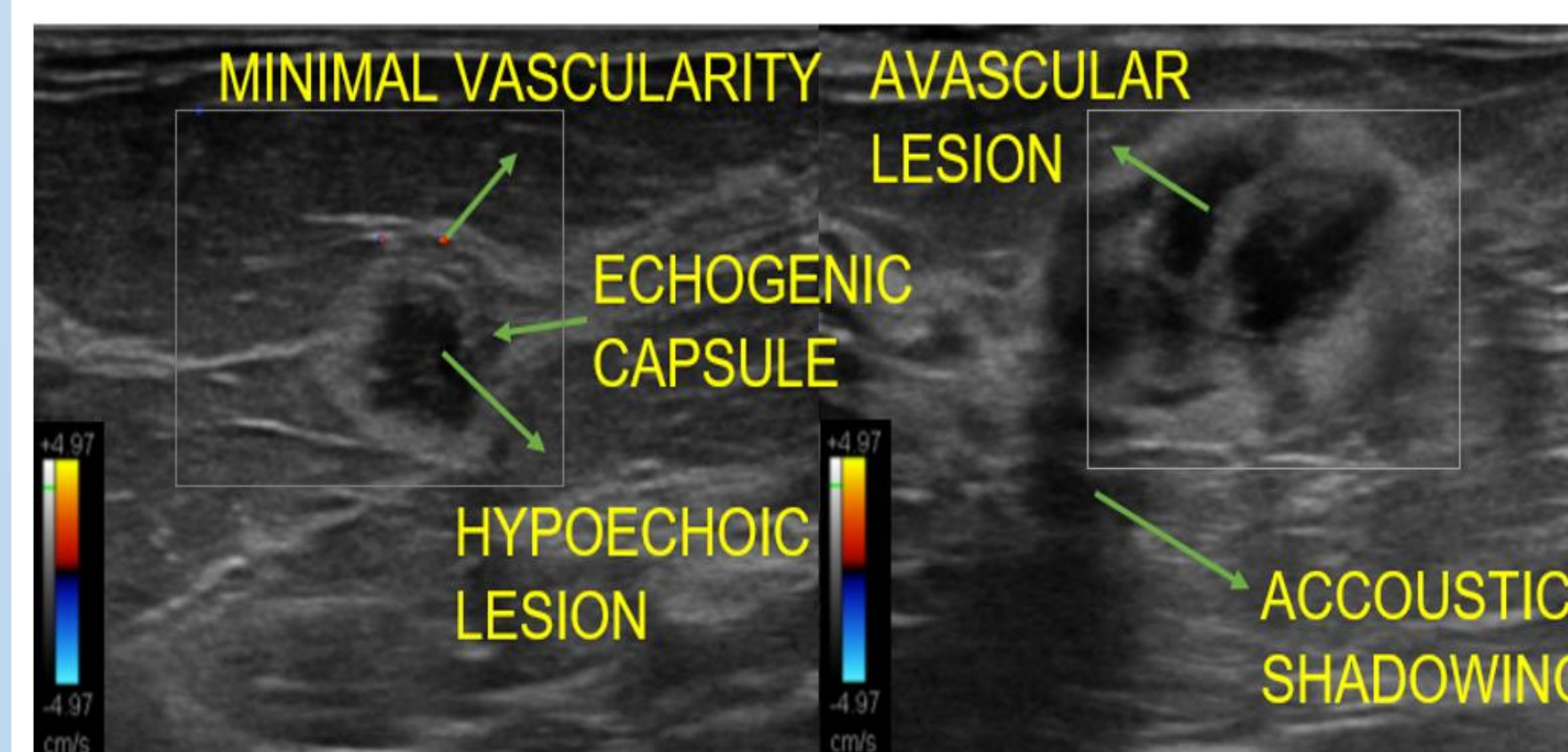
## ULTRASOUND EXAMINATION



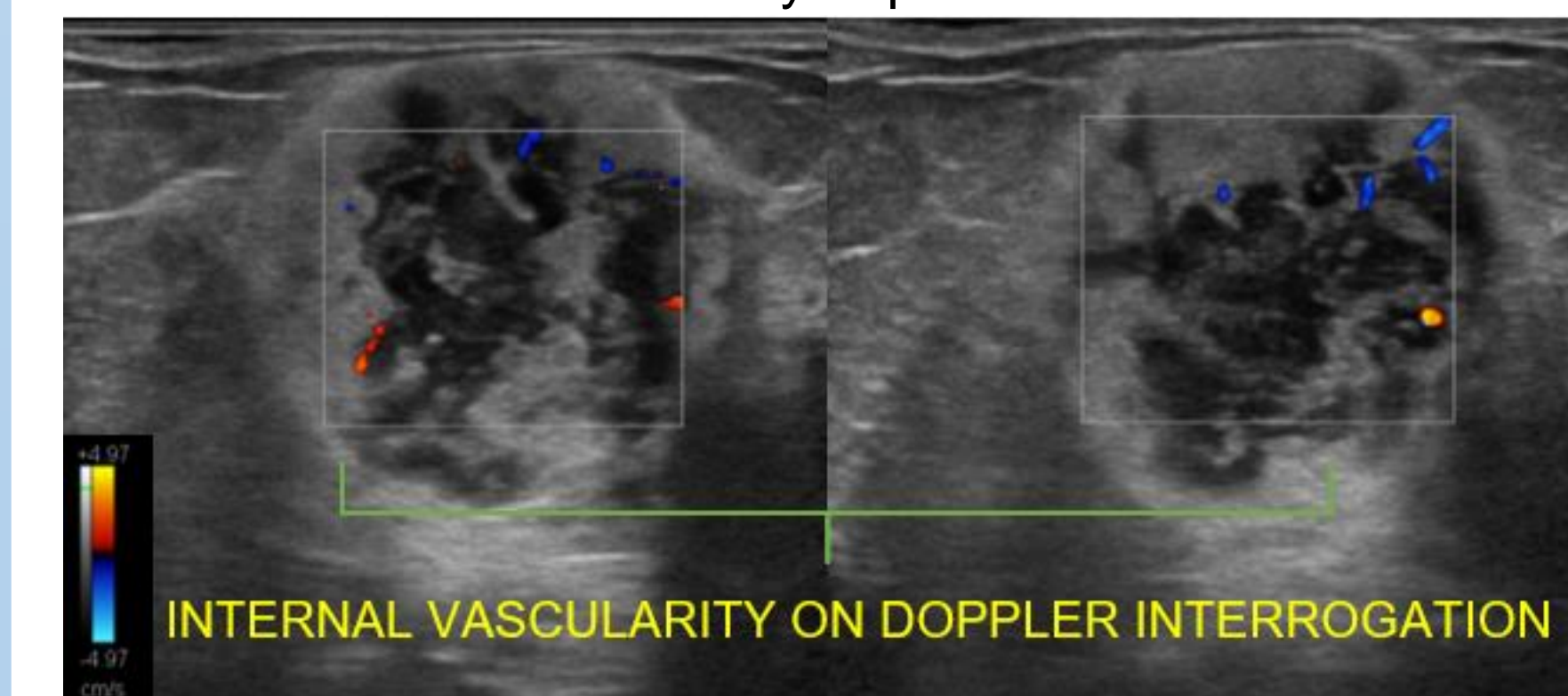
**Figure 2:** A transverse view of the palpable area of concern demonstrates a large well circumscribed lesion with mixed echogenicity throughout and a heterogenous echotexture centrally which may be likely for central tissue necrosis. Well circumscribed borders may mimic benignity (Besina *et al.*, 2013) but its important that potential malignant pointers e.g., heterogeneity, mixed solid/cyst components are not overlooked in its favour.



