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Sustainable healthcare: A future for all

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Selective chemotherapy responses in ex vivo propagated Phyllodes tumour metastasis to bone

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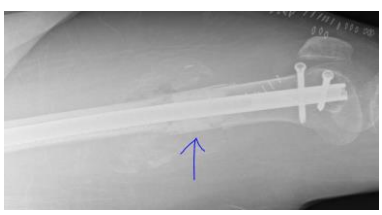
Background

Phyllodes tumour (PT) is a fibroepithelial cancer of the mammary stroma that accounts for 0.3 to 1% of all primary breast tumours and 2.5% of all fibroepithelial breast tumours. Although it has a relatively high tendency to recur, distant metastases are relatively uncommon. The incidence of metastatic disease among patients with malignant PT is estimated at approximately 20–25%. The tumour shows a predilection for lung spread (75%). Bone metastases remain very rare and single series reports approximately 19% incidence. Palliative radiotherapy only, or in combination with doxorubicin, has been employed as therapy. The longest mean survival in patients with bones metastases is reported as 11.8 months. (1)

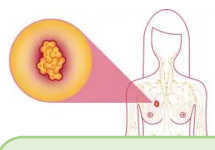
Bone Metastasis of Phyllodes

The PT studied was diagnosed in a 61-year-old female who developed a metastasis to the femur 2 years after initially presenting with primary breast disease. Palliative radiotherapy only, in combination with doxorubicin, is likely to be employed clinically.

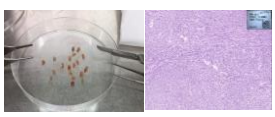


Open biopsy and frozen section of the femur was undertaken via a lateral approach. Once histopathology confirmed metastatic phyllodes, meticulous intra-lesional curettage was performed, an intramedullary femoral nail passed and cementation performed to the surrounding bone defect.

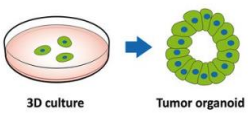
Methodology



Malignant tissue surplus to pathological needs was collected and transferred under sterile conditions to the CPAC facilities at TRI.

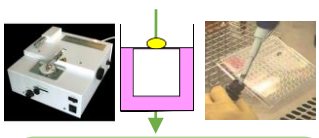


Tissue fragments were fixed for histology, snap frozen for RNA, or processed viably for culture.



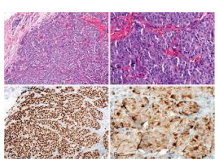
Patient-derived organoids (PDOs) were generated using mechanical and enzymatic methods as established in our laboratory. (2)

PDOs were treated for 5 days with SOC agents eribulin, paclitaxel, doxorubicin or vehicle (DMSO).



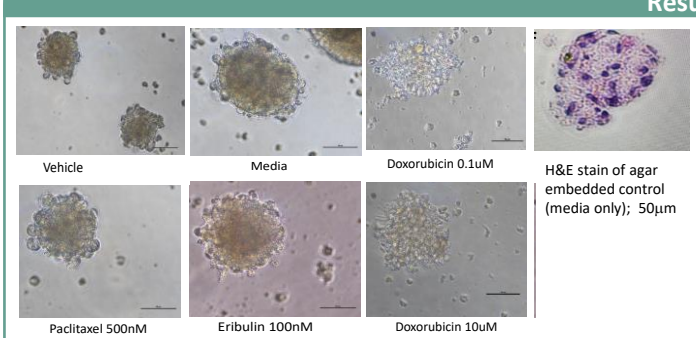
Tissue was also sliced (200 µm) using the McIlwain chopper into patient-derived explants (PDEs) for culture on dental sponge at the air-liquid interface.

Longitudinal MTS metabolic assay.



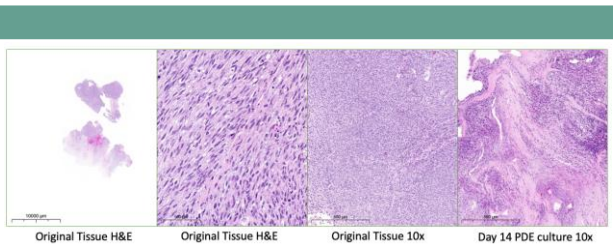
Upon endpoint PDE/PDO samples were fixed for histological and immunohistochemical analysis.

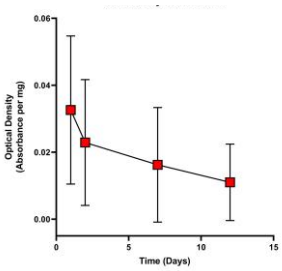
Results



H&E stain of agar embedded control (media only); 50µm

Of the agents tested, only doxorubicin reduced PDO viability as indicated by organoid sphericity and morphological changes.





PDEs showed a 50% decrease in metabolic activity by the second day of culture, with a 32% average viability after 12 days of culture. This informs the possible ex vivo treatment timeframe.

Summary

- Our data demonstrate the potential of PDOs to indicate personalised therapy responses, which may ultimately guide patient cancer therapy.
- PDEs offer advantages in providing an intact tumour microenvironment, including immune cells relevant to immunotherapy, but should be used early.
- The CPAC team are working on increasing PDE longevity.

Clinical Significance

We hypothesise that breast cancer PDOs from clinical samples are representative of clinical responses to patient and provide the basis for a predictive test of personalised tumour responses sufficient to support accreditation.

Reference List:

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2. Thomas PB, Perera MPJ, Alinezhad S, Joshi A, Saadat P, Nicholls C, Devonport CP, Calabrese AR, Templeton AR, Wood JR, Mackenzie NJ, Jeffery PL, Vela I, Williams ED. Culture of Bladder Cancer Organoids as Precision Medicine Tools. J Vis Exp. 2021 Dec 28;(178). doi: 10.3791/63192. PMID: 35037658.

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