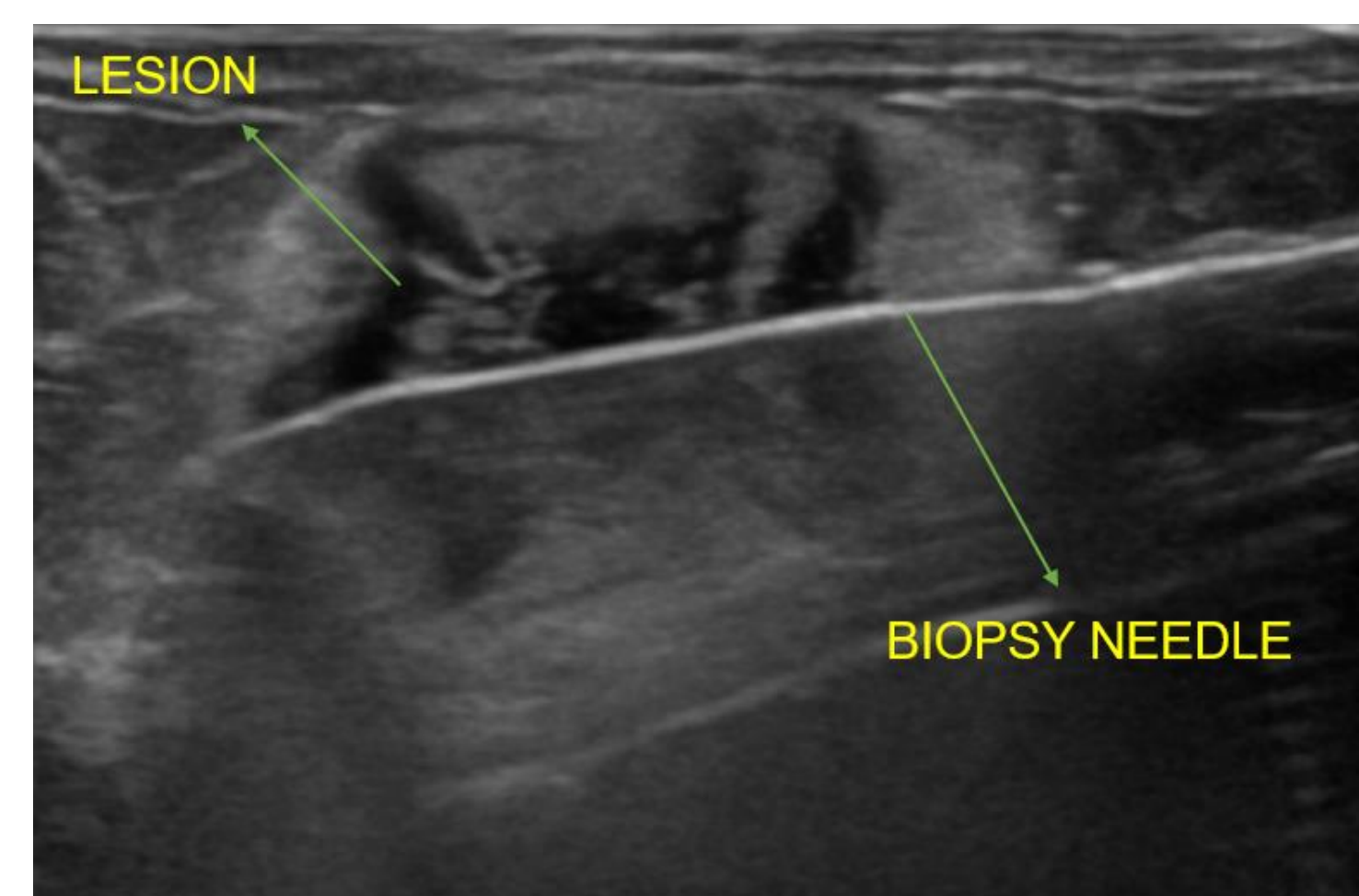
**Figure 3:** On further assessment, multiple lesions were noted bilaterally with irregular and indistinct margins in contrast to the well circumscribed palpable lesion of concern. This is considered a more common appearance of mammary leukemic deposits (Besina *et al.*, 2013). This highlights the non-specific sonographic features of leukemic breast deposits.



**Figure 4:** On Doppler interrogation some lesions were noted to demonstrate little to complete absence of vascularity. Both images also demonstrate varied B-mode appearances like lesion hypoechoicity, capsulation and posterior acoustic shadowing displaying further the non-specific sonographic features of leukemic mammary deposits.

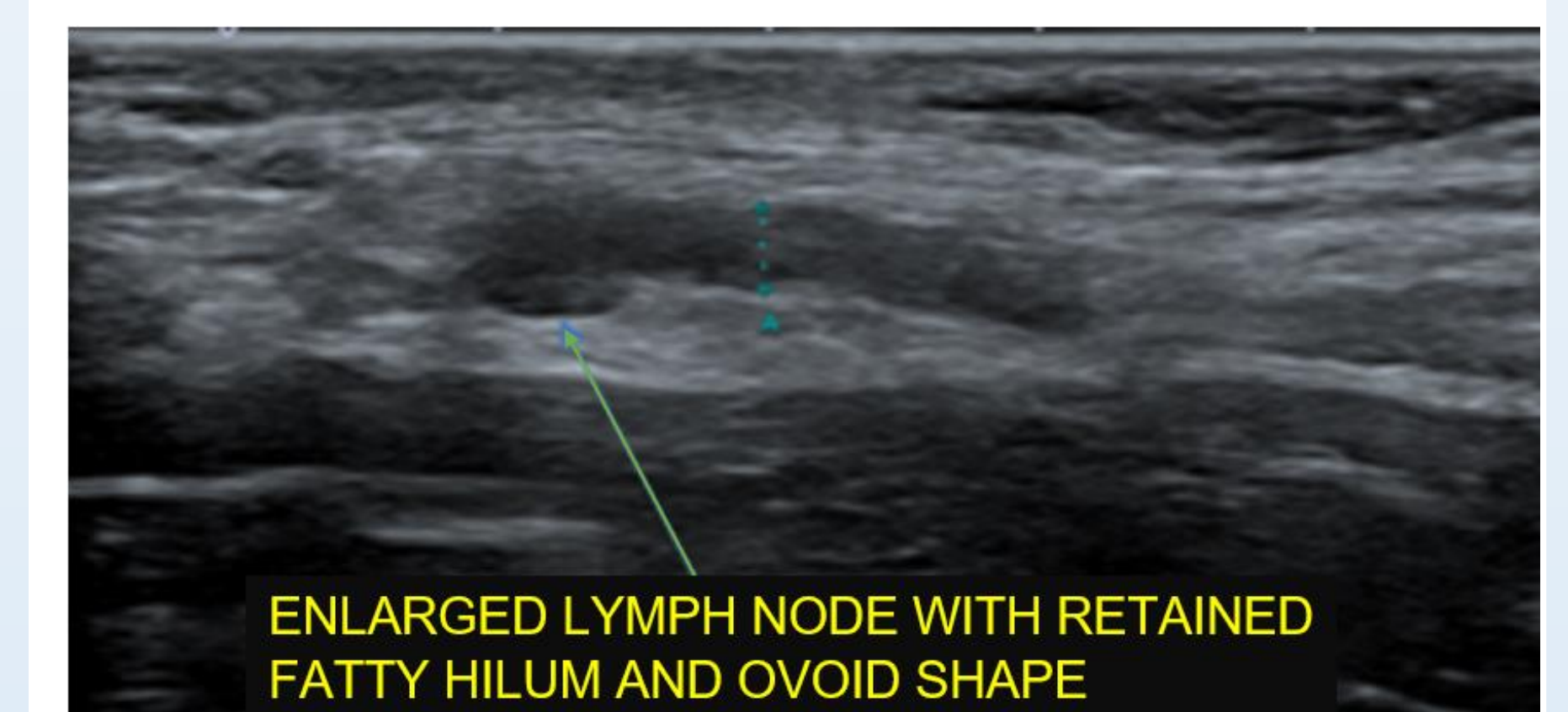


**Figure 5:** Internal vascularity was demonstrated in multiple other lesions bilaterally. Vascularity is not detected in the hypoechoic centres of such lesions and may reinforce the notion of central necrosis within the lesion.



**Figure 6:** US guided biopsies were performed in an attempt to accurately and safely diagnose the above lesions as the target can be well-visualised and vascular anatomy can be avoided to prevent post-biopsy complications e.g., haematomas.

## ULTRASOUND EXAMINATION



**Figure 7:** A transverse view of an axillary lymph node with cortical bulging >3mm. In the absence of obvious abnormal lymphatic appearances, cortical bulging >3mm is one of the earliest changes indicative of malignant lymphatic spread (Ecanow *et al.*, 2013). This appearance warranted US-guided FNA exploration.

## DIAGNOSTICS & TREATMENT

Breast biopsy findings were consistent with lymphoblastic infiltration confirming ALL relapse. Subsequently the patient underwent an US Liver for abdominal complaints which revealed a 4.5cm hepatic mass. Further CT and Nuclear Medicine imaging revealed hepatic and retrocaval nodal and diffuse osseous metastases.

The foundation of ALL treatment with mammary involvement is usually based on multiagent chemotherapy (Kulkarni *et al.*, 2016). Dependence solely on radiotherapy and surgery is found to invariably lead to recurrence within 2 years. Prior to this discovery the patient was in remission for 2 years with successful response to Hyper-CVAD chemotherapy.

In this case the patient responded poorly to initial Venetoclax treatment and participated in drug trials with no satisfactory results. She underwent multiple cytarabine cycles with no satisfactory response and ultimately rejected it. Therefore, the patient was discharged to palliative care and some months later passed away.

**Table 1.** Common Sonographic Features of Leukemic Mammary deposits

Sonographic Appearances Leukemic Deposits
Non-Specific, Varied Appearances
Multiple
Hypoechoic
Heterogenous
Indistinct Margins
Microlobulations
Irregular Outline
Significant Echogenic Components

## CONCLUSION

Extramammary leukemic metastasis usually involves bone infiltration. Mammary involvement is extremely rare. Patient presentation is typically young therefore limiting mammographic evaluation. While US findings are non-specific and varied, it is a safe, well-tolerated, accessible, and sensitive modality in breast lump evaluation. Although a definitive diagnosis cannot be deduced from image findings alone, US further contributes to accurate diagnosis through US-guided tissue sampling which ultimately confirms lesion diagnosis.

## REFERENCES

American College Of Radiology (2016) 'ACR Appropriateness Criteria: Palpable Breast Masses', *Journal of the American College of Radiology*, 14.

Ecanow, J. S., Abe, H., Newstead, G. M., Ecanow, D. B. and Jeske, J. M. (2013) 'Axillary staging of breast cancer: what the radiologist should know', *Radiographics*, 33(6), pp. 1589-1612.

Glazebrook, K. N., Zingula, S., Jones, K. N. and Fazio, R. T. (2014) 'Breast imaging findings in haematological malignancies', *Insights into Imaging*, 5(6), pp. 715-722.

Gogia, A., Mehta, P., Pramanik, R. and Kumar, R. (2014) 'Isolated breast relapse mimicking breast cancer in elderly patient with acute lymphoblastic leukemia', *Turkish journal of haematology : official journal of Turkish Society of Haematology*, 31(2), pp. 203-204.

Karbasian-Esfahani, M., Wiernik, P. H., Yeddu, M. and Abebe, L. (2008) 'Leukemic infiltration of the breast in acute lymphocytic leukemia (ALL)', *Hematology*, 13(2), pp. 101-106.

Keykhaei, M., Masinaei, M., Mohammadi, E., Azadnajafabad, S., Rezaei, N., Saeedi Moghaddam, S., Rezaei, N., Nassernejad, M., Abbasi-Kangevari, M., Malekpour, M.-R., Ghamari, S.-H., Haghsheenas, R., Koliji, K., Kompani, F. and Farzadfar, F. (2021) 'A global, regional, and national survey on burden and Quality of Care Index (CCI) of hematologic malignancies: global burden of disease systematic analysis 1990–2017', *Experimental Hematology & Oncology*, 10(1), pp. 1-11.

Lehman, C. D., Lee, A. Y. and Lee, C. I. (2014) 'Imaging management of palpable breast abnormalities', *American journal of roentgenology* (1976), 203(5), pp. 1142-1153.

Masood, L., Sayeed, S. and Aslam, S. (2021) 'Acute lymphoblastic leukemia simulating breast carcinoma', *The Egyptian Journal of Radiology and Nuclear Medicine*, (no. 1), pp. NA.

Puckett Y, Chan O. Acute Lymphocytic Leukemia. [Updated 2022 Jan 2]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK459149/>

Shin, H.-C. (2016) 'Relapse of Biphenotypic Acute Leukemia as a Breast Mass', *Journal of breast cancer*, 19(4), pp. 455-458.

Wienbeck, S., Meyer, H. J., Uhlig, J., Herzog, A., Nemat, S., Teifke, A., Heindel, W., Schäfer, F., Kinner, S. and Surov, A. (2017) 'Radiological imaging characteristics of intramammary hematological malignancies: results from a German multicenter study', *Scientific reports*, 7(1), pp. 7435-10